

Preventing Breast Cancer:

*THE STORY OF A MAJOR, PROVEN,
PREVENTABLE CAUSE OF THIS DISEASE*

John W. Gofman, M.D., Ph. D.

• – Our estimate is that about three-quarters of the current annual incidence of breast-cancer in the United States is being caused by earlier ionizing radiation, primarily from medical sources.

From Chapter 1

• – This edition includes an additional section, "Response to Critiques of the First Edition."

Section 5

Second Edition: 1996

C.N.R. Book Division

Committee for Nuclear Responsibility, Inc.

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Preventing Breast Cancer ... 1996

This book uncovers the major cause of the recent breast-cancer incidence in the USA. The author shows that past exposure to ionizing radiation --- primarily medical x-rays --- is responsible for about 75 percent of the breast-cancer problem in the United States.

The good news: Since the radiation dosage given today by medical procedures can be significantly reduced without interfering with a single useful procedure, numerous future cases of breast-cancer can be PREVENTED.

The author recommends specific actions to start breast-cancer prevention now, not ten years from now.

Thanks to the talents and generous effort of David T. Ratcliffe, a growing number of this book's chapters (and various other works of the author) are available on the Internet at:

<http://www.ratical.com/radiation/CNR/>

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The HEIR-2 Report (1996)

The Committee for Nuclear Responsibility, Inc. (CNR) is a non-profit educational group organized in 1971 to provide independent analyses of the health effects and sources of ionizing radiation. Authors of CNR publications speak for themselves alone and not for CNR's entire Board, whose members are known for their own independent thinking.

This study, PREVENTING BREAST CANCER, is the second one in CNR's series of reports, "Health Effects of Ionizing Radiation" (HEIR Reports).

The previous report (1990) was RADIATION-INDUCED CANCER FROM LOW-DOSE EXPOSURE: AN INDEPENDENT ANALYSIS, also by Gofman. (See, for example, reviews in Choice, January 1991; in the New England Journal of Medicine, February 14, 1991; in the Bulletin of the Atomic Scientists, January 1992; in the PSR Quarterly, March 1993.)

The third HEIR Report will be a study, covering both males and females, of the causal role of medical radiation in the overall cancer problem --- not in breast-cancer alone.

Research in this field is not commercially viable. Most radiation research, analysis, and publications are sponsored by government grants. CNR neither requests nor would accept any government funding. The low price of the HEIR Reports is made possible by the foundations and individuals who generously support these scholarly works, and by the refusal of the author to accept royalties or payment of any other sort from CNR.

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PREVENTING BREAST-CANCER:

The Story of a Major, Proven, Preventable Cause of This Disease.

John W. Gofman, M.D., Ph.D. 1996.

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PREVENTING BREAST CANCER, SECOND EDITION

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Preface and Acknowledgments

Writing this book has been a happy task. It deals with a very serious problem, with a very happy ending. It would be hard to think of anything more rewarding for this effort than the knowledge that we can begin the task of breast-cancer prevention --- now.

People have often asked me to write a book which has no numbers, no mathematics, no symbols, no equations. I appreciate their fear that they will not understand. We, who have worked on the preparation of this book, think that anyone can understand the fascinating past history of 100 years of the x-ray in the production of breast-cancer.

Simply accept "numbers" the first time through. The story will tell itself that way. And then come back, if you are so inclined, to challenge all the numbers. The numbers are your insurance that this story has real legs.

Three people have made exceedingly large contributions to the book. Many improvements in the writing come from them. Professor Helen Gofman patiently brought the perspective of a pediatrician and a general physician as she meticulously went through the manuscript to tell me where it would not be understood without changes.

Egan O'Connor, our Editor of CNR Books, not only put a rough manuscript into the English language, but provided a clear, cool, critical head in challenging everything placed before her.

John David Gofman, M.D., my son, volunteered to "look the manuscript over," and indeed he did. All the pages, and all the lines. His insights, his advice, his knowledge made a very large difference in the final book which evolved through his and Egan's critical comments and contributions to ideas and style.

Lastly, there is one special place in my heart, for an assist which was absolutely essential. That place is occupied by the superb library of our medical school at the University of California in San Francisco. What a treasure --- a collection so rich as to make the trip back through 100 years of medicine an easy one. And the cooperation of the librarians was superb.

This is the beginning of an effort to prevent cancer in one effective manner. Most of the methodology will be applicable for an effort with cancers other than those of the breast. Indeed, we hope other investigators will make their own studies using such methods as are presented. For the inevitable errors and unclear passages, I take all the credit. We shall try to improve later editions as we learn of such flaws.

John W. Gofman, M.D., Ph.D.
San Francisco, California
Spring 1995.

Spring 1996: This edition benefits by the addition of Section 5 (and its associated references). Sections 1, 2, 3, and 4 are the same in the first and second editions.

In-print books by this author on related topics:

1981, Radiation and Human Health.

Library of Congress Catalog Card Number
80-26484. ISBN 0-87156-275-8.

1985, X-Rays: Health Effects of Common Exams (with O'Connor).

Library of Congress Catalog Card Number
84-23527. ISBN 0-87156-838-1.

1990, Radiation-Induced Cancer from Low-Dose Exposure: An Independent Analysis (HEIR-1 Report).

Library of Congress Catalog Card Number
89-62431. ISBN 0-932682-89-8.
Several chapters of this book are on the Internet at: <http://www.ratical.com/radiation/CNR/>

1994, Chernobyl Accident: Radiation Consequences for This and Future Generations (Russian-language).

ISBN 5-339-00869-X.

Information about the author is located at pp.379-381.

Preview:

Another book (the HEIR-3 Report) is in preparation by this author, for publication probably in 1996 or maybe early 1997. The HEIR-3 Report explores the hypothesis that earlier medical irradiation has caused not only most cases of breast-cancer, but also a large share of the cases of other cancers, in both men and women. The ISBN is 0-932682-97-9, from the Committee for Nuclear Responsibility Books.

#

CHAPTER 1

Our Conclusion: A Large Share of Breast-Cancers Need Not Occur

Part 1. The Bottom Line

We begin this book with our bottom line, because we think the advice of Sara Jeannette Duncan is good: "If you have anything of importance to tell me, please, PLEASE begin at the end!" So here is our conclusion:

Breast-cancer is a largely PREVENTABLE disease, and we reach that good news because of our finding that a large share of recent and current breast-cancer in the United States is CERTAINLY due to past medical irradiation of the breasts with x-rays --- at all ages, including infancy and childhood. Much of today's radiation dosage is preventable, without any interference with necessary diagnostic radiology, and hence many future breast-cancers need not occur.

What do we mean by "a large share" of recent and current breast-cancer?

Our estimate is that about three-quarters of the current annual incidence of breast-cancer in the United States is being caused by earlier ionizing radiation, primarily from medical sources. We will show that the recently growing incidence is not mysterious, and that if we wish to understand why the incidence has been growing, we must look to radiation events in the life of women 15-25-35-45 and more years before breast-cancer diagnosis. Moreover, there is recent evidence about induction of EARLY-onset breast-cancer by radiation (Chapter 3).

There are many stories in this book, but no villains. The cast of historical characters is interesting, impassioned, and sometimes very wise.

No one meant to do any harm. On the contrary. After discovery of the x-ray in 1895 and of radium in 1898, radiation was tried out widely in medicine, right up to recent times, in the hope of RELIEVING a great variety of human afflictions. Some radiation therapies were (and are) clearly effective (and this book is highly complimentary about such uses). Some other therapies, clearly not effective, have been discontinued. But usefulness is not always clear-cut in medicine. For example, users reported benefits which others could not see, regarding one type of x-ray therapy which was used for infants and children from 1911 to almost 1960.

The finding of this book constitutes an example of what can happen from exposing people to new agents, such as x-rays, when no one KNOWS the long-term consequences. Readers will see the innocent enthusiasm, the repeated assurances that the procedures were safe, and the power of the "technological imperative" to suppress the idea that there might be a problem with anything as wondrous and potentially useful as x-rays. This is a story of "disaster creep" --- a massive problem creeping up on society without any recognition.

In science, every important discovery should be challenged and checked by others, and our finding certainly will be. We will welcome the genuine, thoughtful critiques. And we expect our finding to be validated. We arrive at our startling conclusion after UNDERestimating the past dosage of x-rays, and after using conversion-factors (conversion from dose to subsequent cancers) which derive from real-world observations.

There is just no doubt that past radiation exposure accounts for a major share of our recent and current breast-cancer problem. The evidence for our finding is overwhelming --- if one simply looks.

Many will look thoughtfully at the input to this study --- but there will be exceptions. We expect our finding to be automatically rejected by some who merely WANT it to be faulty --- and who will comment upon it without even reading this book.

If breasts could talk, they might say, "Read first, judge second, and please start now!"

Part 2. For Whom Is This Book Intended?

This book is intended for anyone interested in breast-cancer, and its prevention. Interest in the problem is the only requirement. The book is for medical professionals AND for individuals with the greatest personal concern: Women in general --- and their families. Readers do not need to know every medical term in the stories, because the MEANING of the stories will be clear anyway. No medical skill or knowledge is essential to understand what will be presented.

Many chapters will begin with a description of what happened, and will end with specific calculations based on the events. Of course, many readers will skip the numbers. The "easy readers" should feel no guilt for skipping the latter part of various chapters. Lots of professionals, also, read scientific journals without ever examining the calculations and tables there. But numbers are in journals, and also in this book, for a very important reason: To ALLOW people to check for themselves exactly how the quantitative conclusions were reached, and to evaluate the validity for themselves.

Part 3. An Astonishing Statement in a Fund-Raising Appeal

I've recently received in the mail a request for funds to help breast-cancer research. It said: "Breast cancer is THE most commonly diagnosed cancer in American women today. It is THE leading cause of death among women ages 40 to 44, and the leading cause of cancer death in women 20 to 54." No argument about that. Every part of that statement makes it all the more important for women to know precisely why we say that breast-cancer is largely preventable. Then the letter added:

"What's worse, even the best doctors have no idea what causes breast cancer or how to cure it." Cure is indeed problematical, and when successful, the process itself can be highly unpleasant. All the more reason why prevention is so very important.

But how can anyone in 1994 say that "even the best doctors have no idea what causes breast cancer"? This error also went out over NBC national news during October 1994, in the television network's coverage of Breast-Cancer Month. In reality, medical science has clearly known for some 20 years already that ionizing radiation is a prominent and proven cause of breast-cancer. Ionizing radiations include x-rays and gamma rays, as well as beta, alpha, and some other high-speed particles. (Radium is used in medicine as a source of powerful gamma rays.)

We think "the best doctors" do indeed know about the role of ionizing radiation as a prominent, proven cause of breast-cancer, but it is astonishing that both lay and medical sources COMMONLY fail to mention this outstanding fact of medical science: Past

medical exposure to ionizing radiation, 10, 20, 30, 40, and more years back in a woman's life, can cause breast-cancer.

Radiation exposure in the first few months of life may be the most serious in causation of later breast-cancer. In fact, irradiation of the breasts between age 0 (newborn) and age 9-years may cause MANY-fold more cases of breast-cancer, over the subsequent lifetime, than does irradiation of women over 40 years of age with the same amount (dose) of ionizing radiation.

The Current Size of the Problem, USA

Today, it is estimated that one woman out of every nine in the USA will develop breast-cancer sometime during her lifespan. The breast-cancer problem is reflected in the estimates below, of breast-cancer incidence in the USA (derived by the American Cancer Society from government data). The numbers exclude "in situ" cases. The rapidly rising numbers below reflect diagnosis, not death. As so many families know already, diagnosis in itself brings severe consequences, even if a woman dies of something else in the end. The numbers on the right show that the growth of the female population can explain only a small part of the rising incidence of breast-cancer. (The tabulation below is expanded in Tables 1 and 2, which are located after the final chapter.)

1970:	68,000 cases diagnosed;	females of all ages =	104,309,000
1975:	88,000 cases diagnosed;	females of all ages =	110,401,000 est.
1980:	108,000 cases diagnosed;	females of all ages =	116,493,000
1985:	119,000 cases diagnosed;	females of all ages =	122,474,500 est.
1990:	150,000 cases diagnosed;	females of all ages =	128,454,000
1994:	182,000 cases diagnosed;	females of all ages =	133,194,000

Part 4. How Do We Know that Radiation Is a Cause of Breast-Cancer?

Every once in a while, a massive step forward in medicine is taken by the oldest technique in medical practice --- the careful taking by a physician of a patient's medical history. Such an event of landmark proportions is represented by the observations of Dr. Ian MacKenzie, a physician in Nova Scotia, Canada.

In 1961, a woman with a rapidly growing breast-cancer came to his office. He noticed that her cancer had occurred in the upper inner quadrant of her right breast, and that her skin over the right chest wall, breast, and sternum showed signs of dermatitis (skin inflammation).

MacKenzie questioned her carefully about her history, and learned that she had been treated 14-15 years earlier for pulmonary (lung) tuberculosis. In those years, a common practice was to let one of the lungs rest, by collapsing it with an injection of air between the chest wall and the lung. This procedure was called artificial pneumothorax therapy, and in her case, it took place over 46 months. Each time she had a re-fill of air into the chest, the status of the lung was checked with fluoroscopy, before and usually after.

Fluoroscopy is also called roentgenoscopy, in honor of Wilhelm Konrad Roentgen, who discovered x-rays in 1895. In roentgenoscopy, examination of a patient with x-rays takes place while the x-ray beam stays "on," so that the physician can observe what happens when the patient or the patient's organs are in motion. Roentgenoscopy is thus very different from roentgenography, which is the use of x-rays to expose a sheet of film

(or other types of image-receivers) to produce the usual x-ray picture. Roentgenoscopy, requiring no development of film, produces information immediately.

When Dr. MacKenzie obtained his patient's sanitarium records, he learned that she had had at least 200 fluoroscopic examinations during her treatment. The patient remembered that her skin changes began during this period, too. Dr. MacKenzie recognized that she had radiation dermatitis, and he began to suspect that breast exposure to x-rays might also account for her breast-cancer.

To check on this idea, Dr. MacKenzie studied almost 800 women who had been treated for tuberculosis in one sanitarium during 1940-1949. The startling results were published in 1965. Of 510 women who did NOT receive artificial pneumothorax treatment and therefore did not have repeated fluoroscopies, one woman had subsequently developed breast-cancer by the time of Dr. MacKenzie's study. This is a rate of (1 woman / 510 women), or 0.00196. Of 271 women who DID receive artificial pneumothorax treatment with multiple fluoroscopies, 13 had developed breast-cancer by the time of Dr. MacKenzie's study. This is a rate of (13 / 271), or 0.04797. The breast-cancer rate in the irradiated group was (0.04797 / 0.00196), or 24.5 times the rate in the non-irradiated group. In his paper (p.7), Dr. MacKenzie said:

"From the evidence presented, it would appear to be a reasonable conclusion that the well-recognized role played by ionizing radiation in the development of certain other forms of malignant disease can be extended to include carcinoma of the breast in the circumstances presented by these cases." If pulmonary tuberculosis itself were the cause of the breast-cancers, then the irradiated and non-irradiated cases should have had similar breast-cancer rates, as Dr. MacKenzie commented. Dr. MacKenzie's finding caused quite a "stir" in radiation circles.

1965 (March): Ian MacKenzie, "Breast Cancer Following Multiple Fluoroscopies," British Journal of Cancer 1965, Vol.19: 1-8.

Soon thereafter, C.K. Wanebo and colleagues, studying the survivors of the atomic bombings at Hiroshima and Nagasaki, and stimulated by the MacKenzie work, launched an investigation of breast-cancer in those survivors. In 1968, they published confirmatory evidence of human breast-cancer induction by ionizing radiation. In 1969, Myrden and Hiltz extended the follow-up time for MacKenzie's 1965 study. And in 1970, Arthur Tamplin and I used the MacKenzie and Wanebo data to quantify the dose-response for radiation-induced breast-cancer. We showed in *The Lancet* that the breast-cancer risk from ionizing radiation was quite serious indeed.

Proven, and Then Forgotten?

In the years which have followed MacKenzie's 1965 paper, numerous studies have confirmed and quantified the induction of breast-cancer by ionizing radiation. For the convenience of readers, we have identified a number of those papers by prominently flagging them with the symbol "#" in our list of references. Many of these studies have been analysed in Gofman 1981 and in Gofman 1990. In 1994, even further confirmation became available in the latest reports on cancer incidence in the A-Bomb Survivors (Mabuchi; Thompson; Tokunaga).

The radiation-causation of human breast-cancer is not in dispute. Nonetheless, it is commonly forgotten in discussions about the alleged mystery of breast-cancer causation.

Part 5. What about Other Potential Causes of Breast Cancer?

Cancer --- not breast-cancer alone --- is now considered to be a genetic disease. It is thought that a tumor develops in stages from a single cell, as the cell and some of its descendants accumulate a set of several "genetic lesions." A lesion is an injury or loss of function. Genetic lesions are those which occur in the genetic molecules --- namely, in the DNA molecules which control a cell's proper operation, including the accuracy and appropriate rate of the cell's division. Genetic lesions in a cell can occur at any age.

Inherited diseases are properly called genetic diseases. They occur because offspring receive certain genetic lesions in the DNA which they inherit from their parents. (Mother and father do not often transmit the SAME lesions, however.) Inherited genetic lesions are present in the fertilized human egg. Since every cell we have is descended from the fertilized egg, the lesion is present in every cell. By contrast with an inherited lesion, a genetic lesion which occurs in childhood or adulthood is present only in the cell where it took place, and in cells descended from the altered cell, but it is not present as an all-cell lesion. So, inherited diseases are genetic, but not all genetic diseases have to be inherited. The responsible genetic lesions can occur after conception.

With respect to cancer, it is thought that cells become malignant only after they have accumulated several carcinogenic lesions (many estimates range from four to ten lesions). Some of the lesions may be inherited, and others may occur at any age after conception. Individuals who inherit one or more carcinogenic lesions in EVERY cell, have an increased chance that SOME of their cells will accumulate a complete set of the necessary lesions during their lifetimes. Such people are born "predisposed" to develop full-blown, clinical cancer.

Interaction of Inheritance and "Other Forces"

Almost certainly, inherited carcinogenic lesions have a range from weak to strong. The famous lesions are the rare inherited ones which confer a high chance of cancer in a specific organ, with the clinical cancer often occurring at a very early age. We call those "destiny" lesions, and the weaker ones "predisposing" lesions.

The inherited "destiny" lesions are estimated to account for five to ten percent of human cancer. For breast-cancer, the estimate is about ten percent. Even a "destiny" lesion may need help from other forces, in order to create some cells with the COMPLETE set of genetic lesions required for full-blown cancer. By "other forces," we mean to include agents such as x-rays, viruses, or certain chemicals.

An inherited "predisposing" lesion, by definition, needs help from other forces in order to cause a cancer.

Do such other forces, acting in the absence of INHERITED carcinogenic lesions, ever produce the complete sets of lesions required for malignancy? At this time, there is no way to know how often this happens, if ever. It may turn out that cancer almost NEVER develops in the absence of an inherited "head start" ... and almost ALWAYS requires the interaction of inherited lesions with other forces.

The bottom line on inheritance and other forces is this:

A very large part of the cancer problem can be eliminated, if people CORRECTLY identify and eliminate the non-inherited forces which act alone or act in concert with inherited genetic lesions, in producing malignancy. This book shows that

past exposure to medical x-rays is a MAJOR non-inherited cause of the breast-cancer which has occurred, is now occurring, and is already committed to occur in the future in the USA. Readers who follow the stories, chapter by chapter, will end up realizing that medical radiation is surely a non-inherited cause of OTHER cancers, also. How large the share is, for other cancers, remains to be evaluated.

And What about Pesticides, Hormone Pills, Diet, and EMFs?

There is nothing about the finding of this book to imply that ionizing radiation is the ONLY cause of recent breast-cancer.

Many non-inherited forces, including pesticide by-products, hormone pills, diet, exercise, EMFs (electro-magnetic fields and "transients"), and several additional factors, have been implicated by epidemiologic studies as potential contributors to recent rates of breast-cancer. (Epidemiology is a science which tries to find the causes of diseases, by comparing their frequencies in various groups of people.)

Do we dismiss these other forces? Not at all. Even agents and behaviors which cause no permanent genetic lesions may accelerate a developing cancer in several ways --- without casting any doubt upon the multi-step genetic model of cancer development. The power of such promoters may depend on the presence of genetic lesions.

Indeed, we take this opportunity to say that we are particularly concerned about the question of EMFs, to which human exposure is likely to INCREASE in future years. We highly recommend a collection of papers on EMFs and breast-cancer (Slesin 1994).

With respect to ionizing radiation, the proof that extra exposure is a cause of cancer (including breast-cancer) comes from studies where all sorts of ADDITIONAL non-inherited causes may have been operating too. The point is this: In any valid epidemiologic study, those other carcinogens are acting EQUALLY upon the irradiated groups and upon the non-irradiated groups. Thus, the EXTRA cancers in the irradiated groups can be attributed to the extra radiation, but the REST of the cancers are due to something else (such as equal exposure, on the average, of all the study-groups to chemicals, EMFs, or prior exposure to radiation-sources other than the source studied).

There is no inherent conflict or competition between carcinogens. The multi-step genetic model of cancer development "permits" contributions even to a SINGLE CASE of cancer, from heredity, ionizing radiation, viruses, and chemicals (for example). It is correct to say that each contributor CAUSED the cancer, if the case would not have occurred when it did, without that contributor.

The finding of this book is that an estimated 75 percent of recent and current breast-cancer cases would not have occurred as they did, in the absence of earlier medical (and other) irradiation.

#

CHAPTER 2

"Incubation Times" for Radiation-Induced Cancer

Part 1. The Latency Period

The breast-cancers induced in a population, by the radiation received in a single year, are spread out over many years. Some of the breast-cancers induced in a population by ionizing radiation become clinically evident very soon after exposure, but most of them become clinically evident 10, 20, 30, 40, 50 (and probably more) years later.

Women developing breast-cancer today in their 20s, 30s, and 40s, for example, have to consider the possibility that their breasts received radiation during infancy or childhood. In such cases, the radiation exposure would be a prime suspect for causation, especially if they have an inherited predisposition to cancer. Chapter 3 deals with recent evidence for radiation induction of EARLY-onset breast-cancer.

Many more women, developing breast-cancer in their 50s, 60s, 70s, and 80s, may have "paid the price" for radiation possibly received decades earlier --- as early as the 1910s, 1920s, 1930s, 1940s and 1950s. Of course, it will be impossible for many women of such ages (if they are still alive) to find out if they are the individuals who received breast-irradiation so long ago. This book is likely to astonish them with the number of ways in which it could have happened to them when they were too young to remember it --- during their infancy and childhood.

The time-delay, between the radiation exposures and the diagnosis of clinical cancer, is called the "incubation period" or the "latency period."

We know for certain, from the study of the Atomic-Bomb Survivors in Japan, that the latency period varies enormously among individuals. Is this variation explained by differences in age, at the time of irradiation? Not fully. Among survivors who received their radiation exposure in August 1945, the latency period sometimes varies by decades even among survivors who were approximately the SAME age in 1945. The A-Bomb Study tells us beyond any doubt that each exposure to extra radiation has its total cancer-consequences spread out over many years. (Such evidence is shown in Gofman 1990, Table 17-B, for example.)

Is there a limit to the latency period? Yes. It can not possibly be greater than the remaining lifespan of the irradiated group's most enduring member. Thus, the RANGE of the latency period can be greater for a group irradiated during infancy and childhood, than for a group irradiated at age 60.

Part 2. Latency and Today's Breast-Cancer Problem

The "spread-out" nature of radiation-induced cancer has a very important implication for today's breast-cancer problem. If we want to learn what fraction of recent, current, and future breast-cancer is due to medical (and other) irradiation --- and is therefore preventable --- our evaluation has to begin as early as 1920.

For the sake of illustration, let us consider the 1940s. If a large female population of mixed ages received breast irradiation in 1940, 1941, 1942, 1943, 1944, etc., the

breast-cancer rates observed in 1950, in 1960, in 1970, in 1980, in 1990, and very probably in 2000 and 2010 also, will include some breast-cancer cases produced by irradiation in each of those years of the 1940s.

The maximum duration of the cancer latency-period is not yet known. The existing human evidence is reviewed and discussed in Chapter 17 of our 1990 book. The results from the two longest, largest human studies are explored in detail. They are the study of the A-Bomb Survivors and the study of adult patients irradiated for relief of the pain from ankylosing spondylitis (a serious disease of the spine).

The A-Bomb Study is particularly important, because it includes females irradiated at ALL ages, including children below age 10 --- who have the greatest risk from irradiation. The follow-up evidence through 1985 on cancer deaths shows that the radiation effect is certainly not "over" (finished, gone) in 1985 for people irradiated by the bombs 40 years earlier.

No study yet exists which includes the full lifespan of younger participants. For example, A-Bomb Survivors who were under age 10 in 1945 are under age 60 in 1995. Therefore, no one knows whether radiation's carcinogenic effect will endure for the entire lifespan of the youngest irradiated group, or not. Many experts today assume that it will. We, too, use that assumption in this book. Only future follow-ups of the A-Bomb Survivors will reveal this part of the "story" for certain. The A-Bomb Study is a biomedical resource of unique value.

Specifically Breast Cancer: What We Know about Latency NOW

In 1994, the report entitled "Incidence of Female Breast Cancer among Atomic Bomb Survivors, 1950–1985" was published. We will refer to it in later chapters also. Here, our focus is on what it says about a key question of latency:

Can breast irradiation during INFANCY AND CHILDHOOD really cause radiation-induced breast-cancer in ADULTHOOD?

Some physicians seem incredulous. Nonetheless, the answer is "Yes." During the 1970s, the idea was barely accepted --- even as a possibility --- by segments of the radiation community. In 1981, when the evidence was still thin, we predicted that the answer would turn out to be "Yes" (Gofman, 1981, Chapter 7). The subsequent evidence for "Yes" is so strong that it elicits an emphatic statement (below) from an ordinarily cautious source: Analysts at the Radiation Effects Research Foundation, known as RERF. Funded by the governments of the United States and Japan, RERF controls all the databases of the A-bomb survivors. The 1994 report on breast-cancer incidence (just cited above) was done by RERF analysts: Masayoshi Tokunaga, Charles Land, and four more. Near the paper's end, citing their own data and the data of Hildreth 1989, these analysts state (Tokunaga 1994, p.220):

"At this point, there can be little doubt that radiation exposure of breast tissue during early childhood and infancy can contribute to the risk of breast cancer during adult life." (When irradiation causes an elevated cancer-RISK for an individual, it causes an elevated cancer-RATE for a group.)

Part 3. Why Does the Latency Period Vary among Individuals?

We are often asked an intelligent double-question: "Why does the incubation time vary, and why does it take so long for cancer to become manifest CLINICALLY after exposure to a carcinogen such as ionizing radiation?"

The answer to this question has more than one part.

First, we must emphasize that there is no evidence for thinking that ALL cases take "so long." For example, if a thousand cancer cases are "committed" to occur sooner or later, due to genetic lesions induced by ionizing radiation received by a group of people in 1940, some of the cases probably occur by 1945. Some may even occur immediately.

Why do we say "probably" and "may"? Why can't we say for certain? The answer lies in something called "the small numbers problem." The cases committed in 1940 and occurring by 1945 look clinically just like all the other cancers occurring in the years 1940 through 1944. The presence of the cases committed in 1940, therefore, has to be detected by epidemiology. But if the accumulated number of radiation-induced cases (committed in 1940 and full-blown by 1945) is still very small in 1945, relative to the number of cases occurring anyway, their presence can not be proven statistically even if they are really there. This is the common --- and dreaded --- "small numbers problem" in epidemiology.

"Last Straws," "Early Straws," and Luck

One reason for thinking that some cases may occur immediately derives from the multi-step genetic model of cancer development (Chapter 1). Radiation-induced cases could develop very quickly in individuals who have already accumulated several carcinogenic lesions in a vulnerable cell. For such a cell, a radiation-induced lesion could be the "last straw which broke the camel's back." And the latency period could be extremely short.

But compared with "last straws" from radiation exposure, "early straws" must occur more frequently. Individuals with "early straws" from a radiation exposure will develop cancer only after a cell accumulates ADDITIONAL carcinogenic lesions, so their cancers are likely to show a longer latency period than "last straw" cancers. The multi-step genetic model goes a long way toward explaining the variation in the latency period.

It is important to emphasize that ONLY SOME irradiated individuals with "early straws" ever develop a full set of cancer-lesions, and that not everyone who is irradiated by the same dose of radiation develops cancer later. Because luck plays a role, it is not possible to predict WHICH individuals will develop the extra cancers when a group of people receives radiation. Nonetheless, we (and others) can predict the total NUMBER of individuals who will develop radiation-induced cancer from a known amount of radiation exposure, because we have real-world evidence patiently accumulated by numerous researchers over many decades.

How the "Host" of a Cancer Determines Its Latency Period

The length of the latency period almost certainly depends on the "host" of a radiation-induced cancer. As hosts, people vary in the number and strength of carcinogenic lesions which are inherited, AND individuals vary in the number and strength of carcinogenic lesions which are induced by various non-inherited factors, both

before and after a specific exposure to ionizing radiation. So it would be really surprising if latency did NOT vary from person to person, following a specific radiation exposure.

Ionizing radiation is known to induce a great variety of genetic lesions, most especially chromosomal abnormalities. Because chromosomes are the structures produced by the winding of the DNA around specific proteins, chromosomal lesions are GENETIC lesions. It is abundantly clear now that cancer cells generally show chromosome abnormalities of structure, or number, or both. Moreover, the variety of the abnormalities is also abundantly clear. It is very reasonable to expect that the SPEED of cancer development varies with the particular chromosomal damage which is present in a cell. That is one aspect of saying that the "strength" of carcinogenic lesions varies.

Part 4. The Radiation Effect: "Most Cases" vs. "Early-Onset Cases"

About 22 percent of all deaths per year in the USA are due to cancer. As everyone knows, cancer rates generally increase with advancing age. There is a special set of childhood cancers, but they are fortunately rare. As for leukemia in the USA, about 5 percent of it occurs before age 20, so it is NOT predominantly a childhood malignancy.

What we see for cancer in general (with some exceptions) is a rising rate of new "spontaneous" cases per 10,000 adults, as they advance in age. Some of the so-called spontaneous cases are really radiation-induced cases. Nonetheless, in epidemiologic studies of radiation-induced cancer, analysts are observing the consequence when some people have been exposed to EXTRA radiation, while a comparable control-group has not been exposed to the extra dose.

The observed effect of extra radiation is to cause the spontaneous rates ("background" rates) of cancer to increase, by percentages which depend upon the amount of extra radiation exposure and on the age at which the extra exposure occurs. Most of the spontaneous cancer-cases appear during middle-age and beyond, and so do most of the cases induced by extra exposure to ionizing radiation.

Most cases, but certainly not all.

There is very important evidence from the A-Bomb Study of radiation-induced early-onset breast-cancer --- cases occurring before age 35 --- in women who were under age 20 at the time of the bombings. That is the subject of Chapter 3.

#

CHAPTER 3

Early-Onset Breast-Cancer: Evidence on Radiation-Induction

An enormously important issue is breast-cancer which becomes clinically manifest in very young women --- before age 35, for instance. Recent evidence, discussed below, underscores the importance of acting upon the finding of this book, if prevention is everyone's goal. So that all readers (including the "easy readers") can contemplate the meaning of this new evidence, we introduce the units in which radiation doses are measured.

Part 1. Dose-Units, Especially "Medical Rads"

The term "medical rad" is the one which we use in reaching the finding of this book. To show what it means, we have to cover some other units.

RADS. The "rad" is a unit in which amounts (doses) of ionizing radiation are measured, the way "dozen" measures an amount of eggs. Rad is the abbreviation for "radiation absorbed dose." A rad is really just a ratio of energy delivered by ionizing radiation, per gram of irradiated cells or tissue. A rad is 100 ergs of energy per gram --- a definition which NO reader needs to remember. One thousandth of a rad, or 0.001 rad, is a milli-rad. An effort is underway to re-name the rad as a centi-gray (cGy) and to call 100 rads a gray (Gy). We and many others prefer to stick with rads.

ROENTGENS. The Roentgen is a unit for measuring ionization in air; a few reports also use it for doses inside the body. The abbreviation for Roentgen is R (but a small "r" was customary in the older literature). Under common medical circumstances, an entrance dose of 1 Roentgen at the skin gives a breast-tissue dose of about 0.69 rad, when the beam is traveling from front-to-back of a patient. The Roentgen is the dose-unit often used to describe x-ray dosage from fluoroscopy. In the 1930-1935 era, many fluoroscopy machines could generate beams with dose-rates like 100 Roentgens per minute (Braestrup 1969).

REMS. Another unit is called the rem, an abbreviation for "roentgen equivalent, man." The rem can indicate that adjustments have been made for the non-standard "quality" of some radiations. Usually (but not always) the standard is an x-ray of 100 to 400 KeV. An effort is underway to re-name the rem as a centi-sievert (cSv) and to call 100 rems a sievert (Sv).

MEDICAL RADS. Per rad, gamma rays from an atomic bomb are about half as harmful as x-rays from medical irradiation, so 1.0 rad of A-bomb gamma radiation could be called 0.5 rem. We avoid rems in this book by converting all doses into "medical rads." Hence, 1.0 rad of A-bomb gamma radiation is called 0.5 medical rad.

Some Very Common Radiation Dose-Levels

- - NATURAL BACKGROUND RADIATION. The typical annual dose from natural background radiation, excluding doses from inhaled radon, is about 0.1 rem or 100 milli-rems (BEIR 1972, p.50; BEIR 1990, p.18). The dose per year rises with altitude. Because the natural background dose is mostly from gamma and cosmic radiation, its medical equivalent per year is about 0.05 medical rad (50 medical milli-rads). In a

70-year lifespan, the cumulative dose is about 3.5 whole-body medical rads. A whole-body dose is received by all parts of the body, in contrast to a partial-body dose.

The natural dose-rate per MINUTE is of interest, for comparison with dose-rates from fluoroscopy. Nature's dose-rate per minute is (0.05 medical rad / year) times (1 year / 525,600 minutes), or 0.000000095 medical rad per minute from natural background radiation. If we round this off, it is about one ten-millionth of one medical rad per minute. At this dose-rate, only a tiny fraction of cells is irradiated per minute.

- - AIRLINE TRAVEL. The extra radiation dose, from flying between the east and west coasts of the USA, is about 0.3 milli-rem (0.0003 rem) per HOUR of commercial flying. For a ten-hour roundtrip, the extra dose would be about 3 milli-rems (0.003 rem). It would require about 3,300 flying-hours to receive 1.0 extra rem of whole-body irradiation --- equivalent to about 0.5 extra medical rad. Dose-rates from flying vary with altitude and latitude.

Part 2. The Dose Which Doubles the Rate of Early-Onset Breast-Cancer

Ordinarily in epidemiological studies of cancer-development from radiation, one faces the "small numbers problem" : An insufficient series of cases in the relatively EARLY follow-up period to permit a reliable conclusion. So time is allowed to run, to accumulate additional cases ("statistical power"). And then all the cases --- short latency and long-latency cases, combined --- are examined together for such issues as cancer-increase per rad of dose. But WHAT IS LOST, within the accumulated total, is any evaluation of whether the "early-onset" cases are different from the other cases. From here on, the cases diagnosed before age 35 will be called "early-onset" cases.

With follow-up of the A-bomb survivors now complete for 1950 through 1985, there may be enough total cases of breast-cancer to separate the early-onset cases from the others, and to compare them for induction-rate per rad of irradiation. In 1993, Charles Land, Masayoshi Tokunaga, and additional RERF analysts, made a brief report in the Lancet, entitled "Early-Onset Breast Cancer in A-Bomb Survivors" (Land 1993). By extracting the pertinent data from the figure in their 1993 paper, we can tabulate their findings in the nearby box. They are remarkable results, to say the least!

In their 1993 paper, Land et al are reporting exclusively on female A-bomb survivors who received the bomb-exposure before the age of 20 years. Although Land et al do not say so, the number of females who were exposed by the bombs below age 20 was approximately 12,000, and their average age at the time of bombing was about 10 years old (calculated from Gofman 1990, Table 26-F). There are 205 incident cases of breast-cancer, reported between 1950-1985 for this group. The cases are segregated by Land et al into two main groups: Women whose breast-cancers occurred before age 35 years constitute one group, and women whose breast-cancers appeared after age 35 years, the other group. We repeat: All the women were less than age 20 at the time of exposure.

In the boxed tabulation, the entries for "fractional increase ... per rad" indicate a spectacular difference between early-onset cases versus cases occurring at age 35 and beyond. The difference is treated as real (not spurious) in both Land 1993 and Tokunaga 1994. We shall propose an explanation of the difference in Part 4. But here, we will focus on the breast-dose which, if delivered sometime before age 20, can DOUBLE the

● - TABULATION BASED UPON LAND ET AL, 1993.

Average Age When Breast- Cancer Occurs	Number of Breast- Cancer Cases	Fractional Increase in Breast-Cancer Rate over Spontaneous Rate PER RAD
Breast Cancers Occur Before		
Age 35 years	32 years	27
Breast Cancers Occur After	41 years	80
Age 35 years	49 years	85
	57 years	13
Sum of cases, bomb-exposed women		205 cases.

rate of early-onset breast-cancer. This value can not change with any future observation of the A-bomb survivors, because the story for EARLY-onset cases was over when the youngest survivors (newborn in 1945) passed the age of 35 --- in 1980.

The "Doubling Dose" for Early-Onset Breast-Cancer

The dose which doubles the spontaneous frequency of early-onset breast-cancer is the dose which causes a 100 % increase in its spontaneous rate. Therefore, to estimate how many rads would cause a 100 % increase, we divide 100 % by 13.6 % per rad (from the boxed tabulation). Thus, 7.35 rads, received before age 20, is the approximate doubling dose for early-onset breast-cancer.

The doubling dose for early-onset breast-cancer is even lower when we consider medical x-ray radiation, or beta particles of energy comparable to such x-rays. The medical rad has approximately two times the effectiveness of A-bomb radiation from which Land, Tokunaga, and colleagues developed their findings. Therefore, we must warn that the dose of medical rads required to double the spontaneous rate of early-onset breast-cancer must be in the neighborhood of only 3.68 medical rads, received sometime before age 20. As readers will see in Sections 2 and 3 of this book, such doses and far higher ones have been commonly received during childhood from certain medical procedures --- and we do NOT mean doses from radiation therapy after a cancer has already occurred.

Part 3. A Test for Agreement about the Magnitude of Risk

Below, we will show the good agreement between RERF's quantification of risk (by Land, Tokunaga, et al) and our own independent analysis of 1990. The "easy readers" of this book may wish to skip to Part 4 or Part 5, but others will find Part 3 very interesting.

Our analysis used the data on cancer deaths (all types) from 1950–1982 in the A-Bomb Survivors, and the RERF analysis used exclusively the breast-cancer incidence from 1950–1985 among the A-Bomb Survivors. Both analyses (Gofman and RERF) are finding out the "fractional increase or percent increase above the spontaneous rate, per rad" --- a concept which we named "the K-value" simply for the sake of brevity. Tokunaga et al call the same thing "Excess Relative Risk," or ERR.

Based on the linear dose-response in Tables 15-G and 15-H of Gofman 1990, our K-value estimate for females exposed at ages 0–9 years is 0.01922 (the same as 1.922 %). Age 0 means from birth to the first birthday. For exposure at ages 10–19, the K-value is 0.01097 (or 1.1 %). When the two values are weighted by the number of cases, the average is 0.01265, or 1.265 % per rad for exposure at ages 0–19. This value is for ALL types of cancer, combined. For breast-cancer alone, the K-value is 2.524 times the value for combined types (Thompson et al 1994, pages S26, S49, S61). Multiplying the 1.265 % per rad for all cancers, by 2.524 to adjust for breast-cancer alone, we obtain a K-value of 3.2 % per rad for breast-cancer, when bomb-exposure occurred at ages 0–19 years.

The comparable K-value from RERF's own analysis is 2.41 % per rad --- from Tokunaga 1994, p.215, Table VI. RERF's value is derived from observations of cancer incidence, whereas our value is derived from observations of cancer mortality. When our 3.2 % is divided by their 2.41 %, we see that one estimate differs from the other by only 33 %. The two separate analyses are in remarkably close agreement.

The similarity in estimates is supportive of the concept that, when extra radiation induces extra cancers, it induces cancers which are fatal and non-fatal in the same proportion as occurs without the extra exposure to radiation.

Part 4. Early-Onset Cases vs. Later Cases: Why Such a Difference?

If readers look back in Part 2 at the boxed tabulation, they will see the column for "average age when breast-cancer occurs" for 205 of the A-bomb survivors irradiated between birth and age 20. For cases diagnosed at an average age of 32, the percent increase per rad above the spontaneous rate is 13.6 %, whereas the percent increase per rad is DRAMATICALLY LOWER if diagnosis occurs at the average ages of 41 years, or 49 years, or 57 years.

What accounts for the striking difference? Is there some big biological difference between the radiation-induction of breast-cancer for cases which appear before age 35, compared with the radiation-induction of cases which appear after age 35? Is there some altered response (to irradiation during childhood) in the irradiated HOSTS after they pass age 35? Various possibilities are discussed in Tokunaga 1994 (pp.221–222).

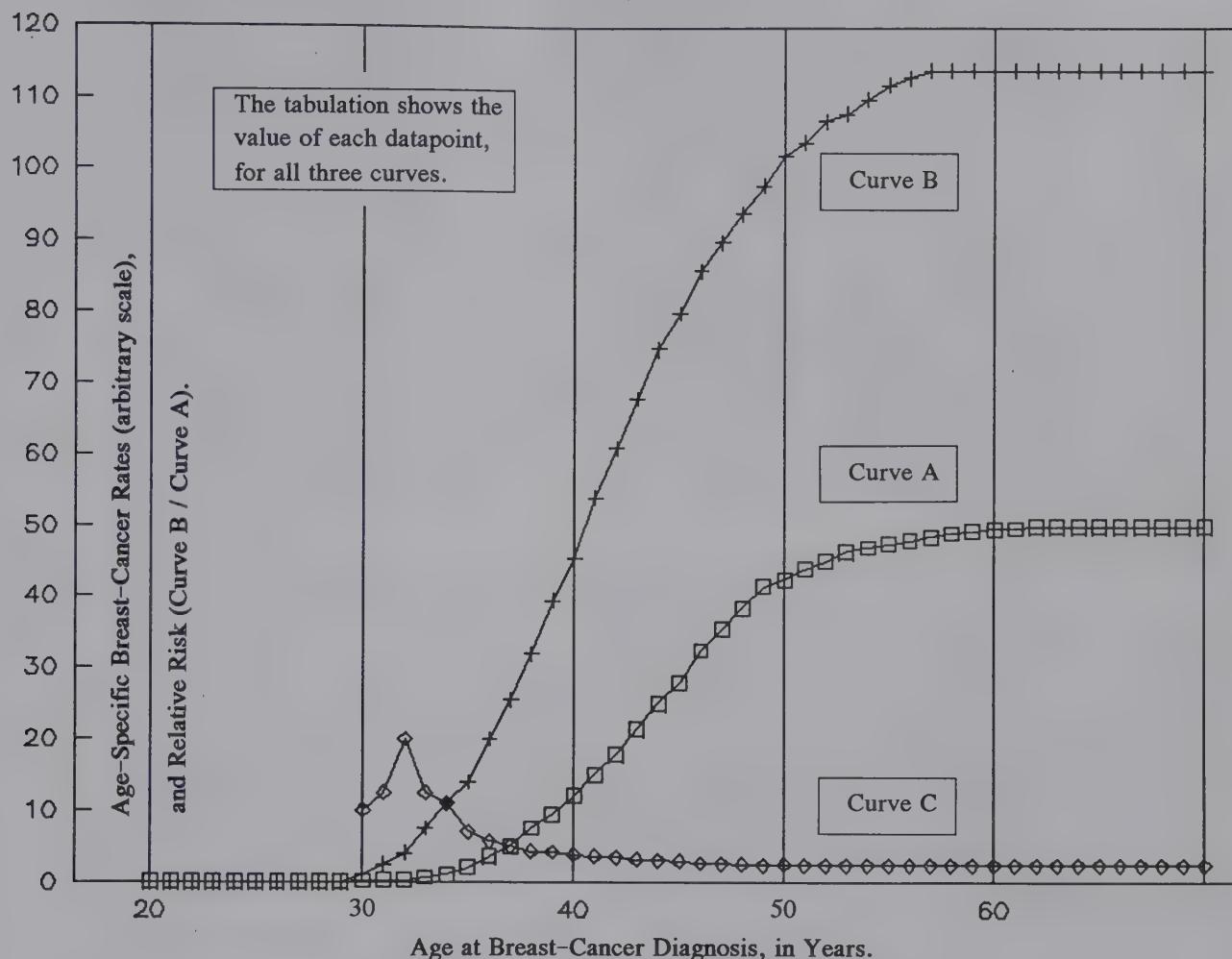
We propose a relatively simple explanation. Our figure, "Three Curves with a Story," demonstrates how the observed difference could arise.

Who Are These Curves?

- – CURVE A: In the nearby figure, Curve A depicts a SPONTANEOUS breast-cancer rate beginning to rise when women reach the age of about 30. We wish to emphasize that Curve A is a "generic" or illustrative curve, with imaginary rates of new cases (per 10,000 women) on the vertical axis. The reality-based aspect of Curve A is its depiction of a rise which is gradual, then steep, and then gradual again.

Three Curves with a Story

- Curve B = breast-cancer rate in women irradiated below age 20, by an unspecified dose.
 Curve A = spontaneous breast-cancer rate in comparable non-irradiated women.
 Curve C = relative risk (Curve B / Curve A).



Age	A	B	C	Age	A	B	C
29	0	0		50	42.5	102	2.4
30	0.1	1	10.0	51	44.0	104	2.4
31	0.2	2.5	12.5	52	45.0	107	2.4
32	0.2	4.0	20.0	53	46.5	108	2.4
33	0.6	7.5	12.5	54	47.0	110	2.4
34	1.0	11.0	11.0	55	47.5	112	2.4
35	2.0	14.0	7.0	56	48.0	113	2.4
36	3.5	20.0	5.7	57	48.5	114	2.4
37	5.05	25.5	5.0	58	49.0	114	2.3
38	7.5	32.0	4.3	59	49.3	114	2.3
39	9.5	39.5	4.2	60	49.6	114	2.3
40	12.0	45.5	3.8	61	49.7	114	2.3
41	15.0	54.0	3.6	62	50.0	114	2.3
42	18.0	61.0	3.4	63	50.0	114	2.3
43	21.5	68.0	3.2	64	50.0	114	2.3
44	25.0	75.0	3.0	65	50.0	114	2.3
45	28.0	80.0	2.9	66	50.0	114	2.3
46	32.5	86.0	2.6	67	50.0	114	2.3
47	35.5	90.0	2.5	68	50.0	114	2.3
48	38.5	94.0	2.4	69	50.0	114	2.3
49	41.5	98.0	2.4	70	50.0	114	2.3

For ages 20 through 29, the spontaneous frequency of breast-cancer is very low (shown as "zero" rate). Then, for ages 30, 31, and 32, we have elevated each data-point (really, data-symbol) SLIGHTLY above the baseline. At age 33, we show the rate of new cases starting to increase in each successive year, with the amount of annual increase greater (steeper) between ages 35 and 50 than between ages 50 and 60, for example. The rates plotted as Curve A are tabulated in the box underneath the figure.

- - CURVE B: Curve B depicts the corresponding breast-cancer rate in a comparable group of women who received breast-irradiation between birth and age 20. Again, we show IMAGINARY rates of new cases (per 10,000 women) on the vertical axis, and we have not specified any particular radiation dose. What we are showing, however, is reality-based: Starting at age 30, the irradiated group shows a rate of breast-cancer which is HIGHER than the spontaneous rate. The real-world observations of a higher rate were discussed in Part 2. Among the irradiated A-bomb survivors who were ages 0–19 during the bombings, there are 27 cases of early-onset breast-cancer --- and all but 2 or 3 of those cases were diagnosed when the women were ages 30 through 34 (Tokunaga 1994, p.214). There are 178 additional cases diagnosed after age 35 in that group.

What we want to explain is why the percent increase per rad is so much higher for the cases diagnosed at the average age of 32 (the early-onset cases) than for cases diagnosed later. Curve C depicts the question.

- - CURVE C: Curve C shows the result when each cancer-rate of Curve B, for irradiated women, is divided by the corresponding (and lower) cancer-rate of Curve A, for non-irradiated women. The values are also tabulated beneath the figure. These ratios are the relative rates, or Relative Risks (RR), which quantify how many TIMES higher the exposed rate is than the spontaneous rate. We plot the RR values as Curve C, which uses the scale of the vertical axis as an "all-purpose" scale (just don't say "per 10,000 women").

At age 32, the tabulation shows that the irradiated rate is 20 times higher than the spontaneous rate. To transform this Relative Risk of 20 into percent increase per rad (K-value), we just subtract 1.0 from the Relative Risk and then divide 19 by the dose in rads. Example: If the average dose which produced Curve B were 110 rads, then the fractional increase per rad for cases diagnosed at age 32 would be $(19 / 110 \text{ rads})$, or 0.173 per rad --- which is the same as 17.3 % per rad.

What Is the "Story" of A, B, and C?

Curves A and B are nice, smooth curves suggesting nothing biologically EXOTIC. Nonetheless, their relationship generates a stunning PEAK in Relative Risk, and therefore in percent increase per rad, for early-onset cases diagnosed at an average age of 32. After its peak value of 20, Relative Risk declines dramatically --- down to 4.3 for diagnosis at age 38, down to 3.0 for diagnosis at age 44, and then remaining above 2.0 for diagnosis beyond age 44.

What is the meaning of this peak for early-onset cases?

When two curves (for irradiated and non-irradiated groups) have been near the zero-rate during a follow-up study, the addition of just a few cancer-cases to one curve earlier than to the other curve has to cause very high Relative Risks --- even when the

higher rates are not very high at all. Such events are illustrated for ages 30, 31, and 32 at diagnosis. At age 29 and younger, the breast-cancer rates are shown as equal in the irradiated and non-irradiated groups. Curves A and B are right on top of each other, at the zero-rate. At age 30, both rates increase a LITTLE (see the tabulated values): Non-irradiated moves to 0.1 case per 10,000 women, and irradiated moves to 1 case per 10,000 women --- a very low rate compared with what is coming later. Nonetheless, this slight change means that the risk goes "overnight" from being equal in both groups, to being 10-fold higher in the irradiated group --- all because of 1 case per 10,000 women. At ages 31 and 32, additional small changes drive the Relative Risk to its peak at 20.

In computing Relative Risks, the spontaneous rates are the denominators of the fractions. As long as the spontaneous rates remain near zero, even modest growth in the exposed rates will generate enormous Relative Risks. The phenomenon does not happen when analysts look at the women exposed at older ages, because the spontaneous rate is already well above zero when analysts begin comparing the irradiated and non-irradiated groups.

The Key: A Baseline Rate Near Zero

For A-bomb survivors irradiated below age 20 and diagnosed with early-onset breast-cancer before age 35, the exceedingly high Relative Risks (and percents increase per rad) are real --- but their initial magnitudes turn out to be temporary. Relative risks compute at a less spectacular level as soon as the spontaneous cancer-rates have their own rapid climb (away from zero) in the denominator of such ratios. We have been able to mirror these observations, in a generic way, with Curves A and B, which generate Curve C. The three curves also mirror the observation that the less spectacular Relative Risk (for cases diagnosed after age 40) persists at an approximately constant level through the 1985 follow-up (see Land's data in Part 2; confirmation in Tokunaga 1994, p.221).

In our opinion, "Three Curves with a Story" means this: Analysts of the A-Bomb Study need not invoke special concepts about the cancers or the hosts, in order to explain the much higher Relative Risk observed for early-onset cancer-cases than for the cases diagnosed at older ages. The observed difference in Relative Risk, due to radiation, can be explained by the fact that both curves rise from a baseline rate which is very close to zero.

True Meaning of "Less Spectacular"

The "less spectacular" Relative Risk really reflects a much greater number of radiation-induced breast-cancers than the peak Relative Risk. In figures like ours, it is the AREA under a curve which reflects the aggregate number of cases observed. The area under Curve B minus the area under Curve A reflects the EXCESS number of cases induced by radiation. Clearly, the difference in the two areas for ages 30 through 35 is very small compared with the difference in the two areas beyond age 35. The "less spectacular" Relative Risk not only endures much longer, but it reflects the multiplication (by radiation exposure) of a much higher spontaneous cancer-rate.

Part 5. The Need for Action

How many women who have developed early-onset breast-cancer over the past half-century KNOW whether or not they were irradiated in infancy?

We wonder. Readers of this book are going to learn about a very large number of female children who suffered the fate of such undesirable irradiation of the breasts --- even before they left the nursery of hospitals where they were born. Others suffered nearly the same fate in their first few years of life.

No one can alter the past. But from the past, we can learn the key to preventing many, many cases of early-onset and later breast-cancer. Prevention.

Time Would Tell ... And Time Has Told

Once upon a time (1977), the United Nations Scientific Committee on the Effects of Atomic Radiation, known as UNSCEAR, speculated that breast-irradiation during infancy and childhood might have "minimal" cancer-consequences because "only a few breast cells" exist to be irradiated before puberty (UNSCEAR 1977, p.389). Since these few cells must be the progenitors of all future breast-tissue cells, we rejected that line of reasoning (Gofman 1981, p.249-250).

In 1994, the issue seems settled. Tokunaga et al (1994, p.215, Table VI) report statistically significant excess breast-cancer rates in the bomb-irradiated women who were ages 0-9 years old in 1945 --- as well as in the group which was 10-19 years old in 1945. Both groups, each analyzed separately for the period 1950-1985, show the excess. And both groups have much higher risks per rad than risks for women who were 20 years of age and older at the time of the bombings.

The Irradiation of Children Today

The era of irradiating children is far from past. The diagnostic use of x-rays can be extremely helpful in pediatric medicine. For example, we are aware that a high number of x-rays may be taken of premature infants and others in neonatal intensive care units (NCRP 1989). The use of x-rays is also high in association with birth defects (especially heart problems). The use of x-rays for children involved in automobile and other accidents can also be high, especially if there are insurance battles and lawsuits.

The task mandated by the evidence in this chapter is not to stop such examinations, but rather, it is to make sure that the frequency and doses are kept to the minimum really NEEDED. In Section 4 of this book, we have some suggestions about what concerned parents, physicians, and medical schools can do.

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CHAPTER 4

Three Key Concepts in Our Analysis

Part 1. Breast-Cancer: Production-Rate vs. Incidence-Rate

The purpose of this chapter is to draw distinctions between three concepts, because the distinctions will make the method of this study readily understandable.

- A. Annual production-rate of breast-cancers by radiation.
- B. Annual delivery-rate (incidence-rate) of radiation-induced clinical breast-cancers.
- C. The "Law of Equality," which refers to the situation when the annual clinical incidence-rate is equal to the annual production-rate, DESPITE the latency period.

Production versus Delivery: Cases on the "Shelf"

The breast-cancers produced in a population, by radiation received during a single year, do NOT all occur exactly 3, 10, 20, 30, 40, or 50 years later. Rather, a certain number are COMMITTED in a single year, and this number is spread out CLINICALLY over many years, as explained in Chapter 2. We shall use the terms "committed" and "produced" as equivalent. The concept of production simply means that, once the irradiation has occurred, some cells of female breasts have experienced an addition of lesions essential for developing breast-cancer. Some fraction of the females who received such lesions will later develop overt, clinical breast-cancer.

We can think of a simple shelf. The irradiation received in a particular year puts "on the shelf" a certain number of future breast-cancers. These are the produced breast-cancers or committed breast-cancers, from this one year of radiation exposure. At some later time, and over a period of many years, those produced breast-cancers come "off the shelf" and are "delivered." By delivered, we mean that they become CLINICAL breast-cancers, or clinically DETECTED breast-cancers.

If readers just keep the distinction in mind between annual PRODUCTION-rate and annual DELIVERY-rate, they will already be well advanced into understanding the method of our study.

Relationship of Annual Incidence-Rate to Annual Production-Rate

Now we come to the third concept: Years when the annual incidence-rate is equal to the annual production-rate, DESPITE the variable and often long period of latency. We will demonstrate the "Law of Equality" in Part 2.

Application of this "law" achieves almost everything! In other words, this concept explains how we will approach the problem of FINDING OUT what fraction of recent, current, and future breast-cancer is due to past irradiation. Readers who intend to follow the method on which our findings rest, will need to grasp this law. The "easy readers" can do without it, of course, or can come back to it after a first "flying read" of the book's more narrative parts. However, we encourage everyone to try Part 2 of this chapter, which is really easier than some readers may imagine.

Part 2: A First Demonstration of the "Law of Equality"

How can annual incidence-rate become equal to annual production-rate, despite the variable latency period? In a problem such as this, it helps a great deal to start with some simplified or idealized conditions, so that the mind is not diverted by real but momentarily deferrable details, to which we will attend gradually.

In our first demonstration, readers should note three key conditions: The same age for everyone who is irradiated, the same number of such people, year after year, and the same radiation dose, year after year. By people, we mean female people, since our focus in this book is breast-cancer.

So, for the first demonstration, we arbitrarily say that the age is 5 years of age, the number of such female children is constant but not specified, and the radiation dose to the breasts each year is a dose which produces (commits) a total of 100 cases of breast-cancer, excluding any cases which occur sooner than ten years after production.

The Various Rows of Figure-A

The first demonstration corresponds with Figure-A. Let us focus on the bottom row of boxes. Each box represents 2.5 cases of clinical breast-cancer. The bottom row of 40 boxes represents 100 clinical breast-cancers PRODUCED by irradiation during 1920. We will pretend that there was no breast-irradiation before 1920, and that 1920 initiates the annual production of 100 radiation-induced breast-cancers.

How do we distribute the cases PRODUCED during 1920? We know that the latency period is variable. For simplicity, Figure-A arbitrarily shows 2.5 CLINICAL cases observed per year, after an initial latency period of 10 years, (1921 through 1930), and this detection-rate of 2.5 cases per year goes on for 40 years. Thus, the bottom row is depicting 40 different latency periods. The irradiation during 1920 has put 100 cases "on the shelf," and every one of those cases labeled "produced" ultimately becomes one which is delivered, labeled "clinically detected." The delivery, from the 1920 production, begins during 1931 and is completed during the year 1970 --- a total of 40 years.

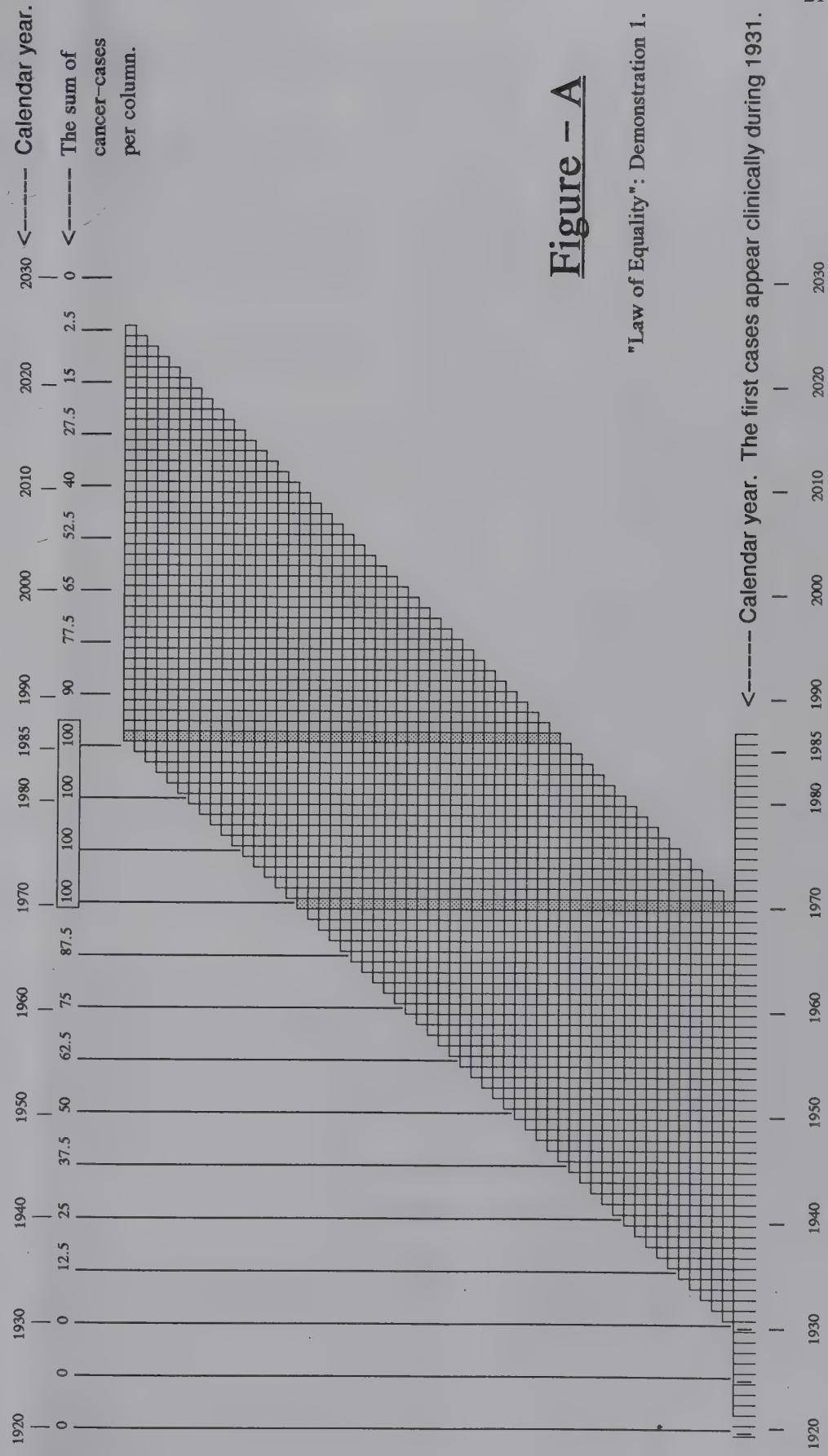
The next row of Figure-A shows that, in 1921, the same thing occurs: The same number of 5-year-olds (who are not the same children as those who were age 5 during 1920) receives the same dose (which puts another 100 breast-cancers "on the shelf"). And Figure-A, with its 56 rows, shows this production-rate continuing every year through 1975 --- an arbitrary "cut-off" date. Because of the initial latency period of ten years, the FIRST delivery from 1975-production occurs in 1986, as shown by the top row.

The Various Columns of Figure-A

Each vertical column depicts the number of CLINICAL breast-cancers detected (delivered) in a specific year. Each box represents 2.5 clinical cases, so the number detected during 1931 = 2.5 cases, but the number detected during 1940 has risen to 25 cases. In 1933, age 18 delivers the bottom box; age 16 delivers the top box.

The key point is that during 1970, the INCIDENCE-rate of radiation-induced breast-cancer reaches 100 cases --- which is equal to the annual PRODUCTION-rate --- and the equality (100 cases) is shown to recur in 1971, 1972, 1973, and in every year through 1986. The columns for these years of equality are the shaded columns and those between the two shaded columns.

- Each box in the grid represents 2.5 cases of clinical breast cancer.
- Each horizontal row of 40 boxes represents 100 breast cancers — the number PRODUCED by a single year of irradiation. So each row represents one year of production. In Fig.A, the group irradiated in 1920 is age-5. In 1921 (next row), it's a new group, age-5, etc.
- Each vertical column represents the number of radiation-induced breast-cancers clinically DETECTED in a single year.
- Both SHADED columns have 40 vertical boxes, as do the columns BETWEEN the two shaded columns. Such columns represent 100 clinically DETECTED breast-cancers per year, in the years 1970 through 1986. These are the columns which demonstrate "the law of equality" under the conditions specified in the text, Part 2.



Statement of the "Law of Equality"

So Figure-A has demonstrated the "Law of Equality": If the same level of irradiation is maintained year after year, and if the number of irradiated females is the same every year, we finally reach the situation where the annual clinical incidence-rate of radiation-induced breast-cancer is equal to the annual production-rate of radiation-induced breast-cancer, and this annual incidence-rate will endure indefinitely, if we maintain the annual production-rate. And this occurs DESPITE the variable latency period for the cases produced in a single year.

Figure-A also shows what happens if the annual production-rate is NOT maintained. We arbitrarily made 1975 the last year of irradiation (with delivery beginning in 1986, after an initial latency). Although the annual production-rate goes suddenly to ZERO in 1976 and thereafter, the annual incidence-rate of radiation-induced cases falls GRADUALLY (that is, the number of boxes per vertical column declines, until there is just one box occurring in the vertical column for the year 2025).

Duration of the Radiation Effect

In Figure-A, the total duration of the radiation effect is 50 years --- 10 years of an initial latency period plus 40 years of "delivery." This initial latency period and total duration were chosen to be only illustrative. We are quite confident that, in reality, there is no MINIMUM latency period, as noted in Chapter 2. And in reality, the duration of the radiation effect may exceed 50 years in people who are irradiated as children. By contrast, the duration of effect will surely NOT exceed 50 years in women irradiated at age 55, because of the natural lifespan of humans.

Part 3. The Law's Validity under Real-World Conditions

Because the "Law of Equality" is central to the method of our study and therefore central to our findings, we intend to prove, below, that the law also applies to real-world conditions.

For example, the law applies no matter what the delivery-pattern may be for the cancers committed during a single year of production. There was nothing "magical" about the pattern illustrated by Figure-A. The patterns in Figures B and C will each be very different from Figure A, in initial latency periods and in speed. Most importantly, we will demonstrate that the law applies to a population of MIXED ages, when the cases committed by a single year's radiation exposure are delivered "from the shelf" at a NON-UNIFORM rate per year. This situation is a very close approximation to reality, and will constitute our final demonstration.

Figure-B: The Second Demonstration

For ease of comparing Figures A and B, we want to keep the total cancers committed per year of radiation exposure at 100 cases, in Figure-B. Nonetheless, we make radical changes from Figure-A regarding the initial latency period (now 30 years instead of 10 years), and regarding the speed of delivery (now 5 clinical cases delivered per year instead of 2.5 cases per year).

In Figure-B, each box represents 5 cases of clinical breast-cancer (not 2.5 cases). The bottom row of 20 boxes represents 100 clinical breast-cancers produced by irradiation during 1920. The first cases are delivered during 1951, and the last ones during 1970. The next row represents 100 clinical cases produced by irradiation during 1921.

- Each box in the grid represents 5 cases of clinical breast-cancer.
- Each horizontal row of 20 boxes represents 100 breast-cancers — the number PRODUCED by a single year of irradiation. So each row represents one year of production.

- Each vertical column represents the number of radiation-induced breast-cancers clinically DETECTED in a single year.

- Both SHADED columns, and all columns BETWEEN the two shaded columns, have 20 vertical boxes. Such columns represent 100 clinically DETECTED breast-cancers per year, in the years 1970 through 2006. These are the columns which demonstrate "the law of equality" under the conditions specified in the text, Part 3.

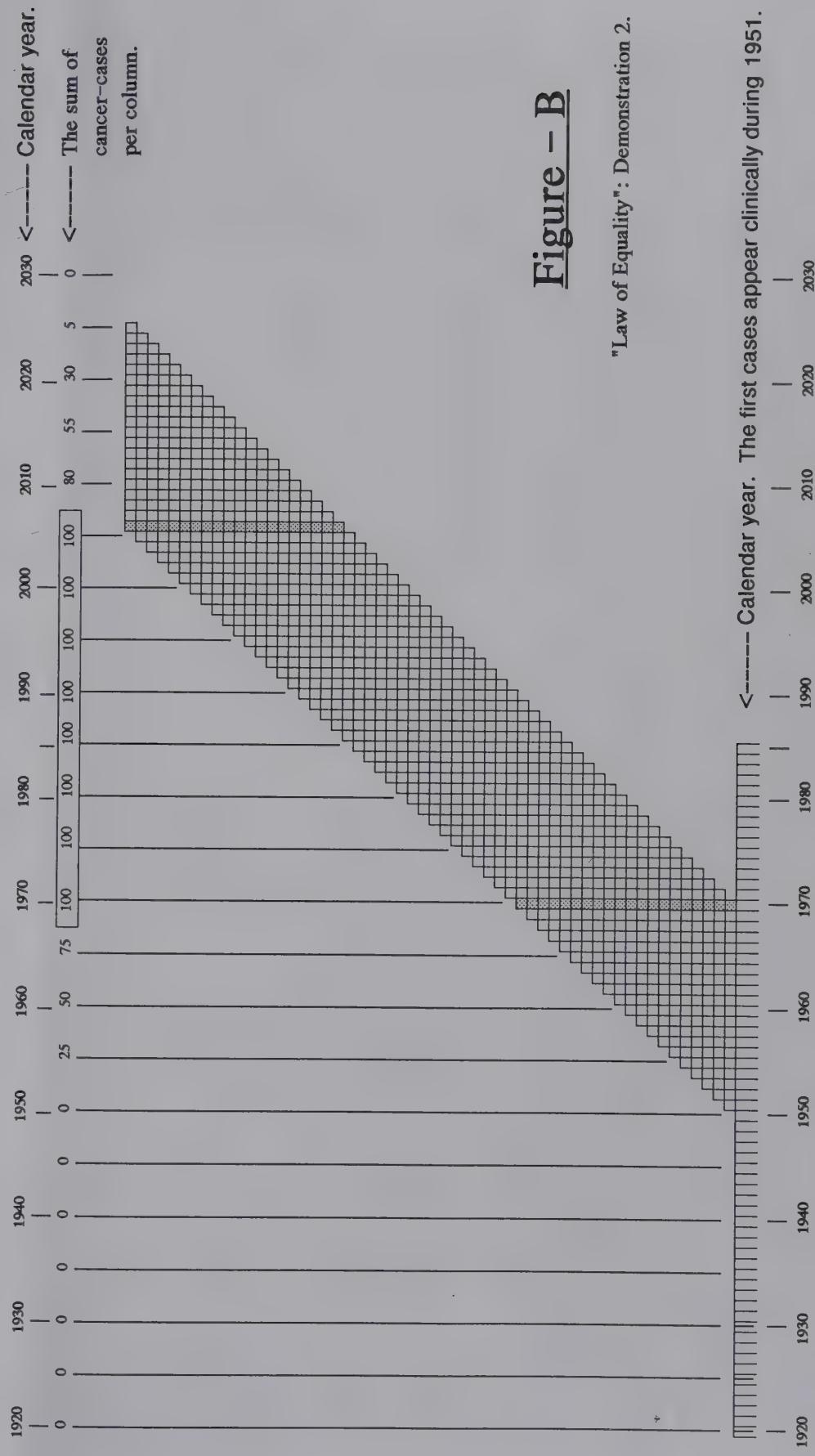


Figure – B

"Law of Equality": Demonstration 2.

Figure-B, with its 56 rows, shows this production-rate continuing every year through 1975 --- an arbitrary "cut-off" date. Because of the 30-year initial latency period, the FIRST delivery from 1975-production occurs in the year 2006, as shown by the top row.

Each vertical column depicts the number of clinical breast-cancers delivered (detected) in a specific year. The number detected during 1951 = 5 cases, and the number detected during 1960 has risen to 50 cases. During 1970, the incidence-rate of radiation-induced breast-cancer reaches 100 cases --- which is equal to the annual production-rate --- and the equality (100 cases) is shown to continue annually through the year 2006, because the annual production-rate was maintained through 1975. Thus, despite a radical change in initial latency period and delivery rate, the "Law of Equality" is validated by Figure-B.

Figure-C: The Third Demonstration

Figure-C deals with the serious problem of cancers delivered "from the shelf" very quickly (in LESS than ten years). Again, we pretend that breast-irradiation first occurs in 1920. The total production of cases which will occur within ten years = 20 cases (not 100 cases). We choose a lower number just to indicate that such cases are outnumbered by cases with longer latency periods.

In our Figure-C, delivery of clinical cases begins after an initial latency period of 3 years, and occurs at the rate of 5 cases per year, so the annual production-rate of 20 cases is delivered over only four years. For cases committed during 1920, delivery begins during 1924 and finishes during 1927. For cases produced during 1921, delivery begins during 1925 and finishes during 1928. The structure of Figure-C is comparable to Figures A and B.

During 1927, the situation is reached where the annual clinical incidence-rate of radiation-induced breast-cancer is equal to the annual production-rate of radiation-induced breast-cancer: 20 cases per year. And this equality continues year after year, as long as the annual production-rate is maintained. So, the "Law of Equality" is validated again. The "short-latency" cases obey the principle with no deviation.

Figure-D: The Key Demonstration

In Figure-D, we treat a far more complex type of delivery of cases "from the shelf." We call this "the key demonstration" of the law, because it so nearly approximates the real-world situation: A non-uniform rate of delivery. However, we want to emphasize that the delivery-pattern chosen for Figure-D is only illustrative of countless possible delivery-patterns.

We return to the annual production-rate of 100 cases put "onto the shelf" --- every year. For delivery of each year's production, we use a nine-year initial latency period, with delivery beginning during the tenth year and distributed as follows:

Four successive years of 15 clinical breast-cancers per year (= 60 cases delivered), followed by eight successive years of 5 clinical cases per year (= 40 more cases delivered).

In Figure-D, each letter represents 5 cases of clinical breast-cancer. Each year of production has its own letter, so that readers can distinguish one year's commitment from the next year's commitment. For example, we can pretend that all the "A" boxes were produced during 1920, all the "B" boxes during 1921, etc. We use 20 different letters,

- Each box in the grid represents 5 cases of clinical breast-cancer.
 - Each horizontal row of 4 boxes represents 20 short-latency breast-cancers —— the number PRODUCED by a single year of irradiation. So each row represents one year of production.
 - Each vertical column represents the number of radiation-induced short-latency breast-cancers clinically DETECTED in a single year.
 - Both SHADED columns, and all the non-shaded columns BETWEEN the two shaded columns, have 4 vertical boxes. Such columns represent 20 clinically DETECTED short-latency breast-cancers per year, in the years 1927 through 1979. These are the columns which demonstrate "the law of equality" under the conditions specified in the text, Part 3.

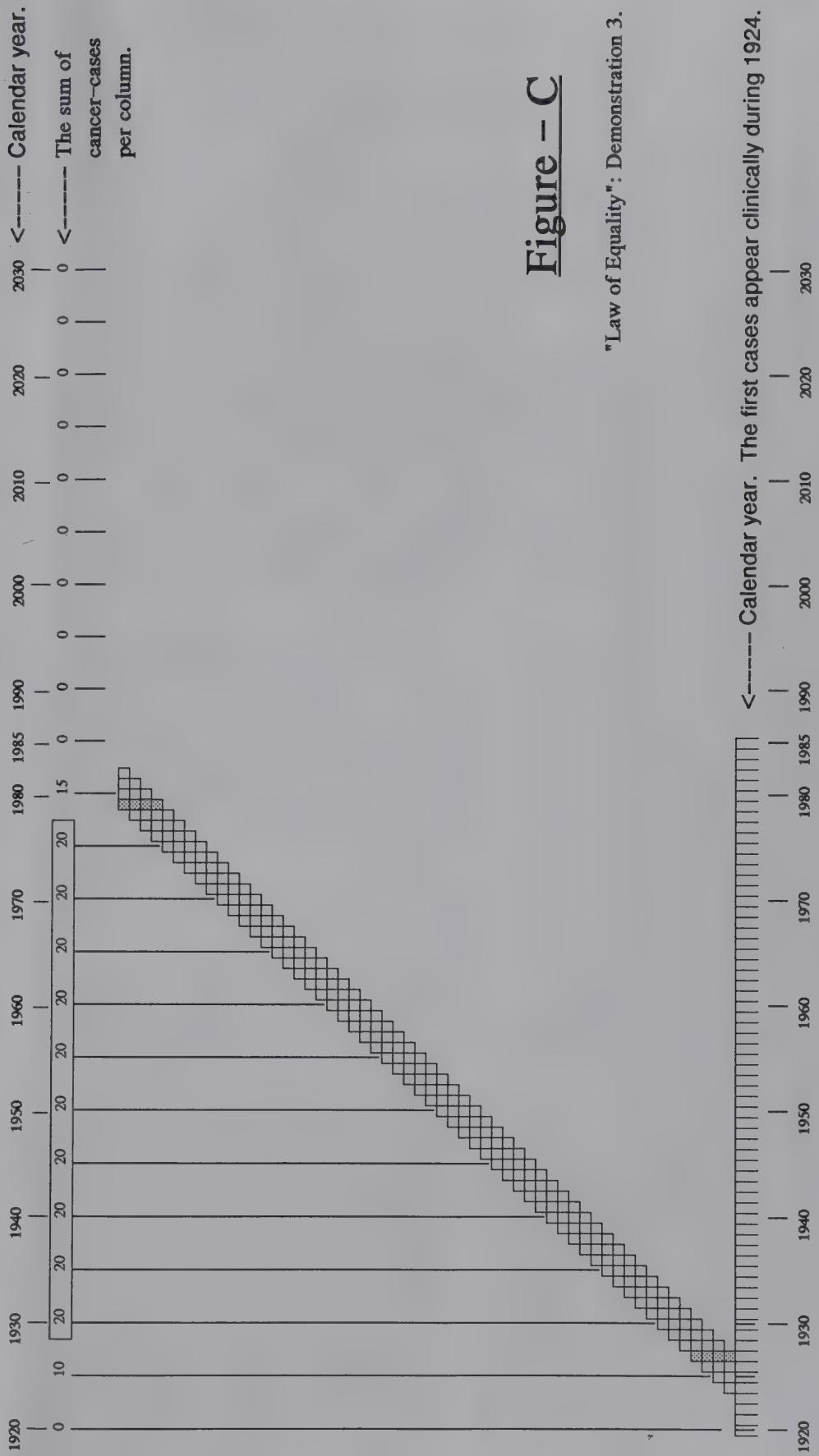


Figure - C

"Law of Equality": Demonstration 3.

Figure - D

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of radiation-induced breast-cancer.

- PRODUCED by one year of irradiation = 100 cases. The annual production is delivered as follows: An initial 9-year latency period, followed by four successive years of 15 clinical breast-cancers per year (= 60 cases delivered), followed by eight successive years of 5 clinical cases per year (= 40 more cases delivered). Thus twelve different latency periods are depicted.

- – Each year of production has its own letter, so that readers can distinguish one year's commitment from the next year's commitment. Figure-D depicts 20 successive years of production (Letters A through T).

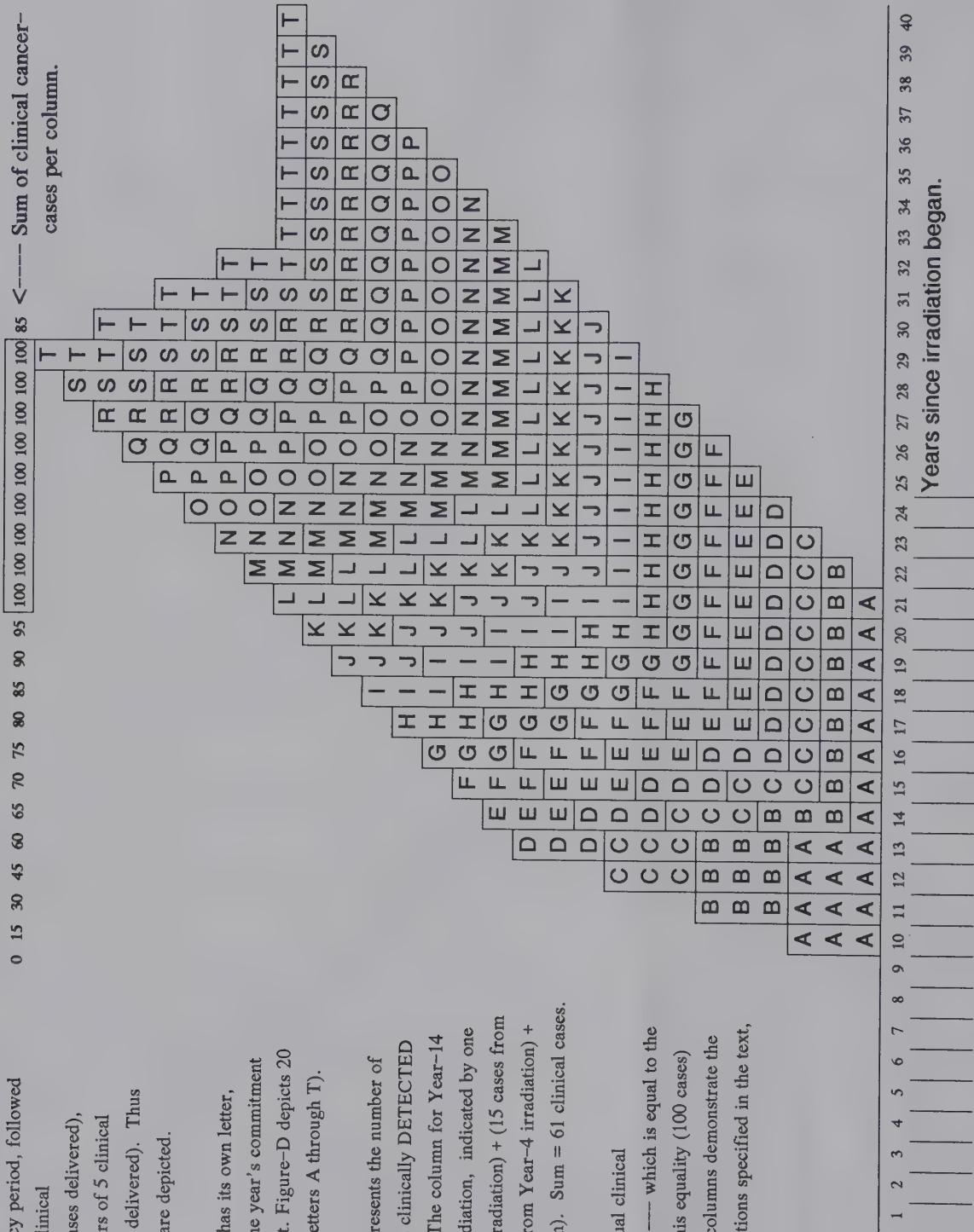
- Each vertical column represents the number of radiation-induced breast-cancers clinically DETECTED during a single year. Example: The column for Year-14 shows (5 cases from Year-1 irradiation, indicated by one 'A') + (15 cases from Year-2 irradiation) + (15 cases from Year-3 irradiation) + (15 cases from Year-4 irradiation) + (15 cases from Year-5 irradiation). Sum = 61 clinical ca.

- During Year-21, the annual clinical incidence-rate reaches 100 cases — which annual production rate — and this equality lasts for nine years. These nine columns describe "law of equality" under the conditions specified part 3.

| Years since irradiation began.

"Law of Equality": Demonstration 4.

Sum of clinical cancer-cases per column.



representing 20 different production-years. The vertical columns have the same meaning as in the preceding figures: They depict the total incidence of radiation-induced breast-cancers delivered during a single year.

Examination of the strange-looking result shows that, during the 21st year, the annual clinical incidence-rate of radiation-induced breast-cancer reaches 100 cases --- which is equal to the annual production-rate --- and this equality (100 cases) continues year after year, for a total of nine years. During the years of constancy, each vertical column has a stack of 20 letters.

During the 30th year, the columns begin to lose height (letters) only because we arbitrarily stopped the annual production-rate. The last production-year represented by "T" boxes is Year-19. Delivery of "T" cases begins in Year-29 (after the latency). In Year-30, there are no "U" cases for delivery because none were produced. If we had NOT stopped the steady, annual production-rate, the constant annual clinical-rate would have continued at 100 cases per year INDEFINITELY.

So, Figure-D proves that the result becomes "neat," despite some interesting irregularities which occur in the annual incidence-rate BEFORE it becomes constant. The "Law of Equality" is validated again.

Part 4. The Final Significance of These Proofs

We have shown in Part 3 that various possible "exercises" each lead to a stable, constant, annual incidence-rate of radiation-induced clinical breast-cancers. The constancy endures as long as a constant annual production-rate endures among a population of constant size. It follows that any COMBINATION of constant incidence-rates will itself become a constant total rate, for all the possible "exercises" combined.

This concept has great importance for handling a population of MIXED ages, which we must do in our analysis.

Suppose that 0-9 year-old children differ from the 10-19 year-olds in radiation-sensitivity, or in the delivery-times for radiation-induced cancer. And suppose these age-groups differ in sensitivity and latency periods from women in the age-group 20-29 years. We could go on describing numerous differences until every age-group is considered.

Despite this diversity, if breast-irradiation is initiated at a certain level into a female population of mixed ages and of constant size, and if irradiation is maintained at that level indefinitely, there necessarily will come a time --- several decades after the initiation --- when the combined annual incidence-rate of radiation-induced breast-cancer in this population becomes EQUAL to the combined annual production-rate of such breast-cancer, despite the mixed ages of the population. And this combined annual incidence-rate will endure indefinitely too, until the annual production-rate is altered.

This means: If we can figure out the annual production-rate from radiation for a specific period of years, then we will know the annual incidence-rate from radiation which will occur decades later --- and thus we learn what fraction of the total breast-cancer problem in those later decades was caused by ionizing radiation.

"The simplest questions are the hardest to answer."

● – Northrup Frye

CHAPTER 5

The Rationale of Our Study: Methods and Materials

Part 1. The Years 1920–1960, and Beyond

Chronic human exposure to ionizing radiation, from natural sources, has been occurring since the beginning of our species. Then along came Dr. Wilhelm Roentgen with his discovery of x-rays in 1895. Just a few years later, human exposure to ionizing radiation began to grow rapidly. Some segments of the population began receiving extra radiation exposures far greater than natural radiation exposures. Soon thereafter, radium and radon also became widely available as radiation sources in medical practice.

We could start our study at the very beginning of such medical irradiation, but it is not essential to go back quite that far. Instead, we go back to 1920. We pick the forty-year period of 1920 to 1960 as the period for which we will determine the annual production-rate of radiation-induced breast-cancers, because we are interested in the much later set of years when the annual INCIDENCE-rate of radiation-induced breast-cancers is equal to the annual production-rate (Chapter 4).

To build up to that point of equality can take decades of steady cancer-production, and to decline from that point of equality can also require decades --- as depicted, for example, by Figure-A of the preceding chapter. Even if every bit of medical irradiation of breasts had suddenly stopped in 1960, decades would still be required for the delivery of all the radiation-induced breast-cancers produced before 1960.

Moreover, irradiation of breasts most certainly did NOT cease in 1960. Even if we assume that the average annual dose-level to female breasts after 1960 fell appreciably below the average level of 1920–1960, we can not ignore the large increase in the average population of women receiving the average annual dose. The two changes would balance each other out and would MAINTAIN the earlier annual production-rate of radiation-induced breast-cancer, to a good "first approximation."

For these reasons, the study of the annual PRODUCTION-rate of radiation-induced breast-cancers during the 1920–1960 period will be adequate for our "first cut" at estimating the annual INCIDENCE-rate of radiation-induced breast-cancer for approximately the years 1960 to 2000.

Part 2. What about Constancy of Population and Dose-Rate?

The "Law of Equality" (Chapter 4) requires both a constant number of persons irradiated per year, and a constant level of exposure, year after year.

We know that the female population of the USA grew during the 1920–1960 period (Table 2, located after the final chapter). So we have calculated an AVERAGE annual population for 1920–1960, which makes the total size the same in every year. Although the age-distribution of the female population may have changed somewhat during the 40-year period, we consider that this is a secondary phenomenon which we ignore in our "first cut" estimate. In Chapter 8, readers will see exactly how we obtained our constant

number of females in each age-year (age 0 means from birth to the first birthday, age 1 means from the first birthday to the second birthday, etc.).

We will often use the term "age-year," in order to prevent a mix-up with "calendar-year."

With respect to radiation-induced cases of breast-cancer, the annual exposure-level of breasts per age-year determines the annual PRODUCTION-rate of breast-cancers in people irradiated at a particular age. And the annual production-rate is what we need, to obtain the annual incidence-rate in later years from the "Law of Equality." Because radiation-sensitivity changes with age at exposure, we must keep the annual production-rate for all 65 age-years distinct in our work, until we are ready to add up the separate production-rates from ALL ages, for a single calendar-year of exposure.

Not even for a single age-year can we expect the annual medical breast-dose to remain constant over a 40-year period. But, as readers will first see in Chapter 8, we can develop an AVERAGE annual breast-dose per age-year which typifies each calendar-year of our 1920-1960 period. Not everyone, of course, received the medical procedures evaluated in our study. When we speak here of the average annual breast-dose per age-year, we mean the breast-dose received by those who were irradiated, adjusted DOWNWARD by distributing their dose (mathematically) over the WHOLE female population of the same age-year.

We consider irradiation of females only below the 65th age-year --- an approximation which introduces a slight underestimate into our findings.

Starting in Chapter 8, we will demonstrate all these abstractions with real-world numbers, and we will show the reasonable approximations forced upon us by the real world, rather than the ideal world described in Chapter 4. Readers who go through this entire book will, we believe, be convinced that the method we use is sound.

Part 3. The Worst Possible Outcome on This Subject

As the method used in this book is also used in the future by ourselves and by others --- to study OTHER cancers, and additional aspects of breast-cancer --- we expect that we and others will be able to sharpen the method appreciably. However, expected refinements of the method would be a horrible excuse for delaying appropriate action to start the prevention of breast-cancer, NOW, in the United States and in other countries too.

We have seen comments, from some physicians who should know better, that "There is speculation about a possible relationship of ionizing radiation with breast-cancer."

There is no basis for such comments. Breast-cancer induction by ionizing radiation is a settled issue. There are a few ASPECTS of the issue which can not yet be settled, such as the full duration of the effect for females exposed below age 10, as already noted in Chapter 2, Part 2. But to suggest that the relationship of ionizing radiation with breast-cancer is "speculative" suggests some defect in a physician's medical training, at this stage of history. There is a reason for emphasizing the point:

The worst possible outcome on this subject would be just to hold hearings, or to appoint some new Presidential Commission, or to say that "Future research may show

radiation to be a cause of breast-cancer." These are the usual substitutes for action on such matters. But there is already more than enough knowledge to say, with certainty, that there will be a reduction in future breast-cancer incidence if people take all the steps needed to reduce medical and other radiation exposures as much as possible.

Ionizing radiation is not just "a cause" of breast-cancer. The evidence summarized in this book indicates that radiation is the major cause of breast-cancer in the United States. We ought to start doing something very constructive on this issue, and not be satisfied with procrastination and SUBSTITUTES for action.

Part 4. Main Sources of Raw Information for This Study

By careful detective work and by studying literature in the x-ray field for 1920 to 1960 (and some later and earlier documents), we have tried to reconstruct the probable radiation dose to breasts for females in each of the age-years, for one average year of the 1920-1960 period. Without the dosage, nothing is possible in any effort to figure out how much of the recent, current, and future breast-cancer problem is due to past radiation.

It has been an illuminating tour through medicine.

We wish to express our gratitude for the existence of collections of the American Journal of Roentgenology and Radium Therapy for that entire period. What an excellent journal! The extensive discussions, following presentation of papers at meetings, are all there --- not only the papers. Thus, one can get a flavor of the times and the debates, not just the data themselves. And the sections covering journals throughout the world were an invaluable source of references needing attention. Timely editorials were very useful in highlighting problems of the period. We are particularly impressed with the series of scholarly papers by Dr. Arthur Desjardins of the Mayo Clinic, on mechanisms of radiation action. In the 1930s, he set out the rationale of x-ray therapy for disorders of various physiological systems, in papers which are fascinating and most useful. Other journals were helpful too, of course. It is quite refreshing to have such a fine window on a past era.

Starting with such literature, we have evaluated as many types of radiation procedures as possible with respect to breast-dose. We wish to state with emphasis that we are trying to evaluate the dosage, but we are NOT evaluating the rationale, success, or failure of the usage. We are not in judgment of the procedures themselves. We are just trying to learn the magnitude of an unintended consequence: Breast-cancer.

During each year of the 40-year period (1920-1960), breast-cancers were being produced (committed) by medical x-rays and radium gamma rays. Some of the radiation was used to treat non-cancerous disorders of the breast-tissues. Most often, the radiation was NOT planned for reaching the breasts, but reached the breasts unavoidably during the planned irradiation of OTHER tissues and organs.

Potential Surprises for Young Physicians Today

There will undoubtedly be some readers of the stories in this book who will be critical of the radiation-uses which occurred in the early period. Of course, 20/20 hindsight is a powerful instrument. But there is little room for latter-day experts to be judgmental, in our opinion. Monday-morning quarterbacking is of no value. What has

value is to gain some wisdom for the future, about the too-rapid introduction of certain technologies, and the too-little appreciation for the long incubation period for certain important diseases.

It would be "poetic license" to say that, in the early period of roentgenology, ionizing radiation from radium or from x-ray machines was tried for virtually any disorder or disease one could name --- but it is no exaggeration to say that it was tried out to seek relief for a great variety of afflictions. It was tried, too, for an affliction of uncertain existence, called "enlarged thymus gland." (The thymus gland, part of the immune-response system, is located in mid-chest, under the sternum, or "breast bone.")

We doubt that many young physicians in practice today would know, for example, that leading institutions would refuse to do a tonsillectomy and adenoidectomy without first ascertaining (with diagnostic x-rays) whether enlargement of the thymus existed. And if it did exist, therapy (with x-rays) was required before surgery would be contemplated.

Many, today, may be surprised to read that bronchial asthma was treated with x-rays, that whooping cough (pertussis) was treated with x-rays, that bacterial pneumonia was considered to be highly effectively treated with x-rays, and that many articles cited x-rays as the treatment of choice for serious inflammatory problems such as carbuncles.

A Regrettable Exclusion from Our Evaluation

There are many types of medical exposure reported in the literature which did not permit us to make quantitative estimates of breast-dose. For this reason, we are confident that the annual average breast-dose per age-year must have been appreciably higher than our estimates. In turn, this is a source of underestimation in our annual production-rate per age-year of radiation-induced breast-cancer, and necessarily in our estimated annual incidence-rate (delivery-rate), occurring decades later. Section 3 of this book discusses the sources of radiation exposure which we know to have existed, but which were not quantified in this investigation.

A Deliberate Exclusion from Our Evaluation

In our search of the literature, we deliberately excluded from our analysis the use of radiation in the treatment of EXISTING malignancies, or in treatment of any other disease known to cause appreciable life-shortening. Our interest is in estimating the annual production-rate of radiation-induced breast-cancer in people who had a reasonable chance of living long enough to develop the disease. We exclude radiation therapy for existing malignancies because we want to avoid blaming radiation for more consequences than would be correct.

Part 5. Conversion-Factors from Dose to Cancer-Production

When we have achieved an evaluation of annual breast-dose in the 1920-1960 period for each age-year, the next step is to convert dose into an annual production-rate of breast-cancer.

There is rather good agreement today about the percentage increase in breast-cancer per rad of breast-irradiation, as illustrated in Chapter 3, Part 3. There is still some disagreement about the exact shape of the dose-response curve, but the disagreement does not make a big difference in this particular study --- partly because

many of the breast-doses from medical procedures occurred at relatively high dose-levels, where we and others have always been in rather good agreement about the magnitude of the radiation effect.

The term "conversion-factor" can be used for any formula which says how MANY radiation-induced cancers result from exposure to each rad of dose.

The number of cases produced PER RAD of dose is always the same, at any total dose, if the dose-response is linear. However, if the dose-response is non-linear, the number of cases produced PER RAD varies with the size of the dose. Our 1990 analysis of the A-Bomb Study shows a supra-linear dose-response, with the most cases induced PER RAD at the lowest doses. As total doses increase, each additional rad produces FEWER cancers (Gofman 1990, Chapters 14 and 15).

Readers will see in this book, starting in Chapter 8, exactly how we adjust the actual breast-doses DOWNWARD, whenever appropriate, so that our low-dose conversion-factors will not overestimate the consequences from higher doses. In other words, we adjust the DOSE rather than the conversion-factors.

The Issue of a "Threshold" or "Safe Dose"

A "threshold" for radiation effect is the hypothesis that NO health-risk occurs from radiation if a dose is below a certain level (the threshold-level). A risk-free dose is a SAFE dose. A dose which creates a risk is NOT a safe dose.

Back in 1970, it was still possible to speculate that a threshold-dose might be found with respect to radiation-induced cancer, although human evidence was already trending strongly against the speculation (Gofman 1969, p.6; Gofman 1971, p.262). In the 1990s, the hope for a safe dose must yield to real-world evidence. By any reasonable standard of biomedical proof, that issue was settled in our 1990 book (Chapters 18 through 21).

Existing human evidence, combined with analysis of the number of ionization tracks created per cell-nucleus from various doses, invalidates older claims that proof of cancer-induction is limited to doses which are greater than 10 or 20 rads. In reality, there is human evidence in the mainstream medical journals of cancer-induction from radiation doses which are close to the lowest POSSIBLE dose and dose-rate --- and some of that evidence happens to come from studies of radiation-induced human breast-cancer.

There is NO safe dose (risk-free dose) with respect to radiation-induced cancer. Every dose counts in the total exposure. The doses received early in life count MORE in the risk of subsequent cancer-occurrence, but all doses count.

Part 6. The "Master Table" of This Book

Near the end of this book, in Chapter 39, is the "Master Table." This table assembles all the findings about annual average breast-dose per age-year, from the chapters of Section 2. So the Master Table applies to a single calendar-year, and to 65 different age-years. The final columns of the Master Table (Columns U, V, and W) apply the conversion-factors which yield the annual PRODUCTION-rate of radiation-induced breast-cancers for each age-year.

The SUM of the annual production-rates for all 65 age-years is, of course, the annual production-rate for all females (USA) during each year of the 1920-1960 period.

From Chapter 4 and from Part 1 of this chapter, readers already know how the 1920–1960 annual production-rate of radiation-induced breast-cancer relates to the recent, current, and future annual INCIDENCE-rate of breast-cancer.

The sum in Column W is a remarkable number. Nonetheless, the number is unrealistically LOW with respect to past exposure-levels, for reasons which will become clear to the readers of Sections 2 and 3.

Overview of the Exposures Evaluated in the Master Table

Below is an overview of the various types of breast-exposure which are evaluated in the columns of the Master Table. The sequence of the columns is arbitrary, and is not related to the size of the consequences.

- – Column C, Enlarged Thymus Gland: X-ray breast-dose, during first year of life (usually during first few months), in diagnosis and therapy of "enlarged thymus" and "status lymphaticus." Chapter 8.
- – Column D, Enlarged Thymus Gland: X-ray breast-dose, mainly during age-years 2 through 15, in screening and therapy for "enlarged thymus," prior to tonsillectomy, adenoidectomy, and other childhood surgeries. Chapter 10.
- – Column E, Acute Mastitis: X-ray breast-dose in therapy of acute mastitis (inflammation of the mammary gland). Chapter 13.
- – Column F, Chronic Mastitis: X-ray breast-dose in therapy of chronic mastitis, a disorder which has many names (including fibroadenosis, chronic cystic mastitis, benign fibroadenoma, or adenofibrosis), and is characterized by lumpy, tender breasts. Chapter 14.
- – Column G, Management of Tuberculosis: X-ray breast-dose in the fluoroscopic monitoring of artificial pneumothorax therapy, for patients having tuberculosis (the Detroit experience). Chapter 15.
- – Column H, Management of Adolescent Scoliosis: X-ray breast-dose from spinal x-rays in the monitoring of adolescent scoliosis (curvature of the spine). Chapter 21.
- – Column I, Mass Screening for Tuberculosis: X-ray breast-dose in mass screening-programs to detect tuberculosis (unlike Column G). Chapter 16.
- – Column J, Bronchial Asthma: X-ray breast-dose in the therapy of bronchial asthma (the Mayo Clinic experiences). Chapter 17.
- – Column K, Pre-Birth Breast-Irradiation: X-ray breast-dose to the fetus as a result of the mother's pelvic and abdominal x-ray examination while pregnant. Chapter 12.
- – Column L, Hyper-Thyroidism: X-ray and gamma-ray (from radium and iodine-131) breast-dose in the radiation therapy of hyper-thyroidism, whether exophthalmic or not. Chapter 20.
- – Column M, Enlarged Thymus Gland: X-ray breast-dose, mainly during age-years 1 through 9, in prophylactic therapy of "enlarged thymus" (the experience of the Massachusetts Eye and Ear Infirmary). Chapter 9.
- – Column N, Whooping Cough: X-ray breast-dose in the therapeutic management of pertussis (whooping cough). Chapter 19.

- - Column O, Fission-Product Fallout: Equivalent medical rads to breasts from radioactive fallout in the 1945-1960 period of weapons-testing. Chapter 25.
- - Column P, General Diagnostic X-ray Exams: X-ray breast-dose from general diagnostic exams, roentgenograms plus fluoroscopic examination. Chapter 23.
- - Column Q, Occupational Exposures: X-ray breast-dose, occupationally incurred. Chapter 24.
- - Column R, Chiropractic Exams: X-ray breast-dose in chiropractic applications, largely from full-spine x-rays used in diagnosis and follow-up. Chapter 22.
- - Column S, Pneumonia: X-ray breast-dose in the roentgen therapy of pneumococcal pneumonia. Chapter 18.

We now begin the stories of the various radiation exposures, which left their "mark" within the breast-cells of so many women.

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About Dr. George Pfahler

In our travels back through the literature of roentgenology in its early years, we met Dr. George Pfahler many times. He was regarded as "the dean of American radiologists" (see below), and readers of this book will find him quoted on several topics.

In 1955, when Dr. Pfahler reached his 80th birthday, there were tributes. One was written by Dr. James T. Case, a past president of the American College of Radiology. Entitled "Dr. George E. Pfahler, An Appreciation," it appeared in the journal CA: A BULLETIN OF CANCER PROGRESS, Vol.5, No.1: 11-13, January 1955. Dr. Case said:

"Fifty-five of Dr. Pfahler's eighty years have been devoted to the science of radiology. An account of his activities and contributions in this field constitutes a veritable history of radiology in America. He is held in respect and affectionate regard by his colleagues throughout the world as the dean of American radiologists. He belongs to the group of pioneers in radiology."

Dr. Case recounted that the Board of Managers of the Philadelphia General Hospital decided to buy a roentgen-ray machine and asked the young resident, Dr. Pfahler, to take charge of it. Dr. Pfahler at first "doubted the propriety of getting into a thing like radiological practice, which he thought had been already pretty much worked over, for the bones had been studied and foreign bodies had been demonstrated." But he did take the responsibility. This eminent physician, who had suggested it was essentially all over for new developments in radiology, finally published about 350 medical articles!

In this book, we "hear" from Dr. Pfahler on thymus disorders, chronic mastitis, and liver measurements. And also:

- - Dr. Pfahler's story about the surgeon and the dentist (p.203).
- - Dr. Pfahler's impassioned warning (in 1925) about mis-users of the roentgen ray (p.206).
- - And Dr. Pfahler's own reflections in 1955 on what had followed from the discoveries of the x-ray and radioactivity (p.260).

CHAPTER 6

The "Enlarged Thymus" Story: Start of a Long Controversy

Part 1. The Thymus Gland and Its Unfortunate Location

We have made a choice concerning which data we shall use for a detailed illustration of the "nuts and bolts" features of our handling of the actual procedures of processing the breast-dose data. And we make this choice for many reasons. Some of the very best clinically-available data needed for the study are those of breast irradiation in female infants under 6 months of age, with breast irradiation occurring BOTH in the diagnosis and the therapy of "Enlarged Thymus," the thymus being a gland lying under the sternum (breast-plate). Moreover, the results are strikingly important in this entire picture, as will be seen. Analysis of this evidence represents a fascinating, exciting, useful effort for humanity's health in the future, if we take heed of its message. But it is also a tragic recounting of how high the price can be for a message, with many, many thousands of women paying the price via breast-cancer.

We shall present the story of the "Enlarged Thymus" problem first in this book. No reader will have any difficulty with this account from history. However, when we come to Chapter 8, there will be some numbers and calculations. None are foreboding. Nevertheless some readers may prefer to leave those calculations for later in-depth examination, if they choose to do so. They can choose to "accept" our numbers on their first time through the book.

How Did the Thymus Gland Get Embroiled in All This, Anyhow?

We are seeking out the extent to which ionizing radiation is a major cause of breast-cancer in our country. Why "pick" on the thymus? It happened that an organ, the thymus, became known as an organ needing diagnosis and needing therapy with ionizing radiation in some cases. But it was a pure accident of fate that the anatomic locations of the thymus and the breasts were such that if the thymus were going to get thoroughly irradiated by x-rays or gamma-rays from radium (and both were used), it was nearly impossible to avoid partial irradiation of the breasts. Undoubtedly there were some private offices and institutions that gave much lower, others, much higher breast-doses than the average in the course of their management of alleged thymus disease.

If the thymus had been located on the thigh, and if we were concerned about breast irradiation, the thymus problem would not have anything to do with the problem of breast irradiation. It is necessary to have the reader understand this, for otherwise the impression could be left that thymus disorders and breast-cancers have some special intimate relationship which we are investigating.

Part 2. The "Enlarged Thymus" Story

This is the story of a set of symptoms and signs which captivated the medical profession for essentially a half-century. A careful reading of the medical literature of that half-century reveals the absolute certainty of numerous experts on OPPOSITE sides of the question of the meaning and ultimate effect of these symptoms and signs. Many

physician-experts in the field reported 90 to 100% cure with ionizing radiation for the variants of the "enlarged thymus" problem, in series involving hundreds of cases. Others reported that the disease being treated did not really exist and had never existed before. All of this went on for a half-century, often with white-hot debate.

Of one thing we CAN be certain: It was an inevitability that female breasts in infancy --- even in the first month after birth --- received a great deal of radiation in the course of this long-ongoing giant medical debate over the questions about EXISTENCE of "enlarged thymus," its appropriate diagnosis, and its appropriate treatment.

After examining the literature of the multi-decade convulsion in the medical-radiological-pediatric-surgical community, it is clear to us that it would be impossible to understand the magnitude of the x-ray dose to female breasts in the 1920-1960 period, without intensive investigation of the "enlarged thymus" story. Friedlander (1907) is widely credited with having reported the first case of a child with enlargement of the thymus treated "successfully" with x-ray. Sidney Lange (1911) brought this to the attention of roentgenologists with a report, quickly noted as important, of successful treatment of four cases of enlarged thymus with x-rays.

Part 3. Dr. Sidney Lange Puts the Enlarged Thymus Problem "On the Map"

This beginning in 1911 came when Dr. Lange, of Cincinnati, published his paper, "X-Ray Therapy of Enlarged Thymus" (in the American Quarterly of Roentgenology, Vol.III, April 1911, 1-22). We quote directly from his paper (p.1):

"It is the purpose of this paper to report four cases of enlarged thymus treated by X-rays, to make a plea for the consideration of enlarged thymus as a separate entity, apart from the so-called status lymphaticus of Paltauf [which we will consider later], and by experiments upon young rabbits to demonstrate the action of the X-ray upon the thymus." And:

- - "Case 1, E.L., male, aged 7 weeks, was referred for X-ray treatment because of cyanosis [blueness of the skin] and inspiratory stridor [stridor is often described as any noise apparently coming from the trachea during breathing, often characterized as "crowing" in nature]. The diagnosis of enlarged thymus was based upon the presence of an abnormal area of dullness over the upper part of the sternum [medically, dullness in the chest means apparent solid or liquid beneath the percussing finger where there should be air-filled tissue]." And:

"The family history strongly supported this diagnosis. A previous child which was normally delivered at full term developed, a few days after birth, a marked cyanosis which persisted without remission. At the age of three months it began to have attacks of suspended respiration, with extreme cyanosis, which attacks were relieved by raising and lowering arms above the head. The child died suddenly in one of these attacks at the age of four months." And (p.2):

"The present baby was delivered normally at full term, weight at birth, 6 1/2 lbs. It was breast-fed. From birth it was noticed that the child's color was not good, appearing dusky and blue at times. When about two weeks old, he began to snuffle in respiration as though there were an obstruction in the nose. The respirations became wheezing in character and at times noisy. After crying, very rapid crowing inspirations would occur, and cyanosis [was] very marked." And:

"When presented for treatment child was seven weeks old, and weighed 8 1/4 lbs. Color was dusky, and at times decidedly blue, especially marked after crying. Mucous membranes were pale, hands and feet cold. The child was very restless, arms and legs jerking, and head and body constantly moving." And:

"The respirations were accelerated and noisy. There was a snuffling in nose and wheezing in chest, alae nasi flared slightly in inspiration, and there was retraction of the jugulum and intercostal spaces."

And, after several intervening paragraphs,

"The skiagram [x-ray picture] which was made with difficulty because of the great restlessness of the child, showed a broadening of the upper mediastinal shadow [the region in which the thymus gland resides]."

Dr. Lange elected to treat this child for enlarged thymus, giving x-ray exposures twice a week, the treatment extending over a period of two months, during which time fifteen exposures of the child to x-rays were made.

We again quote Dr. Lange (p.2):

"The response was prompt. The dyspnoea and cyanosis rapidly improved, appearing at only infrequent intervals after crying and occasionally in morning on awakening. The restlessness disappeared, the child became quiet and playful." And (p.3):

"Two and a half months after beginning treatment, child appeared normal, except after a severe crying-spell when slight duskiness would appear. The skiagram showed a decrease in the breadth of upper mediastinal shadow "

The child was discharged from treatment.

- - A second child was described thusly (p.3): "Stridor so constant and severe that the child could not take food. Attacks of paroxysmal cough and cyanosis coming on at short intervals threatened his life."

The child was immediately treated with x-rays over the upper mediastinum, with exposures made over front and back (age 9 1/2 months at this time).

"Within 48 hours after the first treatment there was slight improvement. This improvement continued uninterruptedly over six weeks, during which 13 treatments were given." And (p.4):

"Cough and stridor had practically disappeared, and the thymic dullness in chest decreased to normal bounds." And (p.4):

"... at intervals of about three months thereafter, the child had three slight attacks of cough and dyspnoea. Each time he was brought to Cincinnati promptly, and given one or two X-ray treatments which at once dissipated the symptoms. One year after beginning the treatment the father reported that child seemed perfectly well."

- - A third child had shown a crowing respiration a few weeks after birth.

Dr. Lange relates that at 3 1/2 months the child was in such desperate condition that when the child was brought into the waiting room, the crowing inspiration could be heard in the next room, although the door between the two rooms was closed. "Ten treatments were given over a period of eight weeks. The improvement was prompt. The crowing subsided and nursing became less difficult."

The child did well, although the mother reported that some wheezing could be heard at times, especially during sleep. Dr. Lange suggests the child should have had a few more x-ray treatments.

- - A fourth child also presented with noisy breathing. Inspiration was audible at all times. An x-ray plate showed a broadening of the upper mediastinal shadow, especially to the left. At page 6:

"Seven X-ray treatments were given which improved the child so much that the mother considered the child cured and although further treatment was advised failed to bring the child in."

Lange wrote the following at page 7 of his 1911 paper:

"Furthermore, it is well-known that the thymus may enlarge in any chronic infection, and that it is regularly enlarged in Addison's disease, and in exophthalmic goiter. Enlargement of the thymus, therefore, may be considered as a separate entity apart from the status lymphaticus of Paltauf, although it is the usual accompaniment of the latter, and the profound influence of the X-ray upon thymic enlargement of whatever origin should be borne in mind. The action of the X-ray upon the thymus is analogous to its action upon the spermatogenic epithelium of the testicles, or if we accept the lymphatic origin of the thymus, it is comparable to the destruction of lymphocytes in lymphatic enlargements or in leukemia."

Part 4. Were There Any Ideas of Mechanisms at Work in This Therapy?

Lange wrote further at page 8 in his 1911 paper:

"In all four cases reported the symptoms were those of actual pressure upon air passages and blood vessels. This question of actual mechanical pressure by an enlarged thymus has been much discussed and doubted by some, notably Paltauf, because of the fact that in many cases of 'thymus deaths,' the thymus while enlarged did not at autopsy seem to be compressing the trachea or veins." And (p.8):

"Drawing my conclusions from the cases reported in the literature, thymus deaths may be grouped under three headings. The first group includes those cases in which there are actual pressure symptoms appearing sometime before death and the post-mortem reveals evidence of pressure upon the mediastinal contents. In the second group, the thymus while enlarged does not produce any prodromal pressure symptoms during life, and the post-mortem shows enlargement but no actual signs of pressure. The fatal issue in these cases is explained by a sudden swelling of the thymus, due to some exertion, as in crying, or due to some interference with the circulation as produced by certain positions of the patient, or as would occur in giving an anesthetic. In these cases, a vicious circle is established. In addition to the swollen thymus, the mediastinal veins become distended and the heart dilated which again react on the swollen thymus, the combination producing death." And (p.9):

"In the third group, the deaths are extremely sudden without evidence of mediastinal pressure of any kind. Upon autopsy the thymus may or may not be enlarged. This group includes the true status lymphaticus of Paltauf, and the cause of death, according to Svehla's theory and experiments, is 'Hyperthyroidism.' And:

"However, the post-mortem state of the gland is not a criterion of its volume and relations during life, for vascular turgescence of the gland during life alters these

relations. The swollen thymus presses upon veins which in turn become turgid and react upon the thymus, thus greatly increasing the mediastinal pressure..." And (p.9):

"Jackson [JAMA, 1907] by bronchoscopy demonstrated actual pressure upon the trachea in a case of enlarged thymus without any accompanying signs of status lymphaticus."

Lange's recommendations at p.12:

"Upon considering the tendency to recurrence after X-ray treatment in each case and noting the experiments of Rudberg showing rapid regeneration following irradiation, it would seem that the X-ray exposures were given too conservatively in these cases. The vague fears of the mother as to the possible harmful effects of the ray, which fears are not infrequently shared by the physician, often cause the X-ray operator to err on the side of conservatism and to treat too lightly and discontinue the treatment too soon." And:

"Therefore, in view of the difficulty often encountered in the diagnosis of thymic enlargements, and in view of the prompt action and the harmlessness of a few X-ray exposures, Roentgen therapy may be rationally employed as a therapeutic test in obscure cases."

The literature decades later was still suggesting x-ray therapy as a therapeutic test "in obscure cases." We might add that mother's intuition may have been written off fifty years too soon, with respect to "possible harmful effects" of this therapy.

Part 5. The Mixed Reception of Dr. Lange's Therapy for Enlarged Thymus

What followed the presentation of Lange's paper became a major war among physicians over the next HALF-CENTURY! Dr. Lange did not suffer from an absence of powerful, prestigious physician following. And on the other hand, the opposition hardly was silent during the fifty-year period following his paper.

At the presentation itself, Professor Henry Pancoast, a "dean" among radiologists and organizer of the University of Pennsylvania department of roentgenology, said (p.16):

"The Society should feel grateful to Dr. Lange for this report on something new. This is a treatment which is undoubtedly of great value."

And in closing his remarks, Dr. Pancoast said (p.17):

"If all we have heard is true, we have here a new and interesting field for X-ray work, especially if the effect of the ray on lymph tissue is what I believe it to be."

And Dr. A.M. Cole, of Indianapolis, said (p.18):

"This excellent paper of Dr. Lange's does demonstrate that the Ray will cause a partial atrophy of the Thymus gland and thereby will cure the train of symptoms associated with its enlargement. I consider this paper one of the most valuable contributions to Roentgen Therapy."

Fond references to "the Ray" are commonly seen in early radiological writings.

The boiling controversy gained momentum from this date forward.

In a 1924 paper, Dr. George Pfahler, widely labeled "the dean" of American roentgenologists, wrote on the subject (and thus lent a whole lot of prestige to the ideas), some 13 years after Lange's plea for more attention to this disorder and its treatment. We quote Dr. Pfahler (at p.39):

"Thymic enlargement is receiving more and more attention throughout the country. I am sure, however, that many cases go unrecognized and, as a result the symptoms are unduly prolonged from lack of treatment. The roentgen ray is undoubtedly the most reliable means of diagnosis, and radiation by x-ray or radium is a specific in treatment. So general is the response to treatment, that if the symptoms do not show definite improvement after a few x-ray treatments or one radium treatment, the diagnosis is almost certainly incorrect, or the symptoms are influenced by some associated pathological condition." And (p.39):

"... On the other hand, thymic symptoms may develop, we believe, even when no enlargement is shown by the x-ray. For by the x-ray we can only show lateral enlargement, and yet it is the anteroposterior pressure which causes the symptoms." And: "For this reason, Dr. [James] McKee frequently sends children for examination and treatment, with instructions that the child shall be treated even if I find no enlargement of the thymus. I believe that this therapeutic test is even more reliable than the x-ray diagnosis. In nearly all such cases the symptoms are relieved by the radiation."

What symptoms? Let Dr. Pfahler answer (1924, p.40):

"Symptomatology. The classical symptoms are dyspnea, cyanosis, and an inspiratory stridor, but if one depends only on this trio of symptoms many cases will go undiagnosed." Dr. Pfahler refers (p.40) to a letter from Dr. Lange saying that he sees at least three new cases each week and often three new cases in one day, and gives me [Pfahler] by letter the recommendation of x-ray examination for any of the following symptoms: "Inability to cry loudly, crowing respirations when crying, noisy respirations or wheezing, noisy respirations during sleep, difficulty in nursing, vomiting or regurgitation, feeble respiration, grunting as though the child wants to have a stool, slow or retarded development..."

Dr. Pfahler cites G.W. Grier recommending the x-ray examination in all premature babies, and cites Lange saying, "Premature infants and infants with enfeebled respiration are stimulated and often tided over by x-ray exposure to the thymus." Much argument ensued in the literature during those early years as to whether there was, or was not, a direct pressure problem accounting for many of the signs and symptoms.

"Uniformly Brilliant Results"

Dr. Pfahler concluded (1924, p.44):

"There is probably nothing in radiotherapy that gives such uniformly brilliant results. The younger the child, the more prompt are the results."

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Note: Journals vary. Some write "X-ray" and others write "x-ray" --- some write "the Ray" and others, "the ray." And in Lange 1911, variation occurs within a single article.

CHAPTER 7

Benefits of Thymus Irradiation: Delusion or Reality?

Part 1. The Pancoast "Imperative" of 1930: Diagnostic Fluoroscopy

Professor Henry Pancoast, another of the grand men of roentgenology, entered this entire fray, particularly with respect to the question of an adequate examination of the chest in seeking a diagnosis in suspected cases of enlarged thymus. Dr. Pancoast laid out the criteria for an adequate roentgenologic examination. His recommendations meant a large radiation dose to the chest and breasts, due to extensive use of fluoroscopy (examination of the patient while the x-ray beam is still "on"). We quote Dr. Pancoast in 1930 (at pages 747-748):

"Every roentgenologic investigation of the respiratory tract in infancy and early childhood for any purpose should include a collective study of the nasopharynx, oropharynx, the neck, and the chest. Thymic cases are obviously referred for examination because of obstructive symptoms, and experience has taught us that obstructions anywhere in the upper passages may produce phenomena simulating those due to thymic enlargement." And (p.748):

"A preliminary fluoroscopic study is always imperative." And: "At any rate, the patients must be fluoroscoped in both the sagittal [front to back], and lateral directions. The neck must be included with the chest. The observer's eyes must be well accommodated before beginning fluoroscopy, and in emergency cases one must wait until the proper time arrives for perfect vision. The child must be crying in a regular manner, or at least, deductions must be based upon such crying, and not on sobbing or irregular or jerky respirations. One looks, of course, for any obviously intrathoracic lesions. The movements of the diaphragm domes must be carefully observed and the relations of the mediastinal shadows to these and any abnormalities at the two phases of respiration carefully noted. One should carefully observe the appearances of the pharynx, larynx and trachea and their relations, especially during the two respiratory phases."

And, of course, Dr. Pancoast wanted a number of roentgenographic exposures (x-ray photographs), both lateral and sagittal.

For the purposes of our study, we must take careful note of the fact that these Pancoast recommendations made the radiation dose to the child at least 10 times the dose from actual roentgen films, and it could be a much higher ratio than 10 between the fluoroscopy and the roentgenograms. This will weigh heavily in our assessment of radiation doses to infants and children.

First of all, it can be commented that Dr. Pancoast was a man of very high repute, and his recommendations for technic were likely to be adopted by the best radiologists. Yet when we consider the comments of Dr. Leddy (1934) about fluoroscopists at the Mayo Clinic counting on speed ("celerity") to keep the radiation dose down, we wonder about doses to doctor and patient in those attempting to follow the Pancoast recommendations in cases of possible thymus enlargement.

One might even wonder if a harried, not-too-competent fluoroscopist --- intimidated by the complexity of the Pancoast requirements --- might take the easy way out and simply give thymus therapy without even attempting the rigorous Pancoast technic. After all, there were all kinds of authorities (we have named some and shall name others) who attested to the "harmlessness" of a few hundred roentgens. And there were recommendations of a "therapeutic trial."

Part 2. "Thymus Phobia": Public Concern over Sudden Death in Infants

We think the practice of medicine, especially with children, was not easy in the first half and more of the 20th century. The phenomenon of sudden infant death without explanation (which is still with us, as this century draws to a close) is no small matter. Families were terrified on hearing of sudden deaths with anesthesia, and of sudden deaths with what seemed to be nothing at all going on adverse to the child's health. Necessarily, that spilled over into physician practice, with justifiable concern over both the tragedy of losing a patient seemingly well and the jeopardy of lawsuits for negligence. So, when the public was "thymus conscious" as a part of the general fear of the sudden infant death syndrome, it was quite trying for physician and families.

This situation helps account for the following kinds of comments from two physicians at a major medical center ---- 37 years after Lange's initial recommendations in 1911 for action.

In 1948, Conti and Patton wrote the following about therapeutic treatment of some cases, for the purpose of alleviating the parents' WORRY (p.892):

"Diagnostic roentgenograms offer some reassurance to patients who are thymus conscious. This is not an undesirable effect. The alleviation of anxiety is a commendable medical achievement." And: "The obstetrician or pediatrician should accede to the wishes of parents who want neonatal roentgenograms of their children. It might even be wise to administer therapeutic dosage over the thymus. Whatever assurance is gained by this apparently harmless and perhaps beneficial procedure will aid in alleviating an anxiety which occasionally becomes a thymus phobia."

And the breast dose grows. And the breast dose grew in another way. Why wait for cyanosis, stridor, anxiety of parents? It became a practice in some hospitals to do roentgenograms in the nursery on every consecutive child to try to detect asymptomatic thymus enlargement, and if found, to treat such "enlargement" with therapeutic radiation. For example:

Conti and Patton, 1948: 7,400 consecutive newborns tested, and some treated.
 Donaldson, 1938: 2,000 consecutive newborns studied roentgenographically.
 Of these, about 18% were then treated with x-rays for enlarged thymus.

Part 3. The Cauldron Boiled Vigorously in the 1920s and 1930s ---- On Both Sides

The non-believers stated that they had never observed the findings of enlarged thymus and had never seen any favorable results. Their position was largely that the reason why sudden death victims might tend to have larger thymus glands than those who died after a lingering illness is that thymus glands shrink markedly in lingering illnesses. Boyd (1932) did a large number of measurements and sponsored this point of view.

The believers continued to find excellent results in their diagnosis and therapy of enlarged thymus glands. They claimed success rates at the 90 % level and were adamantly in favor of the diagnosis and treatment of thymic enlargement.

It is indicative of the tenor of the times to examine what the textbooks are saying. Textbooks can be VERY wrong on many issues. Nonetheless, there is generally widespread support for a diagnostic or therapeutic approach when the textbooks "glow" about an issue in medical management.

The Work and Position of C. Winfield Perkins in the 1920s. Perkins(1925).

Let us listen to some of his comments (1925 p.216):

"The modern indiscriminate method of operating on children of all ages for adenoids and tonsils without preliminary roentgen-ray exploration of the chest for possible enlarged thymus and other chest pathology seems to be unwarranted. How frequently we hear of a sudden death of a child, either in a physician's office or in a hospital during an operation or even several days after operative procedure, the death having occurred without known cause in an apparently healthy child. Post mortem examination reveals an enlarged thymic gland even though the patient may not have presented previous clinical symptoms of this condition. That the life of an apparently normal child can be suddenly snuffed out without known cause is alarming and of grave professional concern."

These are very strong words, and it is hard to mistake what Dr. Perkins thinks of any medical colleagues who are so callous as to permit these deaths to go on occurring. Dr. Perkins goes further (p.217):

"During the past five summers, [at Seaside Hospital of St. Johns' Guild of New York City] 1,000 cardiac roentgen-ray examinations have been made for the cardiac clinic, and 500 examinations have been made to detect possible thymic enlargement in tonsil and adenoid patients. As a result of our investigations a standard rule is posted that no tonsil and adenoid cases shall be operated upon, OR ANY CHILD BE OPERATED UPON, unless prior to such operation the chest is examined for cardiac, thymic or chest pathology [emphasis added]."

And let us see how Dr. Perkins calls upon the textbook (p.217):

"The fact that a child may have an enlarged thymus, which is not accompanied by the characteristic symptoms of stridor, cyanosis, unconsciousness, asthma, and respiratory difficulties is fraught with grave consequences, especially when operative proceedings are contemplated, for such patients are prone to sudden death under anesthesia. Kerley and Graves in their recent textbook, [Practice of Pediatrics, 1924] state: 'It is well proved by a long series of cases carefully studied, by competent observers, that the condition known as status lymphaticus is an entity and is characterized clinically by a lowered vitality or unstable equilibrium of the vital forces, so that accidents or disturbances, otherwise unimportant, such as some slight injury or a light anesthesia, may precipitate failure of the heart and respiration ... Autopsy findings in these subjects usually show a general lymphatic enlargement of the tonsils and follicles at the base of the tongue and in the intestine, and swelling and enlargement of the thymus, especially at an age when it has generally disappeared ... Many of the sudden deaths, occurring during chloroform and ether anesthesia have proved to be due to status lymphaticus.'

When I was a medical student, such material in a textbook of Pediatrics would look quite acceptable to me ---- if I had not investigated to realize that a boiling controversy was going on in the nation between those who agreed with this "textbook

wisdom" and those who accepted NONE of it at all. Words such as "well proved," and "a long series of cases" are potent expressions in a textbook. And so is a warning: "Many of the sudden deaths occurring during chloroform and ether anaesthesia have proved to be due to status lymphaticus."

After all these forceful words, it is no surprise that the following conclusions are presented in the close of Dr. Perkins' 1925 article:

1. All children before operative procedure should be studied both clinically and roentgenologically for enlarged thymus.
2. Sudden death without previous clinical symptoms may result in patients with enlarged thymus from primary anesthesia or mild shock to the system.
3. Roentgen radiation presents a satisfactory method of treatment of enlarged thymus.

The reader might be surprised to learn there was a countervailing medical opinion that none of this was true. But that countervailing opinion was far from strong enough to prevent a great deal of ionizing radiation exposure to the breasts of female infants and children.

How Did Dr. Perkins look at this issue four years later (Perkins, 1929)? We shall quote some of his conclusions (1929 p.261):

"Therefore, a preliminary roentgen examination of chests in children in order to find possible thymic enlargement is in the field of prophylactic [preventive] medicine and should be done when possible at all times. If in a thousand operative cases in children, 50 show definite roentgen evidence of thymic hypertrophy, there is always the chance of postponement of operation, and the institution of roentgen therapy will probably save some lives. According to other observers and reports, 50 cases of thymic enlargement in 1000 cases is a conservative figure. Some of these cases may be status lymphaticus, but there is very little difference as to the question of a possible fatality as the result of shock, either surgical or otherwise. A thymic death is a surgical tragedy and anything that can be done to avert such an outcome should be done immediately and not questioned. I have good reason to believe that there will soon be a demand for a roentgen examination of a child's chest prior to operation and if this is neglected, the physician or surgeon will be held responsible as is now the case in fractures. Into the difficulties of universal preoperative roentgen examination of the thymus as a measure of safety in pediatric surgery, one need not go. The practicability of this step has been I believe proven in many instances. The added advantage of heart and lung examination is without question. It has always followed that when something could be done for the better protection of the patient, it would in the end be demanded and thereby become routine."

Clearly, Dr. Perkins has not changed his opinion. He may even be more forceful than he was four years earlier.

The Work of Drs. Conti and Patton of Pittsburgh, 1948

Thirty-seven years after the publication of the 1911 Lange paper, not only was the issue of "enlarged thymus" by no means settled, a GIGANTIC increment in radiation exposure of human breasts in infants and children had been created, and Conti and Patton reported the following in a paper entitled "Study of the Thymus in 7,400 Consecutive Newborn Infants," American Journal of Obstetrics and Gynecology 56: 884-892, November 1948 (p.884):

"The thymus problem presents today as it has for many decades, a challenge to the physician. Most thoughtful investigators believe that definitions and clarification of the physiology of this gland must precede any stable and scientifically sound solution. Controversy has been the keynote of thymus discussion since 1889."

"At present there seem to be a few points upon which there is agreement."

1. A competent radiologist experienced in thymus interpretation will usually be able to determine whether the gland is enlarged. [Note that 37 years later, there is still a discussion of how to find out whether thymic enlargement is even present.]
2. Many obstetricians and pediatricians believe that respiratory symptoms in the presence of thymic enlargement justify therapeutic irradiation.
3. In the majority of cases where no other pathology is demonstrable the respiratory symptoms will improve with the rapid thymus atrophy which follows roentgen therapy.
4. There has been no positive proof adduced that sudden death in infants can be due to tracheal compression or bilateral recurrent laryngeal nerve paralysis from enlarged thymus. However, many reliable authorities attest to this possibility and submit autopsy proof of cases which showed no postmortem findings except the presence of an enlarged thymus gland.
5. The general public is thymus conscious and has what is possibly unjustified confidence in the efficacy of roentgen diagnosis and treatment.

Dr. Henry Pancoast Speaks on the Thymus Issue, 1930

Henry K. Pancoast, M.D., Professor of Roentgenology, wrote an influential paper, "Roentgenology of the Thymus in Infancy and Differential Diagnosis of Enlarged Thymus and Its Treatment." This paper appeared in December 1930 in the American Journal of the Medical Sciences. Professor Pancoast, highly regarded in roentgenological circles, was then Professor of Roentgenology, University of Pennsylvania, and Roentgenologist to the Hospital of the University of Pennsylvania.

We single this paper out because Professor Pancoast (one of two enormously influential voices during years of the debate) wrote in no uncertain terms about a PROPER roentgenological examination to study the thymus and to differentiate thymic enlargement from other intrathoracic entities (Part 1). We can be sure that nationwide and worldwide his advice was respected and commonly followed by many radiologists and other physicians.

Concerning his views on how the roentgenologist should proceed in problems for the individual presenting clinical evidence of thymic enlargement and upper respiratory tract obstruction, we have the following (p.746):

"The vigorous controversy regarding the exact cause of death in cases of supposed status lymphaticus or enlarged thymus has been waged for well nigh a century. The so-called thymic death has been ascribed to a variety of causes ... The one theory which seems to be most popular at the present time regards the calamity or potential danger as due to the pressure of an enlarged thymus upon the trachea, blood vessels or nerve trunks. A second theory ascribes death to a constitutional defect manifesting itself through an injurious raising of the vagus [nerve] tone, together with a deficiency of the chromaffin system and weakness of the sympathetic system. Another cause of death that has been stressed is a hypersusceptibility to physical and chemical agents. A fourth theory is

anaphylaxis. Finally, a fifth ascribes death to an abnormal thymic secretion of a general lymphotoxemia." And (p.746):

"Personally, as previously stated elsewhere [citing two prior papers], we have followed the trend of most roentgenologists and pediatricians who have seen the wisdom of being on the safe side in the thymic controversy and of recognizing the condition of enlarged thymus as an entity. Our views have been greatly strengthened by the observations and statements of Jackson [THE Chevalier Jackson, regarded as "Dr. Bronchoscopy" in that period]. We believe, therefore, that the potential danger in the infantile thymus lies in its ability to enlarge further and to compress the trachea and the recurrent laryngeal nerves, and to cause other phenomena due to respiratory obstruction. We have observed all of these occurrences roentgenographically and fluoroscopically in the living infant and we have the statements of Jackson upon observation made directly in the respiratory passages during life. Our beliefs and our remarks do not in any way apply to the cause of supposed thymic deaths in adults. We do not believe that compression is a possible cause of death during adult life."

[We insert here the fact that many observers in that era pooh-poohed the idea of tracheal compression in the infants or the adults. But the experience and capabilities of those critics hardly stood up against the views of two highly respected physicians, Henry Pancoast and Chevalier Jackson.]

Back to Dr. Pancoast: At page 746:

"Jackson in 1907 made the following statement: 'It has been my privilege with the aid of the bronchoscope, to demonstrate beyond all doubt on the living patient the purely mechanical nature of thymic asthma in one instance. This, of course, does not prove that every case has this same pathological mechanism, but it does prove the occurrence of that which many ... have denied, namely, that a hypertrophic thymus can compress the trachea sufficiently to obliterate its lumen ... it would seem more accurate to call it thymic tracheostenosis.'" And: "Jackson, in 1915, made the following statement, based upon further observations: 'Thymic deaths under anesthesia attributed to 'status lymphaticus' and 'hyperthyroidism of the blood' are nothing more or less than arrested respiration due to obstructive pressure of the engorged thymus. Artificial respiration is useless, as air cannot be drawn into the lungs, although it can be forced out. After death the engorgement factor is not evident.' In a recent personal communication [to Pancoast], Jackson stated that 'over 300 cases since that time have been observed bronchoscopically, showing compression and the purely mechanical character of wheezing, dyspnea, and the impending asphyxia from thymic pressure.' 'The upper orifice of the thorax is a rigid ring, and coughing, choking, and hard breathing jam the large thymus into this ring and compress the trachea. After asphyxia the thymus shrinks because engorgement is depleted, and at autopsy the thymus is no longer compressing the trachea.' "

Professor Chevalier Jackson is VERY clear concerning his interpretation of what is happening.

Professor Pancoast says at p. 747: "Our roentgenological studies made during two phases of respiration have proven that the thymus is pushed upward during expiration, and it is easy to understand how the apex of the wedge jams up into the narrow, rigid, bony thoracic inlet and compresses other yielding structures such as the trachea, vessels, and recurrent laryngeal nerves." And:

"In view of these observations of an eye witness of actual conditions during life, of the post-mortem findings of the character of the gland which readily lends itself to causing pressure, and the confirmation of both by roentgenologic studies, we, who have almost an equal opportunity to confirm these findings in the living, cannot do otherwise than take the stand that the danger in the thymus lies in the possibility of its causing pressure stenoses under certain circumstances. Even if it cannot be proven that actual death results from thymic compression, we have sufficient evidence to lead us to believe that obstructive phenomena and cyanosis can result. It may be that another factor is essential in the causation of asphyxia and death. We know from experience that at least one such factor is possible, namely, recurrent laryngeal [nerve] paralysis, which is a complication of thymic enlargement, to be discussed later."

Part 4. Was There Really No Way to Tell Whether a Thymus Was Enlarged?

Drs. Jackson and Pancoast have made their positions crystal-clear, in support of tracheal compression by the thymus, and their prestige made a great deal of difference. Many physicians, radiologists and others believed passionately in x-ray therapy of enlarged thymus. Their numerous papers, over several decades, are filled with evaluations of "90% cured," "95% cured," "almost all favorable results." And many of these super-optimistic reports came from very prestigious institutions on the medical scene in the USA.

But it is also true that there was a series of investigators who denied that thymic enlargement ever existed as a pathological-clinical entity. Boyd (1932) was certainly one such investigator. The basis for the argument centered around what the expected weight of a normal thymus gland must be. Those who agreed with Boyd believed that in deaths which followed a lingering or wasting illness, the thymus gland was very, very small. However, in those who died suddenly, in accidental circumstances, with no prior wasting disease, the thymus was not small. So, the controversy centered in a large measure around what the true normal size of a thymus gland should be. Obviously, since pathological material was the source of thymuses, there was real room for differences among pathologists on this issue. There seemed to exist no way to stop the bitter debates about whether a certain size was normal for the thymus gland or whether that size represented enlargement.

Professor Pancoast certainly seemed to practice what he preached. He indicated (Pancoast 1930, p.762) that "We have treated 315 cases of enlarged thymus from 1912 up to April, 1930. Of these 271 have been treated since 1924."

Are roentgenologists today suggesting that Dr. Pancoast consistently deceived himself about what he saw in roentgen studies from 1912 to 1930? Dr. Pancoast is in the top echelons of the famous American roentgenologists.

Part 5. A Pathologist-Coroner with Enthusiasm for "Enlarged Thymus Disease"

I was a student at UCSF Medical School at the time that Jesse Carr was one of our professors of pathology. He was also the coroner for San Francisco. Professor Carr was a flamboyant, enthusiastic lecturer who certainly had his pathology well in hand. He was very popular with the medical students.

In 1945, some 34 years after the 1911 paper by Lange, Professor Carr wrote an extensive (43 page) paper in the Journal of Pediatrics, Vol.27, No.1, July 1945, pp. 1-43, in which he was scathing in his comments about those who denied the existence of thymic enlargement as a real pathological entity.

Professor Carr wrote, at page 2, "Young and Turnbull, in 1931, were sent into this confusing maze of theories by the Status Lymphaticus Committee working under the auspices of the National Research Council of Great Britain, but they emerged unfortunately with little more theory of acceptable character than was proposed before their work and established no new facts concerning the function or development of the gland. In fact, by their stated position, doubting the presence of such syndrome as status thymo-lymphaticus, they probably did more to confuse the issue than they did to clarify it." Real vintage Jesse!

Concerning lymphatism, Carr wrote (p.8):

"Part of the confusion existing in the literature and in the minds of doctors today is perhaps due to a futile ambition to ascribe all deaths in children with lymphatism to one cause. Certainly there is enough material available in the literature to certify that sudden death does occur in this condition with no cytological changes being demonstrable at autopsy other than hyperplasia of the lymphatic tissues and enlargement of the thymus. That not all of these cases point to a common cause of death is, however, equally true, which may mean that at least some and possibly all of the theories of death in lymphatism which we have enumerated are valuable and that the diagnosis of lymphatism should not only not be discarded as both a clinical and necropsy diagnosis but rather could with profit be broadened and extended with qualifications added covering the conditions which upon analysis prove to be more than pure theory."

At the San Francisco coroner's office they had 520 cases of sudden death in children below 10 years of age. After eliminating many cases as being other than thymus-related, Carr says (p.9)"...of this total we can collect 49 cases dying of conditions arising from, or directly associated with, pathological changes in the thymus and lymphatic system. This group offers what we feel to be indisputable examples of death from asphyxia following tracheal compression from an enlarged thymus gland, deaths from partial obstruction by an enlarged thymus during or following anesthesia, cases showing a combination of thymic enlargement, lymphatism, and anaphylaxis, and substantiated cases of adrenal insufficiency associated with thymic hyperplasia."

Then he introduced a new term, "Status Thymico-Asthmaticus." Dr. Carr said (p.9):

"In addition to reporting a series of cases of each of these types, we wish to contribute a new descriptive term which denotes a disease entity frequently responsible for strangulation in the young, namely, status thymico-asthmaticus. Under this heading is presented a series of cases occurring in widely varying age groups where death has occurred from asphyxia and wherein the thymus is enlarged. This enlargement is of lesser degree than in cases dying with acute tracheal compression from an enlarged thymus and associated with it is an hyperplasia of the lymphoid system which instead of being generalized is limited largely to the bronchi and bronchioles. Because the lymphocytic infiltration is in the submucosa, and among the muscle fibrils as well as peribronchial, the term asthmaticus is included. This picture cytologically resembles a developing or existing asthma and the clinical course is differentiated with difficulty from true asthma excepting for the single but very important fact that the status thymico-asthmaticus group show no beneficial response to the injection of epinephrine."

The clinicians and pathologists remained seriously divided on these issues of thymic involvement in illness and particularly in sudden deaths. However, it does appear clear that physicians feared malpractice suits if they failed to include thymic enlargement as a possible diagnosis and if they failed to treat with radiation. The studies were both large and plentiful from around the country reporting large series of cases of infants studied for thymic enlargement and treated for it --- in leading medical centers.

Part 6. A Clinical Study of 2,000 Newborn Babies

The Donaldson Studies at Ann Arbor, Michigan, 1930 and 1938

Some 27 years after Lange's paper, Dr. Sam W. Donaldson published a paper in the Ohio State Medical Journal, entitled "A Study of the Relation between Birth Weight and Size of the Thymus Shadow in 2000 Newborn" (Vol.34, No.5, pages 538-541). He had published a paper on "Hyperplasia of the Thymus" in 1930. That paper dealt with 1,045 patients.

In the second paper, not only did Dr. Donaldson present data on 2000 CONSECUTIVE INFANTS in the St. Joseph's Mercy Hospital, Ann Arbor, Michigan, but he showed the following. In the male newborns (examined 24 hours after birth), 19.3% of babies were regarded as borderline or positive for x-ray evidence of thymic enlargement; in the female newborns, 17.5% were regarded as positive or borderline. This is a much higher incidence than that widely reported elsewhere.

For the females (112 positive and 63 borderline), the following was the procedure: The 112 positive cases were given from two to four treatments of 100 R each, the treatment being given at weekly intervals.

The 63 with borderline positive thymic findings were given one treatment with 100 R --- stated by Donaldson to be a prophylactic measure.

Altogether, about 18 % of all the children born in that hospital during the period of accumulation of 2000 births were given therapeutic doses of x-rays.

Dr. Donaldson was by no means unaware of a deep split in the medical profession concerning whether enlarged thymus was a disease at all and whether it made any sense to treat it with radiation.

Awareness of the Controversy

Dr. Donaldson wrote (p.538):

"It has long been the opinion of many physicians that only those newborn who are above average weight should be examined roentgenologically for evidence of an enlarged thymus. Complicating the picture is the fact that there appear to be two separate and distinct schools of thought regarding the thymus problem. One group maintains vehemently that there is no such problem and that the danger from the existence of an enlarged thymus is negligible if it exists at all. The members of the other school of thought contend with equal firmness that an enlarged thymus is pathological, basing this contention on their experiences with sudden and unexplainable deaths in which the only finding was that of an enlarged thymus, or on their observation of the disappearance, following irradiation, of the classical symptoms attributed to the thymic syndrome."

Donaldson pointed out that even though Lange's 1911 paper was one of the first to describe the effects of roentgen irradiation upon the thymus gland, the textbooks published

as late as 1915 made no mention of the use of roentgen treatment of enlarged thymus gland. They simply ignored the subject, both with respect to therapy and with respect to prognostic significance of an enlarged thymus, according to Dr. Donaldson.

In spite of this "textbook failure," Lange's work became applied early. Newborns whose x-ray exam showed a thymic shadow were subjected to x-ray treatment, and routine pre-operative irradiation of the gland with its subsequent reduction in size was a precaution taken by many surgeons, according to Dr. Donaldson (at p.540).

Results of the Treatments One Month Later

As for Dr. Donaldson's own practice, the detailed observations are indeed fascinating. At page 540, Dr. Donaldson relates:

"All babies in this series with a borderline finding were given one treatment of 100 R, 130 P.K.V. [our kVp] filtered through 4 mm. of aluminum. This amount of radiation was considered to be sufficient to cause involution of the gland in a newborn infant and was given solely as a prophylactic measure. Those with a more marked finding of enlargement and with compression of the trachea were given from two to four treatments of 100 R each with the same factors. Treatments were administered at weekly intervals and checkup films were made 30 days following the last treatment to determine whether or not there had been a reduction in size of the shadow and expansion of the shadow of the trachea." And:

"In practically every case where a re-examination was made following treatment there was found to be a reduction in the size of the shadow of the thymus and an increase in the width of the shadow of the trachea to normal. In a very small percentage of the cases the thymus shadow had not receded to within normal limits, but had diminished in size and appeared denser, suggesting that fibrotic changes had occurred as a result of the radiation and induced involution. Up to the present time, although records are not complete on every child examined, in none of the children in either the treated or untreated group who have died has the death been attributed to a persistent thymus."

Part 7. Delusion or Reality? An Enduring Enigma, in Our Opinion

The reader has quite a platter to choose from concerning what one finds when searching for enlarged thymus glands, and what one finds when assessing the benefit of x-ray therapy of those thymuses found to be enlarged. It is a disturbing matter indeed to witness the disparities in reports on this issue. We go from the "observation" that there is no entity such as a pathologically enlarged thymus gland to the "observation" of marvelous results of the x-ray therapy itself. That is QUITE a range.

Some readers may be ready to assume that the marvelous results "observed" from radiation therapy were just "self-suggestion" by the physicians or the parents. And such readers may be correct. The phenomenon of self-suggestion in medicine is not limited to patients (or parents of very young patients). There is no doubt that physicians, too, sometimes "find" a positive outcome therapeutically for the patients they treat, when there is no such outcome.

But were the immediate benefits of thymus irradiation really a delusion? We are not ready to say so. It seems hard enough for people to maintain their convictions about REALITY if the beliefs are under attack. The physicians who believed in roentgen therapy for alleged thymus disorders maintained the faith decade after decade, despite

vigorous challenge, well-known to them. What were all those physicians "seeing" to sustain their faith in the 1920s, 1930s, 1940s, and 1950s, if not real benefits? The enigma remains, in our opinion.

By contrast, there is no mystery about the public's enthusiasm for the thymus-explanation. When there were babies turning blue and having trouble breathing, parents were desperate for relief. When there were unexpected sudden deaths in young children without any evidence of pre-death illness, the public was primed to be responsive to something like the enlarged thymus concept --- especially with all the reports of favorable (even "brilliant") results from the roentgen irradiation of the thymus.

Under these circumstances, parents did not want to hear from the skeptics. The parents wanted x-ray diagnosis and x-ray treatment for their children --- and they got them.

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1925: "... there is no doubt that a decided enlargement of the thymus exists in a large number of newborn babies and that while it causes no inconvenience in many of these, there are a few of them in whom it will cause serious trouble, or even prove fatal. The number of sudden deaths from enlarged thymus in babies supposedly healthy is sufficiently large to consider this condition a potentially serious one whenever found. Since we do not know which of these babies will develop trouble, or why some do and some do not, the only safe plan to follow is to treat all enlargements as pathological. Fortunately, the treatment is simple and so far as we know harmless, both as to immediate and remote effects."

• - G.W. Grier, "Enlarged Thymus: Differential Diagnosis and Radium Treatment," ATLANTIC MEDICAL JOURNAL pp.502-506. May 1925.

1927: "... from the observation and treatment of a large number of cases, it may be confidently stated that the roentgen ray offers not only a highly satisfactory method of treatment of enlarged thymus, but, in practically all cases, a safe and certain cure."

• - John Remer and Webster W. Belden, "Roentgen Diagnosis and Therapy of the Thymus in Children," AMERICAN JOURNAL OF ROENTGENOLOGY AND RADIUM THERAPY Vol.18: 119-124. August 1927.

"... the one real specific in pediatric medicine ..."

1925

"If there is one real specific in pediatric medicine, I feel it is the radiation treatment of thymic disease. The relief afforded sometimes by only one exposure is so marked that it verges on the dramatic. In a number of instances I have seen infants practically in extremis with stridor, dyspnea, and tetany, react miraculously within a few hours after a single roentgen treatment. The reduction in size of the enlarged thymus gland can be simultaneously followed by roentgenographic study."

And:

"Two conclusions might be stated as almost axiomatic: (1) That failure of symptomatic relief suggests an error in diagnosis, and (2) the effects of properly measured roentgen dosage on the thymus appears so definite that it might be applied as a diagnostic procedure in doubtful cases, much as the therapeutic test is employed in suspected syphilitic conditions."

And:

"Empiricism is so contrary to modern scientific medicine that any therapeutic measure advanced at the present day not based upon experimental and laboratory research and data, must perforce lose much of its value. And yet clinical medicine has struggled through the ages and given birth to its most valuable healing agents purely upon empirical grounds. Assayed in the molten crucible of experience and withstanding every conceivable onslaught of criticism and trial, there have survived many of the most valuable therapeutic aids in medicine based upon what is the true and tried test — the result achieved in the war against disease at the patient's bedside ... "

Mulford K. Fisher, M.D. "Roentgen-Ray Treatment of Chronic Cough in Children."

AMERICAN JOURNAL OF ROENTGENOLOGY and RADIUM THERAPY Vol. 14: 244-246. 1925.

CHAPTER 8

Thymus Irradiation before Age One: Start of Our Master Table

Now we begin the task of estimating the average levels of breast irradiation for a typical year during the 1920–1960 period. At the start, a few reminders from Chapter 5, Part 2, may be helpful.

- – Our Master Table considers 65 different age-years (age at irradiation) for a single, typical calendar year.

- – Because our method is based on a typical year, ideally the population-size and the dose-level would be the same in every year (1920, 1921 ... 1958, 1959). In the real world, no year is just like the years before or after it, with respect to population-size and dose-level. But it is valid to "even out" the differences mathematically, and we do so, to produce one "synthetic" year which can be treated as typical.

Except for some general considerations in Part 4, this chapter deals only with radiation received before age one, and only from diagnosis and treatment of "enlarged thymus" and "status lymphaticus." Thus, this chapter provides the entries for Column C of the Master Table (Chapter 39). Additionally, Part 1 of this chapter describes the origin of the entries for population in Column A of the Master Table, and Part 4 of this chapter provides the entries for natural background radiation in Column B of the Master Table.

Part 1. Average Annual Breast-Dose from the Therapy

We will begin with the 1985 study by Hildreth and co-workers of 2,856 infants who received such treatments in Monroe County, New York between 1926 and 1957. Data from Hildreth 1985 carry over to Hildreth 1989 (which is the next follow-up report).

Actually, however, we must add approximately 375 additional children who were treated with radiation to the thymus during the period under study, but for whom the records were destroyed, so that follow-up could not be conducted on these. Whether followed or not, these additional children must, of course, be included, if we are to approximate that "all" children treated in Monroe County have been taken into account. See Item 3, below.

- – Item 1: What was the place of study? Five hospitals and four private radiologists in Rochester, New York, were engaged in the practice of thymus examination and subsequent therapy when deemed necessary. All of these facilities are in Monroe County, in "upstate" New York. The county is a single well-defined geographic location for which some essential population data are readily available.

- – Item 2: Can we regard the listed participants as truly representative of Monroe County for the relevant period? The answer is "Yes." The authors are quite explicit on this point. They tell us that the initial roster of subjects was developed by searching radiation therapy records maintained by five Rochester hospitals and four private radiologists to identify individuals who were irradiated for this condition in Monroe County between 1926 and 1957. And the report assures us that this series represents nearly all the individuals who received x-ray treatment for this condition. In Item 3, we

point out that the key word here is "almost," since there are some 375 additional children who were treated, but not followed.

- - Item 3: How many persons were treated? 2,856 were treated, with "nearly" half females. Therefore, we use 1,428 as the number of female infants treated. But Hildreth (1989 at p.1281) states: "...As a result, this series includes almost everyone who received x-ray treatment for an enlarged thymus in Monroe County. The only records not reviewed were those of a private radiologist who had destroyed his records on retirement in 1944. It is estimated that he treated fewer than 400 children for this condition..."

Since our analysis seeks to know how many children were actually treated, and not necessarily who were followed, we can not exclude the "fewer than 400" additional treated children. We can simply make the best approximation of how many were treated in this group. We shall use a value of 375 additional children treated, to interpret "fewer than 400."

Since approximately half the treated children were female, we should add (375/2), or 187 female children with thymus irradiation. The total number of female children treated in Monroe County becomes (1428 + 187), or 1,615 female children as the total treated group.

- - Item 4: What ages are represented in the treated group? All the infants were under 1 year of age, with most of them under 6 months of age at treatment. The age between birth and the first birthday is called "age-year 0" in our Master Table.

- - Item 5: What was the total period over which the treatments continued? We are told that the treatments were between 1926 and 1957. We shall return to the duration of the study in Items 7 and 12.

Total Female Infants below Age One, per Year, USA and Monroe County

- - Item 6: We need to know the total population of female children below age one in Monroe County for the average year in the period 1920-1960. We shall get this value in an indirect fashion. The Master Table (Chapter 39) gives the number of female persons in each age-year in the entire USA from age-0 through age-64, in its Column A. Now we must ask how the numbers in Column A were derived.

From the World Almanac, we obtain the female population of the United States for each decennial year, 1920 through 1960. The average for this period is 69,037,400 females, all ages combined. Now we need to distribute the population by ages. In Table 24 of Radiation and Human Health (Gofman 1981), we have the life-table values for the number of female persons in each age-year for a total population of 131,000,000 females (out of a total population of 250,000,000). So for the mid-period of 1920-1960, the entries for Column A of the Master Table are obtained by the following relations:

$$\text{Fraction} = 69,037,400 / 131,000,000 = 0.527 .$$

$$\text{Each entry for Col.A} = (0.527) \times (\text{Entries in Table 24 of Gofman 1981}).$$

The entry for Col.A of the Master Table for age-0 is 905,213 females.

Next, we find out how the population of Monroe County compares with the population of the United States. For this comparison, the year chosen is not crucial, provided the composition by age or other features did not change materially with time. We shall use 1960 data from the 1962 County and City Data Book for this purpose.

In 1960, Monroe County had 586,309 persons (County and City Data Book).
 In 1960, the U.S. population was 179,333,000.
 The ratio, Monroe / USA = (586,309 / 179,333,000).
 This ratio we take as valid for the mid-point of 1920-1960.

So, the number of female infants, age-0 in Monroe County in a typical year between 1920-1960, was: (The ratio Monroe / USA) times (the entry for the entire USA from Col. A):
 $((586,309) / (179,333,000)) \times (905,213 \text{ from Col. A}) = 2,959 \text{ female children, age-0, per year.}$

Total Age-0 Females IRRADIATED per Year, Monroe County

- - Item 7: How many female infants in the age-0 group were irradiated PER AVERAGE YEAR in the Hildreth Study? For 1,615 irradiated in-toto (Item 3), and a 31-year period over which such irradiations occurred, the average PER YEAR = 1,615 / 31 , or 52.1 .

Breast-Dose per Treated Child, and Its Adjustment for Supra-Linearity

- - Item 8: We need the average dose to the breast-pairs for the irradiated children. Dr. Marvin Rosenstein (in Hildreth 1985, p.386) has estimated the average breast-pair dose to be 69 rads for the irradiated children. He provided the distribution of absorbed dose by percentiles, shown in the nearby tabulation. In the righthand column, we show our downward adjustment for supra-linearity, to be discussed below.

%	Dose Range to Breasts	Mean Dose to Breasts	Each Dose, Adjusted for Supra-Linearity
25%	0 to 3 rads	1.5 rads	1.5 rads
25%	3 to 9.5 rads	6.25 rads	5.75 rads
25%	9.5 to 95 rads	52.25 rads	29.78 rads
15%	95 to 212 rads	153.5 rads	65.39 rads
5%	212 to 287 rads	249.5 rads	99.30 rads
4%	287 to 491 rads	389 rads	154.82 rads
1%	499 to 705 rads	602 rads	239.60 rads

From the tabulated data, we calculate that the Mean Dose (weighted) for the entire group = 72.08 rads, before our supra-linearity adjustment. Given that Rosenstein had the actual raw numbers at his disposal, the agreement with his 69 rads is excellent.

Except for 1.5 rads, each of the individual Hildreth/Rosenstein Mean Doses in the tabulation needs a downward adjustment for use in our analysis. The reason for this was first mentioned in Chapter 5, Part 5, when we defined "conversion-factor" as any formula which says how MANY radiation-induced cancers result from each rad of dose. Then we mentioned that the number of radiation-induced cases PER RAD varies with the size of the dose. As the dose per exposure rises, the effect PER RAD declines. The shape of this supra-linear "dose-response" relationship is depicted and discussed in Chapter 40, Part 2, Discussion of Box 3.

Due to the supra-linear bend in the dose-response, we can not use the same conversion-factor for different dose-levels. A great variety of dose-levels occurred, not only in the Hildreth Study but also in other sources of breast-irradiation examined in subsequent chapters. So we had to make a choice in constructing our Master Table. We

● – ADJUSTMENTS FOR USE OF LOW-DOSE CONVERSION-FACTORS.

Whenever a dose per medical procedure is above 5 rads, we adjust the stated dose DOWNWARD by the appropriate factor in Column C. The adjustment factors in Column C prevent an exaggeration of cancer-effect when we use LOW-dose conversion-factors in the Master Table. The adjustment is based on the supra-linear curvature of the dose-response, which is shown by the figure in Chapter 40.

Col.B: These entries are for average increase in cancer-rate per rad (cSv) among 10,000 people. They come directly from Gofman 1990, Table 14-A, Column F --- which matches the figure shown in Chapter 40 of this breast-cancer book. The entries apply to the combined observations for all ages, both sexes, all cancer-sites. However, we are not interested in the absolute values here. We are interested in the RATIO of each entry to the low-dose entry at 5 rads, because the ratio reflects the declining carcinogenic potency of the average rad, as dose increases.

Col.C: These entries are each entry in Col.B divided by 4.716, which is the 5-rad reference value in Col.B. Factors for other specific doses can be calculated from Gofman 1990, Table 14-A.

Col.A Dose per Exposure	Col.B Avg. Increase in Cancer- Rate per 10,000 People per Rad (cSv)	Col.C Adjustment Factor of Dose, for Use of Low-Dose Conversion-Factors
5 rads & below	4.716	1.000
10 rads	3.966	0.841
20 rads	3.335	0.707
30 rads	3.014	0.639
50 rads	2.652	0.562
70 rads	2.438	0.517
100 rads	2.230	0.473
150 rads	2.015	0.427
200 rads & up	1.875	0.398

could (1) use a great variety of conversion-factors adjusted in the Master Table for BOTH dose-level and age, or we could (2) adjust the DOSE downward as needed in various chapters and then use a single low-dose conversion-factor adjusted only for AGE in the Master-Table. Both approaches are equivalent, and we chose the latter one so that each adjustment (dose-level, then age) would be clear.

The nearby box, "Adjustments for Use of Low-Dose Conversion-Factors," provides examples of the way in which the carcinogenic potency or "effectiveness" of the average rad declines, as total dose increases.

We can use the box to make an approximate adjustment for the 69-rad average breast-dose in the Hildreth Study. If we use the Adjustment Factor of 0.517 (for 70 rads), the Adjusted Dose would be (69 rads x 0.517), or 35.67 rads. This is the same as saying that 35.67 rads --- at the same per-rad potency as the per-rad potency of 5 rads --- is equivalent to 69 rads at reduced per-rad potency.

Because Rosenstein (in Hildreth 1985) provided us with the input to the average dose of 69 rads, we could adjust each dose-level separately. The separate adjustments were already shown in the righthand column of the earlier tabulation. From those entries, the average weighted dose is 32.62 rads, adjusted for use with low-dose conversion-factors. So:

Final Adjusted Mean Dose = 32.62 medical rads, adjusted for supra-linearity.

Conversion of Individual Dose to Population-Dose

- – Item 9: Population Exposure. We need now to go through the steps to get the average POPULATION EXPOSURE from this irradiation, rather than the raw individual doses per treatment. In Item 6, above, we calculated that there were 2,959 female children in the age-0 group during a typical year. In effect, we must now distribute the dose received by only 52.1 infants per typical year into the whole population of age-0. There are two steps:

- (a) the calculation of person-rads, and
- (b) the calculation of average dose taking the whole population into account.

Let us start with person-rads. When we have a group of people who each receive a radiation dose, we can calculate a measure which describes the overall harm for the group. Two rads each to 10 persons is twice as harmful as two rads each to 5 persons. We formalize this by writing:

$$\text{Person-rads} = (\text{c number of persons}) \times (\text{d number of rads}) = cd \text{ person-rads.}$$

In our case of infant breast-irradiation in Monroe County, we have in a typical year: 52.1 persons x 32.62 rads = 1699.5 person-rads.

And now the second step produces the average exposure in the entire population of Monroe-County infants in the age-0 group:

$$\text{Population Exposure, rads, } = \frac{1699.5 \text{ person-rads}}{2959 \text{ persons}} = 0.574 \text{ rad per year.}$$

Why There Are No High Doses in Our Master Table

We stop to call the readers' attention to the fact that high doses like 69 rads to individual infants (Item 8) become low doses like 0.574 rads to the AVERAGE infant, after the adjustment for supra-linearity has been made and after the infants who received no dose at all have been included. So there is no contradiction between high doses reported in the narrative parts of this book, and the low doses which characterize the entries in our Master Table.

Part 2. Average Annual Breast-Dose from the Diagnosis

Thus far, we have considered breast-dose received by the infants who received THERAPY for enlarged thymus, but now we must ask about breast-doses received by the

treated children and by ADDITIONAL children in the process of SELECTING specific infants for the treatment, not only in Monroe County, but nationwide. The decision almost always was based upon diagnostic roentgenology.

But the number of age-0 infants irradiated in the diagnostic phase of thymus disorders is uncertain. It makes a very big difference whether it was routine practice in many hospitals to examine every newborn with x-rays, or to examine only the heavy newborns (see Chapter 7, Part 6), or to give prophylactic treatment to asymptomatic infants if the parents were fearful of sudden infant death, or to use x-ray examination only on age-0 infants who were already having overt problems.

We have tried to pin down the pre-therapy facts for the Hildreth Study, in vain. This is not a criticism of the study. Far from it. Sometimes the past just can not be reconstructed in detail. There is another source, much earlier than Hildreth, which describes the pre-therapy "facts" (and lack thereof) quite well, and we shall quote that discussion here. The reference is the paper by James W. Pifer and his co-workers (1963, pp.1338-1339) concerning an earlier follow-up of this Rochester study-group:

"The degree of heterogeneity cannot be determined because the symptoms were diagnosed, and the children treated in nine radiology departments and private offices over the 31-year period. The various diagnostic criteria used to select the cases are unknown and probably varied considerably since each practicing radiologist in the early period had been trained in a different medical center. The diagnosis for one subgroup of children, for example, was based on fluoroscopic examination, while that for another was made by examination of routine roentgenograms of all newborn infants. Also, the indications for treatment differed with each radiologist, pediatrician, or general practitioner. Frequently parents insisted that their child be treated. Some pediatricians fluoroscoped all infants routinely, but probably most children treated in private offices had symptoms at presentation which prompted a radiologic examination. In hospitals, also, indications for treatment varied greatly. In one hospital, only very sick infants were treated, whereas in another hospital, all newborn babies with thymic enlargement, determined by routine roentgenographic examinations, were given therapy, even if asymptomatic. Because of these heterogenic factors, it was impossible to select a control group comparable in all respects except for radiation exposure."

It is clear, for the Hildreth Study, that not all of the treated infants were newborns. Hildreth and co-workers state that "Approximately 90% of the irradiated persons were less than 6 months old at the time of treatment." Also it is unlikely that all newborns were screened in Monroe County, as we will see.

We have estimated (Item 6) that 2,959 female children were born per year in Monroe County, and that 52.1 received therapeutic thymus irradiation during their first year of life. That is a rate of 1.76 %. If every consecutive newborn had been screened by x-ray examination for enlarged thymus, the number receiving therapeutic treatment would have been higher than 52.1 infants per year. Why do we say this? The percentage of newborn infants with "definitely enlarged" thymus was reported to be 11.2 % in Dr. Donaldson's radiologic study of 2,000 consecutively born infants in Michigan (Donaldson 1938). The percentage was reported to be 3 % to 4 % in the Conti-Patton radiologic study of 7,400 consecutive newborns in Pennsylvania (Conti + Patton 1948, Tables 3 and 5). The difference in these two studies may reflect judgments about what qualified as "enlarged," or may reflect different examination technics. In both studies, however, the

rate of treatment for newborns alone was higher than our estimated rate for Monroe County even when infants up to the first birthday were included there.

In any case, we are interested in the TYPICAL situation nationwide. Except for research studies like Donaldson 1938 and Conti-Patton 1948, we will assume that radiologic screening of EVERY newborn was not typical. But then, what WAS the typical way in which infants, age-0, came to receive x-ray therapy for enlarged thymus? We know of no documents which answer this question. We are going to lean toward assumptions which may produce a great underestimate of total breast-dose from the radiologic screening-process of infants at age-0, prior to therapeutic irradiation.

- - Item 10: We consider that Donaldson's earlier studies of 1930 are of consequence in making an estimate. He studied one group of 165 infants recently born and in hospital but referred to the roentgenology department for thymus exam because someone felt that there might be a problem of enlarged thymus. Donaldson's finding was that 41% of these infants were positive for definitely enlarged thymus gland.

He studied a separate group of infants, ranging in age from newborn to six months of age, who were referred to roentgenology from the outpatient department based upon some suspicion about the thymus. In this group he found 40.7 % who received a diagnosis of definitely enlarged thymus gland.

We can round off these results to 40% of both groups. Therefore, we estimate that 2.5 infants were subjected to diagnostic examination by x-ray for each infant subjected to thymus therapy by irradiation. We recognize the likelihood that this may be a serious underestimate of the number subjected to diagnostic examination.

- - Item 11: We are not provided with a dose-value for those undergoing thymus evaluation by x-ray. We shall assume that only half of the diagnostic examinations used any fluoroscopy, and that when fluoroscopy was used, the breast-dose was only 5.0 rads. In other words, we will assume that the extensive fluoroscopic observations recommended by Dr. Pancoast (Chapter 7, Part 1) were NOT in general practice. We will assign an average breast-dose of only 2.5 rads per diagnostic thymus examination. Again, this may well be a significant underestimate. But using these approximations for the diagnostic work-up, we have for Monroe County, per year:

$$\begin{aligned} \text{Persons examined} &= (52.1) \times (2.5) = 130.3 \\ \text{Person-rads (diagnostic)} &= (130.3 \text{ persons}) \times (2.5 \text{ rads}) \\ &= 325.8 \text{ person-rads to breasts.} \end{aligned}$$

These 325.8 person-rads were delivered among 2,959 persons. So population exposure would have been $(325.8 \text{ person-rads}) / (2,959 \text{ persons})$, which means an average dose of 0.110 rads. (In the low-dose range of 5 rads or less, no adjustment for supra-linearity is needed.)

Final average dose (diagnostic) per year, age-0 = 0.110 rads.

Part 3. Average Annual Breast-Dose from Therapy plus Diagnosis

Our total average annual dose is now 0.574 rads from therapy + 0.110 rads from diagnosis, or 0.684 rads per year.

● - Item 12: Did this occur in every year, 1920 to 1960? The Hildreth Study tells about the experience in Monroe County over a 31-year period between 1926 and 1957. No one states or suggests that such irradiations were not going on there before 1926. Knowing as we do that the "enlarged thymus" story was growing, not declining, in the early 1920s, we think it highly unlikely that no radiation therapy for it was done in Rochester, New York, until 1926. We think it would be a mistake to deduct for the period 1920-1926.

At the other end of the time period, the Rochester study does not state that the practice was entirely discontinued precisely in 1957 either in Rochester or nationally. But we do believe that the practice of thymus radiation was declining in those years. We consider it appropriate to make a correction for the decline, and we shall do so in the most radical manner, namely by assuming ZERO dose for the last 3 years (between 1957 and 1960). So we reduce our dose to breasts as follows:

$$\text{Rads, total} = ((37 \text{ years at } 0.684 \text{ rads}) + (3 \text{ years at } 0 \text{ rads})) / 40 \text{ years.}$$

Rads, total = 0.633 rads per year, to be entered into the Master Table.

This entry, 0.633 rads, goes into Column C of the Master Table. There is only one entry in Column C because the age-0 group is the only age-group involved in the Hildreth Study.

Use of the Hildreth Data As Typical for Nationwide Practice

Is generalization nationally from the Rochester experience a reasonable action? In our opinion it is. We have reviewed many other papers and many comments in discussions of papers. Some of these involve studies of thousands of infants tested and treated within a month of their birth in the hospital. And a number of these studies put EVERY child consecutively born in the hospital through the "enlarged thymus" screening. We know of no reason to believe that the Rochester experience was abnormal in radiation dose or in frequency of therapy. On the contrary, what we have read is consistent with regarding the Rochester experience as typical for the nation.

Did Thymus Irradiation Really Induce Cases of Breast-Cancer?

The Hildreth papers are flagged in our Reference list as papers which confirm the radiation-induction of breast-cancer. And Hildreth 1989 is mentioned in Chapter 2, Part 2, when we addressed the question: "Can breast-irradiation during INFANCY AND CHILDHOOD really cause radiation-induced breast-cancer in ADULTHOOD?" Yes. The Hildreth finding is confirmed also by study of atomic-bomb survivors who were infants in 1945, at the time of the bombings.

Part 4. Some General Comments about the Master Table

In subsequent chapters, we will be re-using many of the same steps required to develop the entry for Column C of the Master Table. But in one aspect, the entry in Column C is unusual: It is solitary. There is only one age-year filled in. For this reason, we wish to contrast it immediately with a column which will have every age-year filled in: Column B.

Developing the Entry for Column B of the Master Table

Column B describes the radiation received by everyone over the total body from natural radiation, exclusive of radiation from radon and its daughter products. The

general estimate is that, in the USA, such radiation occurs at a level of about 0.1 rad per year, with some regions receiving nearly double that level. These are rads calculated for radiation more energetic than medical x-rays. Therefore, we have reduced the natural radiation dose to 0.05 medical rads per year (see Chapter 3, Part 1).

Readers will see the identical entry of 0.05 medical rads from the very top of the Master Table to the bottom (from zero years of age through 64 years of age). Of course, there is nothing one can do to remove this source of radiation. Its effects deserve entry into our calculation of total radiation effects. And, of course, natural radiation has not varied from the 1920 period to now.

Developing Entries for the Other Sources of Breast Irradiation

Most of the other entries into the Master Table, which the reader will come to understand, require going through an item-by-item checklist of issues very similar to, but not identical with, those shown here for the enlarged thymus problem in age-0 infants, as reported from Rochester. There are other thymus studies for different age groups (Columns D and M). And there are other totally different reasons for breast irradiation. We shall be going through each of these additional sources in the coming chapters.

The Master Table: Understanding the "Horizontals" and the "Verticals"

All of the entries in the Master Table are for one "synthetic" year --- that year which is the typical year for the entire 1920-1960 period. We feel it is important to repeat this, lest someone be asking "Which year?" and seeking in vain for a particular calendar-year in the Master Table.

We have just illustrated how two COLUMNS (B and C) of the Master Table were constructed. Now let's consider the construction of ROWS. Each row must accommodate all the entries for all types of breast irradiation for a particular age-year. Thus, the row which pertains to entries for age-15 has NO entries for any age other than for age-15. There may be SIMILAR entries for a given source of breast irradiation in other rows, but each row pertains uniquely for one age-year.

Horizontal addition in a particular row is an essential final step after all the entries for breast-dose have been made. The SUM of all the horizontal entries tells us, for a typical year in the 1920-1960 period, what the total breast-dose of radiation is from all the measurable sources, for ONE SPECIFIC AGE-YEAR in the range from 0 through 64 years of age.

Each horizontal row, with all entries of dose summed, provides that information for one age-year at a time. There is no requirement that any particular row have numerical entries in each box along the horizontal row. If there are no available data for a specific source of breast irradiation for a specific age-year, then there will be a BLANK entry in that horizontal row for that radiation source. We do not put zero into such rows. We do not know what the entry might be if all knowledge were available to us. So, for now, we leave such a row blank, with the possibility that some positive entries will be added at some later date, from new information. There are no possible NEGATIVE entries in any such row.

Since each horizontal row finally gives us a sum of all the breast-doses for a particular age-year, it follows that these 65 sums are the annual radiation doses which cause a year's PRODUCTION of radiation-induced breast-cancers, which are put "on the

shelf" to be delivered later. And we know from the "Law of Equality" in Chapter 4 that the number PRODUCED per year will be the same as the number CLINICALLY OBSERVED (delivered) each year, if the annual average radiation dose (in person-rads) is maintained indefinitely.

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The "Take No Chances" Approach with Suspicious Thymuses

1926 "In any suspected case, therefore, even if the radiologist can find no positive evidence of enlargement, therapeutic application of the x-rays or radium should be made until the shadow is reduced to normal proportions or until clinical symptoms have entirely disappeared." And:

"A 'suspected' case may be defined as one which has shown any evidence of respiratory difficulty not clearly due to causes other than enlargement of the thymus. I do not believe that the so-called status lymphaticus can often be diagnosed with certainty antemortem. Suspicion should attach to the child, especially if under 3 years of age, who exhibits widespread lymphatic hyperplasia with or without splenic enlargement. No operative interference on such a child should be attempted without x-ray studies, whether the thymus area is enlarged to percussion or not."

"If all borderline cases are to be suspected, it is inevitable that there will be unnecessary use of the x-rays, both in diagnosis and in treatment. Until diagnostic criteria are available for differentiating the harmless from the harmful thymus, there seems to be no choice, since we are dealing on the one hand with a potentially fatal disease and on the other with a harmless but most efficient preventive and curative measure [emphasis added]."

"In some clinics, the routine preoperative technic for the tonsil and adenoid operation includes a radiographic study. With the criticism that this seems to be an unnecessary precaution, the surgeon who has lost an operative case from thymus asthma probably will not agree."

"Finally, it may be permitted to point out that the very nature of thymus death is calculated to destroy a physician's professional poise. The death of any patient is a cause for more or less self-reproach, but an unexpected and possibly avoidable death is not only a reproach to the physician, but in these days, an excuse for the laity to interpret it as due to professional neglect. From this standpoint, it may be admitted that preoperative study of all patients under 4 years of age by x-rays is justifiable technic."

From J.C. Gittings, M.D. "Thymus Death in Early Life: Its Clinical Differentiation," THE ATLANTIC MEDICAL JOURNAL pp.853-857. September 1926.

CHAPTER 9

Thymus Irradiation to Reduce Sudden Death in Children

Part 1. The Thymus and Sudden Death: A Pervasive Fear in Medicine and in the Public

"A thymic death is one of the supreme tragedies of surgery. An apparently healthy child dies during the administration of an anesthetic, during or after an uncomplicated tonsil and adenoid operation, or, as recently happened, during a simple circumcision. Again, as reported by one of our medical examiners [coroners], a child was standing on the edge of the sidewalk. A runaway horse dashed by and the child dropped dead. At autopsy the condition known as status lymphaticus was found; that is, there was an enlarged thymus and a hypertrophy of all the lymphoid structures of the alimentary canal, these structures being the solitary follicles --- Peyer's Patches and the mesenteric glands. This slight pathology was all that was found to explain the unexpected death." This statement in 1926 is from Dr. Harris P. Mosher, Dr. Alexander S. MacMillan, Dr. Frederic E. Motley (Mosher 1926).

By no means was the concern about disorders of the thymus gland confined to infants under one year of age. Indeed, as we shall see in this chapter and the next, such concern was evident for all ages up through the 'teens. There were long-standing ideas concerning the thymus gland and sudden death; the availability of x-rays did not help to dismiss these long-standing worries, particularly in situations of stress, of which anesthesia and surgery were prime examples.

We continue with a quote from M.L. Janower and O.S. Miettinen, concerning policy at a major institution in Boston, Massachusetts (Janower 1971, p.753):

"From 1924 to 1946, it was the policy of the Massachusetts Eye and Ear Infirmary in Boston to apply prophylactic irradiation in every case in which an "enlarged" thymus gland was diagnosed in infancy. The assessment of the size of the thymus gland was based upon an anteroposterior roentgenogram of the chest taken in expiration with the patient in the supine position. Whenever the width of the superior mediastinum was at least half the width of the heart the gland was characterized as 'enlarged' or 'suspicious,' and the child was given radiation treatment; if the gland was less than half the width of the heart the child was not given radiation. On the basis of these criteria, 1,131 children received thymus gland radiation in the 22-year period." Despite one use of the phrase "in infancy," the irradiated children were an average of 4.7 years of age at exposure.

At the end of this chapter, we will evaluate annual average breast-dose from such treatment of children, ages 1 through 9, for Column M of our Master Table.

Part 2. Enlarged Thymus, with and without Symptoms: Dr. O'Brien

The issues surrounding such treatments were succinctly and well stated by Dr. Frederick W. O'Brien in 1929, at the annual meeting of the American Roentgen Ray Society. We quote O'Brien (1929, p.271):

"For some years now, it has been the routine in certain hospitals to examine all children roentgenologically before submitting them to a general anesthetic. If there is found what is thought to be an enlarged thymus gland, a prophylactic roentgen treatment

is given, because of the rather well-entrenched belief that an enlarged thymus gland is an integral factor of the syndrome of so-called status lymphaticus, a reputed cause of otherwise unexplained sudden death." He also described the controversy:

"An enlarged thymus as a symptom-producing organ, and the roentgenologist's ability to diagnose it, has not gone unchallenged. Status lymphaticus, indeed, as a pathologic entity is declared a misconception."

And the two propositions posed by Dr. O'Brien:

1. Is there a symptom-producing enlarged thymus in infants that can be diagnosed by the roentgen ray and relieved by irradiation?

2. Is there an enlarged thymus without symptoms in infants, children, and young adults, which represents objective evidence of status lymphaticus, and which can be diagnosed by the roentgen ray and should receive prophylactic radiation?"

Uncertainty about Where the Truth Lay

Dr. O'Brien appeared uncertain about where the truth lay. With respect to mortality, he divided the cases as follows (1929, p.273): "Cases of thymic death are readily referred to two distinct groups, those with and without symptoms." About cases with symptoms:

"Accepting the concept of the evolution of the thymus, I do not find any student of the subject who does not concede the existence of a symptom-producing thymus at least in infants. The groups with symptoms usually display the so-called syndrome of thymic asthma, characterized by attacks of inspiratory dyspnea, inspiratory stridor and the so-called Rehn's symptoms, the expiratory swelling of a tumor [meaning a fulness, not a real tumor], the cranial thymus-end in the jugulum." And about cases without symptoms (p.274):

"The other group of so-called thymic deaths occurring in older children in an apoplectiform manner without premonitory symptoms is the one responsible for the current hospital practice to which I have referred of roentgenographing all children before anesthesia." And:

"It has been suggested that these sudden deaths have been due to improper anesthetization and poor operative judgment and technique [see Part 3]. But they occur even without anesthesia and following minor or no surgical procedure at all. These are the cases that are the tragedies of practice and if personal, or under one's immediate authority, cause one to pause."

Prophylactic Irradiation: Claims of Success vs. the Skeptics

Dr. O'Brien continued (p.274):

"Mosher, well aware of the newer concepts, clings to the old idea that the thymus is involved in these sudden deaths, and he has the added argument of no sudden death in his great clinic since his study with MacMillan and Motley (Mosher 1926). They found out of a total of 2,344 children, a positive thymus shadow in 7.5 per cent. Of the positive cases treated by roentgen radiation all were successfully operated on and since employing the routine roentgen examination of the mediastinum, they have had no sudden unexplained death under anesthesia." And (p.274):

"This has been the practice for two years at the Boston City Hospital and the Cambridge Municipal Hospital with both of which I am connected. At the Boston City Hospital, out of a total of more than 2,000 children, there has been but one unexplained death under anesthesia, which occurred recently. There had been no prior roentgen examination and there was no autopsy. At the Cambridge Municipal Hospital, in 526 cases, there have been no deaths. A survey of the chests showed a 'broadened mediastinal shadow' in +6 percent."

We will return to Dr. O'Brien's conclusions in Part 4.

Others were much more skeptical about the 1926 report by Dr. Mosher and colleagues, on the grounds that the absence of deaths was not proof that the roentgen treatment of ostensibly enlarged "silent" thymuses was the real reason for such absence.

Boston: "Nearly All Infants Are X-Rayed Promptly"

During the discussion of Dr. O'Brien's paper, Dr. R.D. Leonard of Boston commented as follows (in O'Brien 1929, pp.276-277):

"We have to construct some theory along which to work, and as our empirical results and our interest and enthusiasm in this theory develops we subconsciously forget that we are working simply on a hypothesis. I think this is something we need to bear in mind in relation to this thymus problem. As we see from these two papers, we know what is generally thought about the thymus gland, but very little has actually been proven." And:

"In Boston, as in various other places, the thymus gland is at the present time a popular subject for discussion. Our obstetricians are very much interested in the thymus gland. Nearly all infants are x-rayed promptly and if any sort of a shadow is seen in the mediastinum, treatment is instituted. In the sudden, unexplained deaths, we recognize the thymus gland as a probable cause. Therefore on account of the present popular interest in the thymus gland, I would add this word of caution that, as far as possible, we as roentgenologists should be sure we know what we are talking about."

The statement by Dr. Leonard strongly indicates that the practice of roentgenographing "nearly all infants" was not confined to research studies. One implication: Our estimate of breast-dose from the screening-process itself --- in Chapter 8, Part 2, Item 10 --- is almost certainly a serious underestimate.

Part 3. The 1914 Edition of "Anesthesia": Dr. Gwathmey

In his 1914 Edition of "Anesthesia," Dr. James Tayloe Gwathmey made some quite illuminating comments about the so-called Status Lymphaticus deaths which occurred in relation to anesthetic administration (p.331):

"Status Lymphaticus. --- Definition. --- Status lymphaticus or thymicus, or lymphatism, is a condition of infancy and childhood, marked by hyperplasia of the lymphatic structures, spleen and bone marrow, and persistence of the thymus gland (Stedman). It has also been defined as a condition of unstable equilibrium, coma, convulsions and vomiting accompanying hyperplasia of the persisting thymus (Gould); and as a morbid state due to excessive production or growth of lymphoid tissues, such as the thymus and thyroid glands, resulting in impaired development, lowered vitality, and sometimes death (Dorland)." And:

"History. --- As early as 1614 attention was called by Felix Plater to the fact that the thymus was enlarged in three cases of sudden death from dyspnea in one family. In 1823, and again in 1829, Kopp mentioned the association of the enlargement of the thymus gland with sudden death. Paltauf, in 1889 and 1890, collected, for the first time, a large number of cases of sudden death in adults, in which there was enlargement of the tonsils, lymphatic gland system, the follicles at the base of the tongue, the spleen, and the thymus gland, with narrowing of the aorta. Kundrat, in 1895, published ten cases of death immediately after anesthesia by chloroform or some mixture containing it, also one case in which ether was the anesthetic. Sudden deaths were noted after this time in many cases in which no anesthetics had been administered. Lymphatic hyperplasia had been found to occur in every chloroform fatality for the past twenty years in the children's clinic at Gratz. The first case recorded in England was reported by Wolff in 1905." And, in commenting on some features of such patients (p.332):

"Pasty complexion, a large amount of subcutaneous fat, and, in adults, a scant amount of axillary or pubic hair are usual; also the hair of the head has a peculiar dry brittle character ..." And (p.332):

"Most patients dying during or immediately after anesthesia have been young people or children, of flabby type, with enlarged adenoids, tonsils, thyroid (usually), and thymus; with narrow, high-arched palate, small mouth and throat, and weak heart sounds. During anesthesia a grayness of complexion or pallor is witnessed, with weak heart action and shallow breathing. Enlargement of the thyroid is said to exist in more than 50% of cases. Enlargement of the tongue is an important factor in diagnosis. The spleen has been found to be greatly enlarged in many cases, also the mesenteric, popliteal, axillary, and inguinal glands. Exophthalmic goiter may also be present, in which event heart failure under the anesthetic is probable. Congenital defects such as cleft palate and cleft kidney are sometimes associated with status lymphaticus. All patients have a pale, thin skin, pasty complexion, and usually subcutaneous fat. The glands of the neck are also sometimes enlarged. The above complex symptoms are noted when, given chloroform for any length of time, much of the anesthetic is absorbed and less secreted than is usual, with a consequent continual poisoning of the system until death occurs several days after the anesthetic. Sometimes delayed chloroform poisoning is mistaken for status lymphaticus. In status lymphaticus, especially in children, patients seem to dread the anesthetic more than is usually the case ..." "

And Dr. Gwathmey offers a strong warning against using chloroform (p.333):

"From the study of a large number of statistics, the fact that chloroform is contraindicated cannot be questioned. Roberts concludes that ether is the safest anesthetic for all of these cases. Unquestionably, chloroform should be avoided in all suspected cases."

A Case Description from Hilliard (1908), as Cited by Dr. Gwathmey (p.334)

"Mortality. --- Harvey Hilliard gives a very complete history of a fatal case of status lymphaticus in a young man aged twenty-one, six feet two inches in height, very thin, and of a highly neurotic temperament. Operation: Circumcision." And:

"The patient was a great smoker of cigarettes and subject to attacks of faintness. The patient had the usual preparation, but was allowed to smoke during the morning, the operation being at twelve o'clock. Hilliard found on examination a rapid pulse, poor chest expansion, and considerable enlargement of the thyroid gland. Chloroform-ether mixture

was the anesthetic. During the induction period, the heart beat very violently. A light anesthesia was maintained. When the prepuce was severed, the patient turned an ashen color and stopped breathing. Rhythmic tongue traction was employed and amyl nitrite vapor, the administrator pressing the lower ribs to restore respiration. This brought the patient round. The anesthetic was discontinued with the idea of discontinuing the operation, when the patient immediately stopped breathing. The usual restorative methods were resorted to, but proved unavailing. Artificial respiration was kept up for forty-five minutes, but the patient did not again come around."

An Alternative Hypothesis about Deaths during Anesthesia

Dr. Gwathmey appeared skeptical about some of the cases alleged to be deaths due to status lymphaticus. At p.336, he cites Yandell Henderson (in *Surgery, Obstetrics, and Gynecology*, August 1911), who felt that unskillful anesthesia is more often the cause of death, and especially in adenoid and tonsil cases, than the status lymphaticus or heart disease. According to Dr. Gwathmey, Dr. Henderson wrote in 1911:

"Writers assume that status lymphaticus was the cause of death, although there may have been no autopsy. Even in those cases in which an autopsy was performed, the pathologist's report sometimes indicates that if he had not been told what to find, he would scarcely have found it."

And Dr. Henderson predicted as follows (according to Gwathmey):

"In many of the very best text-books of pharmacology ... the practice of occasionally interrupting the administration of ether, and of allowing the patient to come for a few moments pretty well out of anesthesia, is expressly recommended. If anesthetists will only realize that this is a procedure which, above all others, should be shunned, the number of cases of so-called status lymphaticus fatalities, under anesthesia will, I believe, show a sudden and marked decrease."

We do not know how many anesthetists looked at Dr. Henderson's advice. But we do know that concern about sudden death in childhood, especially during anesthesia, caused decades of radiation screening and treatment for "Status Lymphaticus" and "enlarged thymus."

Differentiation of Thymus Disorders from Others ... with "Happy Results"

A number of writers (Dr. Henry Pancoast, 1930, in particular) have recorded their opinions that a variety of disorders in the thorax need differentiation from a possible enlarged thymus. Especially has this been true of bronchitis, bronchopneumonia, tuberculous adenitis, sinusitis with associated bronchitis, non-tuberculous lymphadenitis, and possibly other disorders.

Dr. C. Winfield Perkins is another who alluded to possible mis-identifications (1925, p.219): "Many sudden deaths of children FORMERLY SUPPOSED TO BE DUE TO BRONCHOPNEUMONIA [emphasis in original], congenital anomaly of the heart or acute intestinal indigestion, in which autopsies have given little information as to the cause of death, may have been due to unrecognized thymic hypertrophy. Such types of cases have recently been examined, considering the possibility of thymic enlargement, in spite of possible negative roentgen findings, [and have been] treated as such with the roentgen ray with happy results and the disappearance of the cyanosis and dyspnea."

Part 4. The Belief That the Radiation Did No Harm

In Part 2, we featured two pertinent questions of Dr. O'Brien. The second question concerned prophylactic use of radiation therapy for "enlarged thymus." In closing the discussion at the 1929 presentation, Dr. O'Brien made a very strong statement about the safety of thymus irradiation (p.280):

"As to the danger connected with treating the thymus, Hammar has studied the thymus for twenty years and should know something about it. He says there is absolutely no danger from roentgen treatment. The cases he has examined show an emigration of lymphocytes which return rather promptly after the treatment has ceased. That emigration of lymphocytes accounts for the decrease in the shadow" [when it does occur, of course].

This is not the first time we have reported assurances that such roentgen treatments appeared to be harmless (see Index: Safety assurances). And in an earlier paper than O'Brien's, Dr. Roy M. Greenthal was arguing as follows (1922, p.438):

"On the other hand, it seems reasonable to give these patients the benefit of a treatment which we know will reduce the size of the thymus gland. We are aware of the marked reduction in the size of the thymus that can be secured when patients with thymic symptoms are exposed to therapeutic roentgen rays or to radium emanations. We know of no reports of harmful effects following this form of treatment of the thymus and we have never observed any in this clinic."

Possible long latency in development of radiation-induced CANCER simply was not part of the discourse on the presumed harmlessness of roentgen-ray exposure in 1922. Nor did radiation-induction of cancer receive widespread attention for several additional decades.

Prophylactic Irradiation: "Not Only Desirable, but Requisite"

How did Dr. O'Brien answer his second question about screening for enlarged thymus and about prophylactic radiation therapy in symptom-free infants, children, and young adults?

"Since our second query concerns the enlarged thymus without symptoms in children, it is not necessary to consider here tracheobronchial adenitis or lymphosarcoma or thymoma except to say that any of these conditions sufficiently advanced to give a broadened mediastinal shadow would carry with them a very definite clinical as well as roentgenological picture." And Dr. O'Brien continued (p.276):

"I am therefore presuming that the 6 to 7 percent of cases of 'broadened mediastinal shadow' seen in children without symptoms represent at least relatively enlarged thymus glands. No one who is informed thinks for a moment that all of this group represent pathological glands. This group comprises, undoubtedly, those which have not undergone accidental involution from disease, those in whom the rate of chest growth has not kept pace with the thymus, as well as those glands considered potentially a menace."

Dr. O'Brien's emphatic recommendation, about thymic irradiation prior to anesthesia, was tied to the presumed harmlessness of such irradiation (p.276):

"Since there is no evidence that the thymus is not an integral causative factor in the type of death under discussion, and since it is known that involution of the thymus takes place rapidly and without harm (Hammar) following roentgen or radium treatment, it

would appear not only desirable but requisite, until such time as more exact knowledge or experience shall warrant a contrary opinion, to prescribe radiation therapy for those children presenting roentgen evidence of 'broadened mediastinal shadow' without symptoms in whom general anesthesia or surgery is contemplated."

Part 5. Quantitative Analysis of the Massachusetts Eye and Ear Infirmary Data

Here, we shall evaluate the breast-dose received by children of ages about 1 to 9 years old, from thymic irradiation administered due to the fear of sudden death when such children had a variety of chest problems. This will become the entry for Column M of our Master Table. While some of the children had surgical procedures, we shall treat the cases of tonsillectomy and adenoidectomy separately in the next chapter.

We begin with the 1971 study by Janower and Miettinen entitled "Neoplasms after Childhood Irradiation of the Thymus Gland." The average age of the children in their study was 4.7 years old at the time of irradiation, as mentioned already in Part 1. Thus, these children were considerably older than the children evaluated in the previous chapter, about 90 percent of whom were under 6 months of age. The children in the Janower/Miettinen Study represent children with a variety of chest problems plus some head and neck problems, including bronchitis, lymphadenitis, and other disorders which brought them into the Massachusetts Eye and Ear Infirmary.

We shall use almost the same checklist of "items" used in the previous chapter.

- - Item 1: What was the place of study? The Massachusetts Eye and Ear Infirmary in Boston, Massachusetts --- which is Suffolk County. This is a single well-defined facility in a stable location in which essential population information will be available.

- - Item 2: Can we regard the study's participants as representative of Suffolk County for the relevant period? Unfortunately, we have no basis whatever for assuming that all the hospitals and private practitioners referred their patients to this one Infirmary. Nonetheless, we shall make our dose-estimate as if ONLY the children in the Janower/Miettinen Study received such treatment in Suffolk County. For any children of this age-bracket who were treated in other institutions of Suffolk County, we assign ZERO dose.

This means that we shall definitely be underestimating the person-rads of breast-dose for Column M of our Master Table. But our intention is for doses in the Master Table to represent a credible LOWER limit of annual average breast-dose.

- - Item 3: How many persons were treated? Over the 22 year period (1924-1946), there were 1,131 children treated for thymic enlargement.

- - Item 4: What ages were represented in the treated group? Only the mean age was given in the report, a value of 4.7 years. We shall assume that the age-range of those irradiated was from 1 through 9 years of age. We shall assign equal numbers of children to each age-year of the 1-9 year age-range.

- - Item 5: What was the period over which the treatments continued? The total period was about 22 years, starting in 1924 and ending in 1946.

Females of Each Age-Year Irradiated per Calendar-Year, Suffolk County.

- - Item 6: We need to know how many children were present in each age-year for each year of the study. Since 1,131 children were irradiated in the course of 22 years, the

number of children treated per year was $(1,131 / 22)$, or 51.4 children per year. We shall make the approximation that one-half of the children were female, so there were 25.7 female children treated per year of the study.

If we divide this number equally into nine age-years, we arrive at $(25.7 / 9)$, or 2.86 female children in each age-year who received therapeutic radiation at this Infirmary, in a calendar-year.

Total Females Ages 1-9, per Year, USA and Suffolk County

• - Item 7: We need to know the total population of female children in each age-year (1-9) in Suffolk County for the average year in the period 1920-1960. We do this as we did it in Chapter 8 (Item 6).

In 1960, Suffolk County had 791,329 persons.

In 1960, the U.S. population was 179,333,000 persons.

The ratio, Suffolk / USA = $(791,329 / 179,333,000)$.

In the Master Table, Column A, we have the number of females (age-year 1):
 $(892,820 \text{ national}) \times (\text{the ratio of } 791,329 / 179,333,000) = 3,940 \text{ age-1 females.}$

And in this way, the full nine-year tabulation is built.

Age-Year	Females, National: Number in Age-Year	Females, Suffolk Cy.: Number in Age-Year
1	892,820	3,940
2	892,097	3,936
3	891,518	3,934
4	890,657	3,930
5	890,332	3,929
6	890,051	3,927
7	889,806	3,926
8	889,589	3,925
9	889,390	3,925

Breast-Dose per Treated Child

• - Item 8: We need to know the radiation dose absorbed in this "enlarged thymus" therapy. The treated children generally had a cumulative air dosage of 400 Roentgens (4 doses of 100 R each), but we cannot be sure what the distribution was to the breasts. A phantom study, as done by Dr. Rosenstein for the Hildreth Study in Rochester, would have been desirable. Absent that, we shall assume the same irradiation techniques were used in Boston as in Rochester, and that the absorbed breast-dose was the same: About 32.62 rads per child, after adjusting for supra-linear bending of the dose-response curve (see Chapter 8, Item 8). We will use 32.6 rads, below. If most of the Boston children received 400 R (air dosage), our use of 32.6 breast-rads may underestimate the true dose, but this is not provable within the data.

Conversion of Individual Dose to Population-Dose

• - Item 9: We need the average population-dose from this irradiation, rather than the raw individual doses per treatment. We calculated in Item 6 that there were 2.86 female children in each age-year who received therapeutic radiation in Suffolk County, in a calendar-year. We use the same two-step process shown in Chapter 8, Item 9. First, we obtain "person-rads." So for each age-year:

$$(2.86 \text{ persons}) \times (32.6 \text{ rads}) = 93.2 \text{ person-rads.}$$

The second step is to distribute these person-rads, received by only 2.86 persons, into all the children of the same age-year in Suffolk County. We illustrate with the age-1 group:

$$\text{Population Exposure, rads} = \frac{93.2 \text{ person-rads}}{3,940 \text{ females}} = 0.02365 \text{ medical rads per breast-pair.}$$

And we must do this calculation for all nine age-groups.

Age-Year	Females in Suffolk County	Person-Rads	Mean Population Dose, medical rads per breast-pair
1	3,940	93.2	0.02365
2	3,936	93.2	0.02368
3	3,934	93.2	0.02369
4	3,930	93.2	0.02372
5	3,929	93.2	0.02372
6	3,927	93.2	0.02373
7	3,926	93.2	0.02374
8	3,925	93.2	0.02375
9	3,925	93.2	0.02375

• - Item 10: We have considered, so far, only the dose received by those children chosen to get radiation therapy to the thymus gland. This does not tell us what dose was received for those who were roentgenographed, but who did not qualify for radiation therapy. The Janower paper indicates that the criterion used was a certain width of thymic shadow in an antero-posterior roentgenogram. If the Infirmary took just one film and never used diagnostic fluoroscopy, the diagnostic radiation dose to breasts --- distributed over the whole population of those ages --- could have been quite low.

We shall assign a ZERO dose for the "entrance exam" for this series. Of course, this underestimates the doses received, but we prefer an underestimate where there are no usable data.

• - Item 11: Duration. Janower and Miettinen say explicitly that such treatments were given for the years 1924-1946. They do not explicitly say that no such therapy was given in any of the other years of 1920-1960. We are consistently trying to develop a credible LOWER limit of dose, so we will not assume treatments in all forty years. For the period before 1924, we will assume 2 years without activity. And for the period beyond 1924-1946, we will assume no activity during 7 years. So, we will approximate that treatment occurred for 31 years, and no treatment occurred at all for 9 years.

Therefore, we adjust the average annual dose downwards, as follows:

$$((31 \times 0.02368) + (9 \times 0))/40 = 0.01835 \text{ medical rads for age-years 1 through 3, and}$$

$$((31 \times 0.02374) + (9 \times 0))/40 = 0.01840 \text{ medical rads for age-years 4 through 9.}$$

This completes the analytical work for this group, and we make nine entries for nine age-years into Column M in the Master Table.

Use of These Data As Typical for Nationwide Practice

There are sometimes regional differences in medical practice. In our study of the literature, we have looked for evidence of such differences with respect to all chapters of this work. So far, we have not found any reason to think that the Boston data used above were atypical. But if we just suppose that treatment for "enlarged thymus" was more popular in Boston than elsewhere, for age-years 1-9, we should still not worry about any OVERestimate of national breast-dose in Column M. Why not? Because of the undeniable UNDERestimate discussed in Item 2, above.

#

**1922: No Surgery Planned?
Reduce the Thymus Anyway.**

In the debate as to whether infants and children with evidence of enlarged thymus should be irradiated, we have the following (at p.438):

"Because some patients with thymic hyperplasia go through operations or severe illnesses without trouble, does not mean that all will do so. We have no means of knowing beforehand who will be the fortunate ones. It would seem, therefore, that the reduction of an enlarged thymus is indicated in all patients before operation."

As for those not being considered for surgery, Dr. Greenthal concluded that the following should occur:

"How shall we treat nonoperative cases which show thymic enlargement? We have given all these patients roentgen-ray treatments in order to reduce the size of the gland. It is our belief that this, too, is a beneficial procedure."

Why, we ask, did Dr. Greenthal think it was beneficial? The answer centered on one statement:

"It has long been known that some patients with enlargement of the thymus react to illnesses in a violent manner."

Roy M. Greenthal, "The Incidence of Thymic Enlargement Without Symptoms in Infants and Children," AMERICAN JOURNAL OF DISEASES OF CHILDREN Vol.24: 433-440. 1922.

CHAPTER 10

Thymus Irradiation before Anesthesia and Surgery in Childhood

Part 1. The Thymus and Sudden Death: How One Paper Altered Surgery's Course

We think it is worth repeating the first line of Chapter 9 here.

"A thymic death is one of the supreme tragedies of surgery..."

Harris P. Mosher, M.D. (1926, p.1)

Dr. James Tayloe Gwathmey's "Anesthesia" (1914) leaves no doubt about the anesthetists' level of long-time concern about sudden deaths (see preceding chapter, Part 3). The anesthetists and surgeons were concerned about the sudden deaths associated with anesthesia, with even minor surgery, and with the possibility of all these difficulties being brought on by the mysterious constitutional syndrome, Status Lymphaticus. They worried a lot about this long before Dr. Roentgen discovered the x-ray in 1895. According to Dr. Gwathmey (p.331), a connection between an enlarged thymus and sudden death was suspected for centuries:

"As early as 1614 attention was called by Felix Plater to the fact that the thymus was enlarged in three cases of sudden death from dyspnea in one family." Even today, with our plethora of statistical studies, one would sit up and take notice of THAT series of three cases.

What advice was offered by Dr. Gwathmey in 1914 to his colleagues? He provided tips on how to spot the people who might have difficulty with anesthesia, he advised strongly against use of chloroform in all suspected cases, and he passed along Dr. Henderson's warning against interrupting anesthesia.

He said nothing about pre-surgical roentgen treatment of the thymus gland. Friedlander (1907) had treated one case of enlarged thymus with x-rays. In 1911, Lange had published his landmark paper about x-ray treatment of four cases (see Chapter 6, Part 3). But Gwathmey did not mention these. Perhaps he was unaware of them, but the more likely explanation is that Lange's focus was not on anesthesia and Status Lymphaticus, but rather was primarily on the symptom-laden syndrome of respiratory distress and "enlarged thymus."

Although the surgical implications of the 1911 Lange paper appear unrecognized in 1914, the recognition did not take many more years.

Before the mid-1920's, the era spawned by Dr. Lange had arrived. At last surgeons and pediatricians felt they could DO SOMETHING about this dreaded sudden-death disaster --- namely, use x-rays to shrink the thymus gland. Moreover, the Pancoasts and others were teaching the medical profession how one should do a meaningful roentgenologic examination to ascertain whether thymic enlargement truly existed. It is interesting to speculate on what might have happened without the 1911 paper of Dr. Lange.

So now the ingredients were in place for a dynamic rise in activity --- and in breast-irradiation. Diagnosis of enlarged thymus and prophylactic shrinkage were introduced as necessary preludes to anesthesia. Surgeons started to refuse to operate

unless thymus enlargement had been evaluated. And if thymic enlargement existed, surgery was postponed while x-ray therapy of enlarged thymus was conducted (Part 3).

We can best pick up the story by listening to Dr. David Husik.

Part 2. Some Scary Episodes: Their Effect upon Dr. Husik, 1926

In 1926, Dr. David N. Husik's paper reported (p.859):

"It has been my unfortunate and rather sad experience to see three deaths during or immediately following the removal of tonsils and adenoids --- two in children under four years of age whose tonsils were removed under ether anesthesia, and who had apparently recovered from the anesthetic, when they suddenly became cyanotic and died, and the case herein reported under local anesthesia. All three cases were signed out as status lymphaticus, although no necropsy reports were obtained in the two children."

And, after this experience:

"It is my custom now to radiograph the chest of all patients who are referred to me for tonsillectomy --- children as well as adults. This, of course, puts the patient to an added expense, which is not necessary in a good many cases, but my experience teaches me it is safer for the patient, and a comfort to the doctor to know the chest is negative before operating."

Then Dr. Husik relates the following for two leading medical centers:

"It is now the routine treatment to radiograph all children between one and fourteen years of age booked for tonsil and adenoid operations at the throat department of the Massachusetts General Hospital and the Massachusetts Eye and Ear Infirmary. All children showing a broad superior mediastinum are considered as suspicious cases, and are given four x-ray treatments of a third of an erythema dose [an erythema dose was estimated at 300 Roentgens or more, at the time]. The treatments are repeated at intervals of ten days."

Large-Scale Use of the Practice

We are always looking for clues to ascertain when such practices began. The next paragraph, quoted from Husik 1926, was read at the "Symposium on the Thymus Gland," Section on Eye, Ear, Nose, and Throat Diseases of the Medical Society of the State of Pennsylvania, Harrisburg Session, October 8, 1925. Husik is citing results from Drs. Mosher, MacMillan, and Motley from the Massachusetts General Hospital and the Massachusetts Eye and Ear Infirmary, as they were published in the November 1924 issue of "The Laryngoscope" (p.900). Mosher points out (in Mosher 1926) that the numbers published in 1924 cover just the first year's work.

"The total number of children radiographed was 2,344. Of these, 185 (or 7.5 %) showed a positive thymus shadow. Of the 185 positive cases, 110 have been treated [x-ray therapy] and successfully operated on. Ninety per cent of the children treated showed diminution of the broadness of the superior mediastinum."

The number doubles. In their 1926 paper, Mosher and colleagues state the following (p.3):

"The present paper adds the figures for the second year and brings the series up to the present. There have been no thymic deaths during the past two years. Two cases

which the X-ray showed had an enlarged thymus and which had had the regulation treatment with the usual reduction of the gland to normal size gave trouble --- one during the giving of the anesthetic (ether), and one after the completion of the tonsillectomy. The symptoms in both cases were those of extreme shock. Both patients recovered." And, in their conclusions:

"A series of near five thousand consecutive (4820) X-rays shows that 7 % of children in the tonsil and adenoid age --- namely 2 years to 16 --- have an enlarged thymus."

Part 3. Was There a Special Focus on Tonsillectomies?

Although a great deal of attention was centered on preventing thymic deaths during removal of tonsils (and adenoids), we should make it clear that concern extended to ALL types of surgery. We will cite a few examples, to which we have added the relevant emphasis:

- - Mosher (1926, p.1): "A thymic death is one of the supreme tragedies of surgery. An apparently healthy child dies during the administration of an anesthetic, during or after an uncomplicated tonsil and adenoid operation, or, as recently happened, DURING A SIMPLE CIRCUMCISION." Gwathmey (1914, p.334) cites Hilliard (1908) about a fatal case of Status Lymphaticus related to anesthesia. The type of operation: Circumcision.

- - Perkins (1929, p.261) about practice at the Seaside (New York) Hospital: "In any case awaiting tonsillectomy OR OTHER SURGICAL OPERATION, when there was enlargement, operation was cancelled and roentgen therapy was instituted for the purpose of reducing the gland. When the gland was reduced, operation was performed."

- - O'Brien (1929, p.271, p.274, p.276) made repeated references to anesthesia or surgical procedures, without mentioning tonsillectomy: "For some years now, it has been the routine in certain hospitals to examine all children roentgenologically before submitting them to a GENERAL ANESTHETIC." And: "The other group of so-called thymic deaths occurring in older children in an apoplectiform manner without premonitory symptoms is the one responsible for the current hospital practice to which I have referred of roentgenographing all children before ANESTHESIA." And: "... it would appear not only desirable but requisite, until such time as more exact knowledge or experience shall warrant a contrary opinion, to prescribe radiation therapy for those children presenting roentgen evidence of 'broadened mediastinal shadow' without symptoms in whom GENERAL ANESTHESIA OR SURGERY is contemplated."

One Million Adenotonsillectomies per Year

Although concern about thymic death associated with anesthesia and surgery was not limited to tonsillectomies and adenoidectomies, there are reasons that these operations received a great deal of attention. Two reasons.

First, the tonsils are regarded as some of the lymphatic structures of the alimentary canal, which include the thymus, and all of which were considered to undergo hyperplasia in the "Status Lymphaticus" syndrome.

Second, tonsillectomy and adenoidectomy were super-favorites for surgical therapy in the earlier years of this century --- wholly aside from and independent of any considerations of enlarged thymus. John F. Bayley, Jr. (1968 p.918) stated the following:

"Approximately one million children [USA] are subjected to adenotonsillectomy each year. Although this procedure accounts for as high as 44 per cent of all operations in some children's hospitals, no unanimity exists as to the indications."

It should occasion no surprise that the difficulties with anesthetic deaths would be noted more frequently for the most common operation being performed by surgeons of that era.

"A Wise Precaution" for Those with Responsibility and Liability

Dr. Mosher and co-authors make it very clear why the practice of checking and treating thymus enlargement reigned for decades (1926, p.6):

"Since an enlarged thymus is the only available hint that a generalized enlargement of the lymphatic structures of the alimentary tract may exist as well, since this is the only pathological finding at autopsy in status lymphaticus, since deaths from status lymphaticus are more commonly associated with the tonsil and adenoid operation because it is the most common operation in children, it seems a wise precaution owing to our present lack of knowledge of this condition which can express itself so tragically, to learn the size of the thymus and if it is enlarged to reduce it to normal size by the therapeutic use of X-ray before undertaking the tonsil and adenoid operation, in fact before performing ANY SURGICAL OPERATION ON INFANTS AND CHILDREN" (emphasis added). And:

"As one of those held finally responsible when a status lymphaticus death occurs in our hospital, I shall continue to act on the older theory and advise the continuance of the routine X-ray of the chests of children and the X-ray treatment of an enlarged thymus when found."

Part 4. Quantitative Analysis for the Master Table, Column D

Here, we will develop the entries for our Master Table, Column D. The information we use here does not lend itself to all the same steps used in the two prior chapters. However, the principles are the same, and that will become evident as we proceed with the calculation of breast-doses for the Master Table.

- - Item 1: What was the place of study? The entire United States. From the outset, we are going to deal with the entire population instead of a specific locale, such as Rochester or Boston.

- - Item 2: Can we regard the list of participants as truly representative? Since we are going to begin with data for the entire U.S. Population, the issue of "representativeness" disappears.

- - Item 3: How many persons were treated? We shall broaden this question to ask, "How many persons had diagnostic radiation and how many had therapeutic doses to the thymus?" Our final estimate is reached in Items 5 and 11. First we must estimate the annual number of tonsillectomies, in females, for our 1920-1960 period.

Bayley 1968, cited in Part 3, suggests that in some children's hospitals, as many as 44 per hundred of all surgical cases were (in the 1960s) for adenotonsillectomy. Since

Bayley infers 44% as an upper limit, we will approximate that 30 % of pediatric surgical cases were for adenotonsillectomy during the 1920-1960 period.

Next we need to know how many adenotonsillectomies were conducted on female children per average year during that period.

Francis H. Williams presented some data in the year 1928. His data show that 514,240 tonsillectomies occurred per year for a population of 46,750,000 persons (male + female), based on the data for cities with over 10,000 population. We can presume that essentially all of these tonsillectomies occurred in the "tonsil" age-years, 2 through 15.

In 1940, the mid-year of our 1920-1960 period, the population of the United States was 131,670,000 persons (male + female). We shall therefore scale up the number of tonsillectomies reported by Williams, by using the population ratio. So:

$$(514,240) \times (131,670,000 / 46,750,000) = 1,448,341 \text{ tonsillectomies during the 1940 year (midpoint of our 1920-1960 period).}$$

We need to eliminate the male cases, so we divide (1,448,341 / 2), and obtain 724,171 tonsillectomies annually in females of ages 2 through 15.

- - Item 4: Does the ratio of tonsillectomies to all surgeries make any difference in our analysis? It makes a BIG difference. We have shown in Part 3 that pre-surgical evaluation of the thymus was recommended for ALL pediatric surgeries, not just tonsillectomies. If 30 % of all pediatric surgeries were for tonsillectomies (Item 3), how many total surgeries must there have been in FEMALES?

We let x = the total number of pediatric surgeries in 1940, in females.

Percent of all pediatric surgeries which are tonsillectomies = 30 %.

Then: $0.3x = 724,171$ tonsillectomies in females.

Therefore, x, the number of surgeries in toto (including tonsillectomies) will be $(724,171 / 0.3)$, or 2,413,903 surgeries in toto (for females).

The Breast-Dose from Diagnostic Irradiation

- - Item 5: Are we suggesting that all the females in this surgical group are tested by x-ray for thymic enlargement? No, we do not think that everyone was so tested, but it is eminently reasonable, in view of the fear-factor in the general population and also in the medical-surgical population, to estimate that 60 % of the cases were tested by x-ray, nationwide. So:

$$0.60 \times 2,413,903 = 1,448,341 \text{ females who were tested annually for thymic enlargement.}$$

- - Item 6: What is the estimate of radiation dose received by the breasts from the screening procedure?

We have to presume that examination of the thymus was taken seriously. Although we assigned no dose from screening in Chapter 9, Item 10, we believe it would be a big mistake to ignore it here. A pre-surgical situation is quite special in the estimation of parents and physicians.

Considering the level of concern about sudden death, considering the very serious admonitions that a FLUOROSCOPIC exam should accompany every chest examination, and knowing that even pediatricians (but not all) were routinely performing fluoroscopy on children (see Chapter 31), we think it would be absurd for us to assume no use of pre-surgical fluoroscopy. So we will assume SOME use of fluoroscopy, and we will

suggest a breast-dose of 1 rad on the average for the individuals examined nationally. This modest estimate, of course, allows for much non-compliance with the Pancoast "imperative" described in Chapter 7, Part 1.

Dr. Pancoast was not alone in urging fluoroscopy to make a meaningful search for enlarged thymus glands. For example, Dr. C.K. Hasley (1933) concurred vigorously with the Pancoast recommendation. We quote (Hasley 1933, p.477-478):

"This paper is by no means a final analysis of so complex a subject as thymic hyperplasia, but is offered to stimulate a definite routine in the examination, and to encourage --- yes, to urge --- the use of the fluoroscope in making the study. An examination of an infant's or a child's chest should never be considered complete without thorough fluoroscopic study in both the anteroposterior and lateral positions."

- - Item 7: How do we calculate the total person-rads from the diagnostic process?

We have assigned 1.0 rad as the average dose to the breast-pair.

We have estimated 1,448,341 pre-surgical females, ages 2 through 15.

$$\text{Person-rads} = (1,448,341 \text{ persons}) \times (1.0 \text{ rads}) = 1,448,341 \text{ person-rads.}$$

● - Item 8: There are 14 separate age-years in the range of 2 through 15 years. For the Master Table, we need the person-rads separately for each of these age-groups. Therefore, we divide 1,448,341 person-rads by 14, and get 103,453 person-rads per age-year.

● - Item 9: We wish to have the POPULATION DOSE for each of the age-years. We shall show this in a tabular manner at the end of the chapter. Here, we shall illustrate how the tabulation was calculated by dealing with the entry for age-2.

$$\text{Average Population Dose} = \text{Person-Rads} / \text{Total Population.}$$

For age-2 females, Column A of Master Table gives a total population of 892,097 persons.

$$\text{Average Population Dose} = 103,453 \text{ person-rads} / 892,097 \text{ persons} = 0.116 \text{ rads.}$$

- - Item 10: Does this analysis apply for the entire 1920-1960 period?

We have shown that the practice of pre-surgical examination by x-ray was well underway by about 1924-1925 (Parts 2 and 3). Regarding the latter part of the 1920-1960 period, there is some difference of opinion. In the next chapter, we report the opinion of Waldo Nelson (1950), who was not at all friendly to the idea that enlarged thymus was a problem. He estimated that the enlarged thymus "story" was over by 1950. Carr (1945) and Conti-Patton (1948) were certainly not suggesting that it could be over by 1950.

We shall use the estimate that the annual breast-dose from testing, 0.116 rads, applies for only 25 years of the 40-year period, and that the dose was ZERO for the other 15 years. So the adjustment is:

$$((25 \times 0.116 \text{ rads}) + (15 \times \text{zero rads})) / 40 = 0.0725 \text{ rads, overall. This value is found in Column E of the tabulation at the chapter's end.}$$

The Breast-Dose from Therapeutic Irradiation

- - Item 11: We now need to consider the dose received in the course of therapy for the cases of enlarged thymus which were found.

Mosher (1926) reported that in the first 2,344 cases studied, there were 185 positive thymus cases, and of these, 110 received therapy with radiation (see Part 2). We have no reason to suggest that any other studied group during those years would lead to a

different result. And $110 / 2344 = 0.047$, so 4.7 % of those who were studied diagnostically received radiation therapy. This means $0.047 \times 1,448,341$ (from Item 5), or about 68,072 female children per year.

- - Item 12: What was the individual average breast-dose from the therapy?

The external dose was intended to be at least 400 Roentgens per child (see Husik, in Part 2) --- an exposure which may have been even higher than in the Hildreth Study (Chapter 8). But we can not be sure.

What matters is the absorbed dose (rads) reaching the breast-tissue. What fraction of the breast received irradiation is a determination which Rosenstein was able to make for the Hildreth Study by using phantoms. For this chapter on pre-surgical therapy, we have fourteen different age-groups (and body-sizes) to worry about for the fraction of breast irradiated. The fraction may be the same as for the Hildreth Study, but it may not. Following our policy of providing a credible LOWER limit on breast-dose, we will subtract almost 25 % from the dose used in Chapter 8. That dose was 32.6 medical rads, after adjustment downward for supra-linearity of dose-response. For the calculation here, we will reduce it to 25 medical rads.

- - Item 13: What was the annual average POPULATION DOSE from such therapy?

First we calculate the person-rads, which will be the same for every age-year. There were an estimated 103,453 persons per age-group who were tested (Item 8). And if 4.7 % of them were treated for "enlarged thymus" (Item 11), then the number of persons treated in each age-year per calendar-year was $(0.047 \times 103,453)$, or 4,862.3 persons. So:

$$\text{Person-rads} = (4,862.3 \text{ persons}) \times (25 \text{ medical rads}) = 121,558 \text{ person-rads.}$$

$$\text{Average Population Dose} = \text{Person-Rads} / \text{Total Population.}$$

We obtain population-size from the Master Table, Column A --- or from the tabulation at the end of this chapter (Column B). For age-2:

Average Population Dose = $121,558 \text{ person-rads} / 892,097 \text{ persons} = 0.1363 \text{ rads}$ per year from the pre-surgical therapy of enlarged thymus. This value goes into the first row of the tabulation (Column G).

- - Item 14: We need to adjust this radiation-source for duration. We assume that the practice lasted only 25 years out of the 40-year period (see Item 10). So we multiply the per-year population dose of 0.1363 rads by $(25 / 40)$, and enter 0.0852 rads into the first row of the tabulation, Column H. All the other lines of the tabulation are handled similarly.

Combined Population Dose per Year, Diagnosis + Therapy

- - Item 15: The final tabulation-step, before making entries in our Master Table, is to combine the population-dose from diagnosis and from therapy. For the age-2 group, Total Dose = $0.0725 + 0.0852 = 0.1577$ breast-rads per year. This value, entered in Column Eye of the tabulation, is ready for transfer to the Master Table, Column D, for the 2-year-olds. All the other lines of the tabulation are handled similarly, and each line provides an entry for the Master Table, Column D.

The pre-surgical application of Dr. Lange's therapy for "enlarged thymus" caused a big increment of breast-irradiation during the typical year of the 1920-1960 period, as indicated by Column Eye of the following tabulation.

● - ANNUAL POPULATION-DOSE from PRE-SURGICAL THYMUS EXAMS + THERAPY.

Age-Year	Col.A in Group	Col.B Number of Females	Col.C Person-Rads Total	Col.D Average Rads per Exam	Col.E Average Dose in Medical Adjusted for Duration	Col.F Person-Rads Total for Therapy	Col.G Average Dose in Med. Rads per Therapy	Col.H Average Dose Adjusted for Duration	Col. Eye Total Average Dose Exam + Therapy
2	892097	103,453	0.1160	0.0725	121,558	0.1363	0.0852	0.1577	
3	891518	103,453	0.1160	0.0725	121,558	0.1363	0.0852	0.1577	
4	891047	103,453	0.1161	0.0726	121,558	0.1364	0.0853	0.1579	
5	890657	103,453	0.1162	0.0726	121,558	0.1365	0.0853	0.1579	
6	890332	103,453	0.1162	0.0726	121,558	0.1365	0.0853	0.1579	
7	890051	103,453	0.1162	0.0726	121,558	0.1366	0.0854	0.1580	
8	889806	103,453	0.1163	0.0727	121,558	0.1366	0.0854	0.1581	
9	889589	103,453	0.1163	0.0727	121,558	0.1366	0.0854	0.1581	
10	889390	103,453	0.1163	0.0727	121,558	0.1367	0.0854	0.1581	
11	889209	103,453	0.1163	0.0727	121,558	0.1367	0.0854	0.1581	
12	889028	103,453	0.1164	0.0727	121,558	0.1367	0.0855	0.1582	
13	888829	103,453	0.1164	0.0727	121,558	0.1368	0.0855	0.1582	
14	888585	103,453	0.1164	0.0728	121,558	0.1368	0.0855	0.1583	
15	888277	103,453	0.1165	0.0728	121,558	0.1368	0.0855	0.1583	

Notes for these tabulations

Col.B: National average number of females in each age group for period 1920-1960.

Col.C: 1,448,231 females each received 1 rad to breasts in test for thymic enlargement.

Total person-rads = 1,448,231. Person-rads per age-year = 1,448,231 / 14.

Col.D: Average dose in medical rads to breasts for thymus "search" exam, unadjusted for duration.

Col.E: Average dose from Col.D adjusted for less than total duration, 1920-1960.

Col.F: (0.047 x 103,453) persons per age-group TREATED, or 4862.3 persons.

Average dose taken to be 25 rads to breasts. Person-rads = (4862.3 persons) x (25 rads)

Col.G: Average dose in medical rads to breast for thymus "therapy," unadjusted for duration.

Col.H: Average dose from Col.G adjusted for less than total duration, 1920-1960.

Col.Eye: Sum of "search" dose plus "therapy" dose, Col.E + Col.H .

These values are transferred to the Master Table as entries for 2 to 16 year olds, in Col.D.

Part 4 of the text explains the development of this tabulation.

CHAPTER 11

Ending of the Era of Radiation Therapy for Enlarged Thymus

Part 1. Why Did It Stop? Views of Dr. Dewing (1965), Scholar of Radiotherapy

It is not totally clear why the era of radiation therapy for enlarged thymus ended by about 1960. There have been speculations on this subject. In his very readable 1965 book entitled "Radiotherapy of Benign Disease," Dr. Stephen Dewing ventured an interesting opinion on the "coup de grace" for this practice. It is succinct and to the point. We quote from p.149:

"The Thymus: Radiotherapy of the thymus in infancy and early childhood is a matter of historical interest only at the present time. Its rationale rested on associating thymic enlargement or "hyperplasia" (as seen in the chest radiograph) with a clinical picture of respiratory stridor. The known sensitivity of lymphoid tissue and the experimentally demonstrable shrinkage of the irradiated thymus permitted use of very low doses. These were usually of the order of 100-300 R total tissue dose, spread over one to three weeks, the clinical response being the chief guide to therapy." And:

"Nowadays responsible clinicians feel that thymic enlargement is almost never related to tracheal compression, even though theoretically there might be a connection in a rare case. Status lymphaticus, or thymico-lymphaticus, has also disappeared from modern concepts of pathology. The COUP DE GRACE [emphasis in original], however, was the recent alarm raised over possible late carcinogenic effects --- particularly thyroid carcinoma. It would take a bold radiologist indeed --- or a very stupid one --- to undertake therapy of an infant mediastinum today no matter how huge the thymus might appear. Furthermore, the 'proof of the pudding' is that infants are recovering from croup and stridor just as well now as they did in the days when radiation therapy was most in vogue." And:

"One could speculate --- idly --- that the therapy acted as much to quell the inflammation of a tracheo-bronchitis as to shrink the thymus. In this area the modern antibiotics are now doing the same job, and possibly much better." We return to Dr. Dewing in our Chapter 36. He was, in 1965, Associate Clinical Professor of Radiology at New York University Postgraduate Medical School.

Pitfalls in the Words "Very Low Dose" ... and in Dose-Comparisons

Readers may note that Dr. Dewing, in 1965, regarded a dose of 100 to 300 Roentgens as a "very low dose." Today, such doses are commonly referred to as high doses.

Even though a dose of 300 R is not in the ballpark of the thousands of Roentgens used in cancer therapy for specific targets, a dose of 300 R far exceeds the "kerma" gamma-ray doses received by most of the irradiated survivors of Hiroshima and Nagasaki (details in Gofman 1990, Table 9-B).

However, whenever readers attempt to compare doses, they must keep at least three distinctions in mind. First is the quality of the radiation --- for instance, bomb radiation versus medical irradiation, which is usually more serious (see Chapter 3). Second is the difference between partial-body exposure and whole-body exposure, which

is always more serious per rad. And third is the difference between the entrance dose and the dose which actually reaches a particular part of the body (such as the breasts) or an internal organ. For example, the average internal organ-dose received by the irradiated A-bomb survivors was less than 50 rads of whole-body exposure --- and less than 20 rads for most of them (Gofman 1990, Table 13-A). Expressed as "medical rads" (see Chapter 3), those values would be less than about 25 rads and 10 rads, respectively.

Part 2. Don't Blame the Thymus: A Strong Opinion in a Famous Textbook (1950)

In 1950, the Fifth Edition of "Mitchell-Nelson" (the famous textbook of pediatrics edited by Dr. Waldo E. Nelson) emphatically made several assertions to its readers about the thymus story. Its chapter on "The Thymus Gland" was written by Dr. Nelson himself.

Thymus-Size: Accidental Deaths vs. Unexplained Deaths in Infancy

At page 1164, Dr. Nelson described the controversy about "normal" and "abnormal" thymus-size. We quote: "Weight or size of the thymus has been accorded considerable significance in relation both to the production of respiratory obstruction and of sudden death. The data of Hammar and Boyd, in particular, indicate that the weights which had been considered to be those of normal glands have, in actuality, been those of glands reduced in size by inanition and disease. Thymic tissue is extremely sensitive to the general nutritional status of the body. According to Boyd, severe undernutrition or disease (hyperthyroidism and leukemia are exceptions) will reduce the weight of the thymus by one-third within three days. When the weights of the thymus in well-nourished infants dying suddenly from such adequately explained causes as falls from high structures and automobile accidents are compared with those in well-nourished infants dying suddenly from unexplained causes, there are no significant differences."

Difficult Breathing, Sudden Death: "No Relationship" to the Shadow

At page 1165, Dr. Nelson expressed a very negative opinion about obstruction of respiration by the thymus gland. We quote: "Whether the thymus is ever responsible for obstruction of respiration of any significant degree is a controversial point. Once considered as the most frequent cause of laryngeal and tracheal stridor, many clinicians of wide experience now think it is never a factor. It has been shown that laryngeal stridor and attacks of apnea and cyanosis can be explained otherwise in the majority of instances if a careful study is made. The strongest arguments that a thymic enlargement is responsible for respiratory obstruction are the bronchoscopic observations of Jackson and the roentgenologic studies of Pancoast. However, there may well be some doubt that the thymus causes compression of the trachea in any significant number of instances. There is no doubt that the thymus may cause a widening of the upper mediastinal shadow, which may be eliminated by shrinkage of the thymic tissue by roentgen therapy. It is of considerable moment, however, that the size of this shadow bears no relationship to the occurrence of symptoms of respiratory obstruction or to sudden death..."

Pre-Surgical Thymus-Evaluation: "Not Indicated" in Asymptomatic Cases

At page 1165, Dr. Nelson asserted: "The routine roentgenographic examination of infants and small children for evidence of an enlarged thymus as a preliminary to a surgical procedure is now rarely practiced and is not indicated. When there are symptoms of laryngeal stridor, apnea, or cyanosis, a complete examination including laryngoscopy, bronchoscopy, and roentgenologic study of the chest should be obtained. In the majority

of instances some condition other than an enlarged thymus, such as a laryngeal or tracheal lesion, congenital heart lesion, valvular ring, chronic pneumonic infection, or tetany will be found to be the causative mechanism ... Though one cannot say that there are no instances in which an enlarged thymus is the causative factor, it is obvious that it is rarely so, and the instances in which roentgen treatment is indicated are exceedingly rare."

Unexplained Deaths: "Incrimination of the Thymus" Not Justified

Also at page 1165, Dr. Nelson stated: "Lymphatism as a cause of sudden unexpected death is discussed on page 374. It may be stated here that the evidence available does not justify incrimination of the thymus as a cause of sudden unexpected and otherwise unexplained death. The term 'status thymicolumphaticus' and its implication of thymic death should be discontinued because of its inhibiting effect on a more exhaustive search for the real cause of death."

A Lack of Consensus to the Bitter End

At about the same time --- just a few years apart in a fifty-year controversy --- Professor Jesse Carr (1945) was lobbing shells in the general direction of Dr. Waldo Nelson's position in these matters. (See Chapter 7, Part 5.)

Part 3. Is Some Useful Knowledge Buried in an Avalanche of Criticism?

As a life-long researcher in medicine, I feel unsatisfied by the many writers on this entire thymus story.

Let us not rush to judgment on an earlier era. We are profoundly aware of the danger of self-deception which we as physicians can create when medical studies are conducted without double-blinding and the other safeguards integral to the rules of research. And without doubt, much self-delusion goes on right NOW concerning some problems in medicine, so we can hardly be too judgmental about the period of 50 to 100 years ago.

Also, we note that many of the statements made by Dr. Nelson in 1950 had already been made, over and over again, during the height of the controversy in the 1920s, 1930s, and 1940s. How did the physicians who believed in roentgen therapy maintain their faith, if there were no real benefits at all? The enigma endures, we said at the end of Chapter 7.

Dr. Nelson acknowledged that the change in thymus-size as a result of irradiation was a reality --- he just questioned its medical significance. Dr. Nelson said at page 1165, "There is no doubt that the thymus may cause a widening of the upper mediastinal shadow, which may be eliminated by shrinkage of the thymic tissue by roentgen therapy." That is an admission of a central feature of all that has been claimed by the proponents. Then Dr. Nelson assured us, "It is of considerable moment, however, that the size of this shadow bears no relationship to the occurrence of symptoms of respiratory obstruction or to sudden death."

I simply do not think that Dr. Nelson --- or anyone else whose writings I have read --- really has a basis for the sweep implied by the Nelson statement. I have not seen it reconciled with equally emphatic reports, such as the two below from earlier chapters. How did the following statements, for instance, come to be made?

• - Drs. Kerley and Graves, in their Third Edition (1924) of "Practice of Pediatrics," stated at page 471:

"It is well proved by a long series of cases, carefully studied by competent observers, that the condition known as status lymphaticus is an entity and is characterized clinically by a lowered vitality or an unstable equilibrium of the vital forces, so that accidents or disturbances, otherwise unimportant, such as some slight injury or a light anesthesia, may precipitate failure of the heart and respiration."

● – Dr. George Pfahler, one of the early and great roentgenologists, wrote a paper on this subject in 1924 in which he made the following statement concerning roentgen therapy of enlarged thymus (Pfahler 1924, p.44):

"There is probably nothing in radiotherapy that gives such uniformly brilliant results. The younger the child, the more prompt are the results."

"Sleeping Dogs" and "Baby's Bath-Water"

Perhaps it is right for everyone to "let sleeping dogs lie" --- on a story that is long ago dismissed. After all, no one would think of resuming such uses of roentgen therapy today. The health price would be enormous. However, resumption is NOT the issue we are raising. The issue is "throwing out the baby with the bath-water!"

We are warning that some items of knowledge which might be useful may well be buried in the avalanche of criticism of the "enlarged thymus episode" in medical history.

Part 4. Everything Is Connected to Everything, in Medicine as in Ecology in General

The thymus story is a fascinating one --- as a piece of major medical history. What it teaches us, once again, is that ideas have consequences, actions have consequences which are often unintended, and everything is connected to everything else in medicine, as in ecology in general.

An idea developed that the thymus gland might be enlarged and cause respiratory difficulty, even sudden death of infants ---

Roentgen's discovery of x-rays made it possible for the idea to be tested both as to diagnosis and treatment ---

The idea is now long dead, with many saying the marvelous results seen by physicians were never really seen ---

Many thousands of women, whose breasts intercepted some of the x-rays used in this idea's lifetime, are now dead of breast-cancer, others are dying, and more will still die --- unintended consequences of an idea.

CHAPTER 12

Reaching into the Womb: Pre-Birth Breast Irradiation

Part 1. Cancer Production by Prenatal Exposure to Ionizing Radiation

In an important communication in Lancet, 1988, Yoshimoto, Kato, and Schull reported as follows (p.665):

"This study examines the risk of cancer (incidence) over 40 years among the in-utero exposed survivors of the atomic bombing of Hiroshima and Nagasaki, and adds eight years of follow-up to a previous report confined to mortality. Only two cases of childhood cancer were observed among these survivors in the first 14 years of life; both had been heavily exposed. Subsequent cancers have all been of the adult type. Not only did the observed cancers occur earlier in the 0.30+Gy [30+ rads] dose group than in the 0 Gy dose group but also the incidence continues to increase, and the crude cumulative incidence rate, 40 years after the A-bombing, is 3.9-fold greater in the 0.30+ Gy group."

This finding of a significant elevation in cancer rate in those irradiated in-utero is important. However, the total incidence of cancers is numerically small, 18 cases in all, with 16 of the 18 occurring in adults. This suggests, according to the authors, that:

"These results, when viewed in the perspective of fetus doses, suggest that susceptibility to radiation-induced cancers is higher in prenatally than in postnatally exposed survivors (at least those exposed as adults). However, definitive conclusions must await further follow-up studies" (p.665).

It is very early in this study. By 1984 (which was the closing date of the Yoshimoto study), those exposed in-utero were just about forty years old. The cancers are largely yet to come. There were three breast-cancers in the series of 18 cancers in toto, and all three of them were in the ostensibly unexposed category. In view of the random fluctuations of small numbers (and three cases make a severe "small numbers problem"), and in view of what is already known about age-years 0-9 from larger parts of the same study (see Chapter 3, for example; also Gofman 1990), the distribution of the three breast-cancer cases in Yoshimoto 1988 is almost certainly due to pure chance, with no biological meaning. We consider it highly reasonable to assume that breast-cancer sensitivity is about the same for irradiation in-utero as it is for irradiation at 0-9 years of age. Of course, we will continue to observe the on-going follow-up, of the in-utero cohort of A-bomb survivors, to ascertain whether the assumption is strengthened or weakened by continued observation.

Part 2. Proportion of Infants Receiving X-Ray Doses in-Utero (U.S.A)

The most common reason that pregnant women receive x-ray examinations which expose their infants, is to determine whether or not the women will be able to deliver the infants vaginally. The x-ray examinations sometimes take place during labor itself. According to Kevin Kelly and co-workers (1975):

"Roentgenographic evaluation of the relative sizes of the fetal head and maternal pelvis has been used clinically almost since the advent of medical radiography. The

technique was considerably refined by Colcher and Sussman in 1944. Further refinements and variations have been instituted since that time."

Pelvimetry was a routine topic in medical textbooks of the 1930s and 1940s. For example, from Christopher's Textbook of Surgery, Third Edition (1942), we quote Dr. James T. Case, Professor of Radiology at Northwestern University Medical School (p.1635):

"Roentgen measurements of the pelvic diameters can be taken without any special apparatus; the ordinary x-ray equipment of a hospital should be satisfactory. Space here does not permit description of the technic of pelvic and fetal mensuration (see the author's description in Curtis: Obstetrics and Gynecology, Phila., W.B. Saunders Co, 1932, vol.3, p.762)."

(a) Frequency of In-Utero Irradiation: MacMahon's Study

Dr. Brian MacMahon (1962) published a paper entitled "Prenatal X-Ray Exposure and Childhood Cancer." Our major interest here is in his evaluation of the frequency of prenatal exposure to x-rays.

The study-population consisted of 734,243 children born in, and discharged alive from, any of 37 large maternity hospitals in the northeast United States in the years 1947-1954. These hospitals were located in the nine states comprising the Northeast Region of the United States as defined by the U.S. Bureau of the Census. All but three of the hospitals were situated in Massachusetts, Rhode Island, Connecticut, or New York City. The frequency of intrauterine x-ray exposure in the population was estimated in MacMahon 1962 by review of the records of a 1 percent systematic sample.

MacMahon acknowledged that births in these hospitals were not representative of the general population of births in the area, since the included hospitals were not rigorously representative. For example, a special effort was made to obtain the collaboration of three hospitals in which the use of x-ray pelvimetry was believed to have been high, and in general, large hospitals were approached. We shall deal with the bias of this selection-process in a moment.

The MacMahon study concerns x-ray examinations of the maternal abdomen and pelvis in which the fetus received essentially direct whole-body exposure. The majority of such exams are pelvimetry examinations, but flat-plate examinations for twins, placentography and series-studies of the intestinal tract or urinary tract are also included.

The systematic sample comprised 7,346 live births, in which 104 occurred in multiple births and 7,242 in single pregnancies. X-ray of the maternal abdomen or pelvis was recorded in 32 (30.8%) of the multiple and 770 (10.6%) of the single pregnancies. In his Table 2, MacMahon lists 9.9% of all the female children as x-rayed, out of 3,570 cases observed. This is the percentage of special interest to us. For personal reasons, some readers may be interested in MacMahon's finding that first births showed a much higher rate of x-raying than did second and later births. Moreover, this finding has important implications for arranging proper control groups in health studies of in-utero radiation.

MacMahon obtained no estimates of in-utero doses in this series of cases. For doses, we must search elsewhere (Part 3).

(b) Frequency of In-Utero Irradiation: Kelly's Study

Kevin Kelly and colleagues (1975) addressed the question of "The Utilization and Efficacy of Pelvimetry." They reported the following (p.66):

"This study analyzed clinical information from 67,078 single deliveries of 1,000 grams or greater from 16 hospitals [in the years 1969 and 1970]. Pelvimetries were performed during 6.9 percent (4,599) of these deliveries ...". Later (p.68), they reported that pelvimetry accounted for 72% of the pelvic and abdominal x-ray procedures in their study. Thus, the rate of prenatal irradiation was (6.9% / 0.72), or 9.6% --- in remarkably close agreement with the MacMahon findings for a period some 20 years earlier. Like MacMahon, Kelly et al noted that their study-population was not a perfectly random sample, due to some geographic, economic, and racial factors. Also, all of the hospitals providing data were training institutions.

Our Adjustment Downward in the Frequency of X-Rayng

For Dr. MacMahon's purposes (comparing frequency of prenatal X-raying in children having a malignancy, versus frequency in children having no malignancy), seeking out a few hospitals with a high frequency of pelvimetry is not a serious matter. For our purposes, such bias is undesirable. In order to avoid overestimating the frequency of prenatal irradiation, we shall simply reduce the total frequency of x-raying to 75% of the total observed by Dr. MacMahon. This should take care of the possible consequence of MacMahon's selection-process. So:

$$(9.9\%) \times (0.75) = 7.4 \% \text{ of live births had pelvimetry or abdominal radiation.}$$

Part 3. The Question of Radiation Dose to the Fetus in Such Studies

Robert Berman and Benjamin Sonnenblick (1957) have addressed the issue of doses received by the fetus and female pelvis (1957, p. 4):

"The purpose of this communication is to record actual measurements in roentgens of radiation dosage directed to the depths of the female pelvis during the exposure of films for x-ray pelvimetry and hysterosalpingography." Measurements were provided for a total of 28 women, 13 of whom had pelvimetry films taken at or near 38 weeks of gestation.

The total intrapelvic dose of x-ray radiation, as measured in the posterior vaginal fornix in 10 patients who were exposed for the full exam (4 pelvic views), had an average value of 2.9 R, with 6 patients receiving less than 3 R and only one receiving more than 4 R. The total range of doses was 2.1 to 4.4 R.

We shall use the Berman-Sonnenblick estimates for dose, and the MacMahon estimates (adjusted downward by us) for frequency of the examination.

Part 4. Preparation of the Dose Estimate for the Master Table

- - Item 1: In the Master Table we have an entry (in Column A) of 905,213 female infants in the 0-1 age-year group, nationwide. This number is approximately the number of female live-births in the average year of 1920-1960.

- – Item 2: We shall use the reduced value from the MacMahon studies as the frequency of examinations irradiating the fetus (pelvimetries plus abdominal examinations). That value is 7.4 % of live-births per year.
 - – Item 3: Number of infants who received the radiation in the 905,213 live-births = (905,213 births) x (0.074) = 67,000, rounded off, per year.
 - – Item 4: Person-rads per year = (67,000 persons) x (Radiation Dose). For dose, we shall evaluate the two extremes of Berman and Sonnenblick: 2.1 and 4.4 Roentgens. Since this is medical x-radiation, and since these are depth doses measured in Roentgens, we use the approximation here that person-Roentgens are equivalent to person-rads.
- Person-rads = 67,000 persons x 2.1 rads = 140,700 person-rads.
 Person-rads = 67,000 persons x 4.4 rads = 294,800 person-rads.
- The other approximation we make here is that the smaller component in the MacMahon frequency (the abdominal radiation) delivers about the same fetal dose as the dose delivered by pelvimetry.
- – Item 5: We wish never to overestimate radiation dose, so we shall accept the lowest of the person-rad values obtained in Item 4, namely 140,700 person-rads.
 - – Item 6. For the Population Exposure in the Master Table, we need to distribute the person-rads into the entire 905,213 persons:

Thus,

$$\begin{aligned} \text{Population Exposure (in-utero)} &= 140,700 \text{ person-rads} / 905,213 \text{ persons} \\ &= 0.16 \text{ rad per fetus.} \end{aligned}$$

This conservative value, reduced in Item 2 and reduced again in Item 5, is entered into Column K of the Master Table. For this singular entry, we can use the table's first row, because (as noted in Part 1) we will use the same conversion-factor, from dose to breast-cancer, as we use for the year after birth until the first birthday.

In view of Kelly's comment (Part 2), we can assume pelvimetry was in common use for the entire 1920–1960 period.

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CHAPTER 13

Treatment of Acute Postpartum Mastitis with X-Rays

Part 1. The Early Reliance on X-Ray Therapy of Acute Inflammations

In the years before the introduction of chemotherapeutic agents such as the sulfonamides and the antibiotics such as penicillin, there existed a large, developed reliance on x-ray therapy of acute inflammations. Furuncles, carbuncles, cellulitis, pneumonias, erysipelas, and many other acute inflammatory diseases were treated with x-rays. This was true for some inflammatory states other than those caused by acute infections as well as those with an infectious origin.

It may seem to some, today, that these were poor uses of x-ray therapy. Hindsight is so available. However, putting oneself back into those years before chemotherapy and antibiotics --- with the terrifying inability to cope with acute inflammatory conditions --- may lead to a more sympathetic view of such uses.

We shall later discuss (Chapter 18) some studies of acute pneumonias successfully treated with x-rays, after sulfonamides (ordinarily successful) had failed badly.

Why X-Ray Therapy for Acute Postpartum Mastitis Was Delayed in Acceptance

In 1945, Roger Harvey and colleagues of the Strong Memorial Hospital in Rochester, New York, wrote a paper providing some of the useful historical details on the introduction of x-ray therapy in the treatment of acute postpartum mastitis --- a troubling condition vividly described in Part 2.

The reader might wonder why there were not comprehensive reports on this particular application of x-ray therapy at some earlier date. Harvey and colleagues believed they had an answer to this question.

They related that roentgen treatment of acute postpartum mastitis had been successful in Europe, and they listed reports by R. Goetz (1939), J. Granzo (1931), R. Goedel (1937), W.H. Hanne (1936), K. Kautsky (1934), C. Margraf (1936), G.J. Pfalz (1934), A. Pohl (1939), E. Steinkamm (1936), H. Theiss (1935). Also, they related that it had been successful in the few clinics from which it had been reported in the United States, and they listed papers by J.F. Elward and S.M. Dodek (1940), and by H.C. McIntosh (1940).

Harvey and co-workers suggested that widespread acceptance of this method of treatment had been hampered by several specific failings, which they listed (p.396):

- (1) Failure to realize that a co-ordinated plan of management of these patients is necessary even when roentgen therapy is given;
- (2) Failure to prevent simultaneous combinations of conflicting forms of treatment;
- (3) Delay in referring these patients for roentgen therapy until other methods of treatment had failed to relieve the patient.

And they related that in January, 1942, a co-operative plan of treatment of acute mastitis was undertaken by the departments of obstetrics and radiology at their hospital. Since that time, the only breast abscesses which occurred were in some of the patients

initially treated at home and subsequently referred for roentgen treatment, or in patients treated entirely by methods other than roentgen therapy.

For those unfamiliar with such matters, abscess formation represents a failure of treatment, in that surgical drainage is then required to manage this complication.

Part 2. Harvey's Important Words on the Successful Therapy and Its Mystery

In the 1945 paper, Dr. Harvey and colleagues described their methods and experience with roentgen therapy in treating 100 patients with acute mastitis between January of 1942 and June of 1944. This number of patients represented a very aggressive increase in the use of roentgen therapy for this disease in the Strong Memorial Hospital, inasmuch as the paper stated that, in the preceding 16 years of the hospital's existence, a total of only 77 patients had been treated for acute postpartum mastitis by all methods combined.

A Brief Description of the Diagnosis of Acute Mastitis

We quote from Harvey 1945 (p.396):

"The diagnosis of this disease is most accurately made by a combination of subjective symptoms and objective observations. Some patients note pain from cracked or fissured nipples from one to several nursing periods before the onset of mastitis. Then a portion of the breast becomes tender, and fever, aches, and chills occur. Other patients have an explosive onset of their symptoms with high fever, chills, aches, sweats, headache, coryza, and what the patients consider or admit to be a little incidental tenderness of one breast. In the latter group, urine cultures, uterine cultures, chest roentgenograms, and ear, nose, and throat examinations are sometimes in progress before it is realized that a breast infection could account for all the symptoms."

A Comparison of Women Treated and Untreated with X-Ray Therapy

Dr. Harvey's paper compares women treated and untreated with x-rays (p.400):

"The literature on roentgen treatment of acute postpartum mastitis leads one to believe that striking relief from all symptoms occurs immediately after treatment. We have never observed this in treating other infections such as furuncles, parotitis and cellulitis and have not been surprised to find that the same type of interval exists between treatment and effect in this condition. It is granted that a few of our patients have been free from all symptoms two hours after treatment, but in any large series of patients there will be some mild infections which will subside quickly irrespective of treatment. Most of the roentgen treated patients actually do go through some type of crisis 4 to 8 hours after treatment, and thereafter do feel markedly improved. Careful tabulation of the maximum duration of all subjective symptoms and objective findings in the roentgen treated series reveals that the average duration of subjective symptoms is 1.88 days, and objective findings, 2.45 days. In contrast are the figures of the group not treated with roentgen rays in whom suppuration did not occur, with an average of 8 days of subjective symptoms and 10.3 days of objective findings. The group operated on had subjective symptoms from infection for an average of 44.6 days and objective findings for an average of 47.7 days per patient." And:

"No one knows definitely what reaction takes place in an irradiated infection of this type. We do know that the doses of roentgen rays used are infinitesimal as far as ability directly to affect the bacteria themselves."

We believe that this oft-reported finding, of clinical response in infections with doses that could not conceivably prove bacteriostatic or bacteriocidal, remains a mystery today. Harvey and co-workers (p.401) cite Desjardins' suggestion of a speedup of the whole process of defense against local infection.

Harvey's Bottom Line (p.402): Treat Promptly, "Regardless of the Hour"

"Application of roentgen therapy is so effective in the early stages of this disease that treatment should be started as soon as the diagnosis can be definitely made, regardless of the hour. Delay in starting this treatment decreases the chances of recovery without surgery."

Part 3. Analysis of the Quantitative Details in a Much Larger Rochester Series.

In developing our dose-entries for the Master Table, Column E, we will use data from a much larger series than Dr. Harvey's. We will begin with the 1977 paper by Dr. Roy E. Shore, Dr. Louis Hempelmann, and others, entitled "Breast Neoplasms in Women Treated with X-Rays for Acute Postpartum Mastitis." We will follow a "checklist" of items similar to the model in Chapter 8.

- - Item 1: What was the place of study? Rochester, New York, in Monroe County. We are told the following in the Shore Study:

"The 606 women in group A were treated for acute postpartum mastitis with X-rays by Rochester radiologists largely between 1940 and 1955, but a few were treated later. Although X-rays were used to treat acute postpartum mastitis with varying degrees of success, local obstetricians and radiologists claimed the treatment was highly successful if given early. The treatment was considered an emergency procedure and was given day or night as soon as the diagnosis was made."

- - Item 2: Can we regard the listed participants as truly representative of Monroe County for the relevant period? The answer is, "Not sure."

The treatments were done by Rochester radiologists, but we do not have it spelled out that ALL cases treated in Monroe County were included. That is, the Shore Study does not tell us that the coverage was essentially complete, as it was in Chapter 8 for the infants treated for enlarged thymus disease. So, we must leave open the possibility that the true number of persons treated, and hence the true person-rads delivered to breasts, may be underestimated for this series in Monroe County. This means we would also underestimate the nationwide person-rads in the Master Table, Column E.

- - Item 3: How many persons were treated? In the Shore Study, there were 606 women who received the radiation therapy.

● - Item 4: What ages were represented in the treated group? We can approximate that there were 31 different age-years represented. All except one woman were in the age range of 14-44 years at treatment, and the majority were 20-34 years of age (see Item 6).

- - Item 5: What was the total period over which the treatments were performed? According to Dr. Shore and co-workers, the treatments were "largely" between 1940 and 1955, but a few were treated later. Other clinics were using the method well before the Rochester study. We shall use an adjusted value of 20 years out of 40 for duration of such use.

Females of Each Age-Year Irradiated per Calendar-Year, Monroe County

• - Item 6: We need to know how many women of each age-year were treated during one average year of the study. This is a 3-step process which produces the next tabulation.

The first step is to divide the 606 cases into age-BANDS according to the percentages provided by the Shore Study. Column B of the tabulation shows the percentages, and Column C shows the numbers of cases per age-band.

The second step is to divide each number in Column C by 15, because the cases were accumulated over a period of 15 years (Item 5). The result in Column D is the average number of cases treated in one calendar-year. The Master Table always considers a single year.

The third step is to obtain the average number of cases treated in each age-YEAR. So we divide the cases per age-BAND (in Column D) by the number of age-years in the band (Column E). And thus we arrive at a reasonable estimate of cases treated in each age-year during one calendar-year, in Column F of the tabulation.

Age-Band	Percent of Total	Cases	Cases/15	Size of Band	Cases per Age-Year
A	B	C	D	E	F
14-19	4 %	24.24	1.62	6	0.27
20-24	27 %	163.62	10.91	5	2.18
25-29	39 %	236.34	15.76	5	3.15
30-34	20 %	121.20	8.08	5	1.62
35-39	8 %	48.48	3.23	5	0.65
40-44	2 %	12.12	0.81	5	0.16

Females of Age-Years 14-44, per Year, USA and Monroe County

• - Item 7: We need to know the total population of females in each age-year (14-44) in Monroe County for the average year in the period 1920-1960. We will make the estimate with the same method used in Chapter 8 (Item 6) and Chapter 9 (Item 7). We begin with the ratio of the Monroe County population to the U.S. population in 1960, from Chapter 8, Item 6:

The ratio, Monroe / USA, was (586,309 / 179,333,000), or 0.00327.

Then we find the national number of women per age-year (age-years 14-44) in the Master Table, Column A, and we multiply each national number by the Monroe / USA ratio to obtain the appropriate estimates for Monroe County, which are shown in the next tabulation. Since the national numbers of women do not change very much in a five-year interval, we are using one value for an entire age-BAND.

Age-Band	National Number per Age-Year	Monroe County Number per Age-Year
14-19	887,609	2,902
20-24	884,794	2,893
25-29	881,805	2,884
30-34	878,278	2,872
35-39	873,473	2,856
40-44	860,227	2,813

Breast-Dose per Treated Woman

- - Item 8: We need the average dose to breast-pairs from the therapy. Shore and co-workers give the following mean breast-pair doses (in medical rads), and they are so similar that we can take an unweighted average.

Treated at age-years 15-29, mean breast-pair dose = 251 medical rads.

Treated at age-years 30-35, mean breast-pair dose = 239 medical rads.

Mean dose, without any adjustment for supra-linearity = 245 rads / breast-pair.

Adjustment for supra-linearity = factor of 0.398 (Chapter 8, Box in Item 8).

Adjusted mean dose = 97.5 medical rads to the breast-pair.

Conversion of Individual Dose to Population-Dose

- - Item 9: We need the average population-dose from this therapy, rather than the raw individual dose per treatment. This is a two-step process, in which we obtain the person-rads per age-year, and then divide person-rads by the total persons in the county. Because there are so many age-years involved, we will need to make another tabulation.

For the new tabulation, Item 6 provides the information for Column B: Number of women treated per age-year. And Item 8 provides the breast-dose per treated woman for Column C. So Column D, which is person-rads, is Col.B times Col.C.

The total persons (female) in the county comes into Column E from Item 7. By dividing person-rads (Col.D) by persons (Col.E), we obtain the average Population-Dose per Age-Year for Column F. The final adjustment seen in Column G comes from Item 10, below.

Age-Band, Years	Treated Women per Age-Year		Dose in Medical Rads	Person-Rads	Total Women in Each Age-Year	Pop'n Dose per Age-Year	Adjust for 20 Yrs
	A	B			E	F	G
14-19	0.27	97.5	26.33	2,902	0.0091	0.0045	
20-24	2.18	97.5	212.71	2,893	0.0735	0.0368	
25-29	3.15	97.5	307.24	2,884	0.1065	0.0533	
30-34	1.62	97.5	157.56	2,872	0.0549	0.0274	
35-39	0.65	97.5	63.02	2,856	0.0221	0.0110	
40-44	0.16	97.5	15.60	2,813	0.0055	0.0028	

After one more adjustment in Item 10, this tabulation will provide 31 separate entries into the Master Table, since there are 31 age-years represented here (females, 14 through 44 years).

- - Item 10: Duration. The last adjustment, already seen in Column G of the preceding tabulation, is related to the 20 years out of all 40 years (1920-1960) that we should "credit" with this source of radiation. This represents a slight increment in duration over the Rochester study itself, as indicated in Item 5, to take into account the earlier experience of other clinics. In view of extensive use in Europe in the 1930s, it is not conceivable that no American clinics were using the method. Indeed, we have American reports in the year 1940, which had to reflect work done before 1940, as does Desjardins 1931. The entries in Column G above are transferred to our Master Table, Column E. These may be underestimates because of uncertainty in Item 2.

Excerpts (Part 1) from an Important Paper of 1931:

"Radiotherapy for Inflammatory Conditions"

by an eminent roentgenological scholar of the era,

Arthur U. Desjardins, M.D., of the Mayo Clinic, Rochester, Minnesota.

In the Journal of the American Medical Association: 96, No.6: 401-408. Feb. 7, 1931.

The first paragraph follows:

"The value of radiotherapy in the treatment of many acute, subacute and chronic inflammatory processes is not as well-known as it deserves to be. This is apparently because the sound experimental basis and mass of clinical and other evidence on which it rests have not been considered, and because many questionable or wholly unfounded ideas have been advanced as explanations. As in so many other phases of radiotherapy, the first knowledge of the possible value of irradiation in inflammatory conditions resulted from the observation of unexpected benefit following exposure, for diagnostic purposes, of parts of the body which were the seat of inflammatory lesions."

That last sentence is interesting indeed! Many latter-day critics of radiotherapy for inflammations probably do not know that the therapy originated with performance of the method itself, when not expected at all.

There is a section in Dr. Desjardins' paper (at p.401) entitled: "Furuncle, Carbuncle and Other Pyogenic Infections." There he lists 17 specific references "and many others" (between 1906 and 1929) to support these statements:

- - "The influence of irradiation on such lesions, especially when treated during the stage of maximal leukocytic infiltration, which is to say before the stage of frank suppuration, has been demonstrated by Coyle ..." And:

- - "Even now, however, this method of treatment is not used as widely as it might be, probably because its value is not generally realized. A review of all the published reports shows that the majority of patients derive great and prompt benefit. Pain is relieved in about twenty-four hours, although in a small percentage such relief may be preceded by a temporary increase in the pain. The best results are obtained when the lesions are treated early. The behavior and subsequent course of the inflammatory process are greatly altered. Many such lesions never reach the suppurative stage. The advantages of the treatment are that it is most effective during the early stages when other methods of treatment are least effective; it is painless and inexpensive and does not interfere with the patient's activities; it often relieves pain in a few hours, makes hot and other dressings unnecessary or shortens the period during which they must be applied, often makes an operation unnecessary and yields a better cosmetic result ..." And:

- - "Among the inflammatory lesions included in the preceding reports are furuncle, carbuncle, cellulitis and phlegmon, soft tissue abscesses, paranephric and perinephric abscesses, peridental infection, acute adenitis, onychia, paronychia, orchitis, epididymitis, mastitis, suppurative frontal and maxillary sinusitis and otitis media. The report of Heidenhain (1926) included 855 cases; in 76 per cent of these the patients recovered rapidly without surgical intervention. Doubtful results were obtained in 19 per cent."

Following this, the paper describes the excellent results obtained in the treatment of a variety of pneumonias, including a careful statement concerning the phase of pneumonias that DOES respond and the phase known as organization (fibrous tissue growth in the inflamed region) when it is TOO LATE. Amazing insights at that time. Dr. Desjardins said, "Few physicians know that treatment by roentgen-rays may be invaluable in pneumonia."

CHAPTER 14

A Physician's Dilemma: What to Do about Chronic Mastitis

Part 1. Differences between Europe and the USA. Real or Only Apparent?

During the 1920s and 1930s, radiation therapy of chronic mastitis --- with good results --- was reported from Europe. However, there were almost no articles on this therapy of chronic mastitis in the American literature. This is so out of keeping with the reporting of other disorders treated with x-ray, that we have been looking for an explanation.

Was the practice really absent in the United States --- or was there only a reluctance to write about it here?

This is not "just an academic question." When used, this therapy delivered about 375 Roentgens to the irradiated breast (Part 6). Moreover, chronic mastitis appeared to occur far more frequently than acute mastitis (see below). So we must explore various aspects of chronic mastitis in this chapter.

What Is Chronic Mastitis?

Chronic mastitis is one name given to a group of disorders. They have received many names at different times and in different countries of the world. It took a long time to sort out the reality of any differences within this broad grouping of diseases, but it was finally agreed in most quarters that the entity, chronic mastitis, is a single disease with multiple features of manifestation. Cases differ from each other with respect to the prominence and frequency of various signs. At a given time, some cases will prominently display one set of signs; other cases will prominently display others. And with the passage of time, a particular case may shift in the relative prominence of the various possible manifestations.

The real issue, widely discussed and argued, was whether this disorder was really a benign tumor of the breast, or whether it was a chronic inflammatory disease. And if it was chronic inflammation, was it a prelude to malignancy? The various names under which this single disease was listed reflected, for a particular time and place, the leaning of the medical profession toward inflammatory disease or toward benign neoplastic disease.

In 1947, Drs. George Pfahler and George Keefer reported on use of radiation therapy for chronic mastitis in their own Philadelphia (Pennsylvania) practice. In their paper, they described the multiple names for the disease (p.1352, p.1354):

"It has been described as chronic mastitis, mazoplasia, chronic cystic mastitis, fibrocystic mastitis, adenofibrosis, and Schimmelbusch's disease, but Ewing [a great American pathologist] concluded that it begins as an inflammatory process, and then passes through these various changes into carcinoma."

Chronic Mastitis: Far More Frequent Than Acute Mastitis

Swedish physicians appear to have used two designations for this disease, fibroadenomatosis and chronic mastitis. In an earlier work (Gofman 1981), we

summarized the report from Sweden by Baral et al (1977) on cases of chronic mastitis/fibroadenoma treated with radiation between 1927 and 1957 at the Radiumhemmet of Sweden.

We found in the Baral Study that fibroadenomatosis and chronic mastitis together added up to 904 total cases, whereas acute mastitis accounted for only 120 cases. That is a ratio of over 7 to 1. It makes the scarcity of American reports on radiation therapy of chronic mastitis all the more striking. We all know that disease rates can vary from one country to another, but is that the explanation?

Roentgen Therapy for Inflammatory Conditions --- with This Exception?

The scarcity of American reports on roentgen therapy for chronic mastitis (and its various names) is particularly puzzling during years when American roentgenology was reporting success treating the inflammatory response in many other situations (see Chapters 13, 18, 33, 34, and 36). Is there any reason that radiation therapy specifically for chronic mastitis might have been avoided? Or might a widespread USE of it have been a 'verboten' subject in U.S. medical literature? We will consider some possibilities as the chapter progresses.

Part 2. Saving a "Lumpy" Breast versus Missing a Cancer

Chronic mastitis presents itself in several manifestations. Sometimes the prominent feature is recurrent pain and tenderness in the breast, particularly associated with menstrual periods. In some cases, multiple nodules (some tender) are found in both breasts. And sometimes there is even some secretion from the breast, which is worrisome to the observer. Even though Ewing suggested that these features are part of a picture of a disease which ends up as carcinoma of the breast, it is quite clear from the literature that the features of this disease do NOT justify a diagnosis of breast-cancer.

But this disease can present physician-observers with a potentially serious problem. The signs and symptoms are NOT diagnostic of cancer. And any decent physician would surely think of conservation of breasts with a set of signs and symptoms which are not those of malignancy. But physicians know very well that they can not exclude a small carcinoma hidden in a breast which is laden with the lesions of chronic mastitis. Drs. Pfahler and Keefer (1947) stated it well (p.1352):

"We realize that clinical judgment or clinical diagnosis without biopsy or mastectomy cannot be absolutely reliable. Neither can a small amount of tissue removed in these cases for microscopic study or puncture biopsy be reliable for Cheatle has shown that carcinoma is more apt to be found in the small nonpalpable cysts than in the larger ones, and that removal of a large cyst for diagnosis may leave the small carcinomatous cyst in the breast."

And they add: "On the other hand, one is not justified in recommending a mastectomy in every lumpy breast."

The Urge to Stay out of Trouble versus Breast-Conservation

We think this situation was accompanied by a real dilemma for physicians. It would take courage to say to a woman, "We shall watch it, or treat it with radiation for the inflammatory process."

The "what if" is obvious. The physician must think, "There just might be a small cancer developing among those lesions. And if no biopsy or mastectomy is performed,

what will I be able to say if one of these women comes back later with a frank carcinoma --- for which, in retrospect, I should have recommended biopsy or mastectomy? Won't I be severely criticized and vulnerable to a lawsuit? After all, there was prior literature suggesting that chronic mastitis ultimately can end up as a breast-cancer."

But sensitive physicians also must have considered the worth to their female patients of keeping their breasts. It is not a very sensitive physician who would say, "Why not get rid of that breast, so it cannot cause trouble!"

Physicians who believed that biopsy and/or mastectomy could be avoided with safety for almost all patients with chronic mastitis, by treating the condition with radiation therapy, probably felt "way out on a limb." They may have worried a lot about what the critics and lawyers would say if and when one of these cases did indeed develop overt cancer of the breast.

Part 3. Were Women with Chronic Mastitis Afraid to Visit Physicians?

Obviously, the Swedish Radiumhemmet was accumulating a large series of cases of non-malignant diseases of the breast, treated between 1927 and 1957 with radiation without surgery, as reported by Baral 1977. Quite possibly the Swedish culture permitted a leading institution to try to save breasts where it was deemed possible, without huge penalties or disgrace to the physicians.

In Britain by 1928, there had been impassioned articles pleading for the preservation of breasts in cases of chronic mastitis. For example, in the July 14, 1928, issue of the Lancet, J.H. Douglas Webster wrote a strong case for radiation therapy of chronic mastitis, which he entitled "Radiology and Surgery in Cancer of the Breast and in 'Chronic Mastitis'." In his paper, Webster also suggested that some women with chronic mastitis might stay away from medical facilities --- to the women's detriment --- out of fear that breast surgery would be recommended. He wrote (p.65):

"It is an unfortunate tradition among patients that anything wrong with the breast probably means an operation, and I am convinced from many inquiries that the fear of operation is largely responsible for the high percentage of patients who come for treatment not in an operable stage, much less a 'mastitis' stage, but in a frequently inoperable and, so far as we know at present, a practically hopeless condition."

Successes Reported from Radiation Therapy of Chronic Mastitis

In Britain, Reynolds (1932) reported in "Proceedings of the Royal Society of Medicine" a favorable experience in treating 150 cases of chronic mastitis with x-rays.

In Norway, Engelstad and Weyde reported (1944) on a series of successful treatments of "Adenofibrosis Mammae" (in the Norwegian Radium Hospital's material, 1932-1942). Roentgen therapy was used in 123 patients with a favorable outcome in the majority.

In the USA, Drs. Howard C. Taylor and Robert L. Brown (Taylor 1938) commented that "Detailed reports on the effect of roentgen irradiation on chronic mastitis are almost absent in the medical literature." They also stated that "Selected cases of chronic mastitis have been treated by direct roentgen irradiation for several years at the Memorial Hospital [New York City]. It has remained a method to be used only in patients

with severe or persistent symptoms." They did not say how many, or what fraction of cases, were treated by radiation there.

"Improvement" was reported by Taylor and Brown as follows: "... that large doses of roentgen rays do have a definite effect on non-malignant diseases of the breast can best be shown by the unilateral improvement in symptoms and reduction in size when one breast is treated and the other kept untreated as a control." Such a comparison was made at Memorial Hospital in one case, reported at p.519.

Finally, in 1947 Pfahler and Keefer published their first paper on this subject. They reported on 151 cases, accumulated between April 1920 and May 1946, of women treated with radiation therapy for chronic mastitis. It is interesting that Dr. Pfahler was one of the earliest radiologists in America --- and quite obviously, Dr. Pfahler thought well enough of this therapy to stay with it for a very long time.

Part 4. A Strong Recommendation from 1947: Consult with a Surgeon

Notable in the Pfahler/Keefer paper of 1947 is the repeated emphasis on the fact that Dr. Pfahler consulted with surgeons on most of his cases, before going ahead to treat the patients with x-rays. At page 1352:

"During the past twenty-five years --- April, 1920 to May, 1946 --- one of us (Pfahler) treated 151 cases in which the clinical diagnosis was chronic mastitis. In nearly all of the cases the opinion of an experienced surgeon was also obtained. In some cases the patients were sent by the surgeons because they did not feel justified in operating; on the other hand, they did not want to ignore the condition on account of the commonly associated chronic mastitis and carcinoma." And at page 1354:

"There is much danger of mistaking carcinoma for chronic mastitis; therefore, we urge that so far as possible each case be observed or diagnosed by conference between the surgeon and the radiologist, and if in doubt, a biopsy or mastectomy be advised."

In our opinion, Pfahler and Keefer were sending a very clear message to other physicians: "Watch out, there will be criticism of choosing radiation therapy for chronic mastitis, and you should cover your bases with an experienced surgeon, lest there be lawsuits over cancers missed."

What Happened to the Pfahler/Keefer Patients?

Drs. Pfahler and Keefer reported that they did not find a large incidence of breast-cancer in their 151 treated cases. One case only. At p.1352, they stated:

"From the fact that only one of our series of 151 patients with diseased breasts developed cancer of the breast, we must conclude that the clinical diagnoses were extraordinarily accurate or the treatment prevented the development of carcinoma in some of these cases." We need not question this, since the follow-up times were certainly not long enough to ascertain the true breast-cancer rate in the group. Out of 151 treated cases, the follow-up times only on those reported as "Well and symptom-free" were given. These represented 111 of the 151 total cases:

Duration of Follow-Up	Number of Cases	Percent
1 year or less	34	30.8 %
1 to 5 years	33	29.0 %
5 to 10 years	17	15.8 %
10 to 25 years	25	22.6 %
Over 25 years	2	1.8 %

Part 5. The Possibility of a Big Underestimate in Breast-Dose

We see two possibilities worth discussion.

First: The frequency of radiation therapy in America for chronic mastitis, in the 1920-1960 era, may have been at the low level reflected in the 1947 paper by Drs. Pfahler and Keefer --- a frequency which would then represent a very small contribution to x-ray exposure in our Master Table, Column F. This would be good news. On the other hand, we are left to wonder if fear of malpractice suits may have meant that many thousands of women with chronic mastitis lost their breasts unnecessarily.

Second: The possibility exists that radiologists, trying to help women conserve their breasts, silently did a lot more radiation therapy for chronic mastitis than they ever wrote about in the medical journals. After all, at the time, total doses of 400 Roentgens were considered to be harmless (see Index: Safety assurances). So it may have been hard for physicians to deny the women a presumably harmless treatment which seemed to relieve the pain and tenderness and which conserved the breasts. But such physicians may not have wanted to issue an invitation to criticism and lawsuits by writing about it.

If radiologists were using a lot more x-ray, silently, for chronic mastitis, we would certainly want to assess it appropriately in our Master Table, but there is no available way for us to assess it. Following our intention to reach a credible LOWER limit on breast-dose, we will base our estimate on the first possibility discussed above.

In addition, we will assume that NO ONE in Philadelphia except Dr. Pfahler ever used radiation therapy to treat chronic mastitis. This Pfahler-only assumption almost certainly leads to an underestimate in the entries for Column F of our Master Table.

Part 6. Quantitative Analysis for the Master Table, Column F.

- - Item 1: To obtain the dose-estimate from treatment of chronic mastitis, we will use the Pfahler-Keefer series of 151 women treated in the private practice of Dr. George Pfahler, Philadelphia, Pennsylvania (Pfahler 1947), between April 1920 and May 1946 (26 years).

- - Item 2: Do these 151 cases represent the total number of treated women in Philadelphia during those years? Probably not. By using the assumption that they represent the total, we operate in the direction of underestimating nationwide person-rads from treatment of chronic mastitis.

Women of Each Age-Year Irradiated per Calendar-Year

• - Item 3: We shall arbitrarily assign equal numbers of women treated to each age-year, from age 20 through 54 years, in the absence of information to the contrary. The 151 irradiated women, distributed into 35 separate age-year categories, become 4.31 women per age-year. And since these studies were conducted over a period of 26 years, the ANNUAL number of women treated, on average, was $(4.31 / 26)$, or 0.166 per age-year annually.

Females of Age-Years 20-54, per Year, USA and Philadelphia

• - Item 4: We will estimate Philadelphia's population of women in each age-year, for an average year in the 1920-1960 period, in our usual manner. We begin with the ratio of the Philadelphia population to the U.S. population in 1960:

The ratio was: Philadelphia / USA = 2,002,512 / 179,333,000.

This ratio we take as valid over the 1920 - 1960 interval.

Then we find the national number of women per age-year in the Master Table, Column A, and we multiply each value by the ratio. To simplify, we will use one value for an entire age-BAND, and tabulate below.

Age-Band	National Number per Age-Year	Philadelphia Number per Age-Year
20-24	884,794	9,880
25-29	881,805	9,847
30-34	878,278	9,807
35-39	873,473	9,754
40-54	852,293	9,517

Breast-Dose per Treated Woman

• - Item 5: We need the average dose to breast-pairs from the therapy. The average entrance dose was 375 Roentgens, total, delivered in six separate doses.

This total needs conversion to rads. The usual conversion factors for various beam-directions are shown in Chapter 23, Part 3. For front-to-back beams, we will use 0.693 breast-rads per Roentgen. Thus, $(375 \text{ R}) \times (0.693 \text{ rads} / \text{R}) = 260 \text{ rads}$. So, each of the six exposures was about 43.3 rads. A downward adjustment per exposure is required for supra-linear dose-response, as discussed in Chapter 8, Item 8. The adjustment factor for 40 rads is 0.594. In addition, we do not know that the entire breast-area was exposed. We will assume that only HALF was exposed, and adjust downward by a factor of 0.5 too. So the average adjusted breast-dose per treated woman would be: $(260 \text{ rads}) \times (0.594) \times (0.5) = 77 \text{ rads}$ (rounded off).

Conversion of Individual Dose to Population-Dose

• - Item 6: We need the average population-dose from this therapy, rather than the raw individual dose per treatment. We use our customary two-step process: Person-rads, and then person-rads divided by total persons. We can do it all in the tabulation which follows.

A Physician's Dilemma: What to Do about Chronic Mastitis Ch 14

Age-Band, Years	Treated			Total Women in Each Age-Year	Annual Population- Dose per Age-Year
	Women per Age-Year	Dose in Medical Rads	Person- Rads		
20-24	0.166	77	12.78	9,880	0.0013
25-29	0.166	77	12.78	9,847	0.0013
30-34	0.166	77	12.78	9,807	0.0013
35-39	0.166	77	12.78	9,754	0.0013
40-54	0.166	77	12.78	9,517	0.0013

• - Item 7: Duration. We will make no adjustment for duration, because there is nothing in the Pfahler-Keefer paper of 1947 which suggests termination of such treatments after 1946. And the fact that 60% of the patients have follow-up times shorter than 5 years (Part 4, above) suggests that much of the treatment was recent.

In any case, we are talking about very small entries to Column F of the Master Table from therapy of chronic mastitis, as long as we accept the assumptions adopted in Part 5 of this chapter --- assumptions which may result in a serious underestimate of dose from such therapy.

#

Excerpts (Part 2) from an Important Paper of 1931:

"Radiotherapy for Inflammatory Conditions" by

Arthur U. Desjardins, M.D. of the Mayo Clinic, Rochester, Minnesota.

In the Journal of the American Medical Association: 96, No.6: 401-408. Feb. 7, 1931.

Dr. Desjardins asked: "Why is irradiation not used more than it is?"

"The evidence of the therapeutic value of irradiation in inflammatory processes is so abundant and the testimony is so generally favorable that one wonders why irradiation is not used more than it is. Perhaps the very multiplicity of inflammatory lesions in which radiotherapy has been claimed to be effective has led to a not unnatural skepticism. Or, again, failure to utilize the treatment may be due to the excessive fear of ill effects, a fear springing probably from the reading of reports of injury, occurring during treatment for malignant tumors with large doses of irradiation, or of the systemic reaction which so often follows irradiation for lesions requiring prolonged exposure. However, the treatment of inflammatory processes, especially the acute conditions, is an entirely different affair, as will appear presently."

And also he asked (p.404): "What is the mode of action of irradiation?"

"Various explanations have been advanced to account for the influence of the rays on inflammatory conditions, and the very multiplicity of such explanations probably has led many physicians to discredit the clinical evidence or to ascribe it either to overenthusiasm or to psychic factors. Indeed, without a satisfactory and convincing explanation it would be difficult to believe that the same agent could be therapeutically effective against so many different forms of inflammation in different organs or parts of the body. And yet the reason appears to be quite simple and rests on sound and abundant experimental evidence. The natural tendency would be to think that the effect of the rays on inflammatory lesions may be due to a bactericidal action on the infecting organisms, but the almost constant negative results of the large number of experiments undertaken to test the direct influence of irradiation on many kinds of bacteria render such an hypothesis untenable. Since irradiation acts in much the same way and in almost exactly the same time on so many forms of acute inflammation, it is obvious that the inflammatory lesions must have some common factor. What may this factor be?"

The remainder of this paper is devoted to a careful analysis of the world-wide studies of the action of roentgen rays and radium on cells, and of the powerful evidence that the lymphocyte is by far the most radio-sensitive cell. But then, Desjardins asks how does this relate to an action in suppression of the inflammatory process? Much excellent and insightful reasoning leads Desjardins to the conclusion that the roentgen irradiation acts by destroying lymphocytes infiltrating the inflammatory lesion or circulating in the blood vessels which supply the affected area. Why would this have a therapeutic effect? Desjardins suggested that the infiltrating cells contain or elaborate within themselves the protective substances or other means which enable them to destroy or neutralize the bacterial or other toxic products which give rise to the defensive inflammation. And he states:

"If these assumptions are well founded, it seems not unreasonable to deduce that irradiation, by destroying the infiltrating lymphocytes, causes the protective substances contained by such cells to be liberated and to be made more readily available for defensive purposes than they were in the intact cells. There can be little question that the rays act by destroying the infiltrating leukocytes and that the value of radiotherapy depends chiefly on such action."

Whether every idea of Desjardins proved to be correct is not the question at all. It is a beautiful phenomenon to see a critical scientific mind marshalling the worldwide experimental literature plus his extensive clinical experience on this issue, in seeking to understand mechanism of action. It is self-evident, in this author's opinion, that Desjardins was not dealing with an illusion. Moreover, the problem was important. Over time, from staphylococcus to pneumococcus, inflammatory diseases have killed millions.

CHAPTER 15

Management of Tuberculosis: An Eminently Sensible Program

Part 1. A Remarkable Program of Tuberculosis Management: The Detroit Experience

At the 33rd Annual Meeting of the American Roentgen Ray Society in September 1932, a series of superb papers was delivered on the general theme of tuberculosis detection and treatment as a public health problem in the city of Detroit in Wayne County, Michigan. The description covers the period of the later 1920s and the early 1930s. As the papers in that Symposium show, this was a remarkable water-shed period in the medical history of tuberculosis. In this period, it was learned unequivocally that just bed rest, good food, and lots of fresh air was NOT likely to reverse the course of tuberculosis in someone who had already experienced what is called "cavity-formation" in the course of the "adult-form" of tuberculosis, which is generally a re-activation of infection in persons who had been exposed to the tubercle bacillus earlier and had healed the initial lesion of "childhood" tuberculosis.

Once cavitation had occurred --- even not major cavitation --- the person was likely to be spewing tubercle bacilli into the air with coughing, and NOT to be getting anywhere on the road to recovery BECAUSE the cavity failed to close. Unless the cavities can undergo closure, the person continues to cough out tubercle bacilli, the lesion itself spreads IN the affected part of the lung, the disease spreads TO the uninvolved parts of the lung (for example from right to left) and to other people. And the chances of cure were remote. It became understood that some form of "collapse therapy" was the key to recovery from tuberculosis. It was essential to put the affected part of the lung at rest, so that the cavity could heal over. The chest x-ray, properly taken, and read by experts, made it possible to tell what was really going on in the person's lung so far as the tuberculous process was concerned --- and reliance on the physician's stethoscope was NOT good enough. Closure of the cavities meant virtually everything, and this was where the effort needed to be placed.

The possibilities for "collapse therapy" were, in increasing order of effectiveness, (a) crushing the phrenic nerve to rest the diaphragm on one side or the other, (b) cutting the phrenic nerve (since the crushing causes the nerve paralysis only for months to a year), (c) pneumothorax (introduction of air into the pleural space), and (d) thoracoplasty, a surgical removal of some of the rib cage to permit partial lung collapse. We have already discussed the use of pneumothorax as a procedure which involved repeated fluoroscopic examinations before and after air introduction into the pleural space (Chapter 1). That led to very high doses accumulated to the breast tissue, and a high rate of later breast-cancer in those who had been treated with pneumo-thorax.

We should pause here to take note that, while the late results were breast-cancers in SOME of the women who were so treated, the enormous benefit to the entire group of people was that "many lived to tell the tale." What we are saying is that without "collapse therapy" many, many of the people with tuberculosis would have died an early miserable death of tuberculosis. There was little chance of recovery. But with the use of "collapse therapy" and the x-ray guidance in air refills, cavities DID INDEED CLOSE, the spewing of tubercle bacilli stopped, the spread of the disease locally stopped, the spread to other persons and to other parts of the lung of the person infected with tuberculosis

stopped, and recovery processes proceeded. The two keys in all this were (a) stopping of spreading of tubercle bacilli, and (b) insuring (by x-ray evidence) that cavities were indeed undergoing closure. Both were required to assure that progress toward health of the individual and the community, not advancement of disease, was occurring. It behooves us to remember that tuberculosis has been (and could yet again be) one of humanity's greatest scourges.

Part 2. Case-Finding for Tuberculosis in the Detroit Program

Case-finding had been going on with diagnosis of tuberculosis in people who had symptoms, which is already late, and with the vigorous effort to find the contacts of each diagnosed case, because that is THE major place where the additional new cases are to be found.

There was a new program in Detroit: Dealing on a large scale with the apparently healthy persons. Health officials decided to study 35,000 school children, of which 9,000 were of high school age. Starting with one high school examined, with x-rays of the chest in those with positive tuberculin history, they found 14 cases of adult-type tuberculosis --- the really serious immediate threat. Definite symptoms of disease were found in only 3 of the 14. And a major point was that ONLY ONE OF THE FOURTEEN HAD A CONTACT HISTORY. So had only the usual program of just seeking contacts of known cases been in effect, ONLY ONE OF THE FOURTEEN WOULD HAVE BEEN DISCOVERED TO HAVE ADULT-TYPE TUBERCULOSIS. A 14-fold leap in case-finding !

There was one girl, 16 years of age (out of the 14 cases discovered in this high school) who had a very markedly advanced lesion in the left lung. Yet she was well nourished and developed. She played on two of the school teams, and did not have the faintest idea that anything was wrong with her. And in attempting to study the spread of tuberculosis in that school, the officials found that when checked by "home room" in school, in no case were more than 2 cases discovered in any home room, except for that where the 16 year old was, and there 7 of the 14 cases of adult-type tuberculosis were found. So it was clear that where large numbers of children congregate day after day, a definite source of contact with tuberculosis will be found, in this instance an "innocent" source because the source did not know of illness.

From all the 35,000 children investigated, there were two major findings: In the overall high school program, they found the general average to be 0.5%, or one case of adult-type tuberculosis per 200 children examined. They found that 4.9% had childhood type tuberculosis, and an additional 1.5 % were suspects for possible tuberculosis.

Part 3. Development of the Quantitative Radiation-Data for Tuberculosis Patients

Now we will develop entries for our Master Table, Column G. This chapter does not quantify radiation dose from tuberculosis screening procedures --- only from management of identified tuberculosis cases. We start with the data presented by Dr. Henry Chadwick, in his 1933 article entitled "Tuberculosis Problem in Detroit," from the American Journal of Roentgenology and Radium Therapy. The data are for the year 1932.

Determining the Radiation Dose from Fluoroscopic Management of Pneumothorax Therapy

There are two parts to the radiation-dose determination. The first part is to determine the cumulative breast-pair rads for all the female persons who actually received the fluoroscopic doses. The second part is to determine what we have been calling "the population dose," which spreads the dose out into the entire population of Detroit, so that we get an average dose per person in the Detroit female population as a whole.

The First Part of the Calculation of Radiation-Dose

7,383 cases of tuberculosis were on the register in Detroit. Of the known cases, 30% were in hospitals, and 70% were at home (often after a period of sanatorium treatment).

In their two hospitals together, over 2,000 pneumothorax treatments were given each month --- with a roentgenoscopic examination before and after each treatment. So each treatment meant TWO roentgenoscopic exams.

The Massachusetts tuberculosis study (Boice et al 1977, p.830) assigned 1.5 rads of breast-dose for each fluoroscopic exam. If we assign 1.5 rads to the breast for each fluoroscopic examination, this means 4,000 times 1.5, or 6,000 breast-pair rads per month, or 72,000 breast-pair rads per year associated with pneumothorax treatment. We need to exclude the males, so we cut the 72,000 breast-pair-rads in half, to 36,000 breast-pair-rads from the fluoroscopic exams during pneumothorax treatment.

The Second Part of the Calculation of Radiation Dose with Pneumothorax Treatment

We need to know the female population of Detroit in the average year of 1920-1960. We know from Chapter 8 that the female population of the United States was 69,037,400 females, for all ages combined, as the average value in the 1920-1960 period. We ask, "What part of that total female population resided in Detroit, Michigan?"

Detroit had a population of 1,670,144 in 1960 (County and City Data Book 1962). The U.S. Population in 1960 was 179,333,000 persons. The ratio, Detroit / United States is $(1,670,144 / 179,333,000)$. We shall assume this ratio was essentially the same in the mid-period of 1920-1960, and no different for females versus males.

Therefore, female population of Detroit in mid-period of 1920-1960 =
 $(1,670,144 / 179,333,000) \times (69,037,400) = 642,951$ female persons.

$$\text{And, Population Dose} = \frac{\text{(Total Breast-Pair-Rads)}}{\text{(Total Female Persons)}} = \frac{36,000}{642,951} \\ = 0.0560 \text{ breast-pair rads per person.}$$

Average dose per female person in Detroit = 0.0560 rads per person, annually. This entry would apply for every age and we can generalize this to the United States. This is our by-now-familiar "population-dose."

However, we should eliminate the dose to the very young. Collapse management of tuberculosis is virtually absent in the very young children. A reasonable approach is to re-allocate the total delivered dose to all ages except those under 10 years of age by increasing the dose by 10% to those 10 years of age and older. Then the average per person which is effective is 1.1×0.0560 , or 0.0616 rads per person. This will be applied for the entire country.

An Additional Source of Radiation Dosage beyond the Pneumothorax Fluoroscopy

There is an additional item to consider in the Detroit population. We know that 70% of the cases were at home and 30% were at the hospital. And we know that approximately 50 % of the hospitalized cases were not on pneumothorax and hence were not subject to the before-and-after fluoroscopic exam with each refill of air, since there were no refills (Table at p.326 in Chadwick 1933). But those not receiving air refills were nonetheless examined with some regularity to assess the progress of their disease.

One-half of those in hospital would be $(1/2) \times (30\% \text{ of } 7,383)$, or 1,107 persons. These persons would undoubtedly be having a fluoroscopic exam at least 4 times per year, so we have $4 \times 1,107$, or 4,428 exams at 1.5 rads each, or a total of 6,657 person-rads.

And for the 70% at home, we have 70% of 7,383, or 5,168 persons. We feel certain these were watched with fluoroscopic exams at least every 6 months. So this is (2 exams) \times (5,168 persons) \times (1.5 rads per exam) = an additional 15,504 person-rads.

Total additional person-rads = $6,657 + 15,504 = 22,161$ person-rads. We divide by 2 to exclude the males, so the person-rads = 11,081 for females.

The contribution to population dose = 11,081 person-rads divided by 642,951 persons = 0.0172 rads to breasts. And with the 1.1 adjustment factor to leave out those under 10 years of age, we have 1.1×0.0172 , or 0.0189 rads to add to breast-dose of everyone of 10 years of age or higher.

We have no reason to believe that this general experience would have been different with respect to breast-rad dose in other parts of U.S. Therefore, total population-dose would be 0.0616 rads + 0.0189 rads, or 0.0805 rads.

But because the program might not have generated as many person-rads in the first few years of 1920-1960, and because of tapering off in tuberculosis in the 1950s, we shall reduce all these doses by 25 %, and enter the following in Col.G in the Master Table for every female age-year starting with age 10.

$$(0.75) \times (0.0805 \text{ rads}) = 0.0604 \text{ rads per person, annually.}$$

A Word of Appreciation

This book is being completed in 1995 --- some 62 years after the series of papers from the health officials in Detroit who wrote so well on the public health aspects of tuberculosis. We wish to express our deep gratitude, these 62 years later, for their monumental contribution to everyone's opportunity to learn a major set of medical lessons about this unremitting disease, tuberculosis. The specific papers in the series are in the list which follows.

All of them appeared in the September, 1933 issue of American Journal of Roentgenology and Radium Therapy, in Volume XXX, No.3. The editors of the Journal at that time deserve commendation for excellent judgment.

Vaughan, Henry F. Commissioner of Health, Detroit, Michigan "Public Health and Tuberculosis", pp. 300-302.

Brachman, D.S., "The Value of the Roentgen Ray in Apparently Healthy Children of School Age" pp. 303-304.

Douglas, B.H., Superintendent, William H. Maybury Sanatorium, "The Importance of the Roentgen Examination in the Modern Treatment of Pulmonary Tuberculosis," pp. 305-308.

Morgan, Richard, "Artificial Pneumothorax in a Group of Cases of Pulmonary Tuberculosis Formerly Looked upon as Hopeless," pp. 309-314.

O'Brien, E.J. "Collapse Therapy in Early Minimal Lesions of Pulmonary Tuberculosis," pp. 315-320.

Chadwick, Henry D., Detroit Department of Health, "The Tuberculosis Problem in Detroit," pp. 321-327.

#

Preview of Another Use: Skin Disorders

1922

"It is now pretty generally admitted that the roentgen rays constitute the most useful and successful single remedy we possess for the treatment of dermatological diseases. The only competitor for this distinguished position is radium." And:

"That the roentgen rays constitute the most valuable remedy in dermatotherapy, or that the roentgen rays and radium constitute the most useful single agents in the armamentarium of pure dermatology, is shown by the following list of diseases and conditions that are amenable to such treatment, over 80 in number." The list of these diseases is presented.

● — Excerpts from "The Value of Roentgen Therapy in Dermatology," by Dr. George M. MacKee and Dr. George C. Andrews, in American Journal of Roentgenology and Radium Therapy, Vol.9: 241-246. 1922.

1938

In the 3rd Edition of his obviously successful "X-Rays and Radium in the Treatment of Diseases of the Skin," Dr. MacKee states, p.6:

"Over thirty years ago Dr. William Allen Pusey, one of the pioneers of cutaneous roentgen therapy, remarked; 'It is hardly too much to say that roentgen therapy is the most widely useful addition to the treatment of skin diseases that has been made.' In spite of the foregoing paragraphs and the remarkable advance in American dermatology during the past two decades, Pusey's statement may be repeated today. It is the consensus of opinion that x-rays constitute the most important single therapeutic agent in the armamentarium of the dermatologist."

A very persistent therapy — extending over decades.

CHAPTER 16

Mass Screening for Tuberculosis

Part 1. Good Practice vs. Poor Practice in Screening for Tuberculosis

Tuberculosis case-finding in Detroit (Chapter 15) was an eminently sensible and useful program; it used x-ray on ostensibly healthy people who had a positive tuberculin history. Expert use of fluoroscopy was also very effective in detecting the disease (see Chapter 30), but expert use of fluoroscopy was very different from screening based on the crude "photofluorograms" described below --- a massive use of radiation with apparently meagre results.

Catherine Caufield (in her 1989 book, "Multiple Exposures," pp.144-145) relates some statements made to her by Dr. Francis Curry, who was deputy director and later director of public health and hospitals in San Francisco from 1960 to 1970. He is quoted as saying: "What was so horrible about what was happening then is that so many machines had no filters, no coning, no shielding. Many people were getting total body exposures and were getting doses big enough to show clinical symptoms." (That takes doses of the order of 50 rads to the whole body.)

And further (at p.145), Caufield describes the Mass Screening program: "In 1950, San Francisco, like many other cities across the country, established a mass chest x-ray programme intended to detect tuberculosis. The survey used photofluorograms --- photographs of fluoroscope images -- rather than conventional x-rays. If a photofluorogram indicated there might be a problem, the subject was then advised to have a more detailed x-ray examination. More than 40,000 people per year visited the city's clinics or a specially equipped van that toured the city, offering free chest X-rays. 'One reason for the large neighborhood programmes', explained Curry, 'was that the lung associations wanted this type of continuing service. It would help them with their fund-raising. Local groups would have contests to see who had the most members screened. Lots of the black churches did this. Everybody and his brother would go. The same people went over and over again. They were getting a lot of radiation and we were getting [finding] no disease at all.' "

This monstrosity of a 'programme' never should have existed, since good programs had been well demonstrated in 1932. But, as Dr. Curry stated, the neighborhood programs were probably more related to fund-raising than to health improvement or tuberculosis detection.

We can consider here one estimate of the national dose which resulted from such programs with mobile x-ray vans.

Karl Z. Morgan's group at Oak Ridge National Laboratory monitored some of the x-ray devices used in the mass screening and found they were delivering skin exposures of between 2 and 3 Roentgens while the average chest dose from a chest x-ray unit at Oak Ridge was 15 millirads. We recently checked this with "KZ" Morgan personally, and he confirmed these numbers. We presume these x-rays were always taken from back to front [rays entering the person's back and exiting the person's front][except for infants]. Karl Morgan was not able to confirm whether all the exams were taken in this manner. Recent procedure certainly has been to take the exams postero-anterior (back-to-front) [except

for infants]. We shudder to consider the possibility that the reverse was the case in some of the exams, since this would mean an enormous increase in dose to the breasts.

In "X-Rays: Health Effects of Common Exams" (Gofman and O'Connor, 1985), there is a table, Special Table C (at p.404), which permits one to know what the dose in milli-rads is to specific organs when exposure is made to a 1.0 Roentgen, free-in-air source, at a specific beam quality and kilovoltage (2.3 mm Al HVL and 30 keV). The difference between back-to-front (PA) and front-to-back (AP) is enormous.

Specific Organ	Beam AP	Beam PA	Ratio
Breast Pair (Female)	693	37	693/37 = 18.7

The DOSE to the breast-pair is 18.7 times as great for the AP beam entry.

We take the lowest value of Karl Morgan, 2 Roentgens skin dose entering in the back. Our calculation shows that the breast dose is 37 milli-rads for an entrance dose of one Roentgen. So for 2 Roentgens entrance dose, we multiply 2 R x 37 milli-rads per Roentgen, to get a breast dose of 74 milli-rads (0.074 rads). Obviously those having 3 R of entrance dose get a 50% higher dose to the breasts.

The reader may wonder why the doses were so very much higher with the photo-fluorograms than with direct recording on film. In making a photofluorogram, the x-ray beam is "on" a longer time. Direct recording on film requires only a very brief exposure to x-rays, and delivers a sharper, more informative image than a picture from a screen.

Part 2. An Estimate of Doses Which May Have Been Received in Mass Screening

Assuming that 1/2 of the San Francisco population was female, we would have 350,000 female persons.

And accepting the estimate that 1/2 of the 40,000 persons per year who took such examinations were women, we have 20,000 women receiving an average dose of 0.074 rads to the breasts. Probably this is a gross underestimate, considering Dr. Curry's statements.

$$\text{Total person-rads} = (20,000 \text{ persons}) \times (0.074 \text{ rads}) = 1,480 \text{ person-rads to breasts.}$$

Now we concern ourselves with obtaining the Population-Dose, which brings in the unirradiated females of the population of San Francisco.

$$\begin{aligned}\text{Population Dose} &= (1,480 \text{ person-rads}) / (350,000 \text{ female persons}) \\ &= 0.0042 \text{ rads to breasts.}\end{aligned}$$

This mass screening program may have been better or worse in other cities in the United States. We shall make the approximation that the dose of 0.0042 rads applies for all ages from childhood through 64 years. What is not clear is the total duration of the mass screening, since such screening apparently started and ended at different times in different cities. We shall assume, for a conservative underestimate of dose, that the duration was for half of the 40 years from 1920 to 1960. And, therefore, we shall cut the dose down to 0.0021 rads to breasts, for a typical year. This is the dose we transfer to Col. Eye in the Master Table.

CHAPTER 17

Treatment of Bronchial Asthma with X-Rays

Part 1. Radiotherapy of Bronchial Asthma Was Popular for Several Decades

In his 1965 book "Radiotherapy of Benign Disease," Dewing commented as follows:

"Radiotherapy enjoyed a considerable popularity in the treatment of asthma during the first several decades of the twentieth century, and still lingers fleetingly in the recent literature, despite having been largely superseded by medical methods."

- - Item 1: Indeed, Eugene Leddy and Charles Maytum of the respected Mayo Clinic reported their largest therapeutic trial of roentgen therapy of bronchial asthma (over 1000 patients treated) in 1949, having published previous papers on trials by themselves at the Mayo Clinic conducted as far back as the 1931-1934 period. We shall derive our dose calculations for bronchial asthma therapy by ionizing radiation largely from their studies, although numerous other smaller studies are consistent with the Leddy-Maytum studies.

- - Item 2: Source of Data. Eugene T. Leddy and Charles K. Maytum (1949)
"Roentgen Treatment of Bronchial Asthma," Radiology 52: 199-203.

- - Item 3: Doses. After their two early reports on radiation therapy of bronchial asthma, they felt that their usual technic of treatment entailed an excessive risk (p.202), so they cut the dose usually employed in half. And they stated, "In all the cases in which the patients were treated in this manner, the results were satisfactory. This experience led us to adopt the application of a dose of about 250 r to one large anterior and one large posterior mediastinal field. We have now used this method of treatment, which has been termed the 'low-dosage' technic, in more than 1000 cases."

Dewing in his 1965 book lists this as the major study (in size) for bronchial asthma, and he does not suggest ineffectiveness.

Leddy and Maytum regard their results with some satisfaction, although they concede that the beneficial effects are only temporary (months in some cases). Poulsen (1952), in Denmark, cites the Leddy-Maytum work respectfully, and suggests in a 1952 paper that "palliation which may be obtained in roentgen treatment of asthma is utilized in this country to a smaller extent than it deserves, for which reason the following series of cases, although rather limited, is presented." He points out that "the striking beneficial effect obtained in the first two patients with bronchial asthma became known among doctors and patients in the district, and we now often see patients who have requested their doctor to refer them to the Radiological Clinic for roentgen treatment."

Part 2. The Calculations for X-Ray Therapy of Bronchial Asthma

Leddy and Maytum treated over 1,000 patients in their "low dosage" regimen starting about 1941, to about 1946. They estimate that those treated in this manner are about 6 % of the total number of asthmatic patients who have been treated at the Mayo Clinic. So their total number of asthmatic patients is $(100 / 6) \times 1,000$, or 16,667 asthmatic patients in a period of about 5 years. About 70% of the patients "were middle-aged women."

Those asthmatics NOT treated with roentgen therapy (15,667) probably received just the radiation dose from a chest workup, which, compared with the roentgen therapy group, would be negligible. So we shall neglect any such dose to breasts.

Those in the 1,000 treated cases received radiation over two large fields, one anterior, and one posterior. Each field received an air dose of 256 R. We shall assume that this 16 cm square (16 cm by 16 cm) treated region, front and back, irradiated one-half of the breast tissue in each case. We will handle this as 128 R (half the dose) to the complete breasts.

From Gofman and O'Connor (1985):

For the anterior direction, rads / entrance roentgen = 0.693

For the posterior direction, rads / entrance roentgen = 0.037.

Anterior Dose = 128 rads x 0.693 = 88.7 rads.

Posterior Dose = 128 rads x 0.037 = 4.7 rads.

The anterior dose of 88.7 rads deserves adjustment for supra-linearity (Chapter 8).

The adjustment factor is 0.486.

The adjusted anterior dose = (88.7) rads x (0.486), or 43.1 rads.

- – Item 4: Total Dose in therapy of asthma = $43.1 + 4.7 = 47.8$ rads total.

- – Item 5: Person-rads at Mayo Clinic = (0.7 are women) x (1,000 patients) x 47.8 rads = 33,460 person-rads to female breasts.

The Mayo Clinic workers report that for purposes of testing, they studied only their severe asthmatics (about 6 % of their total asthmatic patients). Elsewhere, those physicians who believed in the therapy probably would have extended it to almost all their patients. But non-believers would have used no radiotherapy at all. For the sake of obtaining a "ballpark" estimate of contribution from this therapy to annual average breast-dose, we will estimate that nationwide, about 18 % (not 6 %) of asthmatic patients received such therapy. If this had been the case at the Mayo Clinic, the person-rads would have been $(3 \times 33,460)$, or 100,380 person-rads. The Mayo Clinic experience represented about five years, so PER YEAR, the person-rads would have been 20,076.

- – Item 6: Conversion to annual average population-dose. The next step is always to divide person-rads by total persons. How many persons would be appropriate?

The Mayo Clinic is a special place, attracting patients from all over the country and the world, so we can not derive the number of persons from data for the local county (as we did in Chapter 8, for example). It is difficult to estimate what fraction of the United States population really supplied the asthma-patients for the Mayo Clinic, but we shall use 2 % as a "ballpark" estimate.

Since Leddy and Maytum said that about 70 % of their patients were middle-aged women, we will approximate the age-range as age-30 through age-54. The national number of such women (from the Master Table, Column A) was 21,543,144 for one calendar-year of the 1920-1960 period, and 2 % of that total is 430,863 women. We shall divide the estimated person-rads by that number. So, we have $20,076$ person-rads / $430,863$ persons, = 0.0466 rads.

The last step is to distribute this population dose among 25 different age-years (age-30 through age-54). Per age-year, the annual average breast-dose would be (0.0466 rads / 25), or 0.0019 rads, a relatively minor contribution to breast-dose. There is no basis for assuming that any correction for duration is indicated.

Thus, we make 25 identical entries into the Master Table, Column J, for this source of breast-irradiation.

Part 3. Some Words of 1949 for Contemplation by a Later Generation

As we complete this book in 1995 we realize that a current generation of young physicians might find it laughable that anyone should have thought of treating infections and bronchial asthma with roentgen-rays. The danger is that he who laughs may be doing much worse for his patients.

The Mayo Clinic in the 20th Century is certainly to be regarded as a pacemaker institution. So the reader will find the close of the article by Leddy and Maytum of interest. We quote their words written in 1949:

"Our experience in the treatment of asthma with roentgen rays has been similar in all essentials to our experience in the treatment of inflammatory and infectious lesions, in which our results have improved as the doses of roentgen rays have been lowered. For this reason, we think that a lower dose, possibly in the neighborhood of 100 r, or even less, may be worth a trial in another series of cases of chronic severe, intractable asthma."

Is the reader ready to be sure that Doctors Leddy and Maytum were having an illusion in all that experience? Our use of the data do not depend in any way on whether the therapy had any effect or had none, but we find it interesting in the extreme that at the Mayo Clinic a series of 1,000 patients with severe asthma were treated with roentgen rays --- and few today would believe that the physicians really saw any improvement.

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Part 1

Preview of Another Use: Well-Baby Check-Ups

From Dr. Hanson Blatz, we first learned the following:

"Those of you who have been in the field a long time know that it was once the practice of pediatricians to fluoroscope babies and young children every month and when they had the annual checkup. When we questioned this practice, pediatricians would say, 'Well, the parents expect it. They think if I don't fluoroscope the patients, they are not getting a complete examination'."

Statement in 1970 by Dr. Hanson Blatz, Director of the Office of Radiation Control, New York City Department of Health.

Find that far beyond the credible? Look below. New York City is NOT the only place where this occurred.

Part 2

Preview of Another Use: Well-Baby Check-Ups

Confirmed by Dr. James Pifer and Colleagues!

Dr. James Pifer and co-workers (1963) have described the case material, radiation factors, and study methods in the investigations of enlarged thymus therapy with x-rays in the Rochester studies (see our Chapter 8). Where they described the circumstances which led certain children to become involved in such therapy, Pifer and colleagues stated the following (1963, p.1358):

"... Also, the indications for treatment differed with each radiologist, pediatrician, or general practitioner. Frequently parents insisted that their child be treated. Some pediatricians fluoroscoped all infants routinely, but probably most children treated in private offices had symptoms at presentation which prompted a radiologic examination ..."

That is an eye-opener of the first magnitude. "Some pediatricians fluoroscoped all infants routinely."

That is precisely what Dr. Blatz was telling us had been his experience, too. Well-babies getting fluoroscopy. Regularly. And the information fits the experience of a woman who wrote to me about her own experience as a child in New York City. She could remember being fluoroscoped at every visit to the pediatrician from age 4 through age 12. She had no recall of medical attention, one way or the other, before age 4.

Had this pediatric practice at least been confined to New York State? No way. We then found the same practice, possibly worse, on the other side of the country. Part 3 of this Preview is on page 124.

CHAPTER 18

Treatment of Pneumococcal Pneumonia with X-Rays

Part 1. Pneumococcal Lobar Pneumonia Treated with X-Rays ?

Not many physicians today will really believe that lobar pneumonia was once widely treated with roentgen radiation. Rousseau was one of the investigators who was active in the field of therapy of lobar pneumonia in the early period. Rousseau (1942) has cited a number of publications which had appeared over the years showing favorable and uniform results in treating well-controlled groups of lobar pneumonia cases with roentgen therapy. In the paper by Rousseau and his colleagues in 1942, a series of lobar pneumonia cases is presented. These were 104 cases of pneumococcal pneumonia treated in the winters of 1937, 1938, and 1939. Additionally, a small series of patients was treated, after they had been doing poorly for a period of three to seven days on sulfonamide therapy..

We quote Rousseau et al about these latter cases:

"In this group of cases, it was evident that the course of the disease had not been favorably affected in any way by sulfonamide therapy. The patients were growing rapidly and progressively worse with adequate doses of the drug. By all clinical standards, it appeared that death was inevitable in all cases of this group."

This group of 29 cases showed 22 recovered and 7 died --- which Rousseau and co-workers take as excellent evidence of help from roentgen therapy after sulfonamides had failed. Clinically, their expectation was against any of the 29 surviving.

We shall analyze the Rousseau data below, but first we wish to re-introduce the name of Dr. Arthur U. Desjardins of the Mayo Clinic from pages 96 and 104. Many volumes of American Journal of Roentgenology and Radium Therapy carried scholarly discussions by Arthur Desjardins concerning the facts and the ideas involved in the use of roentgen therapy for every entity in which it was used, including pneumonia. Animal experiments, physiological background, clinical features --- all were treated in a series of articles which the roentgenologists were presenting to say to the skeptics, "We do have a logic for all this." Dr. Desjardins must have been a remarkable scholar, considering the breadth of medicine taken on in his series of essays on roentgen therapy. Mechanism of action was very high on the list of items discussed in the Desjardins articles.

In a 1942 paper in Radiology, Dr. Desjardins made a couple of statements that are worth repeating here, for assuredly some readers are going to wonder about this issue today.

(At page 274) "There is no longer any doubt that roentgen rays often have a beneficial effect on many varieties of acute and chronic inflammation. The evidence is now so abundant that it cannot be disregarded."

(And at page 277) "The action of the rays on acute inflammation cannot, therefore, be attributed to a direct bacteriocidal effect of the rays."

We wanted to bring up the stature of Arthur Desjardins here to show that a leading figure in roentgenology, and a leading figure at the Mayo Clinic itself is speaking to the issue of therapy of inflammatory diseases with roentgen rays. So the reader should steer far away from suggesting that Dr. Rousseau and colleagues were not in mainstream medicine. They certainly were. Not only were they mainstream with respect to the use of radiation therapy of inflammatory diseases, they were from a leading Southern University, Bowman Gray School of Medicine, Wake Forest College, in Winston-Salem, North Carolina.

Part 2. Detailed Consideration of the Pneumonia Studies of Rousseau

- - Item 1: These cases, studied at Bowman Gray, were from North Carolina. The mean age of all these pneumonias was 29.8 years, with a RANGE of ages from 9 weeks to 94 years (pneumococci showing no respect for any age group). For our purposes, we would really love to know how many young children were involved, and we are not using exposure data for persons beyond 64 years of age. In the absence of data, and as a reasonable approximation, we shall assume that 80% of the cases were of ages between 15 and 45 years, and simply leave out consideration of the others. This is conservative, since irradiation of children under 15 would thereby be eliminated from the series. It is consistent with our general policy of seeking a CREDIBLE LOWER LIMIT FOR PAST RADIATION EXPOSURE.

- - Item 2: Estimating population sizes at various ages in the North Carolinians of Forsyth County.

In 1960 U.S. Population was 179,333,000 persons.

In 1960 Forsyth County, of which Winston-Salem is the county seat, the population was 189,428 (County and City Data Book 1962).

We shall illustrate estimation of the female population of Forsyth County in the 1920-1960 period for a single age-year (15 year olds).

The Master Table, Col. A, gives a value of 888,277 female persons at 15 years of age Nationwide in the average period 1920-1960. Therefore, in Forsyth County, we estimate there must be $(189,428 / 179,333,000) \times 888,277$, or 938 female persons, age 15.

For the number of female persons of other ages out to 45 years, in Forsyth County, the same sort of steps have been used.

- - Item 3: There was a total of 104 cases of pneumococcal pneumonia. We shall assume 1/2 of the cases were female, yielding 52 cases of women treated with x-rays for pneumococcal pneumonia.

But we are using 80% of the total group for our calculations. So we reduce that number to $(0.8) \times (52)$, or 41.6 cases.

And we know these cases were distributed over three years, so the number per year must be obtained through division by 3, yielding 13.87 cases per year of accumulation of cases (all ages put together).

The beam was directed anteriorly in these cases, with 200 R over the total breasts. From Gofman and O'Connor 1985 the dose to breasts per R at surface = 0.693 rad.

Therefore, the dose to the breasts was $200 \text{ R} \times 0.693 \text{ rads/R}$, or 138.6 rads. This dose must be adjusted for supra-linearity (Chapter 8, p.58). The adjustment factor is 0.435. Therefore, we reduce the dose to (138.6×0.435) , or 60.3 rads to the breast.

For our 13.87 cases treated per year, person-rads per year = $(13.87 \text{ persons}) \times (60.3 \text{ rads}) = 836.4 \text{ person-rads}$.

We are distributing these 836.4 person-rads into 31 age groups, from 15 through 45 years of age. The entry in person-rads for each of those years will be $836.4 / 31$, or 27.0 person-rads.

Acquiring the "Population Dose" for Forsyth County

In our illustrative calculation for 15 year-old females, we found that in Forsyth County we expect there to have been 938 persons. Therefore, if we distribute 27.0 person-rads into 938 persons, the average dose to the breasts will be $(27.0 \text{ person-rads} / 938 \text{ persons})$, or 0.0288 rads per person (the population dose for 15 year-olds).

From the nature of the calculation, we can see that estimation for each of the additional age brackets, 16 through 45 years, will give average doses slightly higher than that for 15 year-olds, simply because the remaining population is smaller with increasing age. Of course, for our Master Table entries, all doses are to be calculated as demonstrated for our 15 year-old example set.

- – Item 4: Have we underestimated the total radiation dose actually received in Forsyth County, from cases of pneumonias being treated in other parts of the County? We must ask whether the cases reported by Rousseau and co-workers represent ALL the cases treated in the same period, if we are to evaluate true dose received per person, on average.

A careful reading of the paper of Rousseau and colleagues informs us that their group is chiefly interested in the treatment of pneumonia centered around the pneumococcal type. As a result of this special interest, Rousseau and colleagues state that they have eliminated 72 of a total of 176 unselected and consecutive cases of pneumonia. The elimination is solely on the basis of whether or not a pneumococcal etiology exists. The 72 cases are eliminated because the combination of sputum and roentgen examinations led to a diagnosis of atypical bronchopneumonia or to lobar pneumonia due to non-pneumococcal and mixed infections.

As an academic matter, these physicians could construct any series that interested them, but we doubt in the extreme that the 72 cases of acute pneumonia of other etiologies were denied treatment with roentgen rays. So, quite probably a more accurate population dose estimate for our Master Table would be $(176 / 102)$, or 1.73 times as high as the doses entered. Fifty years have elapsed since that publication, so it is not possible to find out just how the additional 72 cases were treated. We shall elect here, for adherence to our CREDIBLE LOWER LIMIT philosophy, not to enter this additional sizable contribution to radiation dose. We are also not including any contribution to radiation dose from radiation treatments that might have been given by other practitioners in the county, again potentially leading to a significant underestimation of dose received.

- – Item 5: It is a reasonable expectation that the 1920–1940 part of the entire 40 years may have seen even higher usage of this type of therapy than is reported for 1937–1939. But surely, after 1945, there were probably very few cases treated this way. Therefore,

before final entry into Master Table at Col.S, all doses will be reduced by a factor of 0.75, reflecting the probable lack of use of radiation therapy in the last quarter of the 1920-1960 period.

The entry at Col. S for our illustrative 15 year old female person is (0.75) x (0.0288 medical rads), or 0.0216 medical rads. As stated above, there is very good reason to think we have underestimated all entries by the factor of 1.73, as a result of eliminating the non-pneumococcal bacterial pneumonias which were probably treated.

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CHAPTER 19

Treatment of Pertussis (Whooping Cough) with X-Rays

Part 1. Whooping Cough: A Very Serious Disease

Lawrence W. Smith and his colleagues of the Boston Floating Hospital delivered the second report from their group on the subject of x-ray treatment of pertussis (whooping cough), with and without additional therapy by a vaccine. Their original paper (1924) had reported on 300 children treated. The current paper (1925) reports on a total of 850 cases of pertussis, which represents an increment of 550 cases treated.

For some perspective on this very serious disease of childhood during that period, we shall excerpt some comments from the paper of the investigators. At page 176:

"The roentgen-ray treatment of whooping cough seems to have passed beyond the experimental stage. The literature of the past year has had a considerable number of reports from Canada, various parts of the United States and Europe, all of which tend to corroborate the feeling which we have concerning its efficacy. Various suggestions as to the mechanism by which the clinical improvement takes place have been advanced, but the general feeling seems to be that it is due to a diminution in the nervous reflex from the pressure of the hilum lymph nodes by a reduction in their size ..."

"These preliminary studies of nearly a thousand cases justify the further investigation of means of treating this serious infection of childhood. It is our hope to extend this work to the various local boards of health, hospitals, and laboratories, with the ultimate expectation of securing a specific means of therapy for pertussis. By such a concerted attack, a thorough survey should be possible and much evidence could be accumulated which is impossible to do from one small group. The roentgen-ray treatment of the disease, which has gained the confidence and support of both the laity and the medical profession to a large degree, offers a means to this end, as it is possible to secure cases for study in this way which it has not been possible to do previously." And:

"For this reason we appeal to the medical profession for furtherance of this work. Whooping cough still occupies one of the chief positions in infant mortality figures. We feel that, by the roentgen-ray treatment of whooping cough, combined with vaccine, as well as the ordinary medicinal agents, we have gone a step forward." And:

"Our own part in this program is comparatively unimportant. Our chief function is to stir up curiosity and interest in whooping cough and to maintain that interest by a constant effort. If we can do this, whooping cough will follow in the footsteps of most of other recognized infectious diseases, as diphtheria, and now scarlet fever, have done."

It would be quite reasonable to suggest that this roentgen-ray therapy of pertussis was indeed in widespread use after all these optimistic reports of good response, and a low mortality. There were, as there always are, some real skeptics concerning the efficacy. We shall assume that the level of use comparable to that in Boston persisted for half of the 1920-1960 period, and slowly went into decline as the protection of an increasing segment of the population by pertussis-vaccination (part of the DPT vaccination program) drastically cut down the number of cases of clinical pertussis requiring management.

Laurie McGinley (Wall Street Journal, November 23, 1994) reports that in the 1930s, before there were widespread immunizations in the U.S., there were 5,000 deaths per year from pertussis.

Part 2. Calculations of the Radiation Dose in Therapy of Pertussis

- - Item 1: Place of Study: Boston, Massachusetts. Study at Boston Floating Hospital. This is in Suffolk County, Massachusetts. We cannot be sure that the Boston Floating Hospital was the only place where pertussis patients were receiving radiation therapy, but it must have been the major one. If we assume incorrectly that it was the only one, we shall thereby only underestimate radiation dose to the population --- part of our conservative underestimate of radiation dose to breasts.

- - Item 2: Total number of children treated is 850, distributed in age as shown in the tabulation box nearby. Our total is 851, because we had to read numbers from Smith's Figure 1.

- - Item 3: Suffolk County population in 1960 = 791,329. USA population in 1960 = 179,333,000. Therefore, for each age-year, to ascertain female children in Suffolk County we proceed as follows: (National number in age-year) x (791,329/179,333,000.) Final entries for female children for each age year are in the tabulation.

- - Item 4: Mean dose to breast-pairs: 100 R delivered anteriorly and 100 R delivered posteriorly. Total dose divided into 4 sessions.

Breast-pair dose, from anterior delivery, $100R \times 0.693 \text{ rad/R} = 69.3 \text{ rads}$.

Adjustment factor for supra-linearity is 0.707 (Chapter 8, page 58), if we approximate 20 rads at each of 4 sessions: $0.707 \times 69.3 \text{ rads} = 49 \text{ rads}$.

Mean dose to breast-pairs from posterior delivery, $= 100 \times 0.037 = 3.7 \text{ rads}$.
Total medical rads delivered to breasts $= 49 + 3.7 = 52.7 \text{ medical rads}$.

- - Item 5: This study provides the total number treated over 3 years. Therefore, the entry for one year is one-third of the total. And taking females as 1/2 of total group, we cut the number per age-year again in half. (See tabulation on next page.)

Radiation Therapy for Pertussis:
Tabulation of Data

Age-year	Number Treated	Treated per Year	Only Females	Suffolk County		Person- Rads	One-half Average	
				Number per age-yr	Rads		Breast Dose	Breast Dose
0	140	46.7	23.3	3995	1230	0.308	0.154	
1	120	40.0	20.0	3940	1054	0.268	0.134	
2	130	43.3	21.7	3937	1142	0.290	0.145	
3	90	30.0	15.0	3934	791	0.201	0.100	
4	103	34.3	17.2	3932	905	0.230	0.115	
5	97	32.3	16.2	3930	852	0.217	0.108	
6	69	23.0	11.5	3929	606	0.154	0.077	
7	35	11.7	5.8	3928	307	0.078	0.039	
8	15	5.0	2.5	3927	132	0.034	0.017	
9	5	1.7	0.8	3926	44	0.011	0.006	
10	5	1.7	0.8	3925	44	0.011	0.006	
11	5	1.7	0.8	3924	44	0.011	0.006	
12	5	1.7	0.8	3923	44	0.011	0.006	
13	4	1.3	0.7	3922	35	0.009	0.004	
14	4	1.3	0.7	3921	35	0.009	0.004	
15	4	1.3	0.7	3920	35	0.009	0.004	
16	4	1.3	0.7	3918	35	0.009	0.004	
17	4	1.3	0.7	3916	35	0.009	0.004	
18	4	1.3	0.7	3914	35	0.009	0.004	
19	4	1.3	0.7	3912	35	0.009	0.004	
20	4	1.3	0.7	3910	35	0.009	0.004	
Total	851							

Illustrative calculation, using data for 0 years of age.

- a. 3,995 female children in Suffolk County in 0 year age group.
- b. Treated female children = 23.3 children.
- c. Mean Breast-Pair Dose in Medical Rads = 52.7 rads.
- d. Person-rads in 0 year age-group = (23.3 persons) x (52.7 rads) = 1,230 person-rads.
- e. Average breast dose = 1,230 person-rads / 3,995 total persons = 0.308 rads.
- f. Cut dose in half to account for decline in use of this therapy over time.

Final dose = 0.154 medical rads. Entries in this column are transferred to the Master Table Col.N, as entries for Pertussis (Whooping Cough) Therapy.

Note: Cases per age-year had to be read off from Figure 1 of Smith et al.

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Part 3

Preview of Another Use: Well-Baby Check-Ups

We must admit that we were quite seriously shaken up by what we learned from Dr. Hanson Blatz and Dr. James Pifer and the woman from New York City. And as we said (p.116), the story went west.

Dr. Franz Buschke and Herbert M. Parker published a very low-key bombshell, in the JOURNAL OF PEDIATRICS (1942) entitled, "Possible Hazards of Repeated Fluoroscopies in Infants." The paper had been read before the North Pacific Pediatric Society, in Seattle, Washington, January 31, 1942.

The opening paragraph follows:

"Recently we became aware of the fact that apparently a number of pediatricians include a fluoroscopy in the monthly routine examinations of infants in their care during the first and second years of life. Since we feel that such a procedure is charged with potential hazards, we welcome the opportunity of discussing the problem at your initiative in this group."

Their beautiful scientific paper has undoubtedly saved many women from breast-cancer's ravages. Such women will never know what they owe to the Buschke-Parker team of wide-awake serious, informed professionals in the radiation field. The details are in Chapter 31.

CHAPTER 20

Treatment of Hyper-Thyroidism and Breast Irradiation

Part 1. Surgery versus Radiation in the Treatment of Hyper-Thyroidism

Hyper-thyroidism was the subject of repeated battles between the surgeons and the radiologists. In the decades 1920-1930 and 1930-1940, an almost endless literature appeared with two separate conclusions, each staunchly defended, (a) hyper-thyroidism is a disorder to be treated surgically or (b) hyper-thyroidism can be better treated in a high percentage of the cases by ionizing radiation, either with radium or x-rays. An occasional author would suggest there might be an intermediate ground, but that was definitely not the rule.

The case made by the radiologists was that there was a definite surgical operation mortality, and that such mortality was highly related to the amount of experience and skill of the surgeon. The radiologists suggested that there was virtually no mortality associated with the radiation therapy (at least not in periods of a decade or so). The surgeons countered with the slowness in response of patients if treated by ionizing radiation, whereas surgery produced almost instantaneous results (not always sustained). Some of the surgeons pointed out that dangerous cardiac deterioration would occur during the weeks and months it took for a full radiation effect to be produced in this disease, which hazard could be avoided by surgery.

The meaning of this conflict in the field is that WE have real trouble ascertaining the frequency of radiation therapy in a given year for a given locale. It is enough of a problem to ascertain the total number of cases treated per year in a given locale because we do not know that all the treating radiologists are reporting their treatment. When we add to the problem --- not knowing the relative number of patients surgically treated versus those radiation-treated --- it becomes difficult to eliminate errors of a factor of two or more. But we do believe we can still get the general order of magnitude of radiation contributions from hyper-thyroidism treatment, by using the work of several authors. We shall explain. Also, in general the error will result in an UNDERESTIMATE of radiation dose, which is consistent with our conservative position.

Part 2. The Principles Involved in Therapy of Hyper-Thyroidism

Hyper-thyroidism is a disorder of great complexity, and it still is not really understood. Many writers use fine distinctions to decide whether a particular patient's disorder deserves the label, Basedow's Disease, hyper-thyroidism, Graves' Disease, or toxic adenoma. It was early pretty well agreed that even if many symptoms were similar, the cases with a defined nodular thyroid plus symptoms should be separated out and should be treated surgically. Over a long period there seemed to exist agreement on this one point. For the remaining cases, some wished to single out those cases with exophthalmic features (protrusion of the eyeballs, so that the patients exhibited the "hyperthyroid" stare). Others did not agree with this feature as a clinical sorter among cases. Most authors cautiously (very cautiously) tended to consider the disorder the result of overproduction and release of thyroid hormone. So, to most workers, sensible treatment meant stopping the FUNCTION of part of the thyroid gland, either by high-dose

radiation, or by surgical removal of large parts of the gland --- with each of these maneuvers intended to lower the subsequent output of thyroid hormone.

This was not wholly agreed to, and in this early period there are papers which doubt the logic of removal of thyroid structure or function. Some advocated pituitary irradiation, others, adrenal irradiation in addition to thyroid irradiation. We quote Read (1949):

"It should be stressed here that roentgen therapy, as well as surgical treatment, is directed at the thyroid. The thymus, of course, is also irradiated and sometimes the pituitary (the adrenals only rarely) thus recognizing the disturbed function of the whole endocrine system in this strange disease."

Some Blamed the Thymus for Hyper-Thyroidism

Our readers may raise an eyebrow concerning the "thymus, of course, is also irradiated." That statement is perfectly correct for the time. Having reviewed many years of early literature on this subject, we know that over and over the physicians considered the thymus in some way responsible for hyper-thyroidism about as much as the thyroid itself. Many, many papers simply described their routine: "irradiate the left lobe, irradiate the right lobe [of thyroid], and then irradiate the mediastinum in order to suppress the thymus gland." Read is by no means alone.

Quigley, for example, (1932) treated his series of patients with radium externally. He writes: "Some cases of exophthalmic goiter are accompanied by persistent thymus. In these it is necessary to irradiate the thymus as well as the thyroid. Care must be taken not to mistake a persistent thymus for a substernal goiter (enlarged thyroid). Here a therapeutic test may make clear the diagnosis, as a thymus always shrinks very quickly after radiation, while the substernal goiter requires operation. Patients with persistent thymus invariably present an unnaturally youthful appearance, seeming to be from 10 to 15 years younger than their real age."

Dr. Quigley's series of 137 cases treated with radium externally, from 1915 to 1927, not only had some breast irradiation from the gamma rays directed downward against the thymus region, but may have had additional exposure from gamma rays coming sideways out of the radium capsule. There are not enough data to enable calculation of breast-dose as a result of the external pathway from the radium applied to the neck.

Williams (1932), in reviewing his experience with radiation treatment of hyper-thyroidism in 200 patients over a period of 15 years, says the following:

"Some good authorities state that there are no contraindications to surgery; others say this idea is very much open to question. In the one opinion, radiation therapy is temporizing, and curative in the other. The cause of the goiter illness begins in the thyroid or elsewhere, subsequently upsetting the thyroid. Goiter histopathology is, or is not, consistent with the symptom complex. The thymus has, or has not, anything to do with the disease..."

Williams does not really tell us whether he explicitly attempted to irradiate the thymus in his roentgen therapy of "goiter illness." His technic section simply relates treatment of an area 10 x 12 centimeters. It is not possible to state how much chest irradiation is received since we do not know the placement of those 10 to 12 centimeters.

This is not too surprising, since many reports indicate that thymus treatment is casually expected in treating hyper-thyroidism.

Menville (1932) queried radiologists all over the USA for their experience, and accumulated data on 10,541 cases of hyper-thyroidism treated with roentgen therapy. With respect to the radiation received by the thymus in such therapy, Menville states:

"The excellent results obtained in the treatment of toxic goiter by irradiation are not alone due to the changes produced in the gland when it is in a state of hyperfunction, but they are also thought to be due in a measure to the irradiation of the thymus gland. It is presently believed that the thymus gland undergoes certain changes in cases of thyrotoxicosis, and also that the benefit received in post-operative hyper-thyroidism by radiation therapy is probably due, to a certain extent, to the irradiation which the thymus gland receives. Schwarz (1928) recommends that the thymic region should be included in the field of treatment while irradiating the thyroid gland, and that the larynx and trachea should be protected."

Part 3. Breast-Dose in Hyper-Thyroidism Therapy: A Division of Time Periods

As we go on to consider the possible assessment of breast-dose from radiation therapy for hyper-thyroidism, we shall divide our considerations into those of the pre-1940 era and those of the post-1940 era. We do this because after 1940, and particularly after 1945, iodine-131 therapy became the leading choice among the radio-therapists for treating hyper-thyroidism. Of course, some surgical therapy continued over all periods.

Approximations to the Breast-Dose in the Pre-1940 Era of Roentgen Therapy

We have already stated that it is difficult in the literature to find a single source of roentgen therapy of hyper-thyroidism where we have confidence that essentially all the cases in a geographic region have been so treated. If any series we use does not include all cases which were treated, we will be seriously UNDERESTIMATING the breast-dose from such therapy. We will still be getting a MINIMUM value for breast irradiation and breast-cancers.

Menville's data provide one reasonable source of treated cases, with some data borrowed from other studies. From the study of 200 cases by Williams, we have the datum that 77.5 % of cases are female, 22.5 % of cases are males. This is quite consistent with Read's data.

Williams' studies also include the datum that 31.5 % of cases are under 30 years of age and 68.5 % of cases are over 30 years of age. If we assign 45 years as average age of those over 30 years of age, and 25 years of age of those under 30 years of age, the average age of all the cases is 38.7 years of age.

Menville received back one report from Illinois of 1,020 treated cases. All other Illinois entries were lower than half this number, so we presume this one entry must be that of a large hospital practice in Cook County. Menville does not give us the number of years over which these cases were accumulated, but since his paper was delivered in 1931, it would be reasonable to say that the cases accumulated over no more than 10 years. This would reduce the number of cases to 102 cases per year. And then accounting for 77.5 % females, we would have (0.775×102) , or 79 female cases treated per year.

Rosenstein's thymus-irradiated children (Hildreth et al 1985), mostly irradiated before 6 months of age, were finally estimated by us to have received 32.5 medical rads to breast-tissue, adjusted for supra-linearity. But we do not believe that the effort to irradiate the thymus in adults would lead to as great a fraction of breast irradiation as in the child. So we shall avoid overestimation, and suggest that the breast-dose in adults treated for hyper-thyroidism was 5 medical rads, as a result of deliberate irradiation of the thymic area. Our choice of less than 1/6 of the breast-dose in the young infants may well underestimate breast-dose in these adult hyper-thyroid cases.

For those under 30 years of age, we estimate 0.315 of cases, or (0.315×79) female cases, or 25 cases. This leaves 54 female cases for the over-30 year age group.

If we distribute the under-30 year cases to age bracket 20 to 29 years, we have 25 / 10, or 2.5 cases per age-year. And if we distribute the 54 cases at 30 years of age or older to those 30 to 59 years of age, there will be 54 / 30, or 1.8 female cases per age-year.

The Person-Rads Calculation

For the under 30 year age group: $(2.5 \text{ persons}) \times (5 \text{ medical rads}) = 12.5$ person-rads to breasts per age-year.

For the over 30 year age group: $(1.8 \text{ persons}) \times (5 \text{ medical rads}) = 9$ person-rads to breasts per age-year.

Arriving at the Population-Dose in Each Age-Year

For all the female categories, the national number of persons per age-year category is <900,000 in the 1920-1940 period.

We accept that these (Menville) cases are from Cook County, Illinois.

In 1960 Cook County population was 5,129,725 persons.

In 1960 U.S. Population was 179,333,000 persons.

We assume the ratio $(5,129,725 / 179,333,000)$ holds for the mid-part of 1920-1940.

Therefore, the national 900,000 women per age-year leads us to

$(5,129,725/179,333,000) \times (900,000)$, or about 25,744 persons/age-year (1920-1940).

Therefore, population breast-dose for the under-30 year age group:

$(12.5 \text{ person-rads}) / (25,744 \text{ persons}) = 0.00049 \text{ rads}$.

Therefore, population breast-dose for the over-30 year age group:

$(9 \text{ person rads}) / (25,744 \text{ persons}) = 0.00035 \text{ rads}$.

Comments on the Hyper-Thyroidism Therapy's Contribution to Breast-Dose

(1) We have reduced the radiation dose to the breast from 32.5 rads to 5 rads, since we are not sure the thymus was as avidly treated in the hyper-thyroid therapy as in direct thymus therapy. We may have been too conservative.

(2) We do not know that one Cook County hospital is the only one doing such therapy and we do not know whether private radiologists may have been doing such therapy. For all we know, we may have underestimated the population being treated by 5 or 10 fold. But we prefer to underestimate than to overestimate.

This completes the assessment for the 1920 - 1940 part of the whole period. We must now assess the 1940-1960 part, with introduction of radioiodine-131 in the therapy of hyper-thyroidism.

Dewing (1965) describes the transition-era very well: "It is extremely interesting to follow the literature of the latter 1920's and early 1930's when surgical and radio-therapeutic claims to control of hyperthyroidism were closely competitive. The issue of RADIOLOGY for March 1932 (Vol. 18) contains a good symposium on the current status of surgical, medical, and radiation management of the disease. An article by Williams contains an excellent general discussion from the radiologist's standpoint and a bibliography of 156 references. Another, by Menville, analyses some 10,541 cases treated by some seventy-five radiologists throughout the United States." And:

"Then, during the 1930's the surgeons pulled ahead for a while. However, as recently as 1949 Read reported a twenty-five year follow up of patients treated with x-ray and concluded that the results were quite equal to those of surgery." And:

"Reichel, in Europe, also reported in 1949 a twenty year followup, and similarly showed that surgery and radiation both gave good results in about 80 per cent of cases." And:

"After World War II the wheel had come around, and artificially produced Iodine-131 at reasonable cost brought radiation to the fore again. Most surgeons, who know all too well the hazards and complications of thyroid operations, are now among the happiest to refer hyper-thyroid cases to another department...."

But this did not mean that x-ray and radium therapy immediately went by the board for hyper-thyroidism --- papers on technics of using x-ray and radium continued to appear in the literature of the 1940's and 1950's.

Part 4. Breast-Doses Incident to the Use of Radio-Iodine-131

For our purposes, we wish to gain an estimate of how the iodine-131 use in the latter third of the 1920-1960 period may have altered our estimate of radiation to the breast in the therapy of hyper-thyroidism.

Dose to the Breast as a Result of Total-Body Irradiation by Iodine-131

Gofman (1981) at pp. 643-644, using data from MIRD Report 5, reported that a value of about 0.71 rads of whole-body radiation is reasonable per milli-Curie of iodine-131 ingested. If we take into account the high energy of the beta particles from iodine-131, we would reduce this estimate to 0.35 MEDICAL rads per milli-Curie.

Suppose we consider a dose of 10 milli-Curies of I-131 --- a common dose. Then, the whole-body dose (and breast-pair dose) is 3.5 medical rads. This is in the same range as the 5 medical rads we took from the thymus part of hyper-thyroidism therapy. BUT we can be quite certain that iodine-131 enjoyed a large surge of use in the 1940-1960 era, and it would be quite conservative to expect that at least 5 times as many persons per 1,000 received radio-iodine for hyper-thyroidism than had ever been the case broadly for x-ray or radium therapy.

We have a dose-reduction factor of $3.5 / 5$, or 0.7 for I-131, and an increased use factor of 5, so the radio-iodine net dose to breasts would be 3.5 times what we estimated above from x-ray therapy. But this is NOT the end of the calculation. We must now take into account the direct EXTERNAL air pathway transfer of gamma radiation from the

thyroid glands being treated TO the breast tissue, without ANY other tissue intervening [except of course some thyroid tissue and some skin tissue]. We are referring to the energetic gamma rays being emitted from the iodine-131 residing in the thyroid gland. Elsewhere (Gofman 1994, Chapter 2), we have calculated a mean effective half-life for I-131 to be 7.16 days. This means that the mean residence time will be Effective Half-life / 0.693, which makes mean residence time (7.16 days / 0.693), or 10.33 days in the thyroid gland. These calculations are for euthyroid persons, and hence will be somewhat different for each hyper-thyroid patient. But for our "range" estimates, 10.33 days as mean residence time is a value we can use.

We are going to calculate dose to breasts from the iodine-131 resident for 10.33 days in the thyroid gland. We shall be estimating rads per hour received by the breast, and multiplying it by the number of hours the radiation continues from the thyroid gland. That number of hours will be (10.33 days) x (24 hours / day) = 248 hours, rounded off.

The I-131 is distributed in a diffusely enlarged thyroid gland, in the two lobes (and some in the isthmus), all of which we can treat as a point source considering its distance of about 20 centimeters from the midplane of the breast tissue being reached by I-131 gamma rays.

Various sources differ in the abundance and exact energies of the various gamma rays emitted by I-131. We shall use the following distribution and the weighted average as calculated from the distribution.

Energy of Gamma Photons	Percent abundance
0.72 MEV	3%
0.64 MEV	9%
0.36 MEV	81%
0.28 MEV	6%
0.08 MEV	6%

Average Gamma Energy per Disintegration = 0.377 MEV.

We agree with Shapiro (1990) on the dose rate for a given flux of gamma rays.

That dose rate due to 100 photons / cm²-sec of Energy E per photon will be (0.172) x (E) milli-rads per hour. Our value of E for I-131 gammas is 0.377 MEV.

If now, we consider a point source of I-131 and a sphere of 1 cm radius, the surface area is 4 x pi x 1², or 12.566 cm².

NOTE: Here and elsewhere in the book, the common symbolic representation of an exponent in modern computer spreadsheets, such as x raised to the y power, is x^y.

For one milli-Curie of I-131, we have 3.7×10^7 disintegrations / sec.

Flux over the spherical surface of 1 cm radius will be

$$(3.7 \times 10^7 \text{ dis/sec}) / (12.566 \text{ cm}^2) = 0.294 \times 10^7 \text{ dis/sec/cm}^2$$

And dose-rate will be $((0.294 \times 10^7) / 100) \times 0.172 \times 0.377$ milli-rads per hour.

This is 1906 milli-rads per hour, or 1.91 rads per hour at a distance of 1 cm from the point source. Shapiro gets 1.86 rads per hour, but he uses only two of the gamma

rays. The literature often gives 2.2 rad / hr but Shapiro points out that this is the result of using a more complete set of gamma rays. We can regard our 1.91 rads/ hour for a one milli-Curie source of I-131 at 1 cm as satisfactory.

But our midplane of breast tissue is about 20 cm from the I-131 source in the thyroid gland, so the dose would be that for photons passing through a spherical surface of 20^2 , or 400 times larger than that for which we had calculated. Therefore, the dose at breast midplane would be 1.91 rads per hour / 400, or 0.00478 rads / hour to the breasts for a one milli-Curie point source in the thyroid gland.

But above, we have calculated the mean residence time to be 248 hours, so the radiation dose would be (248 hours) x (0.00478 rads/hr), or 1.185 rads total dose --- if there is one milli-Curie in the thyroid gland.

We estimate that a frequent dose was 10 milli-Curies administered. And since the hyper-thyroid gland has a higher uptake than euthyroid glands, we can say about 40% of the dose administered will be taken up in the gland. So we will estimate dose to breast as (1.185 rads / milli-Curie) x (4 milli-Curies), or about 4.74 rads to the breast tissue. But since this is quite energetic gamma radiation, we should reduce this to about 2.37 MEDICAL rads to the breasts. And, because some small part of the gamma radiation will be absorbed at the thyroid and in skin, we could round this dose off to about 2 medical rads to breast from the 4 milli-Curies of I-131 deposited in the thyroid gland of hyper-thyroid patients given a total dose of 10 milli-Curies.

Total Dose of Medical Rads from I-131 Therapy of Hyper-thyroidism.

Above we estimated, for the I-131 in the whole-body irradiation that the breasts would receive 3.5 medical rads for a 10 milli-Curie I-131 ingestion. And for the direct gamma transmission in air from thyroid to breasts, we estimate another 2 medical rads, bringing the total dose to 5.5 medical rads. This is very close to the 5 medical rads we estimated from the thymic irradiation part of x-ray treatment of hyperthyroidism. On the other hand, it is quite reasonable to expect that five times as many people per 1,000 got radioiodine as therapy as did those getting x-ray therapy.

So, for under 30 years, instead of 2.5 persons treated per age-year, it would be 12.5 persons. Person-rads = (12.5 persons) x (5.5 medical rads)

And for a population of 25,744 in each age-year, we would have an average dose experienced by the under-30 year group of

$$(12.5 \times 5.5) / 25,744, \text{ or } 0.00267 \text{ medical rads.}$$

And, for over 30 years of age, instead of 1.8 persons treated per age-year, it would be 9.0 persons. Person-rads = (9.0 persons) x (5.5 medical rads).

And for a population group of 25,744 in each age-year, we would have an average dose experienced by the over-30 year group of

$$(9.0 \times 5.5) / 25,744, \text{ or } 0.00192 \text{ medical rads.}$$

Part 5. Combined Estimates, Pre-1940 and Post-1940, for the Master Table

Now to combine the pre-1940 and post-1940 results, we are using the estimate that the early period is 25 years (1920-1944), and the later period is 15 years (1945-1959). Early period is 5/8 of total; later period is 3/8 of total. From Part 3, we have:

Annual population breast-dose, 1920-1944, below age-30 = 0.00049 rads.

Annual population breast-dose, 1945-1959, age-30+ = 0.00035 rads.

For under 30 year age-group, $(5/8 \times 0.00049) + (3/8 \times 0.00267) =$

Mean Value, overall, = 0.00131 rads. Ages 20 through 29 years of age.

For over 30 year age-group, $(5/8 \times 0.00035) + (3/8 \times 0.00192) =$

Mean Value, overall, = 0.00094 rads. Ages 30 through 59 years of age.

These entries are transferred to Column L in the Master Table. (A more refined calculation could be done using the exact population at each age-year, instead of the average of 25,744. But the change in estimate would be small indeed.)

We note that after 1960, the higher results characteristic for use of I-131 treatment of hyper-thyroidism would be applicable.

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1920: "I can truthfully say that a physician makes a grave and deplorable mistake if he allows his patient to be operated on before getting massive doses of x-ray over the thyroid and thymus glands." He is arguing for the superiority of x-ray over surgery for hyperthyroidism.

● - C. Augustus Simpson "A Word to the Roentgen Therapeutist,"
AMERICAN JOURNAL OF ROENTGENOLOGY Vol.7, No.7: 357-358. July 1920.

CHAPTER 21

Management of Adolescent Scoliosis (Curvature of the Spine)

Part 1. How Does Adolescent Idiopathic Scoliosis Come to Relate to Breast-Cancer?

The answer to the title of this Part 1 is in two parts. First, we know of no intrinsic relationship AT ALL between scoliosis and breast-cancer. The second part is that for decades the management of scoliosis was done with frequent x-ray checks of the spine, in the worst possible way for breast irradiation. This led some of the women to develop breast-cancer from the radiation, not from the scoliosis. We shall be discussing some of the opportunities missed (for decades) to prevent such breast-cancer, and some of the elegant work done later to prevent many of the breast-cancers arising from the management of scoliosis.

Scoliosis --- What Is It?

Scoliosis is defined (from the Greek *scolios*, for curved) as a lateral curvature of the spine. There are several possible bases for lateral curvature of the spine, but there is one common entity which concerns us here. That is the entity known as Idiopathic Scoliosis or Habitual Scoliosis. The appellation, "idiopathic," simply means that the cause is unknown. Professor Arthur Steindler, Head of Orthopedic Surgery at Iowa State University, wrote the chapter on "Static Deformities of the Spine" in the 1942 Edition of Christopher's "Surgery."

He wrote at p.463-464:

"The So-Called Habitual Scoliosis or Idiopathic Scoliosis:
This term merely indicates the absence of a definite underlying cause. It implies a general or constitutional predisposition, such as anatomical build and general habitus, or inherited or acquired weakness or relaxation of the spine and its musculature ... The majority of cases occur in females." And (at p.466):

"So-called habitual or idiopathic scoliosis has always received considerable attention from the viewpoint of prophylaxis. It has been called 'school scoliosis' because it is believed to develop during the school age; some investigators have found as high as 20 to 30 % of all school children afflicted with this 'functional' scoliosis as a result of faulty posture. However, the usual prophylactic measures are, as a rule, belated. The critical age is between the third and fifth year, and it is at this time that prophylaxis should be practiced." (Recent investigators cite a later age-band for this disorder.)

The Early History of Treatment

From Dr. Steindler's discussion, it is clear he did not feel muscle training, external or internal splinting were too helpful. External splinting meant braces and internal splinting meant operative fusion of the spine. He certainly was not optimistic about the management of scoliosis. We quote his final conclusions (p. 469).

"This short outline of the treatment serves to emphasize the all-importance of the earliest possible recognition and timely prophylaxis of scoliosis. Until these vital facts have become generally appreciated, there is not likely to be any real progress in the management of cases of scoliosis."

Unfortunately --- during the months and years of the efforts to correct the scoliosis by braces, by casts, by musculature training --- the physicians continued to monitor the patients both with physical examination and with x-ray examinations of the spine. Most unfortunately, the method of taking the spine films in the early period was to have the beam enter the front of the body, and exit through the back (the anteroposterior, or AP, approach). From the point of view of breast irradiation, this was the worst possible approach for part of the x-ray examination. The lateral views which were taken were unfavorable but not as unfavorable as the antero-posterior view.

Apparently very little concern was shown for the steady accumulation of breast-dose from the repeated spinal exams, taken in this extremely unfavorable AP view.

So now the long-drawn out management procedures for scoliosis meant a seriously growing radiation dose to the breasts of adolescent and post-adolescent girls and young women. There was no comment whatever in the Steindler chapter about any hazard of the radiographic aspect of management. We did not expect to find any. The times were such that broadly, the medical profession did not believe that diagnostic x-rays spread over 3 to 6 years could be harmful. Let us be clear; this was a belief, not a demonstration.

A decade later, approximately, the 1950 Edition of Mitchell-Nelson's Textbook of Pediatrics, 5th Edition, has the Orthopedic Pediatrics Chapter written by Dr. Charles C. Chapple. In his brief section on "Scoliosis," the part on Treatment in no way mentions the repeated x-rays associated with management of the disorder:

"Treatment. Nutritional improvement and postural exercises are usually sufficient in the treatment of mild cases, but in the more severe ones, since the scoliosis is liable to become more marked with increasing muscular development, correction by such orthopedic means as exercise and supporting devices is advisable in addition to the treatment of any underlying factor. Many require spinal fusion."

No mention is made of the numerous x-rays which accompanied the use of such corrective devices as braces or casts.

Two decades later, in 1968, "Ambulatory Pediatrics" edited by Dr. Morris Green and Dr. Robert Haggerty, commented succinctly on scoliosis as follows:

"Although complex, carefully fitted bracing may occasionally prevent progression of the deformity, there is increasing evidence that early spinal fusion is by far the most effective method of treatment. Complete correction of the curve is rarely possible, and the purpose of fusion is to stabilize the spine and prevent progression."

There is no mention whatever about the numerous spine films which were taken in the course of such management of scoliosis. Quite obviously the textbooks over three decades, at least, did not consider it worth mentioning that the many spine films were giving a very high dose to the breasts, and that such dosage was really unnecessary.

Finally, in 1979, there was a massive change in the tide.

Part 2. A Spectacular Achievement in Dose Reduction for Scoliosis Patients

Nash, Gregg, Brown, and Pillai (1979), all at Case Western Reserve University, called attention to the serious problem of excessive radiation dosage accumulated by female scoliosis patients during the course of one of the disorder's common treatments, known as the Milwaukee Brace treatment. As Nash and co-workers pointed out,

adolescent girls would be monitored with some 20 x-ray films, plus retakes, or a total of 22 radiographs during the average three-year treatment period. Most films were taken as AP shots. Having made their own measurements, Nash and co-workers estimated an average entrance dose of 1.13 roentgens for the AP shots used, and 1.78 roentgens for the lateral shots. From their estimates of dose to organs, they concluded (p.371) that "given an average of twenty-two roentgenograms over a three-year Milwaukee Brace-treatment program," the risk of breast-cancer due to x-ray radiation rose "from 140 to 290 per million (110 percent)."

Even worse than the conclusion of Nash and co-workers that the monitoring of scoliosis therapy was more than doubling the patient's risk of later breast-cancer, was their additional conclusion that "many scoliosis patients may require more roentgenograms than the average scoliosis patient postulated in this study."

Since these types of therapy had been going on before Steindler's writings in 1942, there is good reason to consider that the entire 1920-1960 period was characterized by this sort of therapy for scoliosis.

Details of the Steps Which Reduced Breast-Dose

Nash and colleagues decided to do something about this situation. They proved in a series of scoliosis patients that shifting beam direction from anterior-posterior to posterior-anterior could reduce the breast-cancer risk by a factor of 28 ! As for the image quality, the Nash team reported that the x-ray films obtained from the PA beam direction proved technically satisfactory for routine scoliosis care.

Additional work of real merit on reducing the risk from x-rays for scoliosis patients has been done by Gray, Hoffman, and Peterson at the Mayo Clinic. In an extensive study (1983), they report on how they used the following combination of measures to reduce dose:

- - : A posterior-anterior beam direction;
- - : Specially designed leaded acrylic filters;
- - : A high-speed screen-film system;
- - : A breast-shield;
- - : Additional filtration in the x-ray tube collimator.

Dr. Gray and co-workers reported at page 5 that the following reductions in breast dose occurred:

"...For the breasts there was a sixty-nine fold reduction from 344 to less than five milliroentgens for the postero-anterior radiograph and fifty-five fold reduction from 277 to less than five milliroentgens for the lateral radiograph."

Part 3. Determining (1920-1960) Breast-Doses in Scoliosis Management

Hoffman, Lonstein, Morin and co-workers (1989) have conducted a followup study of a series of women who had multiple diagnostic x-rays in the course of scoliosis management. We shall make use of some of their data to provide entries for the Master Table, Column H.

They regard scoliosis as a relatively common condition. The prevalence in the general population has been estimated to be as high as 8 %. However, a major determinant of the prevalence reported is the degree of spine curvature used to diagnose scoliosis. The disease is more prevalent in women than in men.

Hoffman and co-workers provide the following [not totally consistent with their estimate above of prevalence of the disorder]:

"Adolescent idiopathic scoliosis afflicts nearly 2 % of the U.S. population, and school jurisdictions in over 50% of the United States have screening programs for children 9-14 years of age. Girls require treatment more often than boys. Once detected, scoliosis requires periodic x-ray monitoring of the spine, especially during adolescence, when the bones are growing at an accelerated rate. The times of breast development and menarche are clinically important because they indicate that the growth spurt has begun or will begin soon. Patients commonly receive anteroposterior and lateral spinal x-rays to monitor the progression of spinal curvature and the effect of treatment."

These school programs certainly are addressing an older group than that suggested worth studying in the Steindler paper, which suggested the critical age to be between the third and fifth year.

We shall use the breast-dose estimates provided by Hoffman et al. in this study (1989).

- - Item 1: This study was done in Hennepin County, in the State of Minnesota. The study population consisted of 1,030 women with a confirmed diagnosis of scoliosis or kyphosis who were seen in one of three hospitals or in one clinic in Minneapolis-St.Paul, Minnesota area. We were not given any assurance that this study included all the cases of scoliosis being treated in Hennepin County during the period under investigation. It is possible that such inclusion existed, but since we do not know, we caution the reader that breast-exposure estimated nationally from these data may well be an underestimate because of the absence of an unknown fraction of the total number of cases.

- - Item 2: The 1,030 women who qualified for inclusion were followed up for 26 years, on average.

- - Item 3: The estimate of dose to the breasts was a mean value of 12.8 total rads (medical rads), acquired over a period of 8.7 years, on average. The examinations were given in the period, 1935 to 1965.

- - Item 4: Since the acquisition of cases occurred over a period of 30 years (1935 -1965), the number of acquisitions per year in Hennepin County must have been, on average, $1,030 / 30$, or 34.3 cases per year.

- - Item 5: Since the average age at diagnosis was 12.3 years, we should assign some of the cases to age groups below 12.3 years and some to age groups above 12.3 years. We shall arbitrarily estimate the distribution of the annual 34.3 cases as in the following tabulation.

Age Group	National Women in Age Grp.	Females in Hennepin	Cases in Age Grp.	Mean Dose Med. Rads	Person-Rads	Avg. Dose Rads, for Hennepin
9	889589	4181	4.9	12.8	62.72	0.01500
10	889390	4180	4.9	12.8	62.72	0.01500
11	889209	4179	4.9	12.8	62.72	0.01501
12	889028	4178	4.9	12.8	62.72	0.01501
13	888829	4177	4.9	12.8	62.72	0.01501
14	888585	4176	4.9	12.8	62.72	0.01502
15	888277	4175	4.9	12.8	62.72	0.01502

- - Item 6: We need to know the number of female persons in each age group during the 1920-1960 period.

The population of Hennepin County in 1960 is 842,854 persons (County and City Data Book 1962). The population of the USA in 1960 is 179,333,000 persons. To calculate the number of female persons in each age group, we multiply $(842,854 / 179,333,000)$ by the number of women nationally in each age group (from the Master Table Col.A) in the average year of 1920 - 1960. This was done and the entries are given under "Females in Hennepin." in the preceding tabulation.

- - Item 7: We know only that there were, on average, 34.3 cases acquired per year, but we do not know the age distribution of the cases. We approximate this by assigning cases to 7 age-years. So $(34.3 / 7)$, or 4.9 cases are assigned per age-year.

• - Item 8: We need to estimate the person-rads of breast-pair exposure for each year. This is the product of (persons irradiated) x (average dose). Since all the cases are taken to be 4.9 per year, and the mean dose of 12.8 rads is used for all cases, the person-rads for all entries is $(4.9 \text{ persons}) \times (12.8 \text{ rads})$, or 62.72 person-rads.

• - Item 9: We have the dose to individuals (12.8 rads), and we have the person-rads represented by the cases. WE NEED, and have not yet calculated, the average population dose for these groups of women. That number is the person-rads injected into the population / the persons in the population. So, we have average dose = $(62.72 \text{ person-rads}) / (\text{number of females in Hennepin, for each age group})$. This, for the first entry into our tabulation, is $(62.72 \text{ person-rads} / 4,181 \text{ persons})$, or 0.01500 rads.

• - Item 10: We must consider the issue of duration before making entries into the Master Table. We have data for 1935 to 1965. We can regard those data as adequately close for 1930 to 1960. The question before us is what we do about the 1920-1930 period for which we have no data.

We suspect, but can not prove, that the dose was higher in that earlier period than in 1930-1960. We, therefore, take the conservative approach of eliminating ANY dose for 1920 to 1930. The final dose adjusted very conservatively for duration is obtained as follows:

$((30 \text{ years} \times 0.01500 \text{ rads}) + (10 \text{ years} \times 0 \text{ rads})) / 40 \text{ years}$, or 0.01125 rads per age-year. This value of 0.0112 is transferred to the Master Table, Column H, for age-years 9 through 15.

We believe the true dose was higher, but using our general rule of conservatism when we can not prove it to be higher, we choose the lowest dose possible, zero dose, for the 1920-1930 time-period in question.

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What motivated Dr. Joel Gray and his Mayo Clinic colleagues to achieve spectacular reductions in breast-dose (see Part 2) for scoliosis patients? They seem to have answered this question, when they wrote (Gray 1983, p.12): "... no level of exposure to ionizing radiation is entirely safe ..."

● - Big Consequences from Low-Dose Carcinogens:
A Warning from the National Cancer Institute (NCI) in 1990

This book (Preventing Breast Cancer) states that low radiation doses do indeed count with respect to breast-cancer totals in the population.

Women will hear from some quarters that when the risk is very low, one can simply dismiss such a risk. Thus, for a given low-level radiation exposure, someone might calculate that radiation will cause a breast-cancer in ONLY one woman out of every 10,000 women receiving that dose. For risks of this size, "Just forget it" is often the advice.

Good advice, or deadly?

The National Cancer Institute (NCI) provides the following warning at page 7 of its 1990 booklet:

"In the human population, large numbers of people are exposed to low doses of chemicals, but the total impact may not be small at all. For example, a carcinogen might cause one tumor in every 10,000 people exposed to it, which may not seem great. But exposure of 230 million Americans would result in 23,000 cancers --- a public health disaster."

Suppose ionizing radiation is the carcinogen for which the NCI is calculating the causation of one breast-cancer in every 10,000 women exposed to a specified "low dose." The female population in 1994 is approximately 133 million, so the number of breast-cancers induced would be 13,300 per year, if the "low dose" is an annual dose.

The nation would be giving only "lip-service" to the goal of preventing breast-cancer, if various ways to prevent 13,300 cases per year were each dismissed because a woman's personal risk "may not seem great" at 1 per 10,000. The NCI makes a good statement (p.11):

"Individually and together, we must make every effort to reduce or eliminate human exposure to carcinogens." And, of course, the NCI starts its booklet at page 1 with the statement:

"Cancer-causing agents also include X-rays, sunlight, and certain viruses." And at page 5, "radiation and radioactive materials" are listed again as proven human carcinogens. The NCI advises at page 12: "Don't ask for an X-ray if your doctor or dentist does not recommend it. If you need an X-ray, be sure X-ray shields are used if possible to protect other parts of your body."

Source: National Cancer Institute (USA), "Everything Doesn't Cause Cancer," 12-page booklet, March 1990 (NIH Publication 90-2039).

CHAPTER 22

Chiropractic Examinations and Breast Irradiation

Part 1. Chiropractic Spine Examinations: How Many ?

In the most recent reprinting (June 15, 1994), NCRP Report No. 100 (p. 16) cites the American Chiropractic Association indicating that, in 1982, chiropractors performed about 10 million x-ray examinations of the spine. And at page 12, NCRP 100 cites the American College of Radiology Manpower Survey (ACR 1982) as indicating that, in 1980, chiropractors performed an estimated 10 million medical diagnostic x-ray examinations, this number being about 5.5% of all the 180 million diagnostic x-ray examinations for the year.

Priscilla Laws, in "X-rays: More Harm Than Good ?" (1977) stated at page 43: "Chiropractors are popular in both Canada and the United States, and a 1971 survey of the Journal of Clinical Chiropractic indicates that more than 10 million x-ray examinations were being conducted by United States and Canadian chiropractors annually. At least two million of those were the type which irradiates the body from the skull to the thigh, including the thyroid, bone marrow, and reproductive organs." This is the examination known as the "Full-Spine Exam."

All of these reports are quite consistent with each other. For total spine exams by chiropractors in 1980, we will use the figure 10 million per year, of which 2 million were Full-Spine Exams (males and females combined).

We have a detailed reference (Bhatnagar and co-workers 1981) on the dosimetry for the Full-Spine Exam.

From that source, the mean dose to breast tissue = 465 milli-rads, including dose to breast from one antero-posterior (AP) exposure and one lateral (LAT) exposure. (These doses, say the authors, are for examinations as performed in one chiropractor's office in the Pittsburgh area.) This publication appeared in print in 1981, but was presented in 1980. We have many reasons to expect that doses in the early period (1920-1960) were higher, not lower than in later periods.

- - Item 1: For conservatism, we shall assume that the breast-dose per Full-Spine Exam was 0.465 rad during the 1920-1960 period.

- - Item 2: We shall reduce the 2,000,000 Full-Spine Examinations for the 1920-1960 period in proportion to population. The average female population for 1920-1960 we have determined is 69,037,400, for all ages combined. And for 1980 (Statistical Abstract of United States) the female population is 116,493,000. Therefore, our adjustment factor for population size is $(69,037,400 / 116,493,000)$, or 0.593. And we must omit males.

We reduce the 2,000,000 Full-Spine Examinations by a factor of two for female population, which gives 1,000,000 exams. Then, reducing this by the factor of 0.593, we end up with 593,000 Full-Spine Examinations by chiropractic in the 1920-1960 period, at an average breast-dose of 0.465 medical rads. This is a start on the problem of the total dose from various spine examinations. Having taken care of Full-Spine Exams separately,

Col. A	Col. B	Col. C	Col. D	Col. E	Col. F	Col. G	Col. H	
Lumbar Projections	Spine Taken	Beam Quality	Entrance HVL, mm, Al.	Average Exposure Roentgens	No. Films per Exam	Rads per Roentgen	Raising Factor	Breast Rads per Exam
	AP		2.37	0.88	1.03	0.693	1.03	0.650
	LAT		2.58	3.20	1.33	0.183	1.25	0.973
	OBL-PA		2.51	1.11	0.46	0.110	1.20	0.067
Total Breast Dose in rads for complete exam ----->							1.690	
Thoracic Projections	Spine Taken	Beam Quality	Entrance HVL, mm, Al.	Average Exposure Roentgens	No. Films per Exam	Rads per Roentgen	Raising Factor	Breast Rads per Exam
	AP		2.37	0.66	1.07	0.693	1.03	0.51
	LAT		2.42	1.46	0.93	0.183	1.11	0.28
	OBL-PA		2.42	0.76	0.12	0.110	1.12	0.01
Total Breast Dose in rads per complete exam ----->							0.79	
<p>Notes: Gofman/O'Connor 1985 provides the factor by which rad doses must be raised when the Half-Value Layer deviates from 2.3 mm Al (Table D). The rads per Entrance Roentgen are also provided there (Table C).</p> <p>Entrance doses for such examinations are provided in Table 3.19 from NCRP 100.</p> <p>The NCRP and Gofman projections and entrance doses are in perfect agreement.</p> <p>Final Breast Rads per Exam are in Col. H, which = (Col.D) x (Col.E) x (Col.F) x (Col.G).</p>								

we now consider the remaining 8,000,000 spine examinations annually. We must multiply this number by (0.5) to get to the value for females only, and by 0.593 to get to 1920-1960 period. So we have (8 million) x (0.5) x (0.593), or 2,370,000 spine examinations additional to the Full-Spine Examinations.

The lumbar spine films are by far the most common spine films aside from the Full-Spine Examination. Using the data from Table 3.7 of NCRP 100, we estimate the lumbar plus thoracic spine exams together will constitute 80% of the spine films other than the Full-Spine Examination. Therefore, we shall reduce the 2,370,000 spine exams to 80% of that value, or 1,896,000 exams divided between lumbar plus thoracic spine examinations.

Part 2. Chiropractic Spine Exams. What Dose is Received by Breasts?

In the 1964 period, thoracic spine exams constituted 0.17 of the total (thoracic + lumbar) exams, and lumbar exams constituted 0.83 of that total.

In the period up through 1963, the "wasted radiation," namely the area exposed relative to the area needed for the x-ray, was about 3.2-fold (NCRP 100 concurs). See also Chapter 23. So the lumbar films can be considered to have had the breasts fully in the field, since there was already high exposure to breasts for this exam even without the wasted radiation. (See 'Lumbar Spine,' p.126 in Gofman / O'Connor 1985.)

Next, we can estimate an average breast-dose for thoracic and lumbar spine exams by combining these two exams in their relative proportions (doses taken from the box).

$$\text{Average Dose} = (0.83 \times 1.69) + (0.17 \times 0.79) = 1.54 \text{ medical rads.}$$

This dose applies for 1,896,000 examinations, which can be handled (mathematically) like 1,896,000 persons.

• - Item 3: Total accumulation of person-rads to the breasts in the United States Population:

$$\text{Full-Spine: } (593,000 \text{ persons}) \times (0.465 \text{ rads}) = 275,745 \text{ person-rads.}$$

$$\text{Other,Spine: } (1,896,000 \text{ persons}) \times (1.54 \text{ rads}) = 2,919,840 \text{ person-rads.}$$

$$\text{Total person-rads, all spine exams} = 3,195,585 \text{ person-rads.}$$

• - Item 4: These person-rads will be distributed into all females between 15 and 64 years of age, a total of 50 age groups. We do not have the precise age distribution of dose, so we shall assume each age group gets 1/50 of the total, which is 3,195,585/50, or 63,912 person-rads per age-year category, rounded off.

• - Item 5: We must next determine the average POPULATION dose in rads. Since we have to deal with 50 different age-groups, we shall demonstrate here how the estimate is made, and in the Master Table (Col. R), the actual calculations of dose will be presented for each of the fifty age-years.

Let us take the national population of women in the 15th year age bracket. That number from Master Table, Column A, is 888,277 women.

If we distribute 63,910 person-rads into 888,277 women, the average dose per woman is (63,912 women-rads) / (888,277 women), or 0.072 rads.

This value will not differ very much from age-group to age-group since the only basis for difference is the decline in population-number with increase in age.

• - Item 6: There is no reason to assume this practice was not carried out throughout the 1920 to 1960 period. Indeed, it was still going strong in the 1980's.

#

● - Safety Claims about Low-Dose Radiation:
A Warning from the National Cancer Institute (NCI) in 1990

This book (Preventing Breast Cancer) states there is no safe dose of ionizing radiation with respect to induction of breast-cancer (or other cancers).

Various women have recounted to us that they have been advised that cancer is the result ONLY of high doses of radiation, and that repair of DNA and chromosome eliminates all the injury at low radiation doses.

What does the National Cancer Institute tell the public? In its 1990 booklet (pp.9-10), it deals with the topic as follows, with question-and-answer:

"Are there safe levels for human exposure to carcinogens? In other words, are there threshold dosages below which we can be sure that no cancer will occur?" And:

"There is no adequate evidence that there is a safe level of exposure for any carcinogen. As far as we know, the frequency of tumor formation goes down as the dosage goes down, but the risk of carcinogenesis may not disappear until the dosage reaches zero. Although high doses are often used in the [animal] tests, we must not assume that only high doses cause cancer. On the contrary, we must assume that low doses will also cause cancer, but at lower rates." And:

"Human cancers have occurred following very low level exposure. Asbestos brought home on the clothing of asbestos workers, for example, has caused fatal cancers in members of the workers' families."

Source: National Cancer Institute (USA), "Everything Doesn't Cause Cancer," 12-page booklet, March 1990 (NIH Publication 90-2039).

Note: For induction of cancer by ionizing RADIATION, there is mainstream evidence (from humans, not from test-animals) disproving any safe dose or dose-rate. See Gofman 1990, Chapters 18-21, 32, 33. In addition, human studies (like the A-Bomb Study) provide evidence of a dose-response --- that is, the frequency of radiation-induced cancer goes down when dose goes-down (and goes up when dose goes up). A dose-response is important in helping to exclude non-radiation explanations.

CHAPTER 23

Major Diagnostic Radiological Contributions to Breast Tissue Dose

Part 1. Sources of Information on Diagnostic Doses for 1920–1960

Gofman and O'Connor (p.11, 1985) tabulated data (originally from Shleien and co-workers, 1977) for medical radiographic examinations (EXCLUDING examinations of the extremities). Note carefully that these data are for a period at least a decade after the close of the 1920 to 1960 period. The key point is that whatever doses such examinations were giving in the 1977 period, we expect and shall show that, for the same numbers of examinations, the doses must have been considerably higher during the period of 1920 to 1960. We shall examine the frequency of various examinations in the post-1960 period and then examine the dose which must be considered to have gone with such frequencies or other frequencies in the earlier period.

All entries expressed as number of examinations per 100 persons (Annually)

<u>Medical Radiographic Examinations</u> (excluding examinations of extremities)		<u>Fluoroscopic Examinations</u> (including spot films and plates)	
<u>Age Group</u> <u>(Years)</u>	<u>Number of exams</u> <u>per 100 persons</u>	<u>Age Group</u> <u>(Years)</u>	<u>Number of exams</u> <u>per 100 persons</u>
Under 15	16	Under 15	1
15–24	42	15–24	3
25–34	56	25–34	5
35–44	65	35–44	9
45–54	72	45–54	12
55–64	73	55–64	13
65–74	73	65–74	15

Since these frequencies are expressed per 100 persons, the size of the total population is not at issue; at issue is the average dose for the various examinations.

How Did Doses During the 1920–1960 Period Compare with Those Beyond 1960?

An absolutely essential introduction which is required to deal realistically with the pre-1960 era consists of several facts and several descriptions of reality concerning x-radiation practice during the pre-1960 period. It will become abundantly clear why this is so.

The Statements of C.B. Braestrup (1969)

C.B. Braestrup was intimately involved in engineering practice in the radiation field in the early period. His report (Braestrup 1969) contains the following statement, according to Shapiro 1990 at page 379:

"Within the first few years of Roentgen's discovery, the application of x-rays in diagnosis required doses of the order of 1000 times that required today [meaning in 1969]. Radiographs of heavy parts of the body took exposures 30–60 minutes long. Maximum allowable exposures were set by the production of skin erythemas (300–400 rad). Thus the skin served as a personal monitor. The Wappler fluoroscope, manufactured around 1930–1935, produced 125–150 R/min at the panel. Skin reactions

were produced and in some cases, permanent injury. To minimize hazard, a 100 R per examination limit was set in the New York City hospitals."

This is truly mind-boggling to hear of the earlier doses with x-ray films and plates. Scientists and physicians in practice today have trouble conceiving of a period where there was no agreed-upon physical or chemical dosimeter to ascertain how much radiation was being delivered. One monitor was, as Braestrup states appropriately, the skin of humans. It was noted that with enough radiation one finally achieves a reddening of the skin, known medically as an erythema of the skin. The early roentgenologists tended to make the assumption that if the skin had not reddened, one could not be near any serious radiation source. And as a number of these early radiologists died, their Journal showed photos of "those who pioneered for their profession and gave their lives in doing so." (See early years of American Journal of Roentgenology and Radium Therapy.)

This dosimeter --- skin --- was crude. Response depended on how big an area of skin had been irradiated. It depended on the voltage across the x-ray tube (which determines kVp of the x-rays coming out). It depended on window thickness of the x-ray tube and on the amount and type of filtration between tube and patient.

It was the erythema dose-unit, which led authors to write about delivering "one-tenth, one-fifth, or one-half an erythema." If one studies those early issues of American Journal of Roentgenology, he(she) will see the controversies about the appropriate use of the erythema doses and the controversies about physical dosimeters that would ultimately replace the living dosimeter.

Early fluoroscopy was in many ways even more mind-boggling, with physician over-exposure, patient over-exposure, and numerous technician and nurse over-exposures due to machines inadequately shielded and beams inadequately collimated. We note the introduction of the Wappler fluoroscope with a bountiful X-ray output, 125-150 R/min at the panel. So the roentgenologists who had become accustomed to a dearth of adequate exposure now found themselves not realizing what could happen in two minutes. Incidentally, the Wappler fluoroscope was a high-quality machine. "Westinghouse liked the machine so well, it bought the company." [Victor Kiam, please excuse borrowing your line.]

It is alarming to consider what these powerful machines meant in terms of fluoroscopic dosage. The statement that skin reactions were produced and in some cases, permanent injury was produced, is chilling, but not unexpected. And to learn that New York City set a 100 R examination limit on fluoroscopy in the New York hospitals should not be assumed to mean that all was well elsewhere. No doubt this is just a reflection of a little MORE concern there than elsewhere.

It is very hard to doubt that average fluoroscopic doses for such procedures as Upper G.I. Series, or Thorax Studies, or Gall-Bladder Examinations (cholecystograms), were at least 2, 3, or 5 Roentgens in the early period --- at a time when legislators tried to limit such exposures per exam from exceeding 100 Roentgens. In Part 3 of this chapter, we surely underestimate exposure by using 3 Roentgens as the entrance dose per average fluoroscopy in 1920-1960.

The Special Problems of Fluoroscopy in Pediatric Practice

Some special problems must be noted for newborns, infants, and children in the pediatric years.

Dr. Hanson Blatz (Blatz 1970), the director, Office of Radiation Control, New York City Department of Health, is cited in Shapiro at page 421 discussing the problem of the prescription of excess numbers of x-rays.

What follows stretches the mind so much, we felt impelled to check. We had known of Dr. Blatz, but had never met him. We telephoned Dr. Karl Z. Morgan, widely recognized as the "father" of the health physics profession. Yes, Karl knew his work well, and Karl gave him an excellent recommendation in the health physics field. These are Dr. Blatz's words from 1970 (as reported in Shapiro 1990, p.421):

"The problem of excessive use of unnecessarily repeated examinations is an abuse that could not be regulated under any circumstances. Popular feeling and professional education have been and will probably continue to be the only effective controls." And:

"And I don't think we should overlook popular feeling. Those of you who have been in the field a long time know that it was once the practice of pediatricians to fluoroscope babies and young children every month and when they had the annual checkup [presumably in the 1940s and 1950s]. When we questioned this practice, pediatricians would say, 'Well, the parents expect it. They think if I don't fluoroscope the patients, they are not getting a complete examination'."

Non-Recorded Doses May Exceed Anything on Record

We now have confirmatory evidence from two sources that what Dr. Blatz described for New York City was also happening in Rochester, New York, and in Seattle, Washington. The observations of Franz Buschke and Herbert Parker (1942) and of James Pifer (1963) are detailed in Chapter 31. Some pediatricians (but not all) were routinely fluoroscoping all their patients at the monthly "well-baby" examination in the first and second years after birth. Buschke and Parker ascertained that exposures from a skillful examiner could add up --- by the second birthday --- to 200 Roentgens of entrance dose, and much more from a non-skilled examiner.

Such information suggests that fluoroscopy in young children could dominate the diagnostic radiation exposure in the 1920-1960 period. It would all depend on what fraction of pediatricians engaged in this practice --- a practice which many of them may not have recorded at all, and a practice for which they surely did not record how long the x-ray beam was on, at each examination.

Do we know of anyone who had fluoroscopy during every pediatric check-up? Yes, we do. While we were doing this study, we happened to hear by letter from a woman in New York who REMEMBERS being fluoroscoped at every pediatric exam from age 4 through age 12. Before age 4, she has no recall one way or the other, and she can not ask her mother who is no longer alive.

The Immature Technology Available in the 1920 - 1960 Era

In the 1920-1960 period, film-speed was much slower than in the post-1960 period. This had several repercussions. It took a longer exposure to make a roentgenogram. And because it took a longer exposure, the effect of motion was very serious for films, and caused bad blurring of images. So there was a high tendency for the roentgenologist to CHOOSE to do fluoroscopy. But MORE fluoroscopy meant even higher doses. A massive improvement became available in the later period, not available in most of the 1920-1960 era, namely fast film-screens which could enhance images in roentgenograms, AND fast film screens which could enhance images in fluoroscopic practice. So on both these counts, the doses in 1920-1960 were necessarily

much higher than in the 1970's and beyond, since lesser exposures became required with the faster film screens.

Part 2. Radiological Doses in the Pre-1960 and the Post-1960 Eras

The Words of Dr. Francis Curry Concerning Practice as Late as in 1960

We have alluded to some of Dr. Curry's comments concerning x-ray exposure from tuberculosis screening. But we must give some more consideration of what some of his remarks must mean for dose estimates for the 1920-1960 era.

Dr. Francis Curry, deputy director and later director of public health and hospitals in San Francisco from 1960 to 1976, is quoted by Caufield at page 144 as follows:

" What was so horrible about what was happening then is that so many machines had no filters, no coning, no shielding. Many people were getting total body exposures and were getting doses big enough to show clinical symptoms. "

If Dr. Curry had this to say about the 1950s, what are we to think about doses in the far more immature era of 1920 to 1950?

We have now covered some of the crucial evidences that indicate we must expect doses for any specific procedure in the 1920-1960 era to be considerably higher than those in the mid-1970s, for which we have some reasonably meaningful estimates of average doses for major diagnostic radiological procedures.

How We Shall Handle the Diagnostic Doses in the 1920-1960 Period

1. We shall assume that the frequency of examinations (diagnostic exams per 100 persons for any age bracket) is the same before 1960 as after 1960. There may be some difference, but we must carefully differentiate between growth in total number of exams which is in part related to population growth (which is large in that period) and the FREQUENCY of examinations per 100 persons in each age category after 1960.

2. The issue of "wasted radiation" is extremely important in our handling of the dose estimates. For these considerations we turn to an important publication of David Johnson and Walter Goetz (1986).

Wasted Radiation in Diagnostic Medical Exposures in the Early Period

It is a fundamental principle of diagnostic radiography today that one never permits the beam of radiation to be of larger total area than the area of the film exposed. ALL RADIATION IN EXCESS OF THAT NEEDED FOR THE FILM IS "WASTED RADIATION" --- EXPOSING THE PATIENT NEEDLESSLY TO RADIATION HAVING NOTHING TO DO WITH DIAGNOSIS. Johnson and Goetz point out that enormous progress was made between 1964 and 1983 in reducing the amount of wasted radiation. For 1964, they found the total dose of radiation delivered in diagnostic work was 3.2 times what was needed for the film. So TWO-THIRDS of the exposure being experienced by the patient added to injury but added nothing to diagnostic efficiency. By 1982, the wasted radiation was almost all eliminated by proper collimation of the beam.

What this tells us is that before 1960, the situation was even worse --- with at least three times as much area of the body exposed as was necessary. In effect, this means

that a diagnostic examination such as Upper G.I. Series undoubtedly exposed the breasts unnecessarily. Examination of the chest exposed several abdominal organs unnecessarily.

In Gofman and O'Connor (1985), for each exam we provided the anatomic limits generally used for each type of examination. Thus (at page 171) we find the following for the Upper Gastro-Intestinal Exam:

"Length of Field: For adults, the field length is 43.2 cm, and extends from 4 cm below the sternal notch to 6 cm below the iliac crests. The field center is 6 cm below the xiphoid process ..."

These dimensions tell us, by reference to anatomical diagrams, which organs are fully in the x-ray beam field, which organs are far away even from the edge of the x-ray field, and which organs are near the border of the x-ray field. When we are calculating the dose in rads to an organ by using conversion factors from entrance dose in Roentgens to absorbed organ dose in rads, we are speaking of the organ dose for those organs FULLY IN THE X-RAY FIELD. And we know about this from the position limits given above under "Length of Field" and its position with reference to body points.

The implication of the work of Johnson and Goetz is that in the earlier days (before 1964) the exposure field was much greater than is the case for exams taken more recently. This means that organs which would be partially in the field by methods used after 1983 could have been totally in the x-ray field before 1964. Organs outside the field by 1984 standards might be partially or totally within the field before 1964.

In Gofman/O'Connor 1985 at page 171, we listed six organs in females which generate most of the cancer risk from an Upper G.I. Exam: Large intestine, kidneys, pancreas, breasts, stomach, and bronchi. But that is according to post-1980 standards of practice. The reason why breast does not head the list of such organs is that the breasts are not fully in the field. So, the estimated cancer risk to breasts is less than it would be if the breasts were fully in the x-ray field.

In the pre-1964 era (and our concern is for 1920-1960), the body parts exposed represented 3 times or more than the area needed to do the examination ---- and that wasted radiation brought the breasts essentially fully in the x-ray field for some exams, partially into the field for other common exams. And for some of the common exams, the position of the beam is sufficiently far enough away, that even with the wasted radiation, we consider that there was essentially no exposure of the breasts in such exams, for example, in the pelvic and hip exams. For such examinations, we shall list the breast dose as ZERO. This will all come together as we consider precisely how the estimates are actually made, in the text which follows.

As we now prepare to estimate the diagnostic radiology doses for 1920-1960, we shall have to take into account for each of the x-ray procedures just what fraction of the organ is in the x-ray field BEFORE we can apply the conversion factor from Roentgens of entrance exposure to rads absorbed by the organ --- in our case, the breast-pair. And we necessarily must take wasted radiation into account. We will let the reader know which organs are regarded as fully in the field and which are only fractionally in the field. Our analysis will give accounting for such differences in developing our final estimates of breast-doses from diagnostic radiology in the 1920-1960 period.

Part 3. Estimation of Diagnostic Radiology Doses for (1920–1960)**Step 1. What Were the Major Diagnostic X-Ray Procedures in Use?**

NCRP 100 provides a listing of the total number of such procedures in the United States, for the 1964 – 1980 period in Table 3.7 at page 15, based upon Mettler's work (1987). Our interest is in the tabulations for the 1964 period, since this is the closest to our 1920–1960 period. We shall need the frequencies listed here for developing a final weighted average dose per diagnostic procedure.

Examination	Number of Examinations (1964) (thousands)	Weighting Fraction
Skull	3,000	0.0442
Other Head and Neck	1,900	0.0280
Cervical Spine	2,900	0.0428
Chest Radiographic	32,400	0.4779
Abdomen (K-U-B)	2,800	0.0413
Cholecystogram	2,800	0.0413
Thoracic Spine	1,200	0.0177
Lumbar Spine	5,800	0.0855
Upper GI	5,500	0.0811
Barium Enema	3,000	0.0442
Pyelogram (Kidneys)	3,300	0.0487
Pelvis	2,100	0.0310
Hip	1,100	0.0162
Total, all listed exams	67,800	1.0000

Excluded are extremities, since those are not tabulated in our frequency per 100 diagnostic exams.

Excluded is Full-Spine, which is primarily a chiropractic exam, and has been treated in the chiropractic chapter, 22.

Excluded are mammograms, which are treated in a separate chapter.

Excluded are CT Scans, which were not available in the 1920–1960 period.

The weighting factors derived here will be applied to the doses per exam to reach our final conclusion of population average dose for 1920–1960. It is not possible to be certain that the relative distribution of exams was the same as in 1964, but any effects of variation of the distribution will not be a major factor in our dose estimation.

Step 2. Determination of the Dose for Each Complete Procedure

The basic data for each exam are provided both in Gofman/O'Connor 1985 and in Table 3.19 at pages 28–29 in NCRP 100. The entries are essentially identical in both sources, except for a minor difference in the estimated average number of films per procedure. We warn the reader that Entrance Exposure in NCRP 100 is given in coulombs per kilogram, whereas in Gofman/O'Connor, entrance exposure is given in Roentgens. NCRP does provide the conversion coefficient to Roentgens, the more familiar unit, by far.

We illustrate the procedure for determining breast-dose using the Upper Gastro-Intestinal Series data. And we shall comment for this and every other examination

whether we regard the organ to be fully in the x-ray field (in 1920–1960 practices) or not. If the organ is fully in the field, the breast-dose will be as calculated. If not fully in the field, we shall provide an estimate of the fraction of the calculated dose to be used.

Upper Gastro-Intestinal Examination

Col.A Beam Direction	Col.B Entrance Dose Roentgens	Col.C Rads to Breasts Rads	Col. D No. of Films	Col.E Beam HVL	Col.F Beam HVL Adjust.	Col. G Final Rads per Breast-Pair
AP	0.640	0.443	0.73	2.80	1.27	0.411
PA	0.547	0.020	1.15	2.86	1.55	0.036
LAT	1.147	0.210	0.05	3.01	1.61	0.017
OBL-PA	0.775	0.085	1.93	2.94	1.59	0.262
Total Avg Dose ----->					0.726 rads	

Explanations:

- - Col. A provides the kinds of directions of the x-ray beam going into the body.
AP (anterior-posterior) means the x-ray beam enters the front of the body and exits through the back of the body.
PA (posterior-anterior) means the beam enters the back, and exits through the front of the body.
LAT (lateral) means the beam enters one side of the body and exits the other side.
Detailed specification gives the information as to whether the beam enters the left side of the body or the right side. So we have LAT-LR and LAT-RL.
OBL-PA (Oblique posterior-anterior) means the beam enters half-way between the back and the side of the body. Had it been OBL-AP, it would have meant a beam entering half-way between the front and the side of the body.

• - Col. B provides the entrance dose in Roentgens. NCRP 100 gives this dose in coulombs per kilogram, which is convertible to Roentgens. We have used the NCRP 100 values, after conversion. They agree essentially perfectly with the Roentgen values for the various exams in Gofman/O'Connor 1985.

• - Col. C provides the dose in rads received by a specific organ for the entrance exposure and for the particular direction, if the organ is FULLY in the field. The values for dose per unit Entrance Exposure are in Table C, p. 404 of Gofman/O'Connor 1985. The entries for Female Breast are as follows (in rads per Entrance Roentgen):

Organ	Beam AP	Beam PA	Beam LAT-LR	Beam OBL-AP	Beam OBL-PA
Breast-Pair					
Female	0.693	0.037	0.183	0.438	0.110

All of these values are for a beam quality ("hardness"), expressed as a Half-Value Layer of 2.3 millimeters (mm) of Aluminum (Al.). This corresponds to 30 keV x-rays.

Thus, for the first line (AP) direction of beam, Col. C is obtained by multiplying 0.693 by Col.B entry in Roentgens.

$$(0.693 \text{ rads / Roentgen}) \times 0.640 \text{ Roentgens} = 0.443 \text{ rads}$$

But this is for one film and a beam quality of 2.3 mm Al. HVL.

• - Col. D provides the average number of films per examination (from NCRP 100). Of course, there are no fractional films. The fractional values reflect the taking of 0 films in some institutions, 1 film in others, 2 films in still others.

• - Col. E provides the Half-Value Layer in mm Al.

- - Col. F provides the adjustment factor for each HVL value.

Since these values are mostly not 2.3 mm Al., it is necessary to use an adjustment factor for all values other than 2.3 mm Al. Such adjustment factors are presented in Table D of Gofman/O'Connor 1985. For the AP direction and an HVL of 2.80 mm Al., the adjustment factor is 1.27, which is the value entered in Col. F.

- - Col.G. This is the final value in rads for organs fully in the x-ray field.

$$\begin{aligned}\text{Col. G entry} &= (\text{Col. C entry}) \times (\text{Column D entry}) \times (\text{Col. F entry}) \\ &= 0.443 \text{ rads/film} \times 0.73 \text{ films} \times 1.27 \\ &= 0.411 \text{ rads.}\end{aligned}$$

Since we consider that the breasts are essentially fully in the field with the wasted-radiation factor of the period 1920-1960, there will be no adjustment for this value of 0.411 rads for the AP view of Upper Gastro-Intestinal Exam.

This general procedure is followed for all other projections, PA, LAT, OBL-PA. The sum of all the rad doses in Col. G represents the total dose to breasts for this particular roentgen examination, for organs fully in the x-ray field.

All other examinations are handled similarly.

We can now calculate what the dose is for all the major diagnostic radiological exams to use for 1920-1960 estimates of combined dose.

CERVICAL SPINE

Col.A Beam Direction	Col.B Entrance Dose,R	Col.C Rads to Breasts	Col.D No. of Films	Col.E Beam HVL	Col. F Beam HVL Adjust.	Col. G Final Rads per Breast-Pair
AP	0.26	0.180	1.45	2.23	0.96	0.251
PA	0.15	0.006	0.04	2.43	1.07	0.000
LAT	0.17	0.031	1.27	2.35	1.02	0.040
OBL-PA	0.20	0.022	0.89	2.35	1.05	0.020
Total Average Dose						0.311 rads

Adjustment for breasts not fully in field = 0.5.

Final Average Dose 0.156 rads

RIBS

Col.A Beam Direction	Col.B Entrance Dose,R	Col.C Rads to Breasts	Col.D No. of Films	Col.E Beam HVL	Col. F Beam HVL Adjust.	Col. G Final Rads per Breast-Pair
AP	0.357	0.247	0.87	2.24	0.97	0.209
PA	0.289	0.011	0.80	2.44	1.07	0.009
LAT	0.186	0.034	0.08	2.98	1.34	0.004
OBL-PA	0.627	0.069	1.20	2.38	1.05	0.087
Total Average Dose						0.308 rads

No adjustments for organ not fully in field.

Final Average Dose 0.308 rads

• - Note: The unseen "trailing digits" in the calculations sometimes cause results to look "off" in very small ways.

SHOULDER (We cut Column C in half, since exam is of one shoulder.)

Col.A Beam Direction	Col.B Entrance Dose,R	Col.C Rads to Breasts	Col.D No. of Films	Col.E Beam HVL	Col. F Beam HVL Adjust.	Col. G Final Rads per Breast-Pair
AP	0.194	0.067	1.45	2.15	0.92	0.089
PA	0.147	0.003	0.04	2.10	0.83	0.000
LAT	0.973	0.089	0.15	2.53	1.22	0.016
OBL-PA	0.306	0.017	0.13	2.30	1.00	0.002
				Total Average Dose		0.108 rads

No adjustments at all for breasts not fully in x-ray field.

Final Average Dose 0.108 rads

THORACIC SPINE (WIDE)

Col.A Beam Direction	Col.B Entrance Dose,R	Col.C Rads to Breasts	Col.D No. of Films	Col.E Beam HVL	Col. F Beam HVL Adjust.	Col. G Final Rads per Breast-Pair
AP	0.663	0.459	1.07	2.37	1.04	0.511
PA	0.516	0.019	0.00	2.50	1.19	0.000
LAT	1.457	0.267	0.93	2.42	1.12	0.278
OBL-PA	0.756	0.083	0.12	2.42	1.12	0.011
				Total Average Dose		0.800 rads

No adjustments at all for breasts not fully in x-ray field.

Final Average Dose 0.800 rads

CHOLECYSTOGRAM (Gall-Bladder)

Col.A Beam Direction	Col.B Entrance Dose,R	Col.C Rads to Breasts	Col.D No. of Films	Col.E Beam HVL	Col. F Beam HVL Adjust.	Col. G Final Rads per Breast-Pair
AP	0.543	0.376	0.48	2.46	1.08	0.195
PA	0.547	0.020	1.41	2.41	1.11	0.032
LAT	0.752	0.138	0.13	2.51	1.20	0.021
OBL-PA	0.744	0.082	1.21	2.52	1.21	0.120
				Total Average Dose		0.368 rads

No adjustments at all for breasts not fully in x-ray field.

Final Average Dose 0.368 rads

LUMBAR SPINE

Col.A Beam Direction	Col.B Entrance Dose,R	Col.C Rads to Breasts	Col.D No. of Films	Col.E Beam HVL	Col. F Beam HVL Adjust.	Col. G Final Rads per Breast-Pair
AP	0.884	0.612	1.03	2.37	1.03	0.650
PA	0.543	0.020	0.03	2.48	1.09	0.001
LAT	3.198	0.585	1.33	2.58	1.26	0.981
OBL-PA	1.109	0.122	0.46	2.51	1.20	0.067
				Total Average Dose		1.698 rads

No adjustments at all for breasts not fully in x-ray field.

Final Average Dose 1.698 rads

ABDOMEN (KIDNEY-URETER-BLADDER)

Col.A Beam Direction	Col.B Entrance Dose,R	Col.C Rads to Breasts	Col.D No. of Films	Col.E Beam HVL	Col. F Beam HVL Adjust.	Col. G Final Rads per Breast-Pair
AP	0.663	0.459	1.28	2.54	1.12	0.658
PA	0.419	0.015	0.23	2.45	1.15	0.004
LAT	2.097	0.384	0.07	2.51	1.20	0.032
OBL-PA	1.221	0.134	0.11	2.44	1.14	0.017
				Total Average Dose		0.712 rads

No adjustments at all for breasts not fully in x-ray field.

Final Average Dose 0.712 rads

BARIUM ENEMA

Col.A Beam Direction	Col.B Entrance Dose,R	Col.C Rads to Breasts	Col.D No. of Films	Col.E Beam HVL	Col. F Beam HVL Adjust.	Col. G Final Rads per Breast-Pair
Barium Enema						
AP	0.760	0.526	1.52	2.95	1.33	1.064
PA	0.771	0.029	0.93	2.92	1.58	0.042
LAT	4.012	0.734	0.49	3.12	1.67	0.601
OBL-PA	1.349	0.148	1.02	3.05	1.66	0.251
				Total Avg Dose		1.958 rads

Adjustment for breasts not being fully in field = 0.33

Final Average Dose 0.646 rads

INTRAVENOUS PYELOGRAM (Kidney Exam)

Col.A Beam Direction	Col.B Entrance Dose,R	Col.C Rads to Breasts	Col.D No. of Films	Col.E Beam HVL	Col. F Beam HVL Adjust.	Col. G Final Rads per Breast-Pair
AP	0.597	0.414	4.51	2.47	1.08	2.015
PA	0.442	0.016	0.20	2.53	1.22	0.004
LAT	0.527	0.096	0.04	2.59	1.27	0.005
OBL-PA	0.915	0.101	0.70	2.59	1.26	0.089
				Total Avg Dose		2.112 rads

Adjustment for breasts not being fully in field = 0.33

Final Average Dose 0.697 rads

CHEST

Col.A Beam Direction	Col.B Entrance Dose,R	Col.C Rads to Breasts	Col.D No. of Films	Col.E Beam HVL	Col. F Beam HVL Adjust.	Col. G Final Rads per Breast-Pair
AP	0.050	0.035	0.10	2.44	1.07	0.004
PA	0.027	0.001	0.92	2.51	1.20	0.001
LAT	0.081	0.015	0.50	2.80	1.47	0.011
OBL-PA	0.120	0.013	0.02	2.49	1.19	0.000
				Total Avg Dose		0.016 rads

No adjustments at all for breasts not fully in x-ray field.

Final Average Dose 0.016 rads

PELVIS exam gives just about 0 rads to breast --- too low in position

Final Average Dose 0.00 rads

HIP exam gives just about 0 rads to breast---- too low in position.

Final Average Dose 0.00 rads

SKULL seems too high to affect the breasts

Final Average Dose 0.00 rads

OTHER HEAD AND NECK

It is reasonable to take the average of skull and cervical spine doses.

$(0.156+0.00)/2 = 0.078$ rads

Final Average Dose 0.078 rads

Now we list the estimated total number of diagnostic x-ray procedures and their dose in order to obtain an overall average dose.

Exam	Breast		Rads Times	
	Rads	Access	Frequency	Frequency
Skull	0.000		3,000	0.0
Other Head and Neck	0.078		1,900	148.2
Cervical Spine	0.156	(0.5)	2,900	451.0
Chest Radiographic	0.016		32,400	518.4
Ribs	0.308		NA	Not calculated
Shoulder (One)	0.108		NA	Not calculated
Abdomen (KUB)	0.712		2,800	1993.6
Cholecystogram	0.368		2,800	1030.4
Thoracic Spine	0.800		1,200	960.0
Lumbar Spine	1.698		5,800	9848.4
Upper GI	0.726		5,500	3993.0
Barium Enema	0.646	(0.33)	3,000	1938.4
Pyelogram	0.697	(0.33)	3,300	2300.0
Pelvis	0.000		2,100	0.0
Hip	0.000		1,100	0.0

Sum 67,800 23181.34

Dose for Average Exam ----> 0.342 rads

Dose to breasts per person = (0.342 rads per exam) x (exams per person).

This follows since we have calculated the mean dose from all exams, excluding exams of extremities.

Medical Radiographic Examinations 1920-1960: Each yielding 0.342 rads to breast.

Age Group	Number of Exams per Person	Breast Dose (Rads) per Person	
Under 15 years	0.16	0.055	
15-24 years	0.42	0.144	
25-34 years	0.56	0.192	
35-44 years	0.65	0.222	
45-54 years	0.72	0.246	
55-64 years	0.73	0.250	
65-74 years	0.73	0.250	

Now we shall consider the additional dose from fluoroscopic exams.

We shall very conservatively estimate the fluoroscopic exposure at 3 Roentgens per exposure, at a beam half-value layer of 2.3 mm Al. In view of the discussions above concerning limiting fluoroscopic exams to 100 Roentgens per exam in New York, it

would be hard to consider 3 Roentgens of entrance dose per average fluoroscopy in 1920-1960 as any sort of OVERestimate. By contrast, the entrance dose from each pediatric fluoroscopy was estimated by Buschke and Parker (1942, p.527) to be 8 Roentgens if the examiner was skilled, or considerably higher if the examiner was inexperienced. Below, however, readers will see that we use ZERO as the annual average breast-dose from fluoroscopy for children below age 15.

For all the other ages, we will pretend that the fluoroscopic beam was never used from front to back (the AP view) --- an unrealistic approximation which clearly results in an underestimate of breast-dose for ALL the age-groups below. Additionally, we will assume that only one-third of the fluoroscopies exposed breast tissue. So we calculate as follows:

For breast in PA view, 0.037 rads per Roentgen for 2.3 mm Al as half-value layer.

For 3 Roentgens exposure, total dose = $3 \times 0.037 = 0.111$ rads.

And assume only 1/3 of the fluoroscopies affected the breast tissue.

Breast Dose from fluoroscopic examinations, = $(1/3) \times 0.111 = 0.037$ rads.

No adjustment for beam hardness is needed at 2.3 mm Al half-value layer.

Fluoroscopic Examinations (including spot films and plates)

Age Group	Number of Exams per Person	Average	
		Breast-Dose in Rads per Person, per Year	
Under 15 years	0.01	0.000	
15-24 years	0.03	0.001	
25-34 years	0.05	0.002	
35-44 years	0.09	0.003	
45-54 years	0.12	0.004	
55-64 years	0.13	0.005	
65-74 years	0.15	0.006	

Final Total Doses to Breasts at Various Ages, Roentgenograms + Fluoroscopic Exams

Age Group	Breast Dose per Person (films)	Average		Rads, Total Breast-Dose per Person
		Breast-Dose per Person (fluoroscopic)	Breast-Dose per Person	
Under 15 years	0.055	+	0.000	0.055
15-24 years	0.144	+	0.001	0.145
25-34 years	0.192	+	0.002	0.194
35-44 years	0.222	+	0.003	0.225
45-54 years	0.246	+	0.004	0.250
55-64 years	0.250	+	0.005	0.255
65-74 years	0.250	+	0.006	0.256

Transfer of Source Data to the Master Table (Col.P)

This final tabulation, taking into account roentgenographic and fluoroscopic exams, exceedingly conservatively stated, will provide entries for every single age-year in the Master Table, Column P.

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CHAPTER 24

Occupational Sources of Breast Irradiation

Part 1. Efforts to Learn About Early Exposure in Radiological Occupations

It would be very difficult to believe that appreciable exposure to nurses, technicians, orderlies, physicians, office assistants, medical residents and fellows did not occur in the 1920, 1930, 1940, and 1950 periods. In the early 1950s we have a very good study from one of the leading institutions, the Cleveland Clinic, done for the purpose of estimating actual worker exposure in a reasonable manner.

Geist, Glasser and Hughes (1953) wrote:

"Within recent years there has been a considerable increase in the use of x-rays and radioactive substances in the diagnosis and treatment of disease. As a result the problem of adequate protection has become greatly magnified."

The Cleveland Clinic and its associated hospital is a very large and prestigious institution. Those who reported the study of worker exposure endeavored to ascertain the doses being received (or not received) by all categories of personnel involved in essentially every activity involving ionizing radiation within the Clinic and the hospital.

The study, involving 84 persons, was conducted over a period of three months. The technique employed for dose measurement was that of film badges. Badges were worn for one week by employees, returned to Tracerlab, Inc. in Boston, and developed by Tracerlab. The results were reported back in milli-Roentgens (mR) per week. New badges replaced the prior badge each week, for a total period of 3 months. We can presume that the measure being obtained is that of whole-body radiation, and that hence the breasts would have received some radiation from anterior, lateral, and posterior entry of x-rays.

A Drawback to the Study

There is every reason to consider that this study was well executed. However, there is a lesson from experience which teaches us that the measured doses were undoubtedly too low for a very specific reason. The employees know that it would be "inappropriate" for management to think they were being careless about doses being received, and would therefore be on their best behavior during the three-month period of such a trial evaluation. Anyone dealing with laboratory procedures knows that when employees KNOW they are under test, the performance is far better than when the test is introduced unknown to the employees. We have had an extensive experience in this regard. There is no way that this particular test could have been done in a "blinded" fashion, so we must assume that the results obtained will show a lower dose than that which truly characterized operations at the Cleveland Clinic before or after the period of testing performance. We will therefore not be overestimating the true exposure by examining these results.

An Urge Which Could Not Be Suppressed

Consider a story from the 1941 paper by Dean Cowie and Leonard Scheele. They did a survey of 45 hospitals (in 24 states) to which radium had been provided for medical use. The purpose of their on-site visits was to study not only the storage and handling of

the radium, but also the exposure of hospital personnel from the administration of diagnostic and therapeutic x-rays (1941, p.769). For example (p.777):

"In spite of adequate shielding, practices were noted that led to overexposure. One technician entered the deep therapy room to talk with the patients or to reposition them after they moved without turning off the high voltage on the tube. It was not possible to ascertain how often this occurred, but during our visit it was done spontaneously several times, and an ionization chamber in the technician's pocket showed that she received 0.75 r during her stay in the room."

It is very likely that this observed behavior represented only the residual "bad behavior" after everyone was trying to display "best behavior" for the evaluators.

Readers who doubt that occupational doses were higher than reported in the Cleveland Clinic Study, may well change their minds when they read some hair-raising stories of how RADIUM in hospitals was often handled --- as observed by Cowie and Scheele in their survey (see Chapter 35).

Part 2. The Actual Conduct of the Survey

We shall trace the various activities evaluated, and record the doses received in each activity. As a reference point, we can note that the so-called maximum permissible dose for exposure of the whole body to x, gamma, and beta radiation was 0.3 R per week, as recommended by the International Commission on Radiological Protection. Geist et al state that whenever the survey revealed that this level was exceeded as measured by the film badges, a further investigation was launched to determine the cause and ameliorative procedures were instituted. Such ameliorative procedures do not reduce exposures in any past activities. And, as a matter of realistic expectations, such ameliorative procedures tend to be forgotten once the test period is over.

The Major Divisions of the Study

The institution is divided into the outpatient Clinic and the Hospital. Separate facilities involving use of ionizing radiation were present in both Clinic and Hospital.

The radiation work is also subdivided by the categories of diagnostic roentgenology and radiation therapy. We shall consider the findings in both of these activities.

We shall describe the work by denoting (a) the department, (b) the number of persons involved, and (c) the estimated annual whole-body dose received for 50 weeks of work per year. The results provided to the Cleveland Clinic by the Tracerlab Company are in milli-Roentgens per week, since the badges were changed weekly. When a badge is returned with no exposure noted, we know that the dose received is somewhere between zero and the limit of detection of dose. Our prior experience indicates that the detection limit is between 10 and 20 mR (milli-Roentgens). We shall assume 20 mR as the detection limit, and record all doses as 10 mR when the report returned indicates no exposure.

Diagnostic Roentgenology in the Cleveland Clinic (Outpatient)

Category	Number	Roentgens per year	Person-Roentgens per year
Radiological Technicians	12	15	180.0
Receptionists	4	0.5	2.0
Secretarial	5	0.5	2.5
Darkroom Operators	4	0.5	2.0
Film Transferers	6	0.5	3.0
Film Distribution	??	0.5	??
Staff Radiologists	5	5.1	25.5
Fellows in Radiology	8	5.1	40.8
Genito-Urinary Technician	1	4.5	4.5
Dental Technician	1	7.5	7.5
Catheterization Lab, Nurse	1	1.1	1.1
Catheterization Lab, Physician	1	4.5	4.5

Diagnostic Roentgenology in the Hospital (In-Patient)

Radiological Technicians	2	2.43	4.9
Surgical Rad. Technician	1	5.0	5.0
Surgical, Cerebral Arterio- graphy, Neurosurgeon	1	6.9	6.9
Surgical, Angiocardiography			
Cardiologist	1	4.6	4.6
Cardiologist assistant	1	4.6	4.6
Radiologist	1	4.6	4.6
Radiologist assistant	1	4.6	4.6
Surgical, Aortography			
Urologist	1	1.6	1.6
Surgical, Cholangiography			
Surgeons	2	3.4	6.8

Therapeutic Roentgenology Departments

Radiologists for x-ray			
therapy and isotope use.	2	4.5	9.0
Fellow in Radiology	1	0.8	0.8
Radium and Radon Handling			
Fellows in Radiology	2	10.7	21.4
Assistant in Biophysics	1	10.7	10.7
Otolaryngology; Radium applicator. Physician	1	3.1	3.1
Ophthalmology, Beta Sources. Physician	1	1.0	1.0

Therapeutic Roentgenology in the Hospital (In-Patient): Continued, next page.

Therapeutic Roentgenology in the Hospital (In-Patient) (Continued)

Category	Number	Roentgens per year	Person-Roentgens per year
Dermatologists, Superficial			
Therapy (100 kv)	1	5.3	5.3
Biophysics, Head	1	1.0	1.0
Assistant	1	1.0	1.0
Total Persons Accounted For:	70	Sum	367.8 Pers.-Roent.

We must presume the remaining persons of the total of 84 were not engaged in operations that might result in exposure.

We may note a couple of features of this tabulation. The outpatient radiological technician data are given only as less than 300 mR per week. But we also have a note that there were nine exceptions, in which this limit was exceeded. We have therefore used 300 mR per week, assuming possible balance between the overexposures and some of the under-300 mR exposures.

Technicians Who Hold Patients While Beam Is "On"

In two categories, for the diagnostic radiologic technicians and the dermatologists, it was noted that exposures were increased by the practice of holding patients during radiological procedures. For the dermatologists, it was explicitly stated that the holding was of infants. The practice of staying with and holding patients was reported also by Cowie and Scheele (1941, p.777):

"A technician in another hospital sat with or held many foreign-language-speaking patients during superficial therapy. She did this on an average of three times weekly and received an average of 1.5 r per treatment. Her daily average on a 5-day basis was approximately 1.0 r."

What Happens without Perpetual Vigilance?

Cowie and Scheele continue (p.777): "A number of other improper practices leading to overexposures were noted, but in the majority of hospitals, practices were excellent. The radiologists in charge in the institutions where overexposure of roentgen-ray therapy technicians occurred had not been checking the work of their technicians and were unaware that these breaks in technique occurred. Close and careful supervision is important."

Part 3. Analysis of the Data from the Cleveland Clinic

$$\text{Mean Annual Exposure} = 367.8 \text{ person-Roentgens} / 84 \text{ persons} = 4.38 \text{ Roentgens.}$$

It would be difficult to estimate how we could extend these Cleveland Clinic data to the national scene directly, but we can place some likely limits on the national doses indirectly with some data from UNSCEAR 1977 (page 243, para.87 and 88). Klement and co-workers (1972) estimated 194,541 medical x-ray workers, and UNSCEAR 1977 (at

p.243) cites a number of 38,000 individuals engaged in radium therapy work, for a total of 232,500 workers, rounded off, in the USA.

The Cleveland Clinic study was done 20 years earlier. A reasonable approximation would be for us to cut the 1972 worker total in half, which gives a total of 116,250 workers engaged in medical x-ray and radium work. We should cut this value in half again, to consider just female workers. Therefore, the estimated early period total for female medical x-ray workers would be 58,125 workers. And we consider this to be a reasonable approximation for the average year in 1920-1960.

We estimate 4.38 Roentgens as the annual exposure based on the Cleveland Clinic results.

$$(58,125 \text{ workers} \times 4.38 \text{ Roentgens}) = 254,588 \text{ person-Roentgens.}$$

We can distribute these person-Roentgens into 25 age-year categories, assuming the workers employed were equally distributed from age 20 to age 45 years.

$$254,588 \text{ person-Roentgens} / 25 \text{ age-year categories} = 10,184 \text{ person-Roentgens per category.}$$

But our interest is in breast-doses. Since these person-Roentgens are for whole-body radiation exposure, and since essentially all film badges are worn on the front of the body, person-Roentgens received from the back are already corrected to rads by the passage through the body before reaching the film-badge. The posterior irradiation, after going through the body, contributes negligibly to the total dose. We shall therefore assign all 10,184 Roentgens to radiation received from the front of the body. But we must now convert the person-Roentgens to person-rads.

$$(10,184 \text{ person-Roentgens}) \times (0.693 \text{ rads per Roentgen}) = 7,058 \text{ person-rads.}$$

We must now convert the person-rads of the exposed workers into the population dose.

For this, we need the value in Column A of the Master Table. Let us illustrate by making the calculation for women in 20th age-year group. Column A entry is 885,914 women.

$$\begin{aligned} \text{Average breast-dose} &= 7,058 \text{ person-rads} / 885,914 \text{ women} \\ &= 0.00797 \text{ rads to the breasts.} \end{aligned}$$

We enter (7,058 person-rads / Column A population) into Column Q of the Master Table for ages 20 through 44 years, to provide the average breast-doses for medical occupational exposure. We consider that this approach represents a conservative underestimate of this dose.

#

1957

Unwelcome Evidence — from the Irradiated Children

Below, we will quote from:

C. Lenore Simpson and Louis H. Hempelmann, "The Association of Tumors and Roentgen-Ray Treatment of the Thorax in Infancy," CANCER Vol.10 No.1: 42-56. January-February 1957.

Simpson and Hempelmann are extremely cautious in stating that their series of children treated for thymus enlargement really were experiencing radiation-caused neoplastic disease. We quote at pages 51-52:

"In all retrospective field studies of this nature, the establishment of suitable control material is a major difficulty. We have pointed out some of the advantages and disadvantages of our controls but feel we have established a definite increase in neoplastic disease among our treated children. We have raised the question whether radiation is responsible for this increase. Although we feel this point will be settled only when further studies have been made, it is of interest to examine the evidence at present available. There are indications from our own data that the tumor incidence varies with the type of radiation given. There are other clinical observations in man, and there is a large amount of evidence from animal experiments indicating that ionizing radiation is cancerogenic."

And at page 52:

"Malignant change occurring in heavily radiated tissue has been recognized for many years, first in the skin of the early radiologists and then in the bones. The part played by radiation in the etiology of such tumors has been recognized because the incidence is high, the tumor is in an unusual site, or chronic radiation damage preceded the onset of the cancer. The extensive literature on the subject has recently been reviewed by Hueper. Prior to the present study there has been little evidence that tumors would follow doses of less than 1000 r. There was also little evidence that radiation could induce thyroid cancer in man."

CHAPTER 25

Weapons-Test Fallout, Pre-1960, and Breast Dose

For our considerations of the 1920-1960 breast-irradiation-doses, we wish to include only doses up to 1960 from weapons testing. For 1960 and beyond, such irradiation will be considered in further research on this topic. While we shall see in this discussion that weapons-test fallout contributes very little to the 1920-1960 breast-doses, the much larger fraction of the fallout in the years beyond 1960 implies that a larger contribution from weapons-test fallout can be anticipated in the post-1960 period.

Since there were no doses of any consequence before 1945, we have 62% of the 1920-1960 period without ANY contribution of fallout to dose. The period 1945-1960, or 38% of the total years, needs an estimate of dose contribution. Whatever that total dose-contribution is, it will be divided by 40 for the total years, 1920-1960.

Two Major Classes of Radionuclides

There are two major classes of radionuclides, those of very short half-lives, and those of relatively long half-lives. For those of relatively long half-lives (such as strontium-90 and cesium-137), the radiation dose PER YEAR is a small fraction of the ultimate dose-commitment. Since we are dealing with YEARLY radiation doses in this analysis of breast-cancer, we need to consider nuclear test fallout doses on a per-year basis. For those radionuclides of very short half-lives, material injected into the stratosphere largely decays before returning to earth, and hence much of the potential dose does not occur.

The Time-Distribution of Fallout Deposition

UNSCEAR 1977 (Annex C) Table 2 (at p.122) provides some of the requisite information. We have there the annual deposition and cumulative deposition of strontium-90 up through January 1976. We shall, of course, use the data for the Northern Hemisphere, since pre-1960 fallout was largely there.

Strontium-90 Deposition

Year	Deposition in Mega-Curies
Pre-1958	1.80
1958	0.63
1959	1.05
1960 to Jan. 1976.	8.65
<hr/> Grand total	12.13

Therefore, we have the approximation that before 1960, 3.48 mega-Curies out of a total of 12.13 mega-Curies, or about 28.7 % of the total, fell out. As a good approximation, we shall state that the cesium-137, the other prominent long-lived radionuclide, fell out quantitatively, before and after 1960, as did strontium-90.

The Short-Lived Radionuclides

The combination of Ce-144, Ru-106, Zr-95, Ru-103, Ce-141, and Ba-140 (plus their short-lived daughters) provide the major share of worldwide exposure in the very early years post-test.

At Table 26, p.153 of UNSCEAR 1977, external radiation from short-lived nuclides is given as 48 milli-rads. As a reasonable approximation for the pre-1960 period, we multiply this value by the same fraction, 0.287, as used for strontium-90. External dose from short-lived nuclides before 1960 is (0.287×48) , or 13.8 milli-rads.

While we believe UNSCEAR has overestimated the correction for body shielding of the breast, we shall, as part of our conservative approach, utilize their values for organ doses directly, and we shall accept 13.8 milli-rads as dose to the breasts for the short-lived gamma-emitters during the 1945-1960 period.

The Long-Lived Radionuclides: Cesium-137 and Strontium-90

At Table 26, the dose contribution from external Cs-137 is given as 62 milli-rads (lifetime commitment). Using our 0.287 factor, we have 0.287×62 , or 17.8 milli-rads. Gofman (1990, Ch.36, p.29) provides the datum that cesium-137 external dose during first 10 years is 20% of the all-time total. And since the pre-1960 period means less than 10 years since deposition, on the average, we can say external Cs-137 dose is less than 20% of total, or less than 20% of 17.8 milli-rads, or 3.6 milli-rads. Let us assign one-half of this value, or 1.8 milli-rads, for the shortness of the exposure period.

Total dose in the early period (before 1960) = $13.8 + 1.8$, or 15.6 milli-rads delivered to breast from all external gamma-emitting sources.

For internal dose from Cs-137, it is estimated that 95% of the total effect is attained in a few years after deposition. The general rule is that internal / external dose, for Cs-137, is 3 / 7. But since the internal commitment is nearly over a few years after deposition, we must use the total external committed Cs-137 dose, which is 17.8 milli-rads, to be multiplied by (3/7), and this gives a value of 7.6 milli-rads for internal breast dose from Cs-137.

So, for the early period, total external dose to breast = 15.6 milli-rads. And for the same period, total internal dose to breast = 7.6 milli-rads. Combined total, internal plus external = 23.2 milli-rads to breast.

What about dose from strontium-90? Up to 1960, we can neglect it. This nuclide, having no gamma ray, delivers no breast-dose when it is external to the body. And the internally deposited strontium would add very little to the breast-dose during this short period of time (pre-1960). However, by also ignoring the external and internal dose from cesium-134 (radiological half-life of 2.06 years), we do underestimate dose here.

The Total Breast-Dose up to 1960

The 23.2 milli-rads must be divided by 40 to obtain the AVERAGE year's contribution to dose in the 1920 to 1960 period.

Therefore, final entry, for all ages, in the Master Table, for fallout from weapons testing is $(23.2 / 40)$, or 0.58 milli-rads per year of high-energy radiation. And since all our entries in the Master Table are in MEDICAL RADS, we first convert to rads, and then divide by 2 to correct to medical rads. The final result in medical rads to transfer to the Master Table, Column "O," is 0.00029 medical rads per year for the average year of 1920-1960 period.

CHAPTER 26

The Beauty Shop as a Source of Breast Irradiation

Beauty shops with x-ray machines, with beauticians as the operators? We realize that this chapter may evoke the feeling, "It just can't be true!" Sadly, it was true. And undoubtedly there have been breast-cancers induced by this particular mis-use of roentgen radiation.

We learned about the use of x-ray machines in beauty shops in a 1930 paper by Dr. Henry Hazen. He is the same person who, in 1921, presented a paper entitled "The Roentgen-Ray Treatment of Diseases of the Skin" before the American Roentgen Ray Society (Hazen 1922). In his 1921 presentation, he both praised the efficacy of roentgen rays in dermatology and warned about the "disastrous results" impending from the post-war rush into roentgen therapy by physicians "with totally inadequate training." Physicians, not beauticians.

We quote Dr. Hazen on both points (1922, p.254):

"Roentgen rays are probably the most useful single therapeutic agent that the dermatologist possesses today. It is of the greatest value in both malignant and benign tumors, keratoses, warts, eczema, acne, lichen planus, some forms of tuberculosis, sycosis and folliculitis of the back of the neck, tinea tonsurans, tinea barbae, some cases of pruritis, granuloma annulare and mycosis fungoides."

And the warning by Dr. Hazen:

"At the same time a word of warning must be issued, for since the war scores of physicians with totally inadequate training are rushing into roentgen-ray therapy and it is certain that some disastrous results will follow ..."

Would Professor Hazen have believed, in 1921, that he might one day encounter something even more troubling than inadequately trained physicians doing roentgen therapy?

X-Ray Machines and Operators with NO Training

In 1930, Dr. Hazen published a paper entitled "Injuries Resulting from Irradiation in Beauty Shops," in the American Journal of Roentgenology and Radium Therapy. We were amazed.

He relates (Hazen 1930, p.409):

"About five years ago a number of beauty shops in various cities installed roentgen machines for the purpose of treating superfluous hair. It is well known that from 1 to 2 mm. of aluminum was used as a filter. However, treatment was given for other conditions than hypertrichosis [excess, unwanted hair]. In my list is one who alleged that she was treated for acne, and another who alleged she was treated for freckles. The ten women who form the basis for this study state that their injuries were received in one or another beauty shop in the East." And:

"In various meetings there have been many reports of damage to the skin alleged to be due to roentgen-ray treatment in beauty shops, but so far there have been no reports of

damage to the gums as a result of this treatment. In this series of 10 cases no less than 7 women have received serious damage to their gums. This fact seems worthy of record."

And Were Breasts Irradiated Too?

We are especially concerned about breasts in the "beauty-shop" problem, because hypertrichosis (unwanted, excess hair) in the nipple-region or in the arm pits is a common phenomenon. To the extent that some beauty-shops used x-rays to remove such hair, appreciable areas of the breasts were surely in the x-ray beam during the procedures.

In earlier chapters, we have already mentioned erythema (reddening of the skin) and the "erythema dose" as about 300 Roentgens. Although Dr. Hazen does not mention breasts, he reports erythema as a prominent feature of his investigation, which means that some beauty-shops were delivering massive doses.

After describing the physical features found in the injured women, Dr. Hazen wrote further (p.411):

"It is worthy of note that in every instance there is the history of an erythema following the third or fourth treatment and of subsequent radiation being given in the presence of it. One can only marvel at the stupidity of the operators, and the fortitude or ignorance of the victims. Any move that can be made to protect beauty-seeking women from their own folly is to be commended. It is amazing that in many communities medical practice acts include only the prescribers of drugs, and permit any type of physiotherapist to apply his trade without let or hindrance, with a total disregard for the potential dangers of the therapeutic procedure."

The "Beauty-Shop Roentgen Department"

There is no way we can provide a set of numbers for the Master Table from the "beauty-shop roentgen department." How many such places were there? How many customers per year were concerned about armpit hair? What was their average breast-dose? How many years did such shops operate? We doubt that anyone could estimate an annual average breast-dose for 1920-1960 from this source.

It is certain, however is that the "beauty-shop roentgen department" did put a number of totally preventable breast-cancers "on the shelf" for delivery, gradually, in subsequent decades.

What we wish to emphasize for readers of this book --- women in all walks of life, physicians, and researchers --- is that here is just one of many examples of radiation exposure to the breasts NOT RECORDED ANYWHERE, except in the genes and chromosomes of breast-cells.

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CHAPTER 27

Yes, We Do Have Your Size: Shoe-Fitters and Breast Irradiation

Part 1. Shoe-Store Fluoroscopy: Enjoyed by Children Almost Everywhere

Two remarkably interesting papers appeared in the New England Journal of Medicine, back to back, in September 1949. We might have anticipated them without surprise in 1929, or in 1939. But they appeared in 1949. Both are well-written and impart quite useful information --- albeit a little late, which is no fault of the authors of the papers.

The first paper is by Charles R. Williams, Ph.D., and is entitled, "Radiation Exposures from the Use of Shoe-Fitting Fluoroscopes." We cite the first paragraph of this paper:

"It is now common practice in many shoe stores and shoe departments of department stores to supplement usual shoe-fitting methods by the use of fluoroscopes known as 'x-ray shoe fitters.' Because this technic has spread rapidly throughout the United States, particularly in stores specializing in children's shoes, it is desirable to know precisely the exposures to irradiation received by customers, as well as by clerks and other persons in the area of x-ray shoe-fitting units." We note that the machines were "particularly in stores specializing in children's shoes."

I recollect having used these "x-ray shoe fitters" during my childhood which was mostly before 1930, in Cleveland, Ohio. The shoe-fitter is a vivid childhood memory for countless people. And when did the shoe-fitter infiltrate small-town America? I learned by casual inquiries that it was present before 1930 even in some small towns. Yet only in 1949 did it become "desirable" to learn something about the radiation doses which it was delivering.

It says a lot about the powerful wish for new technologies to be harmless, that the machine was widely spread throughout the United States BEFORE any attention was given to doses received by children, parents, shoe-store personnel, and non-participating customers. Did no one care any earlier about making some measurements, in light of all the warnings about the hazards of fluoroscopy in medical practice? Such warnings from Leddy (1937), Braestrup (1942), Buschke/Parker (1942), and others, are presented in Chapter 31. For example, referring to one model of medical machine which put out 127 Roentgens per minute, Carl Braestrup warned in 1942:

"Such a unit could be classified as a lethal diagnostic weapon, and yet there are many of these still in use."

Dr. Braestrup was talking about certain medical fluoroscopes. As for the shoe-fitting fluoroscopes, at what rate of Roentgens per minute did they operate? Dr. Williams (1949) reports on that, and we will discuss his findings in Part 3. Here, we will just say that, at the high end, Dr. Williams found shoe-fitters with an output of 348 Roentgens per minute. It will become clear, as we continue, how these shoe-fitters delivered some BREAST-irradiation.

Part 2. For Repeated Exposures, Just Press the Button!

The second paper of 1949 is by Louis Hempelmann, M.D., and is entitled "Potential Dangers in the Uncontrolled Use of Shoe-Fitting Fluoroscopes." Some mothers, seeing that title in 1949, might have said, "And NOW they tell us?"

Let us look at the concluding (summary) paragraph of Dr. Hempelmann's paper:

"It may be said that the type of radiation injury most likely to result from the unsupervised use of low-voltage fluoroscopes in shoe stores is the malformation of the feet of growing children. Such deformities may occur in the absence of x-ray reactions of the skin. Skin damage of the feet of customers and injury of the blood-forming tissues of store employees are possible consequences of the misuses of the shoe-fitting fluoroscopes. These dangers can be controlled by proper regulation of the use of the machines."

But what, in fact, DID regulate use of the machines?

A mother in 1949 might recollect the last time she was in the shoe store with her children, and they were savoring the novelty of examining the bones in their feet as they wiggled their toes. The machine shut itself off after a little while, and all you had to do to start the entire cycle again, was to press a button. And that is exactly what Dr. Williams reported (p.333):

"A push-button automatic timer, which can be set for any predetermined time, is included on most installations. In actual use exposure times have been found to vary from five to forty-five seconds, although twenty seconds appears to be the most popular setting. REPEATED EXPOSURES CAN BE MADE BY RELEASING AND PUSHING OF THE BUTTON [emphasis in the original]."

Also, we learn from Dr. Williams: "More recent models are equipped with three separate switches providing three different intensities --- one for men, one for women and one for children." That can not represent a serious effort to prevent overuse.

Part 3. Foot-Fitters versus Breast-Fitters: How Lucky We Were

The shoe-fitter machines contained a 50 kilovolt x-ray tube, operating at 3 to 8 milliamperes through a 1-mm aluminum filter. The tube was housed in a case lined with lead or steel and containing a fluorescent screen. The kilovoltage was relatively low compared to many medical machines, so deep tissues were less at risk. However, 50 kv is sufficiently high to produce carcinogenic injuries in breast tissue.

The Doses to Feet

Williams established with a series of measurements on 12 separate units that the dose received by the foot was directly proportional to the time that the fluoroscope operated with each button-press. Measurements were done with a Victoreen Roentgen meter placed inside a shoe which was itself put into the opening for the person's foot.

The range of measured dose-rates is indeed astounding to us --- from 0.5 to 5.8 Roentgens per second. So for a twenty-second exposure ("the most popular setting"), doses ranged from 10 to 116 Roentgens delivered to the feet of the customer (p.333). This, of course, was the exposure for a SINGLE FITTING experience, with no extra pushes on the actuating button.

Some of these are really very high output machines --- 5.8 Roentgens per second, inside the shoe, means an exposure of 348 Roentgens per minute, as noted in Part 1.

Ostensible Efforts to Control Exposure

Dr. Williams has a section of his paper entitled "Control of Exposure." The four factors identified as important for dosage are (a) output of x-ray tube, (b) thickness and condition of filters, (c) distance, and (d) time of exposure and number of exposures. The latter two are controlled at the store, if at all.

It turns out that there were some recommendations for dose-limitation before the Williams study. Both the American Standards Association (1946) and the New York City Health Department (1948) had specified that "The maximum permissible dose per exposure shall not exceed 2 Roentgens." And New York City required further that "There shall not be more than 3 exposures in one day and not more than a total of 12 exposures in one year."

Dr. Williams indicated his lack of trust, that these standards would accomplish anything, by his statement (p.334):

"The only attempt to enforce this provision is a requirement for posting of signs on the machines stating : 'REPEATED EXPOSURES TO X-RAYS MAY BE HARMFUL. FLUOROSCOPIC EXAMINATIONS FOR SHOE FITTING SHOULD BE LIMITED TO NO MORE THAN 12 IN ONE YEAR' [emphasis in the original]. These signs should measure at least 7 1/2 inches by 4 1/2 inches and should be posted conspicuously."

For New York, the hope was therefore to limit foot exposure to 24 Roentgens per year, or less. But unless the machines delivering 348 Roentgens per minute were actively eradicated, then twelve exposures per year, of 20 seconds each, would actually deliver nearly 1,400 Roentgens in one year to the feet of customers using them.

Elsewhere, according to Dr. Williams, there were also some modest attempts to limit exposures. The Detroit Department of Health (1948) required that the maximum intensity in the beam must not exceed 12 Roentgens per minute, and that the maximum time of exposure must not exceed five seconds. The Massachusetts Division of Occupational Hygiene joined in this recommendation. So the intention was to limit the maximum dose to 1 Roentgen per view.

But were sales clerks going to control the number of views per customer? And what about customers who visited several different stores before each purchase?

Public Education about Radiation

We do not deny the right of adults to harm themselves, and to pay the price, in full knowledge of what they are doing. But was there ever a meaningful effort to provide full knowledge about the shoe-fitters, or about any other aspect of radiation exposure?

Today it is known, thanks mostly to declassified government documents, that powerful segments of the U.S. Government were actively engaged --- starting soon after Hiroshima and Nagasaki --- in suppressing information which might cause the public to worry about radiation. Radiation from bomb-testing fallout. Radiation from certain aspects of military service. Radiation from working in certain defense industries. Radiation from living nearby. Radiation from working in uranium mines. Under the circumstances, it was probably not a favorable time to start teaching the public to worry about radiation from SHOE-FITTERS.

The Smile of Providence

We can say it is indeed fortunate that the risk of radiation-induced cancer is much lower for feet than for breasts. At least female children were not getting something "fitted" which would give the BREASTS the same dose which their FEET were receiving from those very popular machines.

Providence did smile on people in many ways, we think, as we contemplate the complex obstacle-course laid out for people hoping to stay healthy.

Part 4. The Measured Leakage and Scatter of Radiation

Dr. Williams did a thorough job of examining leakage of radiation in all directions and heights from the shoe-fitter's cabinet-wall, at a number of installations. Except for the back aspect of the shoe-fitter --- which refers to the semi-open side into which the feet entered --- all other areas measured between 3 milli-Roentgens per hour and 60 milli-roentgens per hour. All these measurements were taken right next to the cabinet-wall itself. It is worth pointing out that ambient natural radiation is about 10 MICRO-Roentgens per hour in many U.S. locations, so 60 MILLI-Roentgens per hour is six thousand times as high as natural background radiation. No one should stay in such a region unnecessarily for any length of time.

Scattered Radiation for Customers and Clerks: 100 mR per Hour

In the shoe-fitter, the x-ray beam travels upward from below the feet, and parts of the beam reach the viewing screen above the feet. But some other parts of the beam change direction, because they are "scattered" by the feet, for instance, and by parts of the interior of the fluoroscope cabinet.

Dr. Williams established that, in the shoe-fitter, the opening for the feet was such that radiation was indeed scattered over about a quarter of 360 degrees in the direction of other parts of the shoe-store. If one drew a circle around the machine, one quarter of the circle would describe a region where serious dose was possible due to radiation scattered out of the foot-opening. Moreover, while much of the scattered radiation traveled at right angles to the direct x-ray beam, some of it traveled upward from the opening. Small children walking around could definitely receive scattered radiation to their chests, and so could clerks and parents who were seated, while attending to other feet.

In a diagram (Williams 1949, Figure 2), areas are shown where customers are having preliminary fitting while seated. Such areas showed scattered radiation even higher than 150 milli-Roentgens per hour. We quote Dr. Williams (p.334):

"Figure 2 shows a typical setup in a shoe store. It should be noted that at many of the seats where customers are given preliminary fittings, an area in which clerks may be working, a total daily dose could be received in one hour of operations by anyone in the area." In those years, "a total daily dose" meant 100 extra milli-Roentgens (mR) per day --- a recommended occupational limit per average day back then.

"It Is Obvious ..." Said Dr. Williams

As a result of making his measurements, Dr. Williams wrote in 1949:

"It is obvious from the data shown in the section on scattered radiation that the back (customer's) side of these units should never be directed toward occupied areas within a radius of 25 feet."

We wonder: In how many stores between 1929-1949, and also after 1949, was it "obvious"? And was the scattered dose even higher from some of the earlier shoe-fitter models than measured by Dr. Williams in 1949?

Part 5. A "Ballpark" Estimate on Possible Breast-Dose from Shoe-Fitters

With respect to breast-cancer induced by the widespread popularity of shoe-fitters, three sets of people in the shoe stores deserve consideration: (a) the female children, (b) the young mothers of such female children, and (c) the female workers. In what kind of " ballpark" might their breast-doses fall?

The Female Children and Their Mothers

Suppose we assume that a female child was seated in a region of the shoe-store where the dose from scattered radiation was 100 milli-Roentgens per hour when the machine was "on." We could estimate that time "on" was one-tenth of an hour in each hour. So, potential dose was really 10 milli-Roentgens per hour, or 0.01 Roentgens per hour. And let us assume the child spent a total of one hour per YEAR in this configuration (based on 3 shoe fittings at 20 minutes of such exposure, each). If we assume that the exposure occurred from front to back, then the conversion from Roentgens to rads would be about 0.693 rads per Roentgen for breasts. Under these assumptions, the extra breast-dose might reach 0.0069 rads for this child, each year, as a " ballpark" estimate.

We do not think that every child would have this experience, and we do not know what fraction did have it. Nor do we know how common it was for children to crowd around the machine for "a look" while other children were using it. And we do not know the duration of the Shoe-Store Saga relative to the entire 1920-1960 period represented in our Master Table. There are many uncertainties. Although we make no entry at all in our Master Table for breast-dose from shoe-fitters, there is no doubt that female children and mothers did experience breast-harm from their excursions to the shoestore.

The Female Clerks

We should not disregard the problem of female clerks, since some of them might present an anterior surface or a lateral surface to the scattered radiation, according to the layout of the store. The scattered radiation would be mostly at a low vertical level, but then clerks do sit on a low stool when fitting shoes. The machines were generally operated at 50 kv, so the breast-dose from anterior exposure would need consideration, but breast-dose from posterior irradiation would have been negligible.

Using the information from Dr. Williams, we can make a " ballpark" estimate of breast-dose for the clerks.

Their exposure in the fitting area could be 800 milli-Roentgens per working day (from Part 4). But since some clerks would have their backs to the source, we reduce the anterior exposure to 400 milli-Roentgens. And because the machines were not putting out x-rays all day long, we estimate (as we did above) that the machines operated only one-tenth of the day, which would reduce breast-dose to 40 milli-Roentgens per day or 0.04 Roentgens per day. After conversion to rads, this would be 0.028 rads per day --- for the stated assumptions.

From 200 days of work per year, the breast-dose could be 5.6 rads per year. For an individual woman, this would be a serious annual dose-rate, but after averaging the

exposure over all the women who did NOT work in shoe-stores, the average dose would be reduced a great deal. For the sake of illustration, a 100-fold reduction would mean an average annual dose of 0.056 rads. If we were making entries in our Master Table, we would need to know the appropriate reduction-factor, as well as how many years the shoe-fitters were widely present.

Although we make no entries at all in our Master Table for breast-dose from shoe-fitter fluoroscopy, we are sure that some female clerks did indeed receive injurious breast irradiation. "No entry" in the Master Table does NOT mean "no dose."

Part 6. The "Technological Imperative" --- Expose Now, Regret Later?

In Dr. Hempelmann's paper (1949), he stated in several places that there was insufficient information to enable people to predict the effects of using the shoe-store fluoroscopes. For example, he stated (p.336):

"Little is known of the radiation doses that cause chronic skin damage." And: "There is no published information bearing on the maximum radiation dosage that can be administered to the skin with safety at the intervals at which children are likely to be fitted for new shoes (two to four months)."

Did Dr. Hempelmann believe that the current (and prior) usage of the machines was safe? Clearly not. He wrote (p.336):

"To prevent injury to customers and employees, it is obvious that the use of x-ray machines in shoe stores must be controlled. Proper shielding of the fluoroscope to minimize radiation leakage, education of the users and store officials about the dangers involved in misuse of the machines, and reduction of the foot dosage per viewing must be accomplished. Shielding of a low-voltage fluoroscope is a relatively simple matter. Conspicuous warning signs on each machine can help to educate the public to the dangers of too frequent use of fluoroscopy; restriction of the use of x-ray machines to qualified personnel will reduce the possibility of accidental overexposure. Reduction of the foot dosage per exposure can be accomplished by lowering of the tube output, by adequate filtration and by limitation of the exposure by automatic timing devices. Since the maximum amount of radiation that the foot can tolerate at intervals of several months is not known, it seems advisable to reduce the foot dosage to the minimum that is compatible with satisfactory use of the fluoroscope."

This advice is an interesting illustration of the dominance of the technological imperative. Given what Dr. Hempelmann acknowledged was NOT known about either the skin or the feet (which were the apparent limits of his concern), and given the unrealistic prospects of financing a campaign for "education of the users and store officials" and for "qualified personnel" to operate the shoe-fitter fluoroscope, it seems to us that the ONE question which deserved consideration was simply not asked: "Who needs it?"

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CHAPTER 28

Mammography: Past and Present

Part 1. Patients Often in the Dark about Their Doses

One item has been missing for a long time in the use of medical x-rays: The ability of a patient to find out (a) whether a particular facility knows what it is doing, and (b) what dose of radiation the patient is getting from any particular procedure. Later (Chapter 42), we will discuss whose responsibility it is to obtain such information for patients, for this is not a problem only of the past.

Talking to the general public in Science Digest, two radiation physicists described the situation rather memorably in 1984.

One of them was Dr. Joel Gray (of the Mayo Clinic), whose admirable work on reducing radiation dose for scoliosis patients was already described in Chapter 21. In the 1984 interview, he commented about offices which do not tell patients the estimated dose of radiation which they will receive (Gray 1984, p.96):

"My feeling is that if they won't tell you, they don't know, and if they don't know, they could be among the facilities delivering a hundred times the necessary dose."

The other physicist commented specifically on mammography. Dr. Edward Webster, of the Massachusetts General Hospital, said (Webster 1984, p.96):

"When a woman arrives at a doctor's office for a mammogram, she has no way of knowing whether she's getting three hundred or three thousand millirads."

A Lesson from Recent History: The 1960s and 1970s

If we go back to the 1960s and 1970s, the reality of mammographic doses was startling --- for breast-doses were very high compared with the current levels. Of course, we have no entry at all for mammography in our Master Table, because the table considers only common procedures of the 1920-1960 period.

We will explore, later in the chapter, what it would have meant for women if mammography had become common when the doses were so much higher than today. It did not become common, thanks to some people with a willingness to say "No!" to various pressures to make it common. The history of mammography provides women with a reason to think very seriously about the need for eternal vigilance --- and for "watchdogging" of some technology buffs who are inclined to claim that THEIR pet technology is "safe," without any evidence for such claims.

Part 2. Breast-Doses from Mammography in the 1960s and 1970s

Periodic reports on various aspects of ionizing radiation are issued by UNSCEAR, which is the United Nations Scientific Committee on the Effects of Atomic Radiation. The committee consists of members of the radiation community in interested nations. About mammography, the UNSCEAR 1977 report stated (p.318, para.70):

"Direct radiography of the female breast, i.e., mammography, is of particular interest because the technique is also being used in health investigations. The organization of a number of large population mass-screening surveys caused concern when high-dose techniques were in use and when regular re-examinations were carried out on young women. The justification for such examinations was questioned because of the increase in breast-cancer that might be induced by radiation [references cited]." And:

"In the 1972 report [UNSCEAR 1972] the radiation dose to the breast per mammography examination was reported to be in the range of 10-35 rad. However, since then considerable progress has occurred in techniques for reduction of radiation dose ..." And: with "... the two-film techniques being accepted for screening examinations, surveys can be undertaken with a breast dose of less than 200-300 mrad ..."

So UNSCEAR 1972 reported 10 to 35 rads as the mammographic dose in the 1960s. To make the coming comparison, we will say 20 rads. And UNSCEAR 1977 reported that it was technically possible to reduce doses to 0.2 rads (200 milli-rads) or less by 1977. That is a reduction of 100-fold. But as we shall see (Part 5), a large screening project had been undertaken in 1972 with 10-fold higher doses --- about 2 rads per exam.

Part 3. Breast-Doses from Mammography in Current Times

Improvements continue, and it appears that mammography will finally have sufficient surveillance to insure that low doses become commonplace. The Food and Drug Administration was asked by Congress to set comprehensive standards for the nation's 11,000 mammography clinics, and to issue certification when such standards are met. The FDA requirements, as described in late 1994, include the following:

- - Workers who perform mammography and physicians who interpret the images must be properly trained and experienced. For physicians, that includes interpreting at least 40 mammograms per month. Each clinic must track its accuracy and insure that women with suspicious results are promptly called for follow-ups. FDA-trained inspectors will inspect each clinic annually.
- - Only up-to-date mammography machines are allowed. They must be monitored closely to insure that the images remain clear and that the radiation dose does not exceed 0.3 rad (300 milli-rads, or 0.3 centi-gray) mean glandular dose per view. The standard exam has 2 views per breast (top to bottom, and side to side). So, on the average, internal cells of each breast may receive up to 0.6 rad of absorbed dose per exam --- but actual doses today per exam are often as low as 0.2 rad for each breast.

Part 4. The Estimated Price in Breast-Cancers from Full Implementation of Mammography

Although I consider myself an enthusiast for technological progress, I recognize that the history of applied technology has often been "act now, think later." Part 5 will describe an example. So it would be worthwhile to ask what the price in extra breast-cancer could be from various programs of mammography, if fully implemented in the United States at a current dose of about 0.2 rads per exam. Mammography, of course,

has nothing to do with PREVENTION of breast-cancer. It has to do with detection of a problem NOT prevented.

Because there is no safe dose (risk-free dose) of ionizing radiation, we can be certain at the outset that mammographic programs will cause some number of radiation-induced breast-cancers. The question is: How many?

No one should equate the desire to have a "ballpark" answer, with a desire to obstruct. A desire NOT to estimate the consequences would be peculiar, in our opinion.

So we have prepared an "If-Then" table from which we obtain some estimates (Table 28-A, on the next page). Table 28-A provides estimates from ANNUAL mammography at every age-year, starting with age-30 and ending with age-64. We are well aware that no one today is proposing annual mammograms starting at age-30. We stress that Table 28-A is an "If-Then" table. Its purpose is to enable readers to ask "What if?" about a variety of possible programs with differing frequencies of mammography for different age-groups.

Later, in Part 8, we will also show how to estimate an individual's PERSONAL risk from mammography today.

Part 5. Why Worry about "Only" 2 Extra Rads to the Breasts per Year?

In 1972, the "Breast Cancer Detection and Demonstration Project" (BCDDP) was launched in the United States. It included mammography for the participants. A detailed description of the project was given by Herbert Seidman and colleagues (Seidman 1987). We quote from the "Materials" section of that article (p.266):

"The BCDDP was established in 1972 when the American Cancer Society funded 12 centers to do annual physical examinations and mammography on 5,000 women in each center. The program was later expanded when the NCI [National Cancer Institute] funded additional centers and the number of women increased to 10,000 per center. Screening began early in 1973; by 1975 there were 29 centers in 27 locations that had enrolled more than 280,000 women ages 35 to 74." And:

"Almost all of the centers recruited about 10,000 women each over a two-year period to be screened for breast cancer free of charge at an initial screening and four subsequent annual screenings. Those who joined were screened with a combination of medical history, physical examination, mammography, and thermography."

We doubt that the program could have recruited persons if there were any suggestion made that breast-cancer could be a RESULT for some segment of the women enrolled. Seidman and colleagues reported (at page 266) that about 51 percent of the women who joined the project completed all five screenings.

The Average Breast-Dose Which Was Received in the BCDDP

In 1976, John C. Bailar III reviewed the dosimetry for the mammographic studies in the BCDDP. He reported as follows (Bailar 1976, p.80):

"A very recent survey of the demonstration clinics supported jointly by the National Cancer Institute and the American Cancer Society has shown average doses of about 1 to 5 rads with the use of radiation detectors thought to be significantly more

Table 28-A
An "If-Then" Table For Mammography.
Assumes all women (age-30 and up) in the United States received 0.2 rad
in Annual Mammographies.

Col. A	Col. B	Col. C	Col. D	Col. E	Col. F
Age	Number of Women*	Dose Medical Rads	Person-Rads	Breast-Cancers per 10,000 Person-Rads**	Annual Breast-Cancers
Year					
30	1,670,816	0.2	334,163	44.95	1,502
31	1,669,424	0.2	333,885	44.95	1,501
32	1,667,946	0.2	333,589	44.95	1,499
33	1,666,364	0.2	333,273	44.95	1,498
34	1,664,697	0.2	332,939	44.95	1,497
35	1,662,910	0.2	332,582	26.38	877
36	1,660,984	0.2	332,197	26.38	876
37	1,658,904	0.2	331,781	26.38	875
38	1,656,652	0.2	331,330	26.38	874
39	1,654,176	0.2	330,835	26.38	873
Annual Mammogram-Induced Breast Cancers (30-39 year-olds). Sum =					11,873
40	1,651,443	0.2	330,289	26.38	871
41	1,648,418	0.2	329,684	26.38	870
42	1,645,083	0.2	329,017	26.38	868
43	1,641,422	0.2	328,284	26.38	866
44	1,637,399	0.2	327,480	26.38	864
45	1,632,982	0.2	326,596	26.38	862
46	1,628,151	0.2	325,630	26.38	859
47	1,622,856	0.2	324,571	26.38	856
48	1,617,098	0.2	323,420	26.38	853
49	1,610,858	0.2	322,172	26.38	850
Annual Mammogram-Induced Breast Cancers (40-49 year-olds). Sum =					8,619
50	1,604,120	0.2	320,824	24.56	788
51	1,596,848	0.2	319,370	24.56	784
52	1,588,992	0.2	317,798	24.56	781
53	1,580,517	0.2	316,103	24.56	776
54	1,571,372	0.2	314,274	24.56	772
55	1,561,522	0.2	312,304	24.56	767
56	1,550,950	0.2	310,190	24.56	762
57	1,539,588	0.2	307,918	24.56	756
58	1,527,332	0.2	305,466	24.56	750
59	1,514,026	0.2	302,805	24.56	744
60	1,501,100	0.2	300,220	24.56	737
61	1,483,790	0.2	296,758	24.56	729
62	1,466,720	0.2	293,344	24.56	720
63	1,448,518	0.2	289,704	24.56	712
64	1,429,452	0.2	285,890	24.56	702
Annual Mammogram-Induced Breast Cancers (50-64 year-olds). Sum =					11,280

Notes: Col.D = Col.B x Col.C

Col.F = (Col.D / 10,000) x Col.E

* Column B entries are for the number of women present at each age for an equilibrium population of 250,000,000 total persons. Taken from Table 24 of Gofman 1981.

** Conversion factors taken from Chapter 39, Master Table, Column V.

accurate than those used in the studies cited above. A current average depth dose to breast tissue of 2 rads per film set seems a reasonable and conservative estimate after allowance for the use of xeromammography and other low-dose methods."

The Status of Knowledge at the Time of the BCDDP Initiation

When the Project was initiated in 1972, was there any reason to worry that two extra rads of breast-irradiation every year might CAUSE some breast-cancers?

Seven years earlier, in 1965, MacKenzie had published his findings on radiation-induced breast-cancer (discussed in Chapter 1). In 1968, Wanebo had published his findings concerning breast-cancer in A-bomb survivors. In 1970, Tamplin and Gofman had published estimates, based upon MacKenzie and Wanebo and a relative risk analysis, of a doubling dose for breast-cancer of about 20 to 50 rads. In 1972, the Committee on the Biological Effects of Ionizing Radiations (the BEIR Committee of the National Academy of Sciences, USA) had estimated a doubling dose for radiation-induced breast-cancer of 28 to 120 rads (BEIR 1972, p.141).

Despite all this, a project was launched to give women an extra 10 rads to their breasts (2 extra rads per year for 5 years). It would seem that someone must have had misgivings about initiation of this project, in light of the information on radiation-induced breast-cancer already published and available to the ACS and NCI.

The Breast Cancer Detection and Demonstration Project (BCDDP) was an illustration of the "technological imperative" at work, coupled with all the political propaganda in those years about the "war on cancer."

Mammogram-Induced Breast-Cancers: An "If-Then" Table Based on BCDDP

We will set up another "If-Then Table" to explore the consequences if this program had "carried the day" and had expanded indefinitely, with all U.S. women enrolled at age-35 to receive an annual mammogram thereafter at 2 breast-rads per exam. This is Table 28-B. Since it uses the same population-size as Table 28-A, with a dose ten-fold higher, it shows estimates which are ten-fold higher for the mammogram-induced breast-cancers.

Because of the variable latency period (Chapter 2), the mammogram-induced breast-cancers would not have shown up all at once. Table 28-B estimates the number which would have been put "on the shelf" each year, for delivery later. After a few decades of this program, at two rads per examination, the annual production of mammogram-induced breast-cancers and the annual "delivery" (incidence) of mammogram-induced breast-cancers would have become about equal in number (Chapter 4). And what would the equilibrium number have been?

Ages at Production	Mammogram-Induced Breast-Cancers: Annual "Delivery" at Equilibrium (Chapter 4)
35-39	43,757
40-49	86,187
50-64	112,803
Total	242,747

Table 28-B
An "If-Then" Table For Mammography.

Assumes all U.S. women (age-35 and up) received 2 rads per year in a universal, continuous "Breast Cancer Detection and Demonstration Project."

Col.A Age Year	Col.B Number of Women*	Col.C Medical Rads	Col.D	Col.E Breast- Cancers per 10,000 Person-Rads**	Col.F Annual Breast- Cancers
35	1,662,910	2	3,325,820	26.38	8,774
36	1,660,984	2	3,321,968	26.38	8,763
37	1,658,904	2	3,317,808	26.38	8,752
38	1,656,652	2	3,313,304	26.38	8,740
39	1,654,176	2	3,308,352	26.38	8,727
Annual Mammogram-Induced Breast Cancers (35-39 year-olds). Sum =					43,757
40	1,651,443	2	3,302,886	26.38	8,713
41	1,648,418	2	3,296,836	26.38	8,697
42	1,645,083	2	3,290,166	26.38	8,679
43	1,641,422	2	3,282,844	26.38	8,660
44	1,637,399	2	3,274,798	26.38	8,639
45	1,632,982	2	3,265,964	26.38	8,616
46	1,628,151	2	3,256,302	26.38	8,590
47	1,622,856	2	3,245,712	26.38	8,562
48	1,617,098	2	3,234,196	26.38	8,532
49	1,610,858	2	3,221,716	26.38	8,499
Annual Mammogram-Induced Breast Cancers (40-49 year-olds). Sum =					86,187
50	1,604,120	2	3,208,240	24.56	7,879
51	1,596,848	2	3,193,696	24.56	7,844
52	1,588,992	2	3,177,984	24.56	7,805
53	1,580,517	2	3,161,034	24.56	7,763
54	1,571,372	2	3,142,744	24.56	7,719
55	1,561,522	2	3,123,044	24.56	7,670
56	1,550,950	2	3,101,900	24.56	7,618
57	1,539,588	2	3,079,176	24.56	7,562
58	1,527,332	2	3,054,664	24.56	7,502
59	1,514,026	2	3,028,052	24.56	7,437
60	1,501,100	2	3,002,200	24.56	7,373
61	1,483,790	2	2,967,580	24.56	7,288
62	1,466,720	2	2,933,440	24.56	7,205
63	1,448,518	2	2,897,036	24.56	7,115
64	1,429,452	2	2,858,904	24.56	7,021
Annual Mammogram-Induced Breast Cancers (50-64 year-olds). Sum =					112,803

Notes: Col.D = Col.B x Col.C

Col.F = (Col.D / 10,000) x Col.E

* Column B entries are for the number of women present at each age for an equilibrium population of 250,000,000 total persons. Taken from Table 24 of Gofman 1981.

** Conversion factors taken from Chapter 39, Master Table, Column V.

The BCDDP program was intended to help women. But if it had been expanded and continued, it had the potential to have produced mammogram-induced breast-cancer at the rate of about 243,000 cases every year --- a number to be compared with the 182,000 breast-cancers in 1994 from all causes combined.

Of course, there will be readers who believe our estimate above should not be 243,000 cases per year --- but "only" 50,000 or 100,000 or 150,000 or 200,000. This is not the chapter where we show the basis of the "conversion-factors" in the table's Column E (see Chapter 40). But those who believe that the potential number of mammogram-induced breast-cancers would have been "only" 50,000 cases every year, can surely join in some gratitude to the people who prevented the BCDDP project from expanding and continuing at "only" 2 rads per mammographic exam.

Part 6. The Gradual Development of Mammography: 1913-1964

In a very interesting summary article published in 1964, entitled "Mammography of Cancer," Dr. J. Gershon-Cohen and his colleague, Myron Forman, described the early origins of the mammography technology. Dr. Gershon-Cohen is one of the real pioneers of clinical mammography. We quote from it briefly (1964, p.674):

"Mammography is not new. Fifty years ago, when the science of radiology was still in its 'teens, Salomon in Germany produced credible mammograms of excised breasts (1913). His observations of some 3,000 mastectomy specimens correlated the roentgen findings with the gross and microscopic anatomy of tumors. His descriptions and roentgenograms contain a wealth of interesting information. The differences in the roentgen appearances of the most common forms of mammary cancer were recognized with amazing accuracy and he could differentiate scirrhouous and infiltrating types of malignancy from the circumscribed or the nodular forms. He even described the punctate calcifications seen in many cancers, especially of the duct variety. Finally Salomon is to be credited with the first roentgenographic detection of an occult cancer found in a breast which was removed because of the presence of a large cyst."

Nonetheless, Dr. Gershon-Cohen related that it was only in the later 1920s and early 1930s that references began to appear concerning mammography. Despite excellent work being reported from several clinics in the United States and abroad, he stated that interest in the subject was simply not sustained.

In 1938, Gershon-Cohen and Strickler published a paper on the roentgen examination of the normal breast which emphasized that knowledge of the normal breast at all ages and stages of activity was a prerequisite for recognizing pathologic conditions.

"The Rising Sweep of Interest" in the 1950s and 1960s

Raul Leborgne's work in 1951 was cited by Gershon-Cohen (1964) for bringing to the attention of roentgenologists the importance of punctate calcifications as a pathognomonic [uniquely predictive] sign of malignant processes. Then Gershon-Cohen named a host of workers who stood out prominently with "the rising sweep of interest in this subject during the 1950s" --- all of whom shared in developing techniques and diagnostic criteria.

Speaking of his own institution, Gershon-Cohen cited the collaboration of the pathologist, Dr. Helen Ingleby, as the key event which led to a sustained interest in the subject of mammography. About Dr. Ingleby, Gershon-Cohen stated: "She made notable progress in bringing order out of the chaotic pathologic nomenclature so that the roentgenologist could reconcile his findings with pathologic conceptions."

Dr. Robert L. Egan was cited by Gershon-Cohen (1964, p.679) as another important pioneer in this field:

"More recently, Egan's efforts [1962, 1963] to improve technology and his report of excellent results generated intense interest in the subject. The impact of his work seems to have centered on his preoccupation with technique. It goes without saying that without optimum technique, no substantial reliability can be placed on any roentgenographic procedure. Good contrast and the best possible detail are essential if maximum information is to be obtained from the x-ray film ..."

Efforts to Prove the Value of Mammography

The work described above led to many investigations and consultations between the surgeons and the roentgenologists, to ascertain if mammography could improve the outlook in the breast-cancer problem. At a time when little progress was apparent in therapy, the hope was widespread that perhaps earlier diagnosis of breast-cancer might make treatments more successful.

Radiologists such as Dr. Robert Egan realized that, in order for mammography to be accepted as a valuable technique, capable of providing information over and above techniques already being applied, the radiologists had to prove several things, among which were:

(a) Ability to provide their diagnosis without any knowledge of the clinical findings. They were very wise in setting up this hurdle for themselves, for otherwise it could be stated that they made their analysis of the mammogram AFTER knowing what the clinical picture was.

(b) Ability to diagnose cases by mammogram which could NOT be diagnosed by the clinicians either by history or physical examination or both. This was a major key, for the clinicians were always very worried about their own "false negatives" --- failures to recognize a case as being a cancer when it truly was a cancer.

(c) A low rate of "false positives" from mammography. The more often a mammogram caused a biopsy to be taken, with the finding of a negative result with respect to malignancy, the less useful would the mammogram be.

Gershon-Cohen appreciated the need to have true screening tests of mammography, where no clinical symptoms or signs caused the women to come in for mammography. That is NOT easy to accomplish. But he and his colleagues tried, in January 1956, to set up such a program in the Radiology Department of Albert Einstein Medical Center. All x-ray examinations in the survey were provided free to the volunteers --- with a single condition: Every candidate wishing to participate in the program must be free of breast symptoms. However, one can be at the mercy of the candidates, with respect to their truthfulness about absence of symptoms.

With All This Activity: Why No Entry in Our Master Table?

With only minor exceptions, we found that the studies done before 1960 were not suitable for inclusion in our Master Table. Most of the work involved women who were really under suspicion for possible breast-cancer and were having a mammogram as part of their work-up. As we have said before, we want NOT to count breast-doses administered to women who were already at the stage of clinical breast-cancer. We do not want to consider them as CANDIDATES for radiation-induced breast-cancer. We are trying to evaluate what breast-dose of radiation was being accumulated in the population NOT under study for possible breast-cancer. This, in essence, is why several major studies in the late 1950s were not appropriate for our purposes.

Part 7. Early 1960s: "No Concern about Excessive Radiation Is Entertained"

In 1961, Gershon-Cohen and colleagues made a report on their screening program, mentioned in Part 6. It was entitled "Detection of Breast Cancers by Periodic X-Ray Examinations: A Five-Year Survey." In it, they reported:

"At present 1,055 women still remain in the program [out of 1,312 enlisted in the program]; 257 dropped out after one or more examinations. Each volunteer is examined every six months." What about the dose to the breasts in these repeated mammographic examinations? Gershon-Cohen and associates did indeed consider the safety of their program. They stated:

"Since we find nonscreen films satisfactory for our purposes and since each exposure entails less than 1.5 rad to the breast alone, no concern about excessive radiation is entertained."

It was not even "entertained" in 1961.

By contrast, we have illustrated in Table 28-B that people had better be VERY concerned about doses of 1.5 rads to the breasts twice a year, in any program which enlists large numbers of women. In Table 28-B, the dismal entries in Column F would be 50 % higher from an annual dose of three rads rather than two.

Annual Breast-Doses Well above 10 Rads: Called "Safe"

In 1964, Dr. Robert Egan --- whose work we also admire --- was apparently making the same mistaken assumption about safety as Dr. Gershon-Cohen. Dr. Egan described his evaluation of 1,217 consecutive mammograms on patients who came to biopsy. He used three views, rather than two. And he assumed the total dose was "safe." He stated (p.125):

"Mammography is a highly accurate, reproducible, safe, simple, and non-traumatic roentgenographic technique that provides a new objective approach to the diagnosis of breast diseases. It is the only means by which cancer of the intact breast can be demonstrated before signs and symptoms are present. In a series of 1,217 consecutive mammograms on patients who came to biopsy, 85 clinically unsuspected carcinomas were detected. The mammograms were interpreted without knowledge of clinical findings." And:

"... From all three views, the central point of the average breast receives a total of 3.3 rads. Radiation to the eyes and gonads is negligible. Since only a small volume of tissue, which can be considered an appendage, is in a low-energy x-ray beam, this dose is quite acceptable for use in frequent re-examinations." How frequent? In a 1963 paper, Dr. Egan indicated that this dose would safely allow repeating the examination several times during each quarter year. So he was talking about annual breast-doses well above 10 rads per woman.

Such advice from a pioneer expert in mammography is just the opposite of what might have set the entire mammography effort on a good track, in our opinion. Three rads, in frequent re-examinations, widely practiced, WOULD NOT BE ACCEPTABLE AT ALL to that small-volume "appendage," the breasts. Such a regime, if applied to all women in the United States, would have breast-cancer consequences more than five times the magnitude estimated in Table 28-B.

The Only Target of Our Criticism

We most certainly do not fault Dr. Gershon-Cohen and Dr. Egan for not knowing in 1961 and 1964 what no one knew. Dr. MacKenzie's ground-breaking paper (see Chapter 1) did not even appear until 1965. And we certainly recognize an individual woman's right to accept voluntary medical risks of unknown sizes for herself.

What we fault is something quite different. We fault the policy of making sweeping assertions about safety --- instead of warning everyone about the actual state of ignorance at any given time.

Part 8. How to Estimate a Personal Radiation Risk from Mammography

Women who want a "ballpark" estimate of their personal radiation risk, per mammographic exam, can easily obtain it by borrowing from Table 28-A, Column E. By answering some questions, we will illustrate how to do it.

- - QUESTION ONE. I am age 33. What would be my risk from having a baseline exam at this age?

The lifetime rate at age 33 is 44.95 radiation-induced breast-cancers per 10,000 women who each receive 1 rad (Table 28-A, Column E). But the dose per exam is 0.2 rads, not a whole rad, so the rate will be lower. It will be $(44.95 \text{ cases} \times 0.2)$ per 10,000 women = 8.99 radiation-induced cases / 10,000 women.

To make this fraction easier to grasp, just divide both the top and the bottom of the fraction by 8.99. The result is: 1 radiation-induced breast-cancer per 1,112 women --- or a lifetime individual risk of 1 chance in 1,112. Your chance of NOT developing a radiation-induced breast-cancer from the one exam is 1,111 chances out of 1,112.

- - QUESTION TWO. How does my radiation risk accumulate from a series of several mammographic exams?

If you have 15 exams, you add up the risks from each one. Suppose you have 15 mammograms beginning at age 50. The lifetime rate is 24.56 radiation-induced breast-cancers per 10,000 women who each receive 1 rad (Table 28-A, Column E). But the dose per exam is only 0.2 rad, not a whole rad, so the rate will be lower. On the

other hand, we need to consider 15 exams. Multiplying by 15 is equivalent to adding the rate 15 times, of course. So the rate would be:

(24.56 radiation-induced cases x 0.2 x 15) per 10,000 women = 73.68 radiation-induced cases / 10,000 women. Then divide both the top and the bottom of the fraction by 73.68. The result is 1 radiation-induced breast-cancer per 136 women, or a lifetime individual risk of 1 chance in 136. Your chance of NOT developing a radiation-induced breast-cancer from the series of 15 exams is 135 chances out of 136.

• - QUESTION THREE. How do I combine my risk from the baseline exam with the risk from the later exams?

Using the illustrations above, we just do the addition while BOTH fractions still have a denominator of 10,000 women. So: (8.99 cases / 10,000 women) + (73.68 cases / 10,000 women) = 82.67 cases / 10,000 women. Then we can divide both the top and the bottom of the fraction by 82.67. The result is 1 radiation-induced breast-cancer per 121 women, or a lifetime individual risk of 1 chance in 121. Your chance of NOT developing a radiation-induced breast-cancer from all 16 exams combined is 120 chances out of 121.

Variable Doses, and Variable Risks

The illustrations above use the approximation that "one size fits all." Throughout this book, we are dealing with average doses and average risks. In reality, there is variation around the average values. Neither the dose nor the risk is uniform. For example, dose has to vary with breast-thickness. And even at exactly the same dose, two women of the same age do not necessarily have the same risk of radiation-induced breast-cancer. One reason: Each woman has a unique genetic heritage.

There is debate over whether women born with ONE faulty copy of the gene for ataxia telangiectasia (the AT gene) have a truly elevated risk of breast-cancer and whether they are especially vulnerable to radiation-induced breast-cancer (Swift 1991; Boice 1992; Easton 1994). Resolution will require additional evidence. And the AT gene is just one of MANY genes which --- if faulty at conception --- might predispose their carriers to breast-cancer. For example, let us consider people who inherit genes which mean an elevated rate of non-repair or misrepair of new genetic injuries, including new injuries induced by ionizing radiation. It is probable (but not proven) that such people have a higher rate of radiation-induced cancer, per rad of radiation exposure, than people who inherit a better repair-system.

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"From error to error, one discovers the entire truth."

● – Sigmund Freud, 1856–1939,
founder of psychoanalysis.

CHAPTER 29

Major Surgical Advances and Irradiation of the Breast

Part 1. Major Surgical Advances Go Hand in Hand with Extensive Use of X-Rays

No one can deny the fantastic advances in cardiovascular and other major surgery in the 20th Century.

For example, the ability to correct some major congenital abnormalities in infants and children can convert a very limited and unhealthy life for a child into a life with essentially normal span and normal activity. And at various ages, head surgery, heart-valve replacement, arterial bypass, reduction of luminal obstruction, and peripheral vascular surgery are successfully accomplished, and the procedures are steadily improved.

Most of these surgical triumphs, and many others, have required information gleaned from the use of roentgenographs and roentgenoscopy. A wide variety of studies with catheterization are done under fluoroscopic observation, and observation can require extended periods of time.

It is simply inevitable that such procedures are characterized by much higher radiation doses, often to the breasts, than is the case for usual diagnostic roentgenology. Chapter 32, Part 3, lists average doses to patients as of the 1970s from various radiological investigations of the heart and great vessels. Occasionally, dose-levels in cardiovascular procedures are high enough today to cause "radiation burns," as reported in Chapter 32, Part 5.

Indeed, the currently high levels of dose delivered in some cardiovascular and other examinations are causing concern in the Food and Drug Administration's Center for Devices and Radiological Health (see Part 2).

The Same Benefits with Lower Risk

Surely, no one would consider inhibiting the correction of a major congenital heart lesion, or multiple lesions, which can change misery into happy life for a child. Nor would anyone consider inhibiting a quality-of-life improvement in an adult with a correctable vascular problem. These hardly require discussion. The issue worth attention is avoidance of radiation doses higher than necessary, and prevention of unnecessary injury not only to the patient but also (by scattered radiation) to the nurses, physicians, and technicians.

A child with a corrected heart defect who does NOT later develop an unnecessary breast-cancer is far preferable to one who does develop that cancer. A nurse, technician, or physician who develops an unnecessary radiation-induced cancer represents a serious failure in medicine.

When are unnecessarily high dose-levels of radiation most likely to occur in surgery? Whenever there is inadequate attention to the radiological part of the surgical advance and only a vague appreciation of radiation carcinogenesis.

Part 2. Some Win-Win Advice for Patients and Medical Personnel

On September 30, 1994, Dr. D. Bruce Burlington, Director of the Center for Devices and Radiological Health (Food and Drug Administration), issued a 3-page FDA Public Health Advisory: "Avoidance of Serious X-Ray-Induced Skin Injuries to Patients During Fluoroscopically-Guided Procedures" (Burlington 1994). Under the same title, a 6-page version had been issued by the FDA on September 9, 1994 (FDA 1994).

Readers will soon see that the title of both versions is a bit understated. At issue is protection of numerous medical personnel as well as patients, and protection from far more than skin injury alone.

The Advisory went out to Healthcare Administrators, Risk Managers, Radiology Department Directors, Cardiology Department Directors, and to eleven medical specialty associations. All of us can feel proud of this manifestation of excellence and concern on the part of Dr. Burlington, his associate, Dr. Thomas B. Shope, and their staff at the Center for Devices and Radiological Health. Many lives will be bettered by this timely and valuable guidance to the medical profession, presented in a clear and effective manner.

We will quote from the beginning of the Advisory (Burlington 1994), which spells out the problem AND the wide range of medical procedures at issue, involving not only the heart but also the gallbladder, pancreas, liver, kidneys, bladder, and major blood vessels:

"The Food and Drug Administration (FDA) Center for Devices and Radiological Health (CDRH) has received reports of occasional, but at times severe, radiation-induced skin injuries to patients resulting from prolonged, fluoroscopically-guided, invasive procedures. Procedures typically involving extended fluoroscopic time are:

percutaneous transluminal angioplasty (coronary and other vessels),
radiofrequency cardiac catheter ablation,
vascular embolization,
stent and filter placement,
thrombolytic and fibrinolytic procedures,
percutaneous transhepatic cholangiography,
endoscopic retrograde cholangiopancreatography,
transjugular intrahepatic portosystemic shunt,
percutaneous nephrostomy,
biliary drainage and
urinary/biliary stone removal." And:

"Physicians performing these procedures should be aware of the potential for serious, radiation-induced skin injury caused by long periods of fluoroscopy during these procedures. IT IS IMPORTANT TO NOTE THAT THE ONSET OF THESE INJURIES IS USUALLY DELAYED, SO THAT THE PHYSICIAN CANNOT DISCERN THE DAMAGE BY OBSERVING THE PATIENT IMMEDIATELY AFTER THE TREATMENT [emphasis in the original]."

And in FDA 1994, times between exposure and adverse skin reactions are indicated:

Hours for early transient erythema.
>10 weeks for dermal necrosis.
> 6 weeks to secondary ulceration.

The Cancer Hazard for Patients, Physicians, and Staff

It would be a mistake for anyone to assume that only the patient can receive radiation exposure from "prolonged, fluoroscopically-guided" procedures. Some parts of the original x-ray beam intercepted by the patient, or by any other person or object, become scattered and change direction (for example, see Chapter 31, Part 2). So even procedures which do not irradiate the breasts of a PATIENT can, by scatter, cause some breast irradiation of female medical personnel.

The FDA is well aware of this, and of its implications for patients and medical personnel. We quote from FDA 1994 (p.3):

"Procedures of the type described here may also increase the risk for late effects such as radiation-induced cancers in other tissues and organs. The potential for such late effects should not be disregarded in risk/benefit considerations, especially for individuals with many decades of expected life remaining, such as pediatric and young adult patients, or for procedures involving absorbed dose to radiosensitive tissues such as the breast. These interventional procedures can also result in increased occupational exposure to physicians and staff, and efforts to reduce the exposure to patients will result in reductions in the exposure to those conducting the procedures."

The statement could hardly be more clear and to the point.

Part 3. How Much Radiation Are Patients Receiving in Such Procedures?

The doses received by patients during fluoroscopically-guided procedures are determined by the dose-rate per minute and the total number of minutes the beam is on. We quote FDA 1994 (pp.2-3):

"The absorbed dose rate in the skin from the direct beam of a fluoroscopic x-ray system is typically between 0.02 and 0.05 Gy/min (2 and 5 rad/min), but may range from 0.01 to more than 0.5 Gy/min [1 rad per minute to more than 50 rads per minute] ..." Referring to the rates of 2 rads / minute and 20 rads / minute, FDA 1994 continues: "These dose rates are, respectively, the usual or typical dose rate for normal fluoroscopy for an average-size patient and a dose rate near the maximum which will be permitted for high-level control mode of operation under a recently established Federal limit [cites Federal Register of May 19, 1994, pp.26402-26405]. **THUS, EVEN TYPICAL DOSE RATES CAN RESULT IN SKIN INJURY AFTER LESS THAN ONE HOUR OF FLUOROSCOPY** [emphasis in original]."

Table 2 of FDA 1994 lists twelve levels of skin injury, the absorbed dose from which they can result, and the time to onset of effect:

Effects

Early transient erythema	200 rads	Within hours.
Temporary epilation	300 rads	3 weeks.
Main erythema	600 rads	10 days.
Permanent epilation	700 rads	3 weeks.
Dry desquamation	1,000 rads	4 weeks.
Invasive fibrosis	1,000 rads	---
Dermal atrophy	1,100	> 14 weeks.
Telangiectasis	1,200 rads	> 52 weeks.

Effects (Continued)

Moist desquamation	1,500 rads	4 weeks.
Late erythema	1,500 rads	6–10 weeks.
Dermal necrosis	1,800 rads	> 10 weeks.
Secondary ulceration	2,000 rads	> 6 weeks.

A Set of Sensible Guiding Principles from the FDA

There are probably some people who regard advice from the FDA as unnecessary, since they already know what needs to be done, and some really do. And others clearly do not. Gratefully, we compliment the FDA officials for producing a most valuable set of "General Principles and Recommendations for Facilities in Which Invasive Procedures Are Performed" (FDA 1994, pp.4–5). We reproduce an abbreviated version, below, and call attention particularly to Points 2 and 4:

- – Point 1. "Establish standard operating procedures and clinical protocols for each specific type of procedure performed. The protocols should address all aspects of the procedure, such as patient selection, normal conduct of the procedure, actions in response to complications and consideration of limits on fluoroscopy exposure time ..."
- – Point 2. "Know the radiation dose rates for the specific fluoroscopic system and for each mode of operation used during the clinical protocol ... Calibrate and document radiation output. Record information permitting estimation of the absorbed dose to skin in the patient's medical record."
- – Point 3. "Assess the impact of each procedure's protocol on the potential for radiation injury to the patient ... Counsel patients regarding the symptoms and risks of large radiation exposures and address risks from radiation in the consent form. Justify and limit the use of high dose rate modes of operation."
- – Point 4. "Modify the protocol, as appropriate, to limit the cumulative absorbed dose to any irradiated area of the skin to the minimum necessary for the clinical tasks, and particularly to avoid approaching cumulative doses that would induce unacceptable adverse effects. Use equipment which aids in minimizing absorbed dose with such features as: Indication of cumulative fluoroscopic exposure time. Indication of cumulative absorbed dose to the skin or a related quantity such as dose-area product. Real-time indication of dose rate or related quantity. "Last image hold" or "freeze frame" image display ..."
- – Point 5. "Enlist a qualified medical physicist to assist in implementing these principles in such a manner so as not to adversely affect the clinical objectives of the procedure."

Part 4. Our Own Recommendation about Solving This Problem

If we put radiation THERAPIES aside, it is very likely that fluoroscopy is the most important and least documented radiation procedure today, in terms of cumulative exposure. One might assume that good records are generally being kept of the fluoroscopic radiation dose to patients, broadly. We do not see evidence that this is the case, especially outside radiologic offices. Yet, to record such information is a

requirement, if anyone is ever to know whether medical practice is moving in the right direction on controlling dose in future years --- or in the **WRONG** direction.

The serious problem of high radiation doses delivered by fluoroscopy certainly did not originate with the advanced procedures listed by the 1994 FDA Advisory. Similar problems were addressed by Dr. Braestrup, Dr. Buschke, Dr. Leddy, Dr. Parker, Dr. Pfahler, Dr. Taft, and by others in the 1920s, 1930s, 1940s and beyond (see Chapter 31).

Each generation of new physicians undertaking work in a particular specialty seems to regard roentgenologic hazard as a problem of the past. The assumption apparently is made that roentgenology can be regarded as just a tool in their ever-changing specialty --- not a part which demands their meaningful attention, comprehension, and accountability. That sort of dangerous assumption, to the extent it exists, will result in unnecessary cancers of the breast and other sites.

Possibly the most sensible place for alerting physicians in diverse specialties about the fluoroscopy problem is in the medical curriculum. Do medical schools give all future physicians sufficient warning that roentgenology is a tool which can be very useful, but which seems to return again and again to bite the medical professional in a most unpleasant manner? Future physicians are entitled to receive proper instruction about the unnecessary and unacceptable production of radiation-induced breast-cancer (and other cancers) which will result if they have inadequate respect for one of the MAJOR ways of rapidly building up serious radiation dose.

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● – Confirmation from Another Source

Fluoroscopy was and still is a major source of non-recorded radiation doses — almost certainly THE major source today.

The uncertainty about fluoroscopic doses is a fact which is acknowledged in the most recent report of the United Nations Scientific Committee on Effects of Atomic Radiation, UNSCEAR 1994. That Committee attempted to estimate current average doses from diagnostic medical irradiation in over 20 countries, but it reported difficulty.

Why?

According to UNSCEAR 1994 (p.25): "One cause of uncertainty in these values is the use of fluoroscopy. This procedure results in much higher doses than those from radiography, and its prevalence is both uncertain and changing with time." (No other cause of uncertainty was mentioned.)

To locate discussions of non-recorded radiation doses in this book, see the Index under "Non-recorded radiation doses."

CHAPTER 30

Pre-Employment Fluoroscopic Exams for Pulmonary Tuberculosis

Part 1. Fluoroscopy Can Diagnose Pulmonary Tuberculosis When Physical Exam Fails

We need to keep reminding readers who are relatively young about how important the issue of pulmonary tuberculosis was in the first half of the 20th Century. Two important publications from the Metropolitan Life Insurance Company, one in 1928, and the other in 1929, appeared with some potentially ominous connotations about radiation dose to the breasts.

The paper by Fellows and Ordway (1928) outlined the problem concisely. A number of employees of the Metropolitan Life Insurance Company were diagnosed as having advanced tuberculosis within a year after acceptance for employment, despite a thorough physical examination. It was therefore suspected that cases of unrecognized tuberculosis were being accepted for employment in spite of rigid physical examination and careful questioning.

The Metropolitan Life Insurance Company did not find this to be an acceptable result for a variety of obvious reasons. Casting about for a more accurate means of detecting latent tuberculous disease, the company hired skilled roentgenoscopists [fluoroscopists], well-trained in this type of work, to examine each applicant. This means was employed with a consecutive series of 800 applicants for positions.

From these 800 applicants, accepted after history and physical examination, 8 cases of well-developed pulmonary tuberculosis were found by the roentgenoscopic examinations. Two of these showed calcified lesions, while 6 were classified as having active tuberculosis. These applicants shown roentgenographically to have definite tuberculosis then had repeat physical exams by trained physicians qualified to diagnose tuberculous lesions. In 4 of the 6 cases, these physicians again failed to find abnormal signs in the persons with a definite roentgenoscopic diagnosis of tuberculosis.

This preliminary report indicated that roentgenoscopic examination of chests made by well-trained physicians experienced in this type of work detects tuberculous lesions which otherwise are unrecognized by physical examination alone.

It occasions no surprise that Metropolitan Life Insurance Company pursued the question further. Indeed, one year later, Ada Chree Reid (1929) published a much more detailed account of the Metropolitan Life experience with this problem.

In the years 1924 to 1927, 53 cases of tuberculosis were admitted to a sanatorium for tuberculosis within eighteen months after they began to work for the Metropolitan Life Insurance Company. Presumably, they had tuberculosis at the time of their employment despite a negative physical examination at that time. Reid stated that it is admitted by a number of competent observers that physical examination may miss early tuberculosis in 5 to 10 % of individuals. Cavities may be missed in as high as 50 % of the cases according to Reid's account. The presence of persons with tuberculous cavities in a work force is an open invitation to spread tuberculous disease to healthy individuals (See Chapter 15).

Metropolitan Life Insurance Company reasoned that it would be much more costly to make roentgenograms of everyone to be employed than to have the persons roentgenoscoped. It was felt that the roentgenoscope is a valuable adjunct to physical diagnosis and was employed in the home office of the Metropolitan Life Insurance Company beginning October 1, 1927. From October 1, 1927 to September 30, 1928, 4,883 applicants successfully passed their physical examination. Of these, 59, or 1.214 per cent, were found by roentgenoscopic examination to have tuberculosis. This was confirmed by roentgenograms. Of the 59 cases, 35 reported back in one year. Sixteen were found to have active progressive tuberculosis. The lesions demonstrated varied from minimal to advanced lesions.

There are several points to make concerning these observations. From the human point of view, the major point is to emphasize how lucky those applicants were to have the services of an experienced, well-trained roentgenoscopist and availability of a functioning roentgenoscope. We have no doubt whatever that the lives of a high proportion of those diagnosed with tuberculosis in this manner were saved. Yes, they had an increase in the risk of future cancer, but the roentgen-ray and its use made it possible for them to be alive for decades beyond the discovery of tuberculosis. We have made this point before in describing what collapse therapy of tuberculosis, aided by fluoroscopy, meant in saving lives. This is a different facet of the same problem.

From the radiation exposure point of view, we would need to know how widespread the practice described for Metropolitan Life became in the United States. Surely, other industries must have heard the message and undoubtedly some other industries used the same approach to weeding out prospective employees with active tuberculosis. Unless there is some central recording somewhere concerning how many persons received such fluoroscopic examination, we are unable to ascertain any proper entry into our Master Tables for this radiation source.

Part 2. The Demand for Chest X-rays in Employment Situations

Whatever the case might have been for industries with respect to screening which used the services of a trained expert roentgenoscopist, it certainly was true that employers broadly demanded that new employees have chest films before being accepted for a position. And tuberculosis was THE disease of concern in such exams.

In numerous school districts throughout the country, school teachers had to have an annual chest film in order to receive permission to teach. Unfortunately, the expertise with which such employment examination chest films were read hardly was any match for the type of ability shown by those who did the roentgenoscopy for Metropolitan Life.

The dose received by millions of young women in school systems and in other employment situations is not easily known. To the extent that photofluorography was NOT employed, the average dose may well have been quite low, per examination. The doses, in the main, were not part of those accounted for in hospital x-ray departments or in doctor's offices. As a result, the doses received in such employment examinations are not represented anywhere in our Master Tables. They simply represent a source of breast irradiation for which there is no accounting ---- and hence they represent an underestimate in radiation doses received by the breasts of women in the 20th century.

The number of new cases of pulmonary tuberculosis in U.S.A. decreased steadily in the decades beyond 1950, but that hardly was sufficient for the school board bureaucracies to give up their demand for the annual chest film for school teachers. As a result, school teachers received an unnecessary annual dose of chest irradiation long after the medical need for tuberculosis screening was over. It is a little early to say whether the resurgence in tuberculosis in the 1980s and 1990s will change this screening requirement once again. Diseases such as tuberculosis can hardly ever really be said to be eradicated.

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"Consistency requires you to be as ignorant today as you were a year ago."

● — Bernard Berenson, 1865–1959,
American art critic.

CHAPTER 31

Fluoroscopy: Source of a Big Underestimate in Our Breast-Dose Finding

Part 1. Why We Think Fluoroscopy Has Been Seriously Underestimated

Many times in the chapters of Section 2, we have demonstrated our policy of trying to arrive at a "credible lower limit" of average annual radiation exposure to the breasts, 1920–1960.

In this chapter (and the next), we intend to show why we must regard the real contribution of fluoroscopy to breast-irradiation to be FAR greater than evaluated in our Master Table. We begin with some reminders. In no chapter where fluoroscopy was known to be involved, or considered likely to have been involved, did we ever estimate a fluoroscopic dose to anyone of more than 5 medical rads to the breasts (Chapter 8, Part 2). For general diagnostic fluoroscopy (Chapter 23, Part 3), we assumed that fluoroscopy was never done with the beam traveling from front to back, we assigned a breast-dose of only 0.111 rads per average fluoroscopy, we assigned no population-dose at all for children under 15 years of age, and for frequency of fluoroscopic examination, we used data from the 1970s.

By contrast, some of the reality in approximately the 1920–1960 period was described in 1969 by Carl B. Braestrup, whom we already quoted in Chapter 23, Part 1 (from Shapiro 1990 at page 379):

"The Wappler fluoroscope, manufactured around 1930–1935, produced 125–150 R/min at the panel. Skin reactions were produced and in some cases, permanent injury. To minimize hazard, a '100 R per examination' limit was set in the New York City hospitals."

We can not just walk away from those observations of Braestrup. And we can not believe at all that New York City was Neanderthalia, and that all was very different elsewhere in the country. Braestrup reports that (a) skin reactions were produced, and (b) in some cases, there was permanent injury. Visible skin reactions usually mean an absorbed dose of about 200 rads or more in the skin, and permanent skin injuries require even higher doses (see Chapter 29, Part 3).

"The Thing Speaks for Itself"?

When there was a necessity of limiting each fluoroscopic exam to 100 Roentgens because some people were clearly receiving even more, it might really be a fair statement that "the thing speaks for itself" and that ionizing radiation received in the 1920–1960 period explains the great majority of all the breast-cancers which have been occurring in recent decades.

Of course, that one source of evidence need not "speak" alone. Dr. Francis Curry has already spoken about the use of photofluorograms and fluoroscopy in a 1950 mass screening-program from which "many people were getting [whole-body] doses big enough to show clinical symptoms" (Chapter 16, Part 1).

There is MUCH additional evidence to present about the popularity of fluoroscopy – and its widespread use by unqualified people, as readers will see. Anyone who denies that

medical irradiation has a major role in explaining the breast-cancer problem, really has an obligation to be realistic about fluoroscopy.

Part 2. The Routine Fluoroscoping of Well-Babies

We begin with the topic of routine pediatric fluoroscopy, briefly mentioned in Chapter 23, Part 1.

"Those of you who have been in the field a long time know that it was once the practice of pediatricians to fluoroscope babies and young children every month and when they had the annual checkup. When we questioned this practice, pediatricians would say, 'Well, the parents expect it. They think if I don't fluoroscope the patients, they are not getting a complete examination'."

That statement was made in 1970 by Dr. Hanson Blatz, who was director of the Office of Radiation Control, New York City Department of Health. And there is good reason to believe that pediatric fluoroscopy of well-babies was occurring from one end of the country to the other.

Confirmation from Dr. James Pifer and Colleagues

Dr. James Pifer and his colleagues have described the case material, radiation factors, and study methods in the investigations of enlarged thymus therapy with x-rays in the Rochester Studies of this problem (Pifer 1963). At page 1358, where they described the circumstances which led certain children to become involved in such therapy, Pifer and colleagues stated the following:

"... Also, the indications for treatment differed with each radiologist, pediatrician, or general practitioner. Frequently parents insisted that their child be treated. Some pediatricians fluoroscoped all infants routinely, but probably most children treated in private offices had symptoms at presentation which prompted a radiologic examination ..."

That is an eye-opener of the first magnitude. "Some pediatricians fluoroscoped all infants routinely."

That is precisely what Dr. Blatz was telling us had been his experience, too. Well-babies getting fluoroscopy. Regularly. And the information fits the experience of the woman who wrote to me about her own experience as a child in New York. She could remember being fluoroscoped at every visit to the pediatrician from age 4 through age 12. She had no recall of medical attention one way or the other before age 4, as we mentioned in Chapter 23, Part 1.

Had this pediatric practice left New York State? Indeed it had. We find it on the other side of the country. We will look at the story out west.

More Confirmation, from Dr. Franz Buschke and Herbert M. Parker

Buschke and Parker published a very low-key bombshell, in the Journal of Pediatrics (1942), entitled "Possible Hazards of Repeated Fluoroscopies in Infants." The paper had been read before the North Pacific Pediatric Society, in Seattle, Washington, January 31, 1942.

The opening paragraph follows:

"Recently we became aware of the fact that apparently a number of pediatricians include a fluoroscopy in the monthly routine examinations of infants in their care during

the first and second years of life. Since we feel that such a procedure is charged with potential hazards, we welcome the opportunity of discussing this problem at your initiative in this group."

X-Rays Like a "Powerful Drug" --- Not "Glorified Photography"

The second paragraph illuminates a sorry state of affairs in the level of basic information NOT possessed by the pediatricians --- or even by some radiologists of the time (p.524):

"It is too often not realized that x-rays, in addition to being a useful diagnostic tool, accidentally and unfortunately represent at the same time a powerful drug. As Dr. Case once pointed out, x-ray diagnostic procedures are still considered by many as a kind of 'glorified photography.' Yet every exposure to x-rays actually delivers radiating energy to the body. The output of different diagnostic machines varies within very wide limits, depending upon the milliamperes and kilovolts used, the filtration, the distance between tube and body surface, the time of exposure, and the size of the exposed field. But even many specialized radiologists do not know the actual output per minute of their diagnostic machine."

Buschke and Parker were advising the pediatricians against the practice of monthly fluoroscopy in the routine examination of infants in their care during the first and second years of life. After studying the radiation output of seven randomly chosen x-ray apparatuses in the offices of "reputable pediatricians selected at random," they drew some conclusions of likely doses to infants irradiated in the manner then current. They wrote (at page 527):

"If the average rapid fluoroscopy by an experienced and well-adapted examiner takes twenty seconds, about 8.3 R will be delivered at this rate or 100 R during the first year of life. Actually we know from experience that some of the fluoroscopies last considerably longer."

Fortunately, NOT all pediatricians were using routine fluoroscopy on problem-free babies. We have found no estimate of what fraction did.

"Even in the Best Places ..."

In the seven offices visited, Buschke and Parker found that "none of them knew the output of their machine" (p.525). They found one machine which delivered 35 Roentgens per minute at the supposed operation of 5 milliamperes (Ma.) "The physician in charge, however, reported that the amperage is inconstant and that the amperes would change up to 40 Ma. without change of the controls. In such a case, an amount of about 200 r might be delivered to the infant's body in one minute" (p.525). And they also reported (p.527):

"In another place under the direction of one of the best radiologists we found that the output differed with the operator ... While the physician assumed that he was always fluoroscoping infants with 3 Ma., we found accidentally that one of the technicians when he happened to be at the control would give him 5 Ma., increasing unnecessarily the output from 23 to 38 r. This example again emphasizes that even in the best places there is not sufficient appreciation of the potential hazards, and there is a lack of attention to details with the purpose of minimizing them."

Don't Instruct the Mother While the Beam Is On

Another indication that Buschke and Parker observed appallingly casual attitudes toward the x-ray beam, is reflected in their third recommendations to the pediatricians (p.532):

"3. The exposure time should be kept as short as possible. No discussion of the fluoroscopic findings is permitted as long as the shutter is open. This naturally means that an explanation of the screen picture to the baby's mother during fluoroscopy is not permitted."

Resistance by "the Unbeliever," as Reported by Buschke and Parker

The smaller the child, the more worried were Buschke and Parker about preventing excessive exposure from fluoroscopy (p.525):

"... For the majority of diagnostic procedures used in general practice, the lack of appreciation of these potential hazards is regrettable but probably not a cause of major concern because these procedures in adults and older children are usually limited to fairly small portions of the body. If the small body of an infant is exposed to the same kind of radiation, a comparatively much larger volume of body is irradiated. This risk is naturally increased if such fluoroscopies are done repeatedly in infants at short intervals. For this reason it seems necessary to give even more attention to details of the fluoroscopic procedure with infants in order to eliminate or minimize the possible detrimental effects."

And:

" We will meet, and as a matter of fact have repeatedly met, the objection that never has any damage been observed by those who have used this procedure throughout many years. But as we have already pointed out, the possible effects of doses under consideration here are much more difficult to demonstrate and, it is true, by their very nature can be anticipated only by implications from our general knowledge of radiation biology and from comparison of doses delivered with those used for other therapeutic purposes. IF WE WAIT UNTIL DAMAGE IS PROVED BEYOND THE DOUBT OF THE UNBELIEVER, IRREPARABLE HARM MAY HAVE BEEN DONE [emphasis added]."

What Kind of "Irreparable Harm"?

Buschke and Parker never mentioned breast-cancer (or any other sort of cancer) as the focus of their concern. They wrote this paper in 1942, long before MacKenzie's paper of 1965. Their worry in 1942 about routine fluoroscopic doses was centered on injury to the gonads and to the future DESCENDANTS of the irradiated children (p.527-532). "The doses in question here are well within the range in which such damage might be expected," they warned at page 528. They were concerned about radiation-induction of inherited "disease entities ... such as diabetes, susceptibility to tuberculosis, cleft palate, certain diseases of the central nervous system, etc." (p.529). And they observed (p.530):

"To most clinicians all arguments based on genetic considerations appear somewhat as fairy tales. This is due to the fact that definite conclusions in the field of genetics can be reached only by statistical evaluation of a vast number of observations throughout many generations. Obviously therefore conclusions in regard to human pathology can be reached only in analogy to those obtained by animal and plant experiments."

An Interesting Contrast in Attitudes

In Chapter 28, Part 7, we reported some sweeping assertions in the 1960s about the alleged safety of high-dose mammography --- at a time when clear warnings about the actual state of ignorance would have been appropriate.

Here, we are very pleased to call attention to the wisdom of Buschke and Parker, who showed a very different policy toward acknowledging ignorance and uncertainties. Clearly, they tried hard to warn the medical profession about "irreparable harm" which can be caused by appeasing "the unbeliever."

Buschke and Parker met repeated objections to their warnings about radiation, from physicians who had never PERSONALLY observed any damage clearly connected with fluoroscoping babies within their own limited practices (p.525), or who demanded absolute proof of delayed harm from nearly impossible epidemiologic studies (p.530). In our opinion, such physicians must have received an inadequate medical education. Otherwise, they would have accepted the potential REALITY of some important consequences which can not be proven within a personal practice or even by any real-world epidemiologic studies. Moreover, if they had realized how really hard it is to establish lasting truths in matters of medicine and health, they would have questioned the alleged fact that there was no hazard to the babies from fluoroscopy.

The need to allow for nasty surprises, in the form of unidentified long-term consequences, is well illustrated by the fact that Buschke and Parker apparently did not even imagine the menace of radiation-induced breast-cancer. They were pleading for reduced radiation exposure on other grounds.

Some Advice to Women and Their Families

You are going to hear soothing words many times about many marvels: "Never has any damage been observed by those who have used this procedure throughout many years."

We can offer this advice: When you do hear this, distance yourself from the source, and have a hard look at the type of evidence offered in support of the statement. Will you gain enough, by making the extra effort? Not always. But you may want to consider one illustration of real benefit, presented in Part 3.

Part 3. What Harm Could the "Unbelievers" Do? A Quantitative Analysis

Sometimes, a few numbers can tell a story not easily related in thousands of words. This is one such occasion.

We will do an "if-then" exercise to answer the question: What harm could the "unbeliever" pediatricians have done, by the routine fluoroscopy of well-babies? We will limit the analysis to radiation-induced breast-cancer. Of course, we are using the term "unbeliever" as Buschke and Parker did (Part 2), to denote pediatricians who refused to believe that there might be delayed hazards from such repeated fluoroscopies.

The "If-Then Scenario" per Million Female Infants

- - 1. Start with 1,000,000 female infants.

- - 2. Do the pediatric fluoroscopy each month for 24 months with an average dose of 8.3 Roentgens of exposure per exam. This means a total exposure in the first two years of life of 24×8.3 , or just about 200 Roentgens. These figures come from

measurements by Buschke and Parker, who say the average dose per exam was probably higher than 8.3 R because the duration probably exceeded 20 seconds (Part 3).

• - 3. While Buschke and Parker suggest that most of these fluoroscopies were done with the beam entering the back, we can be sure that some were done with the beam entering laterally or from the front. Nonetheless, we will assume that all were done with the beam entering the back --- which reduces the hazard to the breasts.

• - 4. Elsewhere in this book (in Chapter 23, for example), we use a factor of 0.037 to convert Roentgens to breast-dose in rads, for back-to-front beams. Because of the very small body-size of babies, this factor will underestimate the breast-dose. Nonetheless, we will use it without any adjustment. So for these infants, we will approximate a breast-dose of (200 R x 0.037 rads per R), or about 7.4 rads during the first two years of life.

• - 5. The conversion-factor (from dose to breast-cancer), comes from Chapter 39 --- the Master Table, Column V. Its origin is explained in detail by Chapter 40. The conversion-factor for age-1 and age-2 is:

92.74 radiation-induced breast-cancers per 10,000 person-rads.

Extra Cancers of the Breasts	$(7.4 \text{ rads per person}) \times (1,000,000 \text{ persons}) \times \frac{92.74 \text{ breast-cancers}}{10,000 \text{ person-rads}}$
=	68,628 radiation-induced breast-cancers among every million women who were fluoroscoped as well-babies in the monthly regime described by Buschke and Parker. The estimate is that these 68,628 women per million will develop a breast-cancer in their lifetime even if they were never exposed to any additional medical radiation. The rate of 68,628 women per million women is 1 out of 15.

"I Never Saw Any Damage in My Own Practice"

The lesson of the "if-then" scenario is the ratio --- 1 out of 15 --- not the absolute number (68,628). We have no way of estimating the absolute number without knowing how many million female infants experienced the full regime of well-baby fluoroscopy over the years. We do know that the maximum number "enrolled" by pediatricians in such a regime each year could not possibly exceed the number of females born per year, which was about 905,000 per year in the USA during the 1920-1960 period (from the Master Table, Column A).

Women are quite upset that 1 in 9 of them are currently going to experience breast-cancer. Our "if-then" scenario indicates that those "unbeliever" pediatricians who scoffed at the Buschke-Parker advice created a situation where they could be responsible, among their former patients, for a lifetime rate of breast-cancer which is about 1 in 15. Of course, the "unbeliever" pediatricians never PERSONALLY saw any damage at all.

Can we justify a statement that women and their families owe an enormous debt of gratitude to pioneers like Buschke and Parker, who probably reduced the number of well-babies who received routine fluoroscopies? Obviously, the answer is, "Yes."

Part 4. An Additional Expert Who Reported Hazards and Tried to Prevent Them

Carl B. Braestrup, of the Physics Laboratory of the Department of Hospitals of the City of New York, was persistent in the early years in attempting to limit the hazard of exposure both to patients and staff. Some of his relevant comments in a talk before the New York Roentgen Society in April 1941 (published in 1942) are presented below.

A Certain Fluoroscope Called "A Lethal Diagnostic Weapon"

Describing his experiences with many, many fluoroscopes, Braestrup stated (pp.210-211):

"During the past years we have measured the R [Roentgen] output of large numbers of fluoroscopes, USING THE SETTINGS AT WHICH THEY ARE NORMALLY OPERATED [emphasis added] ... and have found a very wide variation ... Attention is called particularly to test B-116, where the R per minute at the panel was 127, that is, an erythema dose would be reached in about three minutes. SUCH A UNIT COULD BE CLASSIFIED AS A LETHAL DIAGNOSTIC WEAPON AND YET THERE ARE MANY OF THESE STILL IN USE [emphasis added]. This particular one was changed to reduce the output, and the results are shown in test B-129."

We recommend that readers hold these observations of Braestrup in mind as we later describe (Chapter 32) how the virtues of fluoroscopy were extolled in a "blitzkrieg" campaign for more fluoroscopy in the decades of the 1920s and 1930s, and beyond. Responsible people like Braestrup and others seemed to face the attitude: "First use, then learn."

Mobile Fluoroscopic Units: In Surgery and at the Bedside

Braestrup expressed great concern about the mobile units used in hospital radiology. He stated the following (p.213):

"Of the various types of radiologic equipment, the mobile unit probably has been responsible for more radiation damage than any other piece of apparatus. THESE ACCIDENTS HAVE IN MOST CASES OCCURRED WHILE THE MOBILE UNIT WAS USED FOR FLUOROSCOPY BY SURGEONS, WHO APPARENTLY DID NOT REALIZE THE HIGH OUTPUT OBTAINED AT SHORT DISTANCES [emphasis in the original]. Measurements show that at the shortest possible distance, about 8 cm., the R per minute is as high as 1000 without filter at 85 kv. and 5 ma. [milli-amperes]. To avoid these excessive doses it is recommended that all mobile units be provided with fixed cones or a frame arrangement preventing the target-skin distances from being less than 30 cm (12 inches). In addition, the aperture should be provided with a fixed filter of not less than 1.0 mm. Al." And:

"A considerable amount of bedside radiography is done in the larger hospitals, and it is therefore important to consider the protection of the operator of the mobile unit. Tests show that the average stray radiation at the technician's position, 1.5 meter from the tube, is about 0.0044 R per 100 ma.second exposure [milliampere-second exposure]. It is advisable to rotate the technicians doing mobile work, or have them wear lead rubber aprons."

Braestrup's very basic recommendations about the mobile fluoroscopy units were necessary --- even though medicine in 1941 was about 40 years into the Roentgen era. What does the need for such advice imply about casual use of fluoroscopy by unqualified

people --- and the massive, never-recorded doses which may have been delivered by fluoroscopy to female breasts in the 1920-1960 period?

Measurements of "Stray" Radiation from X-Ray Equipment

Braestrup did measurements for "the average ray-proof tube" to establish how much stray radiation would be received by by-standers at a distance of 1 meter from a patient's midline, at right angles to the central beam. He reported his findings as follows (p.209):

"In evaluating the significance of the tube protection, it should be borne in mind that the direct stray radiation --- that originating from the tube --- is only a small part of the total stray radiation received under actual operating conditions. Measurements show that the scattered radiation from the patient is many times as high as the direct stray radiation from the average ray-proof tube." And he provided a startling demonstration of this in his Table 5, entitled "Comparison of Direct and Scattered Stray Radiation":

Field Diameter cm	Type of Stray Radiation	Stray Radiation at 1 Meter Roentgens per hour	Ratio
0 (lead placed in aperture)	Only Direct	0.01	1.0
8	Direct+Scattered	0.03	3.4
35	Direct+Scattered	0.72	80.0

Exposure of the Radiologic Staff, Nurses, Orderlies, Parents, and Residents

Braestrup warned about irradiation of non-patients, as follows (p.212):

"Unfortunately, it is not always possible for the staff to remain behind protective barriers during the exposure. Patients, particularly babies, often have to be supported or held while the x-ray tube is energized, dental units are used without protective screens, and the cystoscopist is exposed to secondary radiation ... This amount of stray radiation makes it advisable for members of the radiologic staff never to expose themselves to scattered radiation if the work can be entrusted to nurses and orderlies who are not normally exposed to the rays."

The reader might be outraged by this apparent concern for the radiologic staff but not for nurses and orderlies. We think Braestrup's words give the wrong impression of what he meant. In reality, the philosophy which has pervaded radiology departments is simply that the procedure IS GOING TO GET DONE, so someone in addition to the patient may have to take a dose in the process. Members of the radiology staff get dosed every day in their work. By contrast, the nurses or orderlies who bring a patient down to the radiology department only rarely would get a dose in the manner suggested by Braestrup. Others have suggested strongly that parents should do the holding of babies and children when necessary in the x-ray department.

Did these exposures actually occur in our hospitals? They most certainly did, and for many decades. We can vouch for such exposures having occurred in the hospitals of the University of California, San Francisco, and of Stanford University. In the former, Professor Helen Gofman, as a resident in pediatrics during the years of World War Two, held infants who were receiving radiation. She related that the reason given was that the

department was short of staff. In the Stanford case, a radiation technician stated that she commonly held infants who were to be x-rayed because she did not expect to have children. Her reasoning was that the younger nurses and technicians might still be planning a family and therefore should not receive the radiation.

One More Type of Unrecorded Breast-Irradiation

In this way, many young women in their 20s, 30s, and 40s received a radiation dose to their breasts during x-ray procedures, without it being recorded. When they held the children and others needing help, they very rarely had film badges or dosimeters. Their radiation dose does not find its way into our Master Table. So this represents one more source of dose underestimation in our analysis.

Part 5. Fluoroscopy and the SELF-Injury of Non-Expert Physicians

In 1937, Dr. Eugene Leddy of the Mayo Clinic wrote an editorial entitled "The Dangers of Roentgenoscopy: Summary and Recommendations" which appeared in the American Journal of Roentgenology and Radium Therapy. Although the editorial concentrates on the SELF-injury of physicians from doing fluoroscopy (roentgenoscopy), it also conveys a great deal about the frequent use of fluoroscopy nationwide, often by general practitioners and surgeons. Dr. Leddy was well qualified to write such an editorial, in view of his study of radiation-injured physicians (Leddy 1936), which we will also describe.

Examinations of Patients "Generally Include Roentgenoscopy"

At page 924, Leddy stated: "In fact, roentgenologic methods of diagnosis are so important that no investigation of a patient is considered complete without roentgenologic examinations, which generally include roentgenoscopy. These studies often are carried out by a general practitioner or surgeon in his office because of lack of facilities for expert study nearby or because the physician sees no need to refer the patient to a roentgenologist. In many localities it is cheaper and more convenient 'to have some pictures made' in 'an x-ray laboratory' operated by a layman than it is to have the appropriate examinations made by a roentgenologist."

"... Careless, Indifferent, or Even Ignorant Use of the Roentgenoscope"

Leddy worried in the 1937 editorial that conditions were getting worse, not better: "From data available from the Bureau of Census and from manufacturers, it has been impossible for me to find out the number of roentgen machines in use in this country. But various estimates which have been given to me indicate that perhaps 2 to 5 per cent of all physicians in this country have roentgenologic equipment of some kind in their offices. When one considers the number of diplomates of the American Board of Radiology in contrast to the number of physicians and others who 'do a little x-ray work' one can estimate roughly the magnitude of the risk of injury that those in this latter group run from casual and nonexpert roentgenologic procedures. With such a great number of roentgen machines in use, one wonders whether injuries by roentgen rays will not be even more common in the immediate future than they were in the tragic days of the pioneers in roentgenology." And:

"It is well known that the majority of physicians who suffered injuries which sometimes led to their death sustained these injuries in the course of roentgenoscopy [fluoroscopy]. The story of the tortures endured by physicians who had extensive roentgen burns has been often and well told. One needs but to read the masterpiece by

Brown, 'American Martyrs to Science through the Roentgen Rays,' to appreciate the tragedy likely to follow the indiscriminate, careless, indifferent or even ignorant use of the roentgenoscope."

Ten Years of "Shockingly Little" Literature on Protection against Radiation

Leddy's editorial expressed fear about injuries in the future: "Because the American literature of the past ten years contains shockingly little about protection against radiation in roentgenoscopic procedures, I am fearful about injuries in the future and hope that they may be minimized by the work of suitable committees."

And once again, he reported on the complete ignorance among a number of physicians who used the fluoroscope:

"In my studies on the causes of roentgen injuries among physicians it was brought out that many of them did not realize that the changes in the skin of their hands were due to roentgen rays, and they exaggerated the already existing injury by their treatment."

Leddy's Study of Physician Injuries and Their Meaning

In a 1936 paper, Leddy reported on the Mayo Clinic's experience with physicians who came to the Clinic for advice on, or treatment of, roentgen-ray dermatitis. The number was steadily growing:

5-Year Time Period	Number of Physicians Seeking Advice for Roentgen-Ray Dermatitis
1919-1923	7
1924-1928	13
1929-1934	35
Total	55

Leddy had a great interest in learning how these injuries occurred. What did he find?

"A Good Strong Dose" from the Office Clerk

Eight of the 55 physicians seeking advice or treatment had been injured while themselves undergoing roentgen therapy for BENIGN dermatoses, such as eczema, psoriasis, acne, or pruritus [persistent itching]. These are among the leading skin conditions which were commonly treated with roentgen rays (Chapters 33 and 34).

Only one of the eight was treated by a radiologist. In that case, the physician had been treated by a radiologist for a benign condition, with good results. But then he insisted that the radiologist repeat the treatment too many times, and an injury had resulted.

One other physician prescribed his own treatment: He asked his office clerk to give him "a good strong dose." She did. An ulcer resulted. The six other physicians in this group were treated by some doctor who had a roentgen-ray machine and 'did some x-ray work.' In no case was the treatment given by a qualified dermatologist.

Fluoroscopic Self-Injury: "Shocking, Although Hardly Surprising"

"Aside from the 10 physicians who suffered injuries while undergoing roentgen treatment, the other 45 sustained injury from using the roentgenoscope in their practice. Almost always this consisted in reducing fractures or removing metallic foreign bodies

under roentgenoscopic control. A few physicians had used the roentgenoscope in examining the chest in tuberculosis surveys or had sustained their injuries while conducting gastrointestinal roentgenoscopic examinations. Of these 45 physicians, 44 were not radiologists. The only radiologist who was injured had been a pioneer in the work, and at the time he was subjected to excessive irradiation the possibility of injury therefrom had not been considered" (Leddy 1936). And:

"It is shocking, although hardly surprising, that out of a total of 45 physicians who were injured by using their own roentgen-ray machines, 44 were not radiologists. As has been stated, they were either surgeons who used roentgen rays in their work or general practitioners who used the roentgenoscope to facilitate the examination of patients."

Some Implications of Dr. Leddy's Statements

Although Dr. Leddy's focus both in 1936 and 1937 was on self-inflicted injury of physicians who were not trained in proper use of the fluoroscope, it seems realistic to infer from what he wrote that such users would also have exposed their PATIENTS (and staff) to much higher doses than necessary. And Dr. Leddy indicated that the non-radiologists "doing a little x-ray work" greatly outnumbered the radiologists.

Part 6. Stories Which Qualified Roentgenologists Told Each Other: 1943

In 1943, Alfred DeLorimier and colleagues gave a paper at the 43rd annual meeting of the American Roentgen Ray Society. It was entitled, "Protective Features Provided with the United States Army Field Roentgenoscopic Equipment." The paper elicited a lively (published) discussion, from which we provide some illuminating comments and stories.

The Doctor and the Dentist Who Went Shooting Together

Dr. Robert Taft, of Charleston, South Carolina, discussed the paper at p.659:

"... I am glad to say that the pendulum has swung in the right direction in regard to roentgen-ray protection and I am delighted to see papers of this kind presented. There is only one thing wrong about a presentation of this kind. IT DOES NOT GET TO THE RIGHT MEN [emphasis added]. The members of the American Roentgen Ray Society know something about roentgen-ray protection. Where these papers ought to be given is back home in our local medical societies where men are fooling with small roentgen machines without knowing what they are doing." And:

"I have only to quote briefly a paper of our esteemed colleague, Dr. Pfahler [one of the giants of early radiology], from the American Dental Journal a number of years ago. Very briefly, if I remember the story, a physician and a dentist went out shooting. There was a minor accident. One of them got a small shot in his finger. They came back and proceeded to remove it fluoroscopically under the dental roentgenographic machine, as a result of which both of them had to have so many fingers amputated that the dentist had to quit dentistry and the surgeon had to give up surgery." And:

"Those things go on happening and I know of many cases that have happened after Dr. Pfahler wrote that paper."

"The Beautiful Nurse with Her Toe on the Foot Switch"

At the same discussion, Major Theodore S. West commented about misleading advertisements for x-ray equipment:

"Colonel DeLorimier and his associates have made a great contribution in this investigation of roentgen-ray hazards. I have been greatly interested in the matter of roentgen-ray protection for many years, and it is my belief that many of the younger roentgenologists do not fully appreciate the hidden dangers of the agent with which they work, and they are inclined to expose themselves to an unsafe amount of radiation. And:

"... I heartily agree with Dr. Taft that this work of Colonel de Lorimier's should be broadcast to the medical profession at large, and not be presented only to roentgenologists who are at least supposed to realize the dangers. Roentgenologic apparatus is now being purchased and used by an increasing number of physicians who had not had adequate training or instruction, and who do not appreciate the dangers." And:

"Advertisements for apparatus seem rather to emphasize the innocuousness of the roentgen ray. I recall a picture in one of the recent journals showing the patient cozily snuggled in bed, the mobile roentgen unit in position, the kindly doctor along side, and the beautiful nurse with her toe on the foot switch. No protective apron or gloves, not even a reasonable distance protecting anyone from the scattered radiation."

Time for a Better Brochure?

Major West continued: "I have recently seen several cases of severe roentgen burns resulting from the use of the fluoroscope for guidance in setting fractures or extracting foreign bodies. The victims in four of these cases, were physicians who 'didn't realize the danger'." And:

"It seems to me that it is the responsibility of the radiological societies to make an attempt to educate the profession at large on this matter. Perhaps a brochure on the subject could be published by the combined societies, and, in cooperation with the manufacturers of roentgen-ray equipment, given to every purchaser of a roentgen-ray apparatus. This may be a big order, but I believe it is our job to see that some such work is done."

Part 7. The Meaning of All This regarding Our Underestimation of Dose

We should think a great deal about these remarks provided by men of experience, as we consider the possible true doses which patients, on the average, were getting from various fluoroscopic procedures in the 1920-1960 period. It is absolutely clear, in our opinion, that we must regard the real contribution of fluoroscopy to breast irradiation to be FAR greater than evaluated in our Master Table.

We believe, but can not prove, that the real annual average breast-dose from diagnostic fluoroscopy alone, probably exceeded everything evaluated in the Master Table for 1920-1960.

- - From Dr. Braestrup (Part 1), we have established that fluoroscopic exams gave such high doses that a limit of 100 Roentgens per exam had to be set by the City of New York. The Wappler fluoroscope manufactured around 1930-1935 produced 125-150 Roentgens per minute at the panel. Braestrup considered certain types of fluoroscopes to be "a lethal diagnostic weapon" (Part 4).

- - From Dr. Leddy (Part 5), we have established that "no investigation of a patient is considered complete without roentgenologic examinations, which generally include roentgenoscopy." Such a statement indicates that fluoroscopy must have been

exceedingly common. Also from Leddy, we established that non-radiologists who used these machines greatly outnumbered the specialists in radiology.

● - It would seem foolish indeed to believe that the frequency of fluoroscopies was only whatever was RECORDED in the 1920-1960 period. Whose crystal ball is good enough to divine the real frequency during years when just about any physician could purchase and use a fluoroscope with no need to measure the doses or report the number of fluoroscopies to anyone?

● - From Drs. Blatz, Pifer, Buschke and Parker (Part 2), we have established that an unknown fraction of pediatricians gave routine fluoroscopic examinations to healthy babies during each routine check-up ... and that sometimes parents insisted on it. Our "if-then" analysis (Part 3) indicated that radiation-induced breast-cancer would be delivered --- decades later --- to about 1 out of every 15 female babies who actually received the 2-year regime described by Drs. Buschke and Parker.

● - From the experts cited in this chapter, we have established that, in general, the general practitioners, pediatricians, and surgeons who used fluoroscopy did not appreciate the dangers. It is realistic to infer that their patients received radiation doses which were much higher than necessary.

● - How did all this come about? In the next chapter, we will describe the blitzkrieg and "promotional hype" for fluoroscopy in the 1920s, 1930s, and beyond.

#

1925: A Leading Figure in Radiology Warns about the Amateurs

"Physicians who have made a life study of roentgenology or radium therapy are familiar with the dangers involved, and in many instances have suffered for their early ignorance of these dangers."

And:

"In recent years, among the general profession and the untrained enthusiasts who have purchased roentgen-ray machines or radium there is an astounding sense of security, and a profound ignorance of the dangers involved. They seem to think that the dangers have all passed and that now these powerful agents are made safe for anyone to use. The diagnostic value of the roentgen ray ... and the therapeutic results ... and the enthusiastic propaganda of commercial salesmen have created a great demand for and a wide distribution of these machines."

And:

"As a result, many institutions, many physicians, and even laymen have installed such equipment. They have given much more consideration to the financial investment than to the mental equipment necessary to do justice to the patients or themselves. As a result the health and lives of both the patients and the operators are jeopardized."

And:

"Warnings have been sounded repeatedly, but especially have we urged caution during the recent years. We still have the memories of the damages done twenty and twenty-five years ago, but in the hands of the untrained or careless, the dangers are a hundred times as great today. In the hands of the well-informed, trained and careful, these agents are almost perfectly safe."

● – Excerpts from an editorial entitled "The Dangers in Roentgenology and Radium Therapy," by Dr. George E. Pfahler, in the American Journal of Roentgenology and Radium Therapy, Vol. 13: 276–277. 1925.

In the remaining paragraphs, Dr. Pfahler recommended that local radiological societies teach the unqualified, and that states require a special license to permit any physician to use roentgen rays in diagnosis or treatment.

CHAPTER 32

Hard-to-Find Doses from Fluoroscopy and Other Sources

Part 1. Some Seriously Unwarranted Early Optimism Concerning Fluoroscopic Hazard

Preston Hickey, M.D., of Ann Arbor, was one of the illustrious radiologists of the early period. In 1922 he addressed the American Roentgen Ray Society. He made some points which, in retrospect, should scare us all --- especially with what came to pass.

In his published paper (Hickey 1923) we find the following:

"A more liberal use of fluoroscopy in the removal of foreign bodies is also traceable to the army training. No longer is the hand or foot extensively mutilated in long-continued efforts to find a needle or a bullet. Operation under fluoroscopic control is now perfectly safe by the intermittent method, and results in easy removal, with a minimum of laceration of tissues." And:

"The extensive use of the fluoroscope in the manipulation and control of fractures is also a step in roentgenologic progress." And:

"Another outcome of the development of war activities has been the diminution in the size of machines. With the self-rectifying tube and the bed-side type of transformer, the internist is now able to do adequate fluoroscopy and still not encroach on valuable office space. In planning or installation of x-ray outfits in buildings where the price per square foot is high, this constitutes a very important item. Practically very little floor space is needed for the electric part of an x-ray outfit." And:

"It is interesting to note also the large number of internists who have placed fluoroscopes in their offices, not with the idea of specializing in x-ray work, but simply wishing to have conveniently at hand an x-ray control of their physical findings. Here again, the simplified apparatus which has developed from war-time practice is conspicuous."

It would be a gross understatement to say that Dr. Hickey was a bit optimistic about the virtues of these machines getting into the hands of those totally untrained to handle them appropriately. (See Chapter 31, where Leddy, Taft, and West make highly relevant comments many years later.)

Part 2. Ardent and Sincere Advocates for the Fluoroscope

Dr. Louis Faugeres Bishop must certainly be cited as the advocate of advocates for fluoroscopic investigation. And he undoubtedly had the expertise to know the benefits in experienced hands. He gave a talk at the Medical Society of the Greater City of New York in 1922 [published].

We single this paper out, not only for its advocacy of fluoroscopy, but because his focus is heavily on the use of the fluoroscope in diagnosis of diseases of the heart. There appeared to be a whirlwind of interest in all aspects of heart measurements, heart motions, and heart disease diagnosis via heart roentgenography and fluoroscopy in the

1920s and 1930s. Many children and young adults received appreciable doses in a variety of large scale studies of cardiac measurements by fluoroscopy.

Dr. Bishop is very critical that in the early years of this century, lots of attention was paid to dimensions of the heart, and x-ray measurements of the size of the heart, but very little attention was given to what he regarded as more important features of heart disease.

We quote Dr. Bishop at page 489:

"It was the custom at that time, if any of you remember, to speak of enlargement of the heart as a matter of importance from a point of view of treatment and to measure the benefits of treatment by supposed reduction in the size of the heart ... Curiously enough the fluoroscopic diagnosis of the activities of the different chambers of the heart and the probable auricular and valvular defects as well as the discovery of congenital lesions was passed over lightly. The idea that this method could compete with the ancient and honorable institution of auscultation and percussion [listening with a stethoscope and thumping on the chest] never entered the mind of even so skillful a worker as Franz Groedel." And:

"Nevertheless, unconsciously they gained a great deal of skill and I remember how often the younger Franz Groedel could independently conclude by sight what his father had determined by history, auscultation, and a general examination of the person. In fact, it is extremely easy to distinguish a mitral heart from an aortic heart and many other important points." And:

Every Doctor's Office Needs One --- a Fluoroscope, That Is

"Fluoroscopy, I venture to assert, will become a routine measure in every physician's office before very long."

We interject here, "Many women can be most thankful that this prediction did not materialize in QUITE the fashion that Dr. Bishop predicted."

We quote further from Dr. Bishop:

"For several years I have examined with the fluoroscope every patient who has come to me. I have at the same time recorded the picture with a film. The fluoroscopic examination which allows me to observe the relative activity of the various chambers of the heart and the pulsations of the large vessels, has furnished me with a real impression of the condition." And:

"Although a series of x-ray plates furnish a permanent record, many people are excluded from the benefits of an x-ray examination entirely on account of the labor and expense involved, thus making it a rather formidable matter. As a result, physicians are deprived of the training which comes only from repeated examinations. In my opinion there is nothing that can take the place of fluoroscopy as a short cut in the diagnosis of cardiac disease ... (to his closing sentence of this paragraph)." And:

"I venture to say at this time, what I do not believe ten years from now any one will deny, that in the detection of minor impairments of the heart the fluoroscope is vastly superior to the stethoscope, and when it is supplemented by the electrocardiograph, at least 30 % of otherwise unknown conditions are added to the factors that must be considered." And:

"Medical students are now receiving an intensive training in the anatomy and physiology of the heart so that facts which are at present known to only a few will be a matter of course to the next generation of physicians. In the interim, it behooves our larger institutions to adopt fluoroscopy as a routine matter because it will reveal a large per cent of unsuspected impairments and will thus save an immense amount of labor in drawing inferences without sufficient data. It will also occasionally reveal a condition of the abdomen or chest which calls for prompt operative intervention and as a result save life."

One must contemplate the radiation dose to the chest (and breasts) from the following description of Dr. Bishop:

"The fluoroscope gives only a general view of the thorax. When the chest is placed behind the screen and the roentgen tube is charged one sees the shadow of the mediastinum outlined on the clearer borders of the lungs. The heart pulsations are clearly perceived and the respiratory movements are interpreted by the vertical displacement of the heart, by the raising of the ribs, by the outline of the thoracic cavity, and by the raising and lowering of the diaphragm. The anterior and posterior mediastinal spaces are shown by rotating the body of the patient from right to left and left to right. These appear clearly because of the slight density of the tissues and it is easy to observe the outline of the denser organs as well as to discover additional shadows of pathological origin. Finally, examination in the dorsal or lateral positions complete in a very short time a series of observations of the thoracic shadows as a whole."

We surely admire a man who so obviously loves his work, but we might choose a different physician if breast-cancer were to be avoided.

In re-assuring us that some of the shadows seen during the examinations do not interfere too much, Dr. Bishop states:

"The mental process of discounting a distortion of the shadows due to the nearness of the tube in fluoroscopy is much easier than one would suppose. I have records of 2000 such examinations. In each instance I studied the heart with the fluoroscope and subsequently in a teleoroentgenogram. I believe that I have acquired the faculty of mentally discounting the larger shadows of the fluoroscope. At any rate the observation of the heart with the fluoroscope enables me to form an opinion of the condition that is usually confirmed by collateral investigations."

Requires Personal Skill ... But Should Become "a Routine Procedure"

"The one disappointing element in this subject of fluoroscopy is that the question of personal skill comes in and training of the observer is necessary. It is always the ideal of scientific work to substitute some mathematical formula or instrument of precision that will eliminate the personal equation. In cardiology nothing is more popular than the arithmetical formula, but so far it has failed to be useful." And:

"Fluoroscopy, however, is capable of systematic development and of very definite interpretation. It is particularly valuable in proving and disproving a negative diagnosis. Striking instances appear in daily work where pretty good men pronounce a heart normal when the fluoroscopic examination, even to the casual observer, shows enlargement or deformity of the cardiac image." And:

"I particularly advocate fluoroscopy as a routine procedure in the examination of large numbers of patients to determine which are deserving of detailed cardiologic study and which are not."

We would add that this sort of program would certainly add materially to the breast-radiation-doses in the population. But we can be sure that Dr. Bishop was an influence, and that many persons did have fluoroscopy in offices and in hospital practices, and only rarely might the radiation doses be available for us to add to the totals for our Master Tables.

Other Major Advocates for Fluoroscopy, Particularly in Relation to Studies of the HEART

If other advocates were not so eloquent as Dr. Bishop, they were nonetheless enthusiasts in recommending MORE fluoroscopic studies. Some prominent ones were:

J.G. VanZwalfenberg: A plea for more use of the fluoroscope in examination of the heart and great vessels.

American Journal of Roentgenology 1920, Vol. 7: 1-6.

Charles Martin: An enthusiast for extensive fluoroscopic studies of the heart.
American Journal of Roentgenology 1921, Vol. 8: 295-315.

Gonzalo Martinez: Spoke of the advances in heart and great vessel diseases because of fluoroscopy. American Journal of Roentgenology 1921, 8: 491-496

Rolla G. Karchner and Robert H. Kennecott: Fluoroscopy of heart steadily growing because the method is so precise for heart measurements, American Journal of Roentgenology 1922, Vol. 9:305

Clarke, T. Wood, 1924, "The value of gastrointestinal x-rays in the diseases of children." Archives of Pediatrics, December 16, 840-844.

The enthusiasm here is for fluoroscopy of the gastro-intestinal tract in children, rather than for the heart. The plea suggests that a thorough gastrointestinal examination by the roentgen ray is a valuable adjunct to the clinical examination and blood, stool, and stomach analyses in the clearing up of gastrointestinal abnormalities in children. Clarke felt that the same roentgenoscopic [fluoroscopic] attention to the child's abdomen is indicated, such as that which is becoming more universally accepted as a routine procedure for the adult.

Other Roentgen Exposures for Which Population Doses are Difficult to Assess

- - In 1925, W.W. Wasson wrote "Radiography of the Infant Chest, with Special Reference to the Progression of the Chest and Determination of the Normal," Radiology Vol. 5, November: 365-398. We cite Wasson's justification for his study of infants. He had developed what he considered a technique for roentgenography of the adult chest, which he considered portrayed quite accurately the minute structure of the adult lung. The same technique was adapted to infants, and Wasson felt that the same principles held true.

Therefore, he launched a study "of the infant at birth before any changes in the lung have taken place." Then he roentgenographed babies during the first two weeks after birth, "and every four weeks thereafter until they were three months of age, then every three months until one year of age, and every three months thereafter unless conditions warranted more frequent roentgenograms. The chest is roentgenographed in the

anteroposterior and lateral positions, usually recumbent, at both inspiration and expiration. THE SERIES AT PRESENT INCLUDES 56 babies [emphasis added] varying from a few weeks to three years of age. The series is also supplemented by group studies of varying ages and by a considerable post-mortem series."

While these studies did not include roentgenoscopy, the two types of roentgenograms used are the worst in terms of exposure to the breasts. And there were many, many shots taken over time at ages of great sensitivity to breast-cancer induction.

This was an era when "studies" of heart and great vessels each involved examination of hundreds, and even over a thousand persons, by roentgenoscopic and/or roentgenographic methods to acquire data for the "normal." We are not being judgmental about issues such as informed consent. Rather, our problem with these studies is that they do not fall anywhere into a defined group from which we can readily ascertain the population radiation dose to the breasts, which surely occurred, and can not be overlooked.

- - In the 1920s, George E. Pfahler, the very eminent Philadelphia radiologist, decided he needed some measurements on liver size in the normal state: 1926, "The Measurement of the Liver by Means of Roentgen Rays Based upon a Study of 502 Subjects," American Journal of Roentgenology and Radium Therapy, Vol.16 (6): 558-564.

We let Dr. Pfahler describe his study himself:

"No accurate roentgenological measurements seem to have been made previously to indicate what measurements may be accepted as standard or what may be considered even relatively normal. Therefore, with the hope of determining the practical value of such measurements and with the hope of establishing at least a relatively normal standard, I have been making routine measurements in every abdominal examination in my private laboratory, and have had made at two of the hospitals (Medico-Chirurgical and the Polyclinic Hospitals, of the Post-Graduate Medical School of the University of Pennsylvania) with which I am connected, 324 similar examinations upon subjects who are in general good health, but who came to our clinics because of some minor accident such as a broken wrist, or ankle, etc. From this group I believed I could obtain a more accurate estimate of the normal for various ages, height, weight, and thickness than could be obtained from a study of any group of students or nurses who would be likely to show much less variation."

The exams appear to have been postero-anterior roentgenograms, not fluoroscopy. Studies such as these leave a legacy of persons carrying a radiation dose which is obscurely recorded, but which still contributes to the production of breast-cancer.

- - In 1925, L.R. DeBuys and E.C. Samuel wrote, "Growth of the Heart, Roentgenographic Observations." American Journal of Diseases of Children, 30:355-358.

This is a continuation of an earlier study of the shape of the heart at various ages. The authors wished to convince themselves of the correctness of their earlier impressions, and have therefore extended their studies up to the thirty-ninth month after birth.

They took roentgenograms within the first twenty-four hours after birth and thereafter every three to six months out to 39 months. Only true antero-posterior roentgenograms were considered acceptable. They made 623 observations on 400

persons, extending over the entire 39-month period. No fluoroscopy was involved.

Incidentally, from the point of view of breast-cancer, their exams were the worst, in terms of dose to the breasts. This work is from the Department of Pediatrics of Tulane University.

• - In 1928, Edith M. Lincoln and Ramsay Spillman wrote, "Studies on the Hearts of Normal Children II. Roentgen-Ray Studies," American Journal of Diseases of Children, Vol. 28: 791-810.

Lincoln and Spillman state: " Many studies of this kind have been made on adult hearts. The literature on the size of children's hearts is not abundant, and a considerable amount of the work was done on small groups and on children in clinics who did not have obvious organic heart disease." And:

"The study was made over a period of seven school years and was based on yearly roentgenograms of 246 of the same group of normal school children ... All the roentgenograms were made with the child in a standing dorsoventral position, at a distance of 6 feet. The exposures varied from three-eighths to three-fourths of a second, with the central ray passing approximately through the fourth dorsal vertebra..." These children ranged in age from 2 years to 13 years.

The taking of the x-ray postero-anterior is of lesser harm with respect to breast irradiation. We would like to say here that we realize fully that a small series of children so studied is not going to have an impact on national breast-cancer rates. The aggregate impact of innumerable studies of children and adults by fluoroscopy (which was not done in the Lincoln study) may not be insignificant --- depending upon how many studies and how much time was spent under the fluoroscope. We have no access to such information for the relevant period, so that if the net dose is an appreciable increment, there is no way to add it to the Master Tables.

• - A good example of our concern is the work of Robert O. Moody, Roscoe Van Nuys, and W.E. Chamberlain of Berkeley, California (Moody 1923, 1928). Their two reports are cited here of roentgenoscopic and roentgenographic studies first of 600, and then of 1,200 healthy students at the University of California. These investigators were conducting extensive studies of the anatomical features (size, etc.) of internal organs. We do not get an estimate of the radiation dose, but with roentgenoscopic studies being done, this is an issue of some importance. If many studies of this sort were being casually done, the person-rads to the breast and other tissues could be significant for our concerns. One cannot have many studies of 1,800 young persons, 400 young persons, 1722 roentgenograms of 246 normal children, etc. without adding to the radiation exposure of the population during the relevant period of our study. The numbers of cases we report here are by no means inclusive --- we have no idea of the number of similar studies that may well have gone unreported.

Cinematography in Studies of the Heart

A "close relative" of roentgenoscopy, in one sense, is the use of cinematography. In the American Journal of Roentgenology and Radium Therapy, Vol. 13: 508-509, 1925, work in France by Lomon and Comandon is cited, "The Roentgenologic Cinematograph." We quote a paragraph from a summary of this article:

"The practical use of cinematography in recording the cardiac contractions is described in some detail. Aside from the immediate value of such pictures, there is also the future use of these in watching the changes in heart contractions at stated intervals; comparison of these pictures may be of much value in following the condition of certain cases. In the method described, 25 roentgenograms can be made per second." The article states that under the conditions used, erythema results only after 20 seconds of exposure. "Because of the extreme heat and tension on the tubes," the writers established 5 seconds as the maximum exposure. In this time, at least 2 complete cardiac cycles were obtained. "From 17 to 18 images per second seem to give the best results, although 25 per second are possible."

Let us consider this procedure. An erythema dose would have been in the neighborhood of 300 R of skin exposure. The authors say 20 seconds produce an erythema, but therefore they limited exposure to 5 seconds. So we have a skin exposure of 75 R. For an anterior entry of the beam, this would be a dose in the neighborhood of $(0.693 \text{ rads/R} \times 75 \text{ R})$, or about 52 rads to the breast. This would have to be regarded as "a new dimension" in doses associated with roentgenography, although not so rare with roentgenoscopy. Since this publication was in 1924, we shall be interested in the future to try ascertaining just how frequent such exams might have become in the United States in the many decades which followed.

Part 3. Fluoroscopy as a Major Problem Refuses to Disappear

There existed so much good work in the 1920s, the 1930s, and the 1940s by people like Leddy, Braestrup, and Blatz, it seemed reasonable to believe that fluoroscopy, the outstanding hazard of radiology, would at least not be the problem in the second half of the 20th Century that it had been for the first half of the century.

But that simply did not happen and is not happening today. A large part of the problem of fluoroscopy is its enhanced use in techniques of medicine and surgery in the diagnosis and treatment of blood vessel disease and heart disease. It simply requires no disclaimer concerning the very wonderful advancements in surgical therapy which have characterized the second half of the 20th Century, especially with the life renewal of children with otherwise lethal, or severely crippling congenital heart problems.

Unfortunately, we need to be concerned that we are building into our society future breast-cancers as a result of the chest-dose to the female children undergoing the surgery. Who would not be happy to accept decades of full happy life in exchange for the risk of a later cancer? We need to be concerned since we may not see the ultimate decline in breast-cancer rates that would otherwise accompany the elimination of such practices as thymus irradiation.

The evaluation of the status of population exposure from high dose individual exposure in connection with cardiovascular therapy and other radiation sources will be a focus of the study of breast-cancer risks being generated in the 1960-2000 period, as a follow-on to the study of the current breast-cancers occurring by the thousands as a result of the radiation exposure during the 1920-1960 period.

Just as a matter of keeping our eyes on the problem, let us examine the order of magnitude of doses which CAN be involved in this second half of the 20th century. We look at Table 9, page 312 in the UNSCEAR Report of 1977. Table 9 is described as

"Mean Energy Imparted to Patients During Radiological Investigations of the Heart and Larger Vessels."

Method of Study	Area cm ²	Time minutes	Filter mm Al	Dose per Procedure Roentgens
Fluoroscopy	200	1.5	0.5	7.5 to 10
Radiography				
Direct	1200		0.5	0.25 to 0.5
Lateral	800		0.5	0.50 to 1
Tele	1200		0.5	0.3
Kymography				
Direct	720		1.0	8
Lateral	720		1.0	12
Electrokymography	50	10	1.0	25
Angiocardiography	1200		1.0	0.5
Heart				
Catheterization	100	22	1.0	30-232
Heart				
Catheterization, with Image Intensifier	400	22	3.0	21
Cine	400	22	3.0	12.5

It is clear that the field of diagnosis and therapy of heart and vessel disease will need an on-going careful look with respect to the issue of breast-dose to patients, nurses, technicians, and physicians.

Part 4. What Can Be Done about Radiation Dose in Fluoroscopy Versus What is Done

Gofman and O'Connor (1985) discussed in detail some excellent work which demonstrated the possibilities of lowering seriously excessive doses in fluoroscopy. The fact that this good work was being done in the late 1970s and early 1980s testifies to the ongoing aspect of less-than-satisfactory progress in dose management in fluoroscopic procedures. Considering the earlier lack of appreciation of the cancer-producing ability of low doses of ionizing radiation, it occasions no surprise that relatively little attention was given to the possibility of extensive lowering of radiation doses in fluoroscopy.

Dr. Kenneth Taylor and colleagues (1979) did a study of 30 radiological facilities in Ontario, Canada, where they found that excessive dose-rate and excessive total time accounted for a huge range in entrance doses for several common fluoroscopic examinations. Their key findings on dose-rate follow here.

Before: Facilities using high fluoroscopic exposure-rates obtained no better diagnostic quality than the facilities using low dose-rates.

After: The radiologists were just as satisfied with the diagnostic images after Taylor and colleagues lowered dose-rates as they were before.

Intensifying Screens: Excessively high dose-rates were closely associated with the use of older cadmium-sulfide intensifier screens; in terms of reduced dose-rate, cesium iodide types were preferable.

Fluorography: With modern image intensifiers, the radiologist can take a 70 to 100 mm film rather than a larger radiograph during fluoroscopy. Taylor and co-workers found that a common cause of high doses was the use of full-sized film, when the 70 mm to 100 mm picture from the image-intensifier system produced satisfactory diagnostic information.

Proper Maintenance of Fluoroscopy Equipment

There are several special tests which Taylor and colleagues used in checking the output of x-ray equipment. Some of these tests, now available through radiological physicists, show up serious additional sources of unsuspected and unnecessary exposure to patients.

As we shall relate, a patient can receive more dose while the fluoroscope is "off" than while it is "on," if its decay performance has been checked in only routine ways.

In their work, Taylor and colleagues found that one of the important features requiring measurement was the waveform of the x-ray yield as a function of time. In one machine, a malfunctioning milliampere stabilizer resulted in a continuous increase in milliamperage --- and therefore in x-ray dose to the patient --- during the course of an exposure. In another, too high a temperature for the tube filament was used, which resulted in an initial high peak exposure, followed after the first second by falling temperature and dose, thanks to control circuits. But even though the fluoroscopist stopped the exposure at 4 seconds, the x-ray yield continued, due to the gradual discharge of the high-voltage circuit. The dose did not fall to zero until 12 seconds after "termination."

As Taylor states (1983, p.656):

"The initial spike and the long decay should not have been present and more than doubled the dose to the patient. Furthermore, the radiation emitted during the tail could not be seen because the television tube is automatically blanked at the termination of fluoroscopy. Thus the patient was being irradiated without the radiologist's knowledge. Usual methods of quality control that measure steady-state conditions do not detect these transients. These transients are commonly found in fluoroscopy but are seldom investigated. The long decay can be eliminated by using higher mA and lower Kv or, better, by discharging the high tension circuit with a load resistance that is automatically connected into the circuit at the end of fluoroscopy. Ironically, the conscientious radiologist who might use high kV and a series of 2-second exposures would in fact deliver to the patient three times the radiation in the 'off' periods as in the 'on' time."

And:

"This is a serious problem, since half the machines in clinical use studied in our survey had one or both of these faults present." [Emphasis added.]

If half the facilities in a survey in Toronto, Ontario, Canada --- an advanced center --- were showing such equipment defects, it is clear that we were, at least in 1983, far from having eliminated serious overdoses in the highest-dose part of radiological practice, namely fluoroscopic procedures. It is clear that this situation needs evaluation in detail and suggests that greater use needs to be made of the services of qualified radiologic physicists. It is fortunate that such individuals are available to maintain some quality control in this area.

The Critical Importance of Beam Size

The risk from fluoroscopic examinations need not necessarily be higher than from the routine films of the same examination. If the beam size during fluoroscopy can be kept small, the area fluoroscoped is small, and hence the risk from small-area fluoroscopic exams can be lower than the risk from larger-area films taken of the same region.

Part 5. In Fluoroscopy It Appears We Win Here, and Lose There.

We hope that Taylor's sage advice in 1983 has made a large impact on diagnostic use of fluoroscopy, and it would be good to be re-assured that this is the case. But we recently learn that while practice is quite good in Radiology facilities in institutions, recent reports indicate that all may not be well in departments which now have their own fluoroscopic equipment, which they operate, without adequate training in radiation safety requirements.

In 1993, Kathleen A. Greer, Associate Editor of "Advance for Radiological Science Professionals," prepared a report of some discouraging findings on this subject.

The report cites a presentation by James B. Spies, M.D. of Sibley Memorial Hospital in Washington, D.C. and Louis K. Wagner, Ph.D., a professor at the University of Texas Medical School in Houston. Their report was "Radiation Injuries During Fluoroscopy: An Unrecognized Risk," presented at the annual meeting of the Society of Cardiovascular and Interventional Radiology in October 1993. These doctors were addressing reports of injuries to patients during fluoroscopy in facilities where there was a lack of training and where patients received either high-dose or lengthy fluoroscopic exposure. The facilities considered to be inadequate are fluoroscopic equipments being used in cardiology, urology, neurology --- regarded by Drs. Spies and Wagner as "just a sampling of other specialty groups performing fluoroscopy."

"Our current concern is that there may not be an awareness of the potential for radiation injury, but it [the potential] exists," Dr. Spies said.

"There is little evidence of radiology personnel involved in fluoroscopy procedures in which radiation burns occurred, but there is documentation of such injuries, primarily during cardiology procedures," Dr. Spies said.

As Yogi Berra, the famous baseball player of the New York Yankees, said: "Deja Vu All Over Again."

It is discouraging to be hearing the same kind of reports we were speaking of earlier for the 1920s, 1930s, 1940s. The genie leaks out of the bottle in the most inauspicious ways.

It is our opinion that the status of fluoroscopy, as a threat for breast-doses which could increase breast-cancer appreciably, is an open question in this second half of the 20th century. These illustrations cropping up, of fluoroscopy in some institutions being able to cause radiation burns and hair loss without anyone even knowing that a problem exists, are disturbing in the extreme. The problem may not be large, but that surmise requires evidence, not wishful thinking.

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1931: Roentgenology Fights for Recognition ... and against the "Dishonest and Incompetent Elements" in the Field

Dr. Haenisch, Part 1.

In 1931, Professor Dr. George Fedor Haenisch of the University of Hamburg, Germany, was honored by the American Roentgen Ray Society to deliver the Annual Eugene Caldwell Lecture. His title: "Roentgenology as a Specialty." (American Journal of Roentgenology, Vol.26, No.6: 821-833, December 1931.)

At that time, roentgenology was fighting hard for its recognition as a medical specialty, rather than as a bunch of "picture-takers." But other types of physicians liked doing their own roentgenology. Pediatricians, general practitioners, surgeons, and many others --- as related in Chapters 31 and 32. Unqualified users of "the ray" did not even know they were harming themselves, let alone their patients. Dr. Haenisch's lecture suggests that the scene was similar in Germany. We quote from it:

"The harm, however, which resulted from a too rapid expansion of the art and the consequent faulty, insufficiently prepared training, was not the worst ... Much more disastrous was the fact that incompetent and dishonest elements grasped this specialty. These, in some instances, were unscrupulous physicians who were guided merely by the expected pecuniary advantages and who, unhampered by clinical and roentgenological knowledge and experience, 'sold x-ray pictures,' paying the referring physician rebates or commissions, or tempting him by allowing a percentage of the fee. In other instances laymen, with or without the connivance of dishonest physicians, saw in the purchase of x-ray apparatus a get-rich-quick scheme at the expense of innocent patients ... In passing I may mention that there existed unscrupulous individuals who unloaded poor apparatus on the inexperienced physicians."

Not a pretty picture. In addition, there were the eternal "turf wars" within universities and hospitals. Dr. Haenisch described them, too (at p.828):

"Opposition against the independence of roentgenology is however not confined to the universities alone. While many large hospitals have recognized the advantages of a central roentgen department under the direction of an independent specialist ... representatives of other specialties believe they must have their own roentgen laboratories so as to avoid a separation of the roentgen examination from the clinical examination as a whole."

And nearly 65 years after this lecture, non-expert users of "the ray" are still a problem (summary in Chapter 42).

CHAPTER 33

Dermatology: More Underestimation in Our Finding

Part 1. "Rave Reviews" for Radiation in Treating Skin Disorders

The lucky readers who have not had skin disorders may tend to dismiss them as trivial, because they are rarely fatal. If there are such readers, we urge them to look at photographs in any dermatology text, in order to appreciate how severe and disabling skin disorders can be. Photographs, however, can not convey either pain or intense itching (pruritus), and these invisible aspects of many skin disorders are very serious ones, too.

From 1900 out to 1955-1960 at least, dermatologists made extensive use of radium and x-rays in the treatment of skin disorders. By itself, dermatologic practice may account for radiation doses of real consequence for female breasts. It is very difficult, however, to find studies which provide sufficient information for quantitative analysis (see Part 3). Thus, there is no entry at all in our Master Table for this source of breast-exposure.

We emphatically warn readers against assuming that the absence, in our Master Table, of any dose-estimate is a suggestion that the average annual breast-dose for females was negligible. On the contrary, it is possible that dermatologic radiation exposure of breast-tissue was greater than the combined sources of breast-dose evaluated in the Master Table. The fact that we have counted no dose at all from dermatologic irradiation is another source of underestimation in our finding.

Dermatologists never deny their extensive use of what they call "superficial x-ray therapy" --- which differs from therapy with the very low-energy radiation known as "grenz rays," also extensively used by many dermatologists (see Part 3). In 1922, Dr. George MacKee, one of the great figures of dermatology, published a paper with Dr. George C. Andrews, from which we quote:

"It is now pretty generally admitted that the roentgen rays constitute the most useful and successful single remedy we possess for the treatment of dermatological diseases. The only competitor for this distinguished position is radium. In a general way, what one agent will accomplish, so will the other." And:

"That the roentgen rays constitute the most valuable remedy in dermatotherapy, or that the roentgen rays and radium constitute the most useful single agents in the armamentarium of pure dermatology, is shown by the following list of diseases and conditions that are amenable to such treatment, over 80 in number." There is a small number of superficial malignancies in the list of 80, but by and large, this is a very long list of benign dermatoses which were being treated with ionizing radiation therapy. Dr. MacKee describes one use which is abundantly confirmed by scanning the literature of the times. Dr. MacKee:

"That the roentgen rays and radium are excellent antipruritics has long been known. In cases of persistent, localized, essential pruritus of undiscoverable etiology they are the only remedies that will with a reasonable degree of certainty effect complete relief [of the itching]. The relief may endure for a month, for several months, or for longer periods. Permanent results are uncommon. Occasional failures are noted."

One gets a good feeling of real integrity in reading the works of Dr. MacKee --- not only in this paper, but also in his classic text, discussed in Parts 2 and 4 below.

Part 2. A Candid Appraisal in 1938 of Actual Benefits

In 1938, Dr. George MacKee published the Third Edition of his book, "X-Rays and Radium in the Treatment of Diseases of the Skin." (The First Edition had been published nearly 20 years earlier.) Dr. MacKee's reputation in dermatology worldwide was one of the best in his time.

His 1938 book, published in the middle of the 1920-1960 period of our current interest, is especially illuminating --- and full of sound and sensible comments about medicine, dermatology, and what therapy is possible with ionizing radiation. Below, we quote some passages from his Preface to the 3rd Edition. Having noted that the dermatologist must know a lot about internal medicine as well as external medicine, Dr. MacKee continues (p.5):

"The foregoing paragraph is a preamble for the statement that x-rays are now employed less frequently in dermatology; and it is possible that they will be used still less frequently in the future. Dermatologists whose training has been inadequate are likely to use x-rays indiscriminately. On the whole, however, there is an increasing disposition on the part of dermatologists to employ x-rays only when necessary or when definitely indicated; in other words, with discriminating judgment. This trend is most noticeable among the older dermatologists and is the result of accumulated experience; also among well-trained young dermatologists who are capable of guidance." And (p.5):

"Thirty years ago certain dermatoses were treated with x-rays because there was no other equally efficacious remedy. Since then other methods of treatment have proved equal to or superior to x-rays in these particular affections ..." (An affection is an ailment, a disease). And (p.5):

"For a number of years, long ago, the author did not fail to cure a case of lichen planus with roentgen rays [lichen planus is a skin disorder described in our Chapter 34]; therefore, they were supposed to be almost a specific; at least they were considered the method of election. Now it is known that x-rays frequently fail to cure and in some instances they do not even modify the course of the affection. Today we know that many cases of acne vulgaris, eczema, and many other dermatoses respond better to conventional dermatological investigation and therapy than they do to roentgen therapy alone ..."

Nonetheless, Dr. MacKee still considers x-ray therapy efficacious for many skin disorders, as indicated in our Chapter 34. As in 1922 (above), he says in 1938 (p.6): "It is the consensus of opinion that x-rays constitute the most important single therapeutic agent in the armamentarium of the dermatologist." MacKee does not disassociate himself from the consensus. He continues (p.6):

"Considerable attention has been devoted [in this book] to the historical aspect. This is deemed advisable because modern skill could not exist without the efforts of predecessors in the same field of endeavor. The young roentgenologist of today knows little of the difficulties, technical and professional, encountered and overcome by the older roentgenologists; nor does he appreciate how much is owed to the roentgenologists of the past, many of whom lost their lives in an endeavor to advance the science and art of roentgenology. These men possessed the pioneer spirit to succeed and the spirit of service. Their work is an inspiration; their names should not be forgotten." And he adds (p.7):

"We are still in the pioneer period ... In the therapeutic field we are badly in need of scientifically controlled experimentation and carefully compiled statistics. We still depend too much upon impressions and beliefs."

In a short Preface, MacKee opted to allude twice (p.5, p.7) to changing observations and to excessive reliance on "impressions and beliefs." We find him refreshingly candid. A man of great experience and accumulated wisdom, a man who has built a worldwide reputation as the "dean" of x-ray and radium therapy in dermatology, seems to be saying in effect: "We are not really getting some of the results we used to THINK we had. We did a lot of self-suggestion, and I'm not afraid to say so." This is our interpretation of his remarks, especially in view of possible self-deception in parts of the "enlarged thymus" story (our Chapters 6 - 11).

Part 3. The Problem of Dosage, and a "Safety" Claim in 1952

There is nothing intrinsically special about the use of radio-therapy for benign skin afflictions which makes it difficult to assess irradiation of the breasts, for our Master Table. There are many sources (including MacKee) which cite typical dosages for various therapies. We cite one paper below. Nonetheless, the problem for us is two-fold:

First, we need a reasonable way to estimate what fraction of such treatments actually reached BREAST-tissue, and second, we need a reasonable way to estimate what fraction of female persons in the population received the various therapies per age-year and per calendar-year.

Because we do not presently have a reasonable way to solve these problems, we just exclude the entire topic of dermatology from the Master Table of this edition. However, for interested readers, the next chapter surveys the skin afflictions for which radio-therapy SOMETIMES caused irradiation of the breasts, and some which ALWAYS did, including x-ray therapy for eczema of the nipple and breast, and for intertrigo under pendulous breasts.

The Development of "Grenz Rays"

There is one aspect of dermatology which undoubtedly prevented the breast-cancer price from being as severe as it would otherwise have been. In 1925, Dr. Gustav Bucky began to emphasize his ideas concerning "infra-roentgen" or "grenz rays." These are low-energy radiations of the region between ultraviolet and roentgen-rays, with a wavelength of 1.5 to 2.0 Angstroms (Bucky 1927, p.645). They have low penetration power. All their energy is absorbed within about two millimeters of tissue, which means that they do not penetrate beneath the skin.

These radiations, also called "super-soft roentgen rays," have an average energy of only 6 to 10 kilo-electron-volts or KeV (Eller 1927, p.437). It is important to know these energies, in order to know the important distinction between "super-soft roentgen rays" ("grenz rays") versus "superficial roentgen rays." In terms of penetrating power (and irradiation of breast-tissue), there is a world of difference.

Why do we accept Eller's energy-values as reliable? For a very good reason: The laws of physics. Visible light, ultraviolet light, x-rays, and gamma rays are all composed of photons, which are packets of electro-magnetic energy traveling at the speed of light. The relationship between the energy of photons and wavelength is the following (from Gofman 1981, p.12): Photon energy in kilo-electron-volts (KeV) = (12.398

KeV-Angstroms) divided by (wavelength in Angstroms). If we use 1.5 Angstroms as the wavelength of "grenz rays," the formula yields 8.3 KeV as the photon energy. If we use 2.0 Angstroms as the wavelength, the formula yields 6.2 KeV as the photon energy. So Eller's values are in harmony with the laws of physics.

The use of "grenz rays" in some aspects of dermatologic therapy became popular and widespread. There is no doubt that their use surely protected breast-tissue, whenever higher-energy x-rays would otherwise have been used for therapies involving the breast.

However, according to the source below, it was NOT customary to use "grenz rays" in the treatment of most skin disorders.

A Safety Claim about Entrance Doses up to 1,400 Roentgens

Early suggestions, that the use of x-ray therapy by dermatologists might be harmful, brought an emphatic denial in 1952 from Marion Sulzberger, head of the Department of Dermatology at New York University. First we will cite his statement about safety and benefits, and then we will show that his reference to treatment by "superficial" x-rays (up to 1,400 roentgens) does NOT mean treatment by "grenz rays." Dr. Sulzberger states (1952, p.639):

"After more than 30 years of experience, the large majority of qualified skin specialists in the United States feel certain that the use of superficial roentgen-ray treatments in the described fractional doses and within the stated limits of maximum dosage is not merely safe and justifiable but is, as a matter of fact, among the best therapeutic measures in selected cases of many benign dermatoses. For it is the recorded dermatologic experience that such treatments 'cure' or materially benefit many patients with skin eruptions which fail to respond to other accepted forms of treatment, thus lessening the periods of disability and often also the risks of permanent physical or psychological damage that would otherwise result from the dermatosis."

We would have no quarrel whatsoever with Dr. Sulzberger's claim of benefit from such use of x-rays. But his claim that such treatments were SAFE (risk-free) is mistaken in a very big way.

How do we know that his reference to "superficial roentgen-ray treatments" could NOT mean "grenz rays"? We compare the kilovoltage (below) with the kilovoltage for "grenz rays" (above). Dr. Sulzberger points out carefully what qualified dermatologists did in "customary practice" for "most dermatoses" (p.639):

"In most dermatoses, the customary practice is to administer to any one area no more than 85 R weekly or 42.5 R once to twice weekly, up to a maximum total dose of about 1,400 R. These figures are based on dosages measured in air. The usual quality of irradiation used ranges from 60 to 100 kv [kilovolts], with half-value layers of about 0.5 to 1 mm aluminum; only in exceptional cases will the voltage used go as high as 120 kv, with half-value layers up to 3 mm aluminum. ["Half-value layer" describes the quality of a beam; an x-ray beam with a half-value layer of 3 mm Al is a beam whose average energy is such that a sheet of aluminum 3 millimeters thick would cut the beam's intensity in half.] For many years this quality and dosage of low-voltage roentgen-ray treatment have been used by dermatologists in the therapy of a great variety of entirely nonmalignant, non dangerous, benign skin conditions --- among them acne vulgaris, 'eczema,' psoriasis, 'neurodermatitis,' and severe and 'intractable' itching of diverse areas."

• - ABSORBED BREAST-DOSES per ROENTGEN of ENTRANCE-DOSE.					
For x-rays of 0.5 mm Al., half-value layer.			For x-rays of 1.0 mm Al., half-value layer.		
Breast Thickness: 4 cm 6 cm 8 cm			Breast Thickness: 4 cm 6 cm 8 cm		
Absorbed Breast					
Rads per One					
Roentgen of					
Entrance Dose	0.284	0.204	0.161	0.406	0.315
					0.250
Absorbed Breast					
Rads per 85					
Roentgens of					
Entrance Dose	24	17	14	34	27
					21
Ch 33, Part 3: Details in text.					

Magnitude of Individual Doses to Breast-Tissue

Our focus is on the risk of radiation-induced breast-cancer, so we shall limit our comment to the BREAST dosage when such treatments involved the breast. The nearby box shows the absorbed dose per roentgen of entrance dose for breasts of various thickness (measured under mammographic compression) and for half-value layers of 0.5 and 1.0 mm Al. We derived the values from the work of Hammerstein (1979, especially Figures 4 and 5), for an x-ray tube having a tungsten target. These doses, plus somewhat lower doses from x-ray tubes having a molybdenum target, are from Gofman and O'Connor 1985 (Table 5, p.220).

Either set of values, or values in the same "ballpark," suffice to make our point: The beams described by Sulzberger as customary are NOT stopped by the skin, and they are irradiating breast-tissue at serious levels:

The lowest value in the box's second row is 14 rads of breast-dose from a SINGLE treatment. Moreover, according to Sulzberger, treatments were repeated weekly, "up to a maximum [entrance] dose of about 1,400 R." If we use the lowest entry in the box's upper row, that would mean approximately: $(0.161 \text{ rad} / \text{R}) \times (1,400 \text{ R}) = 225 \text{ rads}$ of absorbed breast-dose for mature breasts. For female children, with all the breast-cells still close to the skin, the breast-dose per roentgen of entrance dose would be even higher.

It may well be, as noted at the outset of this chapter, that dermatologic practice accounts for more breast-irradiation than everything evaluated in our Master Table. The fact that we have NO contribution from dermatology in that table is most definitely a source of underestimation in the table's sum of radiation-induced breast-cancers per year.

Part 4. Comments of an "Insider" about the Years 1895 to 1938

The study of the x-ray, and what it might and might not do in medicine, has now endured through about a century of human experience. In 1938, Dr. MacKee looked back on the early decades, with the eyes of an insider, and what he tells us and what he warns us against are still relevant --- over 50 years later.

In Chapter 1 of MacKee's 3rd edition (at pages 15-16), we find frank and open criticism of those who used radiation technology in an overtly irresponsible manner. He calls them "radiomaniacs" --- a memorable term for which the context is provided below. In 1938, Dr. MacKee sees three phases in the years since the 1895 discovery:

"The history of roentgen therapy can be divided roughly into three eras --- optimistic, pessimistic and realistic; this is particularly true of this country [USA]. At first enthusiasm and carelessness overcame caution. Many physicians installed apparatus and attempted to employ the x-rays for practical therapeutic purposes, without making a study of the subject. Even the scientific and conscientious workers did not at first realize that they were dealing with an exceedingly dangerous agent. It was natural, therefore, that many patients received serious injuries." And:

"Not only were patients injured, but operators, by repeatedly testing the penetrating power of the rays by inserting their hands between the tube and a fluorescing screen, developed an erythema [a morbid redness of the skin] which in many instances led to serious sequelae. These facts, together with the discovery by Brown and Osgood that sterility was produced by the x-rays naturally caused the operators to be a little more cautious. However, optimism reigned until about 1906." And:

"During those years the rays, to a large extent, were empirically used and they were tried out on nearly every chronic disease. The literature was misleading, as it was full of case reports of wonderful cures, the occasional paper from the pen of a good man being ignored or overlooked by the average x-ray operator of the period and in spite of repeated warnings from capable men, the 'radiomaniacs' held the reins."

The Pessimistic Period

Dr. MacKee goes on to describe the disappointments which came with the realization that cancer was not to be conquered by x-rays and that the "x-rays proved practically useless in pulmonary tuberculosis. This was another great disappointment" (p.16). After describing some "very curious theories" concocted during the period, MacKee comments (p.16):

"In fact, the literature contained many erroneous and even dangerous theories. The unverified accounts of marvelous results, the injurious effects observed as time went on, the fact that there was no satisfactory method of estimating the amount of radiation administered, and the fact that the earlier claims were not substantiated, finally resulted in the period of depression or pessimism which lasted from about 1906 to about 1910 or 1912." And:

"During this period there were a number of scientifically inclined roentgenologists who recognized both the advantages and limitations of the x-rays and who also recognized the necessity of standardizing the work and of devising accurate methods of measurement."

The Realistic Period

At the end of Chapter 1, Dr. MacKee is describing his contemporary period of roentgenology, which was "realistic" in his view. He closes the chapter with two paragraphs (at page 18) whose optimism is worth pondering:

"In addition to the accomplishments of scientifically inclined physicians and electrical engineers, it must not be forgotten that many physicists, biologists, chemists, and physiologists persistently investigated the x-rays and radioactive substances from the very moment of their discovery. The work of these men paved the way for most of the improvements in the technic of recent years and, of course, as a result of their tireless endeavors we now possess a fairly reliable conception of the nature of the x-rays and of the radioactive substances." And the final paragraph:

"At last the value and limitations of the x-rays in the treatment of disease have been fairly well established; especially is this so of cutaneous affections. The improvement in technic, increased knowledge regarding possibilities and limitations, the recognition that roentgenology is a specialized subject, and especially the fact that radiodermatitis can be avoided with a reasonable degree of certainty, have caused a gradual restoration of confidence and this confidence will be permanent if the work can be kept out of the hands of unscrupulous, overenthusiastic and careless individuals."

"If," says MacKee. He alludes to an eternal and universal human problem, occurring in not just ONE occupation or society.

Part 5. The Relevance Today of Dr. MacKee's Lessons

Dr. MacKee would surely be horrified, we think, to learn the sad consequences from excessive radiation administered during the subsequent decades, even in the hands of the best-intentioned physicians and scientists. New technologies having a biological impact can be introduced ONLY AT SOME LOW RATE, or else the price can be tremendous in life and health before the cause is recognized. We believe Dr. George MacKee would very probably be in the forefront of those agreeing with such an opinion today.

1942: An Enthusiast for More Use of Medical Radiation

In 1938, Dr. MacKee held the opinion that "We are still in the pioneer period" of radiation therapy (1938, p.7). The spirit of the times is clear also in the famous text, "Christopher's Surgery."

In 1942, its Third Edition provided Chapter 36 entitled "Roentgenology: Diagnostic and Therapeutic Roentgenology in Surgery." The author of the chapter was Dr. James Thomas Case, Professor of Radiology at Northwestern University Medical School. After listing some radiation therapies of probable interest to surgeons, Dr. Case explicitly tries to inspire expanded use and exploration "of this rapidly developing method of attacking certain diseases" (Case 1942, p.1636):

"Many lesions of a benign character respond to radiation therapy, such as tuberculous glands of the neck, abdominal tuberculosis and some cases of joint tuberculosis, interstitial fibroid tumors when not larger than a three or four months' pregnancy and metropathic hemorrhages. Toxic adenomas [a type of tumor, usually benign] when not too large usually respond well, but the treatments must be continued over a period of three to five months, all the doses being suberythema [below the dose

which causes morbid reddening of the skin --- about 300 R] and with adequate filtration. Furuncles, carbuncles, cellulitis and erysipelas respond promptly to minimal doses. Recently the employment of x-ray in small doses in the therapy of gas gangrene has appeared very promising. Buerger's disease and Raynaud's disease respond nicely to roentgen therapy over the lumbar sympathetic system, often averting the need for amputation. The only worthwhile treatment for leukemia is roentgen therapy, which is also useful in erythremia, Hodgkin's disease and lymphoblastomas of any type." And then:

"No attempt has been made in the foregoing to cover adequately the field of roentgen therapy, but rather to arouse the physician's natural investigative instinct to look at more length into the possibilities of this rapidly developing method of attacking certain diseases."

People Will Learn, One Way or the Other

Some medical uses of radiation were and are enormously helpful to patients. But not all of the uses. In 1938, Dr. MacKee was warning his colleagues against self-deception and carelessness with respect to certain uses of radiation. We have little doubt that many physicians who caused breast irradiation in the course of their roentgenologic work would prefer --- with the benefit of hindsight --- to have used much lower doses or not to have done it at all. We know some of them personally.

From the point of view of a student, not a critic, we wish to comment on the importance of LEARNING from the Dr. MacKees and from past experience in general, in order to avoid tragedies in the future. It would be appalling if medicine were unwilling to accept, or to make, an honest evaluation of the cancers induced by medical irradiation.

There are some reasons for optimism. For example, certain practices with x-rays are long out of use, in dermatology and other aspects of medicine. On the other hand, some other uses are increasing. It will require real vigilance with respect to radiation technologies and their uses, in order to insure that the lessons of the past ten decades succeed in preventing an equal amount of cancer-causation in the future. And the vigilance needs to come from an educated populace, especially women.

People will learn, one way or the other, that they themselves are the ones most likely, by far, to have an intense and enduring concern for the health and well-being of themselves and their own family.

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CHAPTER 34

Treatment of Skin Disorders: Overview by Dr. MacKee

Over 80 skin disorders were commonly treated with x-ray or radium therapies by 1922, as noted in Chapter 33, Part 1. We want to give readers an idea of what conditions were treated this way, and why such treatments could cause irradiation of breast tissue in specific cases. A good way to do this is by providing some relevant samples of treated conditions from Dr. George MacKee's excellent book, "X-Rays and Radium in the Treatment of Diseases of the Skin," Third Edition, published in 1938. Dr. MacKee was then Professor of Clinical Dermatology and Director of the Department of Dermatology (skin and cancer unit) of the New York Post-Graduate Medical School and Hospital, Columbia University.

The samples will come from Chapters 28, 29, 30, and 31. These four chapters alone required 100 pages in MacKee's book, so it should be self-evident that we are not attempting to be comprehensive here. The co-author of Chapter 28 was Dr. George M. Lewis; the co-author of Chapters 30 and 31 was Dr. Fred Wise.

Part 1. Diseases due to Fungi: Unplanned Breast-Irradiation

In their Chapter 28, "Diseases due to Fungi," MacKee and Lewis begin by listing ten skin conditions due to pathogenic fungi which are "more or less amenable to treatment with x-rays or radium" (p.441). We will mention only two of them, below.

Tinea Capitis (Ringworm of the Scalp)

The use of x-ray therapy for tinea capitis was first suggested in 1897, but early practice resulted in a discouraging frequency of permanent alopecia (baldness, loss of hair), "due to excessive dosage" (p.441). However, control of dosage was achieved and the practice was widely used. For example: "We and our associates have employed the combined method of dose estimation (Chapter XVII) in this work for over twenty years. The heads of over 3,000 children have been depilated without a single case of permanent alopecia" (p.455).

Dosage: The "Skin Unit" or "Erythema Dose"

On the subject of dosage: "Three hundred r (1 skin unit, unfiltered) is the epilating dose ... This is a safe dose, but it must not be exceeded except in cases where the toleration is known to be greater. In children under two years of age and in infants, the dose should be 225 r (3/4 skin unit)" (p.455). In those days, a "skin unit" (also called an "erythema dose") was defined as 300 Roentgens at about 60 KeV (p.455).

Beginners: Don't Try It !

MacKee and Lewis urge against use of this therapy by novices (p.455): "The beginner should not attempt the x-ray treatment of this disease until his apparatus and technic have been standardized and repeatedly checked, and he has had experience with the x-ray treatment of various cutaneous affections. He must be certain of his epilating or erythema dose which are the same and correspond with the skin unit (300 r at about 60 kv)," at which point MacKee and Lewis cite three earlier chapters in their book.

Breast Irradiation from the Procedure?

MacKee and Lewis make no comment about external scatter to the breasts. However, Modan and colleagues studied use of this method on 10,834 irradiated children in Israel (Modan 1989, in *The Lancet*). They claim that, using phantoms, they ascertained a dose of 1.6 rads to the breasts from such treatments.

Actinomycosis: A Leading Clinical Problem

According to another text, actinomycosis was the principal fungus disease of clinical importance. This other text, featured in our Chapter 36, is "Radiotherapy of Benign Disease" by Dr. Stephen B. Dewing (1965, p.28).

Dewing reports that "actinomycosis affects primarily the mouth, jaw, and neck regions. It also occurs in the chest and abdomen, as do the other fungus diseases." So direct breast irradiation must occur in treatment of some cases. MacKee and Lewis (p.484) provide a photo of a patient very disfigured by the affliction on her jaw, and report (p.483):

"From personal observation and a review of the literature, we are of the opinion that the x-rays or radium rays are not only indicated in this stubborn and serious disease but that such treatment is superior to any other." They provide a photo (p.485) of the same patient after two x-ray treatments, and the improvement is breathtaking.

Part 2. Eczema, Including Eczema of the Nipple and Breast

In many parts of the literature, aside from MacKee, we encountered numerous reports of very successful therapy of "eczema" by x-rays. The definition of eczema changes, and we will return to that topic in a moment.

According to MacKee, as early as 1900, x-ray therapy was recommended for treatment of chronic eczema (p.489). Moreover, "Very early the opinion was unanimous that in most instances the lesions of eczema disappeared rapidly under the influence of very small doses [of x-rays] and in practically all cases the itching was relieved quickly. At first it was thought that the clinical cure might be permanent but later it was found that recurrences were common" (p.489). And: "Modern writers are perhaps even more enthusiastic than were the earlier authors. The results are better today because of greater ability to select cases and because modern technic practically precludes injury. All modern text-books on dermatology and roentgen therapy call attention to the efficacy of irradiation in the treatment of eczema, especially the chronic types" (p.489).

What Is Eczema? MacKee's Reply (1938)

"To most dermatologists today the word eczema means an eruption that at some stage of its evolution is exudative, either clinically or histologically. It begins with erythema. If evolution is uninterrupted, this is followed by edema and often by vesication, erosion and exudation and, finally, by crusting and desquamation. The development may be slow or rapid; any one stage may be evanescent or prolonged; or the disease may end at any stage either spontaneously or because of therapy" (p.490).

If the cause of the skin eruption is an external factor, some dermatologists prefer to use the term "dermatitis" instead of eczema. Others use the term "eczema" whether the cause is external, internal, or a combination. Comments MacKee (p.490):

"There is, therefore, some confusion relative to the terms eczema and dermatitis, also as to the etiology of the various eruptions comprising the eczema group. Hence we hear of occupational eczema, contact dermatitis, dermatitis venenata, intertrigo, eczema intertrigo, eczematoid ringworm, parasitic eczema, eczema marginatum, dermatophytosis, etc." And MacKee follows this with a very sensible statement (p.491):

"Now as a matter of fact it makes little difference what we call a thing as long as we understand its nature and cause."

Dermatitis Venenata

MacKee suggests (p.491) that dermatitis venenata "may be defined as a reaction of the skin caused by external contact with substances to which the skin or the patient has become sensitized or allergic." Just about any part of the body can be involved.

According to MacKee (p.492):

"The x-rays are not indicated in the majority of cases of dermatitis venenata. If the case is properly diagnosed and the cause removed the eruption as a rule will disappear quickly; especially is this true of the acute types. At times, however, the diagnosis is exceedingly difficult; often quite impossible until after prolonged observation." He states that, although a few doses of 38 to 75 R at weekly intervals can hasten involution of acute eruptions and can reduce itching, "The detection and removal of the cause is the main requisite, otherwise the eruption is likely to persist or to recur repeatedly" (p.492).

MacKee points out (p.492) that YEARS can elapse before identification of the offending agent. Meanwhile, "the erroneous belief that irradiation is of distinct service" can occur if the offending agent sometimes decreases, by chance, soon after a patient receives an x-ray treatment for the problem.

Infectious Eczematoid Dermatitis

Infectious eczematoid dermatitis is defined by MacKee (p.494) as "a dermatitis secondary to a discharging ulcer, sinus, boil, abscess, etc." It spreads mainly by peripheral extension. MacKee himself "has seen eruptions begin at the margin of an ulcer and later involve most if not all of the body surface. In cases of this kind, when the symptoms are acute --- edema, erythema, exudation and burning pain --- x-rays have been of little benefit until the affection has become subacute." And: "In the less acute types, when the eruption is papular or squamous, with or without more or less exudation, and severe itching, x-rays may prove more efficacious than any form of treatment." But again, he points out that permanent cure is provided only by finding and removing the initiating cause.

Dermatophytosis Involving Armpits and Pendulous Breasts

"The term dermatophytosis, for convenience, may include any eruption of eczematoid appearance that is caused by fungi, and dermatophytide may include all eruptions caused by sensitization to fungus products" (MacKee, p.495). MacKee reports his experience that only some cases "do very well" under fractional x-ray treatment (p.496).

The armpits and the region under pendulous breasts are explicitly included by MacKee in a listing of areas which can become involved with this type of dermatitis (p.495).

Neurodermatitis

Under this term, MacKee includes lichenification, lichenified eczema of nape of neck, and lichen simplex. There are two types of neurodermatitis: circumscribed and disseminated (MacKee, p.497).

Circumscribed lesions have sizes from that of a dime to that of a palm. There can be few or many. Although the neck is a common location, the lesions can be "scattered over the body" and may occur "on almost any part of the body" (p.497). According to MacKee, "Most authors agree that irradiation, either x-rays or radium, is usually very effective in the circumscribed types of neurodermatitis" (p.497).

The disseminated neurodermatitis is also known as atopic eczema or atopic dermatitis. It tends to pick the flexures and flexor surfaces, but it can be generalized over the body "and even almost universal" (MacKee p.497). "There is usually a family history of hay fever and asthma and the patients are often sensitized to various substances." And: "The subjective symptom is itching which may be intense and which often precedes the appearance of the eruption."

Does radiation therapy help? MacKee reports with his usual candor (p.499):

"The effect of irradiation on this type of neurodermatitis is uncertain. The treatment practically always causes some relief, but it very frequently fails to cause complete disappearance of the eruption; especially is this true in children and adolescents. Even when the eruption does disappear recurrences are common. Nevertheless the x-rays are a valuable adjunct to general medical and conventional dermatological treatment. The fact that they will lessen the itching and directly or indirectly improve the eruption in the majority of cases of this stubborn affection, is all that is necessary to justify their use. Furthermore, there is always the possibility of complete relief which may even be permanent."

MacKee's Warning against More Than 1,500 Roentgens, Total

"As this affection [disseminated neurodermatitis] usually persists, intermittently, over a period of many years, x-rays are indicated, as a rule, only to help get the case under control during a severe exacerbation. The physician should guard against the accumulative effect of repeated courses of treatment by keeping adequate records. It is preferable to avoid a total of more than about 1,500 r on any part of the body during the life of the patient" (p.499).

Intertrigo Involving Armpits and Pendulous Breasts

Intertrigo is defined by MacKee (p.502) as "an inflammation of the skin situated in locations where there is moisture, warmth, friction and where it is difficult to keep the parts clean ... The usual sites are the crural region, the axillae, the anal region, and the breasts (under pendulous breasts). The eruption usually consists of redness, maceration, erosion, exudation and itching or burning."

MacKee thinks most cases will clear with hygiene and locally applied remedies. But if the problem persists in spite of such treatment, he suggests that "fractional irradiation may be beneficial" (p.502). And: "To irradiate the skin under the breasts it is necessary for the patient to elevate the breasts with the hands. All unaffected parts should be shielded." If MacKee's recommendation was followed, the dose to breast-tissue from that treatment could have been rendered small.

Eczema of the Nipple and Breast of Women

Radiotherapy for eczema of the nipple and breast is obviously a procedure where shielding is impossible for the breast-tissue lying beneath the afflicted area. We have seen several reports in the literature of this special eczema of the breast. MacKee says (p.505): "Here the first requisite is to be certain that the case is not one of Paget's disease. If eczema of the nipple and breast (omitting the possibility of Paget's disease), does not disappear as a result of one or two months' irradiation, it is inadvisable to continue the treatment for fear of injury to the underlying glands."

MacKee's Summary: "The Best Remedy We Have"

At the end of his chapter on eczema, MacKee sums up (p.508): "Considered as one of many remedies used in the treatment of eczema, omitting types of eczema for which there are specific remedies, and visualizing the disease in a very general way, it is the author's opinion that x-rays are the best remedy we have for eczema. In a general way it is our best antipruritic and our best resolvent agent for this purpose. However, too much must not be expected."

It is a common refrain in medicine: "The best we have is not as good as we wish." So, MacKee's opinion that "x-rays are the best remedy we have" was probably influential in the continued use of x-ray therapy for various eczemas.

Part 3. Psoriasis, Including Treatment via Thymus Irradiation

Early in their chapter on psoriasis, MacKee and Wise comment as follows (p.510): "There is hardly a dermatologist or roentgenologist who has not written or spoken (medical society meetings) of the use of x-rays or radium in the treatment of psoriasis. Consequently the literature dealing with the subject is voluminous."

The statement heightens our concern about the possibly high breast-doses contributed from this source alone.

"Psoriasis may begin as a generalized eruption of discrete, rapidly evolving, lentil-sized or split-pea sized, red, conical, scaly papules. This is psoriasis guttata," they report. And (p.510): "The eruption may undergo spontaneous involution in a few weeks or months, but it is more likely to persist and evolve into the nummular, inveterate or other chronic types." And (pp.510-511): "At times, also, the eruption becomes universal, and it may then assume characteristics that compel a diagnosis of dermatitis exfoliativa. These unusual examples may occur spontaneously or they may be the result of improper treatment, either medicinal or by irradiation."

X-Ray Therapy: Often Effective, but Needing "Extreme Caution"

Mackee and Wise have high praise for x-ray therapy, provided it is appropriately used (p.511): "Before attempting to treat psoriasis with x-rays or radium the reader is urged to study the disease in some standard treatise on dermatology. The roentgenologist should know how the disease may behave when left alone and how it may act under the influence of various kinds of treatment." And: "It is doubtful if any therapeutic agent or combination of agents can compare with x-rays (intelligently employed) in general efficacy for the treatment of the lesions of psoriasis, provided the case is one that is suited for x-ray treatment." And: "In spite of the excellent results obtained with x-rays in the

treatment of psoriasis, irradiation is by no means the method of election. Extreme caution and judgment in the use of the x-rays and in the selection of cases for such treatment are necessary, not only in order to obtain good results but in order to avoid bad results."

Treatment of Psoriasis by Irradiation of the Thymus Region

MacKee and Wise provide a brief discussion (pp.513-514) of treatment of psoriasis by irradiation of the thymus gland with x-rays or radium. They note that "In the United States, most dermatologists have abandoned this method of treatment"; they do not say how widely or for how long it was used. The patient "may receive a fractional dose (137 r) once weekly." MacKee and Wise cite some papers reporting very good results (for example, success in 65.8% of the cases) and some other papers reporting failure (few improvements).

Part 4. Lichen Planus, Involving "Almost Any Part of the Body"

This disorder, lichen planus, is treated by MacKee and Wise in their Chapter 31. "Lichen planus usually develops slowly and runs a chronic course. The sites of predilection are the flexor surfaces of the forearms, the inner aspects of the thighs, the glans penis and the buccal mucosa; but almost any part of the body may be involved; the eruption, in fact, may be generalized ... The elementary lesion is a pinhead-sized, flat-topped, shiny, smooth, more or less polygonal, sometimes umbilicated papule. The color is lilac --- violaceous. The subjective symptom is itching, which may vary from mild to intense" (p.524).

A Challenge to "the Consensus Opinion"

"Lichen planus, treated or untreated, may last for months or years. Individual lesions may persist or the eruption may continue to exist through the formation of new lesions, the older lesions undergoing spontaneous involution. It seems to be the consensus of opinion that the spontaneous cure of lichen planus is uncommon. This, however, is not our impression. While not desiring to make a definitive statement, personal impression is that many cases of ordinary lichen planus will disappear without treatment in from six months to a year or two" (pp.524-525).

Radiation Therapy: "Variable and Capricious" Results

"Lichen planus responds in a variable and capricious manner to roentgen therapy. As a general rule, the acute and subacute varieties of eruptions, whether occurring as isolated crops or as widespread exanthems, undergo fairly prompt involution as a result of a series of fractional doses of unfiltered radiation. On the other hand, patients whose eruptions are resistant to treatment, even when such treatment is pursued up to a 'dosis tolerata,' not infrequently are encountered by most dermatologists" (p.525).

"Strange to Say," We Didn't See What We Thought We Saw

In this chapter, as in his Preface, Dr. MacKee seems to allude with some awe to the physician's potential for self-delusion (see our Chapter 33, Part 2). Referring to the observation, above, that radiotherapy for lichen planus fails "not infrequently," MacKee and Wise say (p.525):

"An interesting side-light in connection with this observation is that during the initial period of fifteen to twenty years in which irradiation therapy had been used, the general impression prevailed that the disease is in most cases readily amenable to such therapy. Strange to say, in the past ten years or so, experience has demonstrated the fact that we were too optimistic in this regard. Cases are encountered in which the eruption not only is refractory to radiation therapy, but in which fresh lesions appear during active treatment long after the stage of acute development of the eruption. (In some instances, this holds true also with respect to medicinal therapy.) Hence one should be guarded in making prognostic pronouncements in relation to all varieties of lichen planus."

Their comment reminds us how it has often happened in medicine that a new pharmacologic therapy has been introduced with initial, peer-reviewed reports which positively glowed about the fabulous results observed. The key word is "observed." And yet after a couple of decades, some of these therapies have been discarded --- as ineffective. Is there really any profession which is immune to the pitfalls of wishful self-delusion?

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"Universal acceptance of a procedure [in medicine] does not necessarily make it right."

● – George Crile, Jr., M.D. (from p.9 in
ONCOLOGY TIMES Vol.15, No.2: Feb. 23, 1993).

CHAPTER 35

Breast Exposure by Radium: More Underestimate in Our Finding

Part 1. Roentgenology Versus Radium Therapy

We are almost always speaking of radium-226 when we discuss radium therapy, although there are other nuclides of radium. Broadly speaking, there are no major differences between the health effects of x-rays and those of the gamma rays emitted from a source of radium-226. Both gamma rays and x-rays are photons, and photons are the agents which "kick" some electrons in tissue into high-speed travel.

There is one difference of consequence, however, in the interaction with tissue. The higher energy of the gamma photons from radium-226 "produces" some electrons in tissue which are much more energetic than the electrons "produced" by medical x-rays (a "ballpark" comparison would be 200 KeV initially vs. 40 KeV). The more energetic the electron, the greater the distance between its interactions with tissue along its pathway. The electrons set in motion both by gamma rays and by x-rays gradually slow down, because they transfer energy to the molecules of tissue. On the average, the energies of electrons from gamma radiation are much higher than they are from medical x-rays, and therefore we assign about 2-fold less biological effect from a rad of gamma radiation than from a rad of medical x-radiation.

The Gamma Rays Associated with Radium-226

We have become accustomed to speaking about the gamma rays emitted by radium-226. In truth, only a small proportion of decaying radium nuclei give off a gamma ray (a few percent). Nonetheless, a source of radium-226 is a potent source of gamma rays primarily from the short-lived daughter products of radon-222. Radon-222 is the first decay product produced by emission of an alpha particle from radium-226. While the radium-226 has a half-life of some 1,600 years, the half-life of radon-222 is only approximately 3.8 days. In the decay of radon-222, there are some very short-lived daughter products which do indeed emit very energetic gamma rays. So long as the radon-222 does not escape the confinement with its radium-226 parent, the radon's daughter products build up quickly to a maximum value which determines the gamma ray intensity associated with its radium-226 source.

The Parent-Daughter Relationship of Radium-226 and Radon-222

The very long half-life of radium-226 and the very short half-life of radon-222 provided investigators and therapeutic radiologists with a tool widely used in the earlier days. If one pumped the gaseous radon-222 away from the solid radium-226, the greatest bulk (by far) of the gamma rays from short-lived daughters of radon-222 went with the radon-222. The combination of radon-222 and its daughters, having almost all of the highly energetic gamma rays, was taken off and used to treat patients. This in no way diminished the supply of gamma rays, since a new batch of radon-222 built up within a couple of weeks to nearly its full intensity. So one always had the radium source undiminished (except by its extremely slow decay), and one had short-lived gamma sources over and over again to use for therapy.

Any Contest Between Radium Therapy and Roentgen Therapy?

It is a fair statement to say that what we can accomplish in radiation therapy with the gamma rays from a radium source, we can also accomplish by having a source of x-rays. It is pretty much a matter of convenience and a question of which tissues and organs one wishes to irradiate.

We can quote from the text by Dr. George MacKee (1938, 3rd Edition, p.399):

"There appears to be little if any difference between the biologic and therapeutic action of x-rays and the gamma rays of radium. They seem to be equally efficacious, regardless of the disease, providing conditions are as suitable for the one as for the other. Gamma rays can be used in locations that are inaccessible to x-rays --- mouth, nose, vagina, and external auditory canal ... On the other hand, the x-rays are more suitable and more efficient in generalized dermatoses, or for the treatment of diseases that cover large areas."

We keep in mind one difference. A specified number of rads delivered by the gamma rays from radium-226 will be approximately one-half as effective in the biological effect as the same number of rads delivered by medical x-rays. In the parlance we are using in this book, one rad of gamma rays from a radium source (or the gamma rays from an atom-bomb source) is said to be equal to one-half a medical rad, delivered by medical x-rays.

A review of the radiation journals of the early decades in this century will show that roentgenologists were divided as to whether they preferred to use radium or x-rays in treating a specific disease. This division was largely because of personal convenience rather than because of any fundamental difference in efficacy. Many said explicitly that there was not much reason to choose one over the other in the therapy of benign disease.

An interesting exception is proposed in a paper by G.W. Grier (1925), concerning the treatment of enlarged thymus. We quote:

"Theoretically, then, radiation is an ideal treatment, and in practice this has been found to be the case. The rapid improvement of these cases after radiation is often astonishing. While the roentgen ray is widely used for this treatment, I have abandoned it in favor of radium, and for the last four years have treated all my cases in this way. The advantages of radium are that the response to treatment is somewhat quicker and that it can be more easily applied without disturbing the patient. It is very difficult to keep a baby accurately placed under an x-ray tube unless it is held by others who are in a certain amount of danger from exposure to the rays or to high voltage currents. The restraint of the child is also undesirable as it may precipitate paroxysms of strangulation from the crying and struggling incident to it. The radium can be applied in the baby's bed without any disturbance and the relief is surprisingly prompt."

Do the Cases Treated with Radium Lead to Underestimation of Breast-Dose?

It is hard to know what actual dose in medical rads was utilized in the radium therapy of enlarged thymus. But we can suggest that each case treated with radium simply substitutes for a case treated with medical x-rays. And, roughly, we can approximate that the dose to breasts in medical rads might have been the same from both the x-ray treatments and the radium treatments.

If, however, there are cases treated with radium over and above those where radium was substituted for x-rays, then there really would have been an increment to breast-dose which we have not taken into consideration.

Also it is quite possible, for example, that in further searches we might encounter some dermatological cases where only radium was used, and where we might be able to determine the total national breast-dose increment from this source. Then we would surely wish to correct the underestimate in dose to breasts for the 1920-1960 period, since we had previously missed this application of radium therapy.

Part 2. Handling of Radium in Hospitals: A Remarkable Report in 1941

The handling of radium sources is a totally different kind of problem from the handling of x-ray machines, with respect to hazard to patients, to relatives of patients, to medical personnel, and to "innocent" bystanders such as secretaries, stenographers, janitors, and others.

A remarkable publication in 1941 teaches us that in the very middle of the 1920-1960 period of our interest, the lessons of danger from handling radium were exceedingly poorly learned --- poorly learned in a number of hospitals where this would not have been expected so many years after the work of the Curies.

The Investigations of Drs. Cowie and Scheele in 1940-1941

Drs. Cowie and Scheele of the National Cancer Institute related their experiences in evaluating radiation protection in 48 hospitals (3 originally and 45 hospitals added to the list). This came about as follows. The National Cancer Institute Act authorized and directed the Surgeon General of the United States Public Health Service to purchase radium and to loan it to institutions for cancer research or for the treatment of patients. So, 9.5 grams of radium were bought in 1938 and were loaned to 48 hospitals in various parts of the United States.

Since it was necessary that most of the institutions to which radium had been sent be visited with reference to the renewal of the loans for a second year, it was decided that practices of protection ought to be looked at, in connection with renewal of the loans. The co-operation of the hospitals was sought and obtained in order to make the survey possible.

The "Quality" of the Hospitals Studied

The 45 hospitals surveyed, after a preliminary study of 3 hospitals, were scattered among 24 states all over the country. Twenty of them were state, county, city, or city-county institutions; 20 were operated by non-profit associations; and the remaining 5 were church-owned. Twelve of the institutions were university hospitals, and 3 more were teaching hospitals affiliated with medical schools. The hospitals were relatively large, 32 of the total having over 200 beds. The investigators pointed out that they felt this group of hospitals might show typical, if not slightly above average, equipment and practices in matters of protection against high-energy radiation.

The observations reported by Drs. Cowie and Scheele provide us with no basis for believing that unintentional breast irradiation, from the handling of radium, was a small problem at mid-century. Indeed, the findings may suggest a major, previously unestimated source of additional radiation exposure to breasts. We shall go over some of the details of the Cowie-Scheele findings in Part 3.

Part 3. Storage Systems: Protecting the Radium Rather Than the Personnel

In their survey, Drs. Cowie and Scheele investigated how radium was stored in the various hospitals. On storage methods, they rated 16 hospitals as excellent, thirteen as intermediate, and 16 as allowing "definite overexposure."

The Meaning of "Excellent" and "Tolerance Dose" in 1941

A rating of "excellent" meant that personnel were highly unlikely to receive more than the "tolerance dose" from normal work-habits around radium sources in the hospital. Drs. Cowie and Scheele pointed out, however, that such dose-levels were "nothing more than arbitrary guides" and were not any assurance of safety. We quote them from page 768:

"Various amounts of radiation have been set as 'tolerance doses' for roentgen-ray and radium workers by protection committees. These vary from 0.1 to 0.2 Roentgens per day to the entire body. The commonly accepted standard in the United States is 0.1 Roentgen, but in reality little is known of the amount and timing of radiation necessary to cause the commonly recognized injuries. Much attention has been focused on blood changes as an index of exposure, and it is partly on this basis that the present official tolerance doses were set, with full recognition that they are nothing more than arbitrary guides. While exposure of the entire body to less than 0.1 Roentgen daily may not cause blood changes, it may cause other local damage. Genetic effects may have no threshold, and it is believed the number of changes increases with increase in dose above zero."

Readers will note that there was not a word about radiation-induced cancer from occupational doses up to 20 Roentgens every year --- and of course no worry about breast-cancer. All this activity was going on for decades before Dr. MacKenzie's ground-breaking paper of 1965.

Exposure of Stenographers: Storage of Radium in the Business Office

Drs. Cowie and Scheele reported the following observations (pp.769-770):

"Eleven of the forty-five hospitals visited stored their radium in main-business-office safes. This place was used because of the intrinsic value of the radium, the fact that these safes offered the best safeguard against theft, and because the superintendent or an office clerk could be made responsible for checking the radium as it was taken out or returned, thus helping to prevent its loss. In a few of these cases the amount of lead was adequate, but in many it was not and varied from one-eighth to one-half inch in thickness, with amounts of radium stored in excess of 100 milligrams, and as high as 500 milligrams. In these same instances, stenographers often worked from 7 to 8 hours per day within 5 to 6 feet of the radium." They continued:

"The use of main-business-office safes created another exposure hazard in several cases. As a rule, the night supervisor of nurses did not have the combination of the safe; hence, when radium was removed from a patient after the close of business hours, it often was kept in the nurse's desk inadequately protected. In other cases the radium was locked in wooden or steel drawers in the office to await the arrival of the hospital superintendent or someone else who would place it in the safe. In one instance, because of the failure to take 125 milligrams out of the drawer the first thing in the morning, a number of people worked near it for a half day without protection." And:

"In several additional hospitals the people responsible for the radium in the office admitted that they were often very busy and failed to put it away. In one of these hospitals, 150 mg. of radium in two small lead cylinders, each less than one-quarter inch in effective thickness and containing 75 mg., was returned at 9 in the morning by a nurse and was given to a stenographer who, because she was very busy and had not been instructed in the dangers of exposure to radium, placed the cylinders on her desk instead of putting them in the safe where there was an adequate lead container. She had been exposed for 5 hours on the occasion when the authors [of this report] discovered the situation and [she] stated that she often kept the radium on her desk but did not know that there was any danger of overexposure since it was in lead containers. In hospitals where adequate lead carriers were used, the storage of the radium in the office safe did not lead to overexposure, because the radium was placed in the carrier when it was removed from a patient at night." And:

In one hospital "500 mg. of radium was stored and assembled beside an ordinary plaster-and steel-lath wall on the opposite side of which was a desk at which a stenographer sat for 6 hours each day. She was 5 feet from the radium during this time and received a tolerance dose [0.1 Roentgen of whole-body exposure] each hour she spent at the desk."

Exposure of Nurses: Storage of Radium in the Medicine Cabinet

In addition to nighttime exposure of some nurses, as described above, nurses would be exposed in other ways. "The worst example" was described by Drs. Cowie and Scheele as follows (pp.770-771):

"While the lead thickness of the storage container was adequate in many instances when the radium units were stored unassembled, the practice of placing assembled applicators outside the lead safe because the space in the lead container was not large enough to hold them, caused a number of cases of temporary overexposure. The worst example of this was the storage of a dental compound applicator, containing 100 mg. of radium and used for a few hours daily, in a small enameled basin in the medicine cabinet of the nurses' office. Nurses sat within 3 feet of this applicator when charting and stood within 1 foot of it when they prepared drugs for distribution, and they received over 0.5 Roentgens per hour of such work done."

This was equivalent to the full "tolerance dose" for five days --- in one hour.

Of course, the stenographers and nurses who were exposed in such ways by the careless handling of radium --- during years before and after the Cowie-Scheele survey --- did not have doses which would show up as entries in formal records available for study. But some of the genetic molecules in their BREASTS did accumulate a record of radiation exposure, unfortunately.

Part 4. Transport Systems: Sometimes by Hand, Pocket, Towel, or Jar

Drs. Cowie and Scheele also reported on how radium should be --- and really was --- carried around in hospitals (p.775):

"Overexposure may occur during transportation of radium in a hospital ... Because the time involved in handling carriers containing radium is short and because they are heavy, recommended hand-carrier thicknesses are usually 0.5 inch or more of lead for quantities of radium up to 100 milligrams." And they provided a photo at p.775 of an "excellent hand carrier [with] lead 0.75 inch thick." They continued: "When larger amounts are to be carried, thicker transportation devices should be provided, and it is usually necessary to put wheels on such carriers because of their weight." And they provided a photo at p.776 of a "radium carrier on wheels with minimum lead thickness of 1.5 inches."

But:

"In 21 institutions there were no carriers or they were 0.125 inch or less in thickness. Five [of the other 24 hospitals in the survey] had carriers 0.125 to 0.5 inch thick, and the other 19 had carriers 0.5 inch or more in thickness. However, the fact that an institution had an adequate carrier did not mean that this device was used. In 5, excellent carriers were provided, but because it was easier not to carry them and because no one had directed that radium should always be transported in them, they were unused."

Then the really casual treatment of radium is revealed:

"A nurse and radiologist in one institution carried applicators in their hands; and at another, for lack of a carrier, a resident carried applicators in his pocket. In several instances radium was transported in towels or carried by threads intended for use in anchoring the applicator after insertion. In a few cases the applicators were carried to and from the place of use by thumb forceps."

And Drs. Cowie and Scheele provided a third photo:

"Figure 5 shows a bottle used as a carrier in one of the institutions visited." The photo, showing what many people would call a glass jar with a lid, is captioned "Small glass bottle used for carrying radium."

Assembly of Radium Applicators: Participation by Nurses and Technicians

Another way in which radium exposed hospital personnel was during its assembly into applicators. Drs. Cowie and Scheele reported (p.772):

"The Advisory Committee on X-ray and Radium Protection has recommended that preparation of radium applicators and similar operations should be done behind a lead L-block of a minimum thickness of 2 inches (5 cm). The authors found that 14 hospitals in the 45 had no L-blocks. Of those remaining, all had blocks; however, 4 were from 0.0625 to 0.25 inch thick, 6 were from 1 to 2 inches thick, and 21 were 2 or more inches thick." Moreover (p.773):

"The average person assembling applicators is not adept at this work. As a rule, applicator assembly is an occasional job, therefore no one works at it sufficiently often to develop any real skill." And:

"The assembly of applicators is a task usually assigned to residents, internes, technicians, and nurses. These people frequently had little knowledge of the dangers of overexposure and occasionally had too little direct supervision. In six cases, the lumen of rubber tubing used for tandems was so small that considerable time was spent inserting

radium units covered with lubricating jelly into it. It was found that such procedures could not be carried out without holding the rubber tubing or radium unit in the fingers or in the very short forceps."

Part 5. Radium-Handling's Contribution to Breast-Cancer

Need we even WONDER whether radium-handling contributed to the breast-dose in the 1920-1960 era? If Drs. Cowie and Scheele could uncover so much ignorance and mal-handling of radium sources at hospitals in one on-site survey, what was the aggregate effect from years of such behavior?

How large? Since most of the doses were unrecorded, there is no way to generate meaningful information for the Master Table.

But there is no doubt at all that radium-handling made SOME contribution to breast-cancer among the irradiated hospital personnel. And many years after their exposure, when some of these unfortunate women were having mastectomies, their histories might give no hint about occupational radiation exposure --- because their prior occupation might well say "Stenographer."

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1931: "There Is No Such Thing as 'Minor Roentgenology' ... Secondary or Superficial Attention to It Will Not Do"

Dr. Haenisch, Part 2.

In 1931, Professor Dr. George Fedor Haenisch of the University of Hamburg, Germany, was honored by the American Roentgen Ray Society to deliver the Annual Eugene Caldwell Lecture. (American Journal of Roentgenology, Vol.26, No.6: 821-833, December 1931.) Some excerpts from it, additional to those on page 218, are presented below.

Dr. Haenisch described the consequences of x-ray machines in the hands of the general practitioner (p.829):

"He cannot afford to install large and complete roentgen equipments, because that would not pay, besides he would not be able to operate them or obtain the utmost service from them. He must therefore be content with small, nay the smallest, apparatuses such as are INCESSANTLY PRODUCED and ZEALOUSLY OFFERED FOR SALE BY THE MANUFACTURERS in their efforts to increase their business [emphasis added]. The small apparatuses are sufficient for definite purposes and are useful in the hands of the experienced, otherwise they aid in the production of incapable roentgenologists." And:

"When roentgenology will have become universal among the general practitioners the consequent lowering of the demands upon apparatus and upon the operator's skill and knowledge will result in a deterioration of the quality and in an arrest of the progress and of the development of the art. It is imperative, however, that roentgen diagnosis and therapy be developed to the highest perfection so that they may be of benefit to the patient. We must not be content with incompetent mass production. The advocates of universalized roentgenology must come to a realization of the responsibility which they are assuming by prematurely placing roentgenology in the hands of every general practitioner. The resulting injury may perhaps never be remedied." And:

"We roentgenologists, however, who can foresee the consequences must energetically combat the indiscriminate distribution of inferior apparatus and the consequent deterioration of roentgenologic work because ours is the responsibility for the development of roentgenology." And:

"The physician must recognize that there is no such thing as 'minor roentgenology' in analogy to minor surgery. The difficulties are not readily apparent, the inexperienced does not realize the sources of error, the pitfalls and obstacles which might cause his downfall even in the simplest roentgenogram of a hand or foot, to the detriment of his patient! The nature of roentgenology is such that secondary or superficial attention to it will not do."

Similar warnings in this book can be re-located from the Index under "Danger (potential danger) of x-rays" and under "Unqualified users of x-ray equipment."

The point: There is ample reason to think that non-recorded x-ray doses were very high in the 1920-1960 period.

CHAPTER 36

Radiotherapy of Benign Diseases: Overview by Dr. Dewing

Part 1. Additional Types of Breast-Irradiation Not Evaluated in the Master Table

For anyone seriously interested in the endeavor to reconstruct annual average breast-doses during the 1920-1960 era, a welcome addition to the available sources is the 1965 book by Stephen B. Dewing, M.D.: "Radiotherapy of Benign Disease." The book addresses its topic in a most comprehensive, lucid, and fair manner, and the bibliography is excellent. In 1965, Dr. Dewing was Director of Radiology at the Hunterdon Medical Center in Flemington, New Jersey, and Associate Clinical Professor of Radiology at the New York University Post Graduate Medical School in New York City.

Dr. Dewing's Defense of Benign Radiation Therapy

Dr. Dewing wrote the 1965 book because he had often felt frustrated that no single source provided the details of radiation therapy of benign diseases --- just when the physician wanted those details urgently. And he acknowledged some related concerns in his Introduction (p.ix):

"I admit to a strong sympathy for the under-dog. I would like to correct what appears to be an unfair downgrading of benign therapy. The real point is that radiation therapy of benign conditions is a healthy and respectable subject in its own right." And (same page):

"It has been said that radiation therapy has been used promiscuously, on every disease there is, and probably so. Give credit for zeal! The same can be said of any new drug. Certainly, quite a few conditions have departed from our repertoire through discovery of more effective methods, or due to poor results. But the scope of benign radiotherapy remains very extensive, and new applications continue to appear. Old ones die hard too. The therapist ought to be prepared to treat tuberculous cervical lymph nodes, carbuncles, erysipelas, or other such unusual lesions. Even if many such diseases seem rare, there will always be some patients who need radiotherapy --- either because there is no better treatment, they do not respond to simpler measures, or they are sensitive to a specific drug." And he makes a related comment in his first chapter (p.4):

"Discussion of radiation therapy of many benign conditions seems to arouse a skeptical, or amused, or contemptuous, or even hostile attitude in many physicians unfamiliar with it. Part of this block may be expressed as a suspicion of empiric therapy generally but much more is due to natural preference for the modes of drug or surgical treatment that they know and trust --- radiation is very strange to them."

We might find ourselves in a totally friendly disagreement with Dr. Dewing on a number of his statements --- particularly concerning the harmlessness of certain procedures --- and we think Dr. Dewing would also find himself in disagreement with some of his own statements, in the light of subsequent information. We certainly find ourselves in disagreement with some of our own past opinions as new information and insights develop.

Our Application of Dr. Dewing's Book in This Chapter

We are trying to identify all sources of past breast-irradiation, and Dr. Dewing's book reveals many which will probably surprise readers. They occur in his section on treatment of inflammatory conditions.

Because our interest (in this book) is limited to irradiation of the breast, our application of Dr. Dewing's book will not convey the full scope of his work. For example, he has very interesting chapters on radiation therapy for "Disorders of Function and Overgrowth" (mostly of the uterus), and for benign disorders of the eye (presented with the collaboration of Dr. Manuel Lederman). Also, we will skip over his coverage of radiation therapy for benign skin disorders (presented with the collaboration of Dr. Ralph W. Grover), because we have already covered that topic in our Chapters 33 and 34.

By itself, Dr. Dewing's book has clear limits for our effort, because he focused on the 1950-1965 period. Dr. Dewing was explicit about the time-period in his Introduction, at page "x":

"No effort has been put into developing the historical aspect. Descriptions of the earliest explorations of any particular subject have been sacrificed to brevity and concentration on current technics. In regard to a number of diseases which were once regularly treated with radiation, but now are not, no time or space has been allotted to them." And: "The material is drawn from a review of the American and major European radiologic journals since 1950. Numerous other foreign and domestic sources have been used as the occasion warranted, but material prior to 1950 has usually been cited only when intrinsically important or when little significant on the subject has appeared since."

Despite these limitations with respect to our particular endeavor, we are very pleased to acknowledge that Dr. Dewing's excellent book taught us a great deal. We shall try to pass along a selection of information which is relevant to the task at hand.

Part 2. The Observed Efficacy of Radiation Therapy for Inflammatory Disorders

Dewing at p.22: "The application of radiation to inflammatory conditions dates from radiology's earliest days. Partly as a result of the observed skin erythema (and epilation) from diagnostic or accidental x-ray exposure, and partly from comparison with the currently popular ultra-violet light treatment, physicians were tempted to experiment with treatment of skin diseases (both inflammatory and other) as early as the period 1896-98." And:

"The empiric approach, with small to moderate doses, was so rewarding that the method continued to develop. Over the next 30 to 40 years it was extensively applied to a wide variety of inflammations." And:

"Naturally, a theoretical basis for treatment was sought. It was found quite early that to kill or halt growth of bacteria required doses of many thousands of roentgens (10,000 R and up); far beyond even the range of cancer therapy. This meant that any direct effect on microbes could be ignored in a field where a few hundred roentgens were clinically effective. Besides, a direct effect on infectious organisms would have done nothing to explain favorable results in sterile non-infectious inflammations."

"The practical fact remains that radiation does something to the inflammatory process. If applied early enough it may even abort it; later it tends to accelerate

resolutions with either absorption or drainage. Pain relief is usually a prominent feature, too, roughly paralleling the reversal of inflammatory activity."

"It is interesting that after reviewing all the theories they ended up just about where they started: this or that MAY happen, but there is no real proof. Again, we are left with the empiric situation that we have a therapy that works --- works well enough, whether or not we know why, to make it useful and valuable in practice."

The Two Major Classes of Inflammatory Diseases

Dewing at p.23: "Inflammations can be divided conveniently into those which are caused by infection with some micro-organism, and those which are not."

In the summaries which follow, we will use the same division.

Part 3. Inflammatory Conditions Caused by Infections: Radiation Therapy

We are interested (here) only in the conditions for which radiation did cause or may have caused breast-irradiation.

It would be hard to say too often in our book that we do not pass judgment on these therapies with radiation. They were used --- and that is OUR central fact. We need to know the extent to which their use irradiated female breasts, for the purpose of evaluating breast-dose and its contribution to the recent, current, and future breast-cancer problem.

● - Pyogenic (Pus-Forming) Infections

Dewing at p.23: "Therapy of the pyogenic infections has undergone a considerable revolution since the sulfonamides ushered in the antibiotic era in the latter 1930's. Before that the surgical principles of appropriately applied heat, soaks, drainage, and occasionally excisions, were the standard measures, plus native resistance and nursing care. With these the milder infections usually ran their course and the patient recovered. But up to the time when antibiotics entered the field radiotherapy also played a significant role in the tougher problem cases, and even in the routine ones when given a chance. It still does have a place, though a greatly reduced one, in exceptional situations."

We continue to seek evidence from which we can someday make a calculation of dose to breast-pairs from the following infections which were once commonly treated with radiation: Anthrax, diphtheria carriers, erysipelas, mastoiditis, pneumonia (additional to Rousseau's series, which we covered in Chapter 18), and gonococcal arthritis.

"Some infections have been almost completely eradicated by the widespread use of chemotherapy," says Dewing. "An example is acute osteomyelitis in children, which as recently as the 1930's was far from uncommon but nowadays is a rare disease. Radiation therapy was used quite often for it, and scattered articles describing such treatment have continued to appear, as recently as 1960."

We would very much like to know the extent to which osteomyelitis and its therapy involved breast irradiation.

Acute infections, such as cellulitis, furuncle, and carbuncle were commonly treated by radiotherapy, but rarely so treated by 1965, when Dewing's book was written. These particular infections, especially in the neck, the axillae, and the chest definitely could have delivered appreciable doses of radiation to the breasts.

● – The Fungus Diseases

These are already covered in our Chapter 34.

● – Tuberculosis of the Lymph Glands (Not the Lung)

We have dealt with certain aspects of pulmonary tuberculosis in earlier chapters, and we have calculated annual average breast-doses from some of the collapse therapies (Chapter 15). Here we wish to deal with a totally different aspect of tuberculosis infection, namely tuberculosis of the lymph glands.

We think Dewing has stated the situation well, and we quote him directly (p.38):

"Tuberculous lesions of practically every organ and every type have been treated with x-ray, with at least fair to good results. Most of these are of purely historical interest now, though therapy of peritonitis and salpingitis lingered on into the early years of the antibiotic and chemotherapy era. The status of radiation treatment of tuberculous skin lesions will be noted in the section on dermatologic conditions." And:

"Tuberculous lymphadenitis, however, is a particular situation where radiation was actually a treatment of choice right up to the time when specific anti-tuberculous drugs took over the dominant role in therapy of tuberculosis generally. Lymphadenitis (chiefly cervical, though axillary and inguinal involvement has been occasionally seen, and successfully treated) is becoming a rare condition in the United States, like other extra-pulmonary forms of the disease." In this context, cervical refers to the neck region, not the neck of the uterus.

Elsewhere in the literature also, we have found many glowing comments in one paper or another about successful treatment of tuberculous lymphadenitis with x-ray. As a result, we continue to try to find a reliable source from which one could evaluate radiation dose to the breasts, particularly from cervical and axillary lymph node therapy with radiation.

● – Viral Infections: Herpes Zoster as an Illustration

Dewing at p.39: "Herpes Zoster is a virus infection of the central nervous system which most often attacks the posterior root ganglia of the spinal nerves, but may attack cranial nerves as well. The disease is self-limited, but is usually extremely painful, and is often succeeded by an indolent post-herpetic neuralgia which may linger on for years, and be quite disabling. There is no specific medical treatment, but radiation therapy has been found empirically to produce marked symptomatic relief in most cases." And:

"Most treatment is directed to the seat of the infection, in the posterior root ganglia, and uses conventional deep technic. However, there is a fair sized body of opinion which advocates treating the skin lesions with superficial x-ray, usually in combination with therapy to the spinal ganglia, but also sometimes alone."

We are quite concerned about this combination therapy, since both aspects of it can lead to breast irradiation. As yet we have not uncovered a source of quantitative information on the breast-dose from the management of herpes zoster.

Part 4. The Sterile Inflammatory Conditions: Radiation Therapy

Dewing deals with a mixed group of disorders, which he classes together because (a) there is a predominant element of inflammation and (b) there is no, or at most a minor,

role of infectious agents in the disorder. (It turns out that peptic ulcer does not qualify on the latter.)

● – Arthritis and Para-Articular Painful Conditions

Dewing at p.42: "All forms of arthritis have been given radiotherapy at one time or another. In many cases results were equivocal, and the method was gradually abandoned for such diseases as gout and rheumatoid arthritis."

Nonetheless, we would like very much to know what radiation dose might have been received by breasts, throughout the years of trial, in this effort to treat arthritis. Dewing states:

"Today there seems to be little scope for radiotherapy in joint affections, as such. But there are a multitude of PARA-ARTICULAR aches and pains which are often great problems clinically. A few can be pin-pointed, like bursitis or calcific tendonitis, but many defy accurate diagnosis, and may never be brought beyond the practical fact that one has a patient who has pain, call it fibrositis or what you will. After exhausting all the local injections, internal medications, ultra-sound, and diathermy, quite a few of these come to the radiotherapist's doorstep." And:

"Not all of them can be helped, of course, but one has a duty to make a good try. I have had a patient tell me that she had gone through two years of fairly typical calcific tendonitis of the shoulder, frittering along with various ineffective treatments. It was cleared up in a few days when she fell, almost by accident, into the hands of a radiologist who recognized the situation and what might be done about it."

Disorders such as this worry us concerning the possibility of breast irradiation. Unless great care was used with coning and collimation of the x-ray beam, treatment of various disorders of the shoulder could well have provided appreciable breast irradiation. It may prove impossible to assess this particular source of exposure, and the impossibility will contribute to underestimating the role of x-radiation in the etiology of breast-cancer.

● – Osteoarthritis and Para-Articular Pain

Dewing at p.43: "There will always be a group of patients with pain in or about certain joints, with negative or equivocal physical findings. The radiographs will show evidence of osteoarthritis, or other deformity residual from various types of joint damage --- e.g., trauma, infection, aseptic necrosis, or slipped epiphysis. Some of those who are not controlled by other means will be referred for a trial of radiation..... Any joint may be the site of damage and symptoms, but the commonest affected are the knees, hips, and cervical spine."

We are concerned about the possible breast irradiation from cervical spine therapy in this situation.

● – Ankylosing Spondylitis (Marie-Strumpell Disease, von Bechterew's Disease)

Dewing at p.45: "Therapy has been rather non-specific, however, and it was early learned empirically that radiation was remarkably effective in reducing or eliminating pain." And: "Just what radiation does to the disease process (and how) is obscure. Certainly pain relief is real to the patient, and such relief is claimed for approximately 80 per cent of cases in most reports."

"Treatment technic has included 'wide field' therapy to the whole trunk, looking for a humoral effect, mediated through the sympathetic nervous system." And:

"Most authors, however, have assumed a direct effect on the inflammatory process, and simply aimed their fields at the affected areas. These may include the sacro-iliacs and entire spine, or some portion of these fields, if the involvement is more limited."

We are quite concerned that some of the cervical and dorsal spine irradiations can have provided appreciable breast-dose. A quantitative estimate of annual average breast-dose from treatment of this disorder may become possible someday.

I can offer some comments to readers who may be skeptical about the relief of pain by x-irradiation in persons with ankylosing spondylitis, although the world-wide experience is so large, no one should really doubt it.

When I was an intern in medicine, one of my patients with ankylosing spondylitis was admitted for another course of radiotherapy. At the end of each day on the wards, I visited this scholarly man for long discussions about many things. And of course we spoke about his ankylosing spondylitis, and the empiric status of our knowledge. I never forgot his statement: "Try to think of spending each day of your life in severe pain for 24 hours a day, and then you will have a good idea of what my life has been for 20 years. The x-ray therapy has given me respite on more than one occasion and I am immensely grateful for the existence of this therapy."

● - Bursitis, Tendonitis

Dewing at p.48: "This condition enjoys a bewildering variety of nomenclature: bursitis, tendonitis, calcific tendonitis, calcifying tendinitis ... and simply: painful shoulder." And: "The common denominator appears to be a sterile inflammation of more or less chronicity in muscle tendons attaching near joints, with more or less calcium deposit in the involved area." And of particular relevance to our concern with breast-irradiation:

"The shoulder is the joint area most often affected by tendonitis (about 60 %).

Because the shoulder joint was the prime area treated, we have justifiable concern about breast irradiation as a result of inadequate coning and collimation, particularly in the early decades.

With respect to efficacy of treatment, Dewing states: "Without becoming involved in these arguments [as to efficacy], I would like to present a position that seems to me conservative: there is the patient, in more or less pain. The experience and evidence are at least suggestive that radiation therapy relieves this pain, no matter HOW it acts. Does one have the right to refrain from treating? I am perfectly willing to let other (non radiation) methods be tried first, and if they work, that is fine. I get most of my patients AFTER failure of other therapeutic attempts anyway. I believe that the risks of radiotherapy are negligible and one has nothing to lose by making an honest effort."

We note his belief that "the risks of radiotherapy are negligible" from such treatment.

● - Tietze's Syndrome

Dewing at p.58: "Tietze's syndrome consists of a painful swelling of costal

cartilage, with signs of (sterile) inflammation. It is self-limited and benign." Costal cartilage belongs to the ribs.

Dewing suggests that response to radiotherapy was equivocal. We are not concerned (here) about whether or not the response was favorable, but rather our concern is that painful disease of the costal cartilages involves exactly a region which could mean major radiation dose to breast tissue during therapeutic efforts. Every additional disorder whose radiation therapy involved breast irradiation adds to the total breast-dose --- which adds to the number of radiation-induced breast-cancer cases.

● - Burns: An Interesting Report from Romania

At page 59, Dewing cites an unusual area of study, namely the use of x-rays to TREAT electrical and thermal burns. The idea was reported (1959) by two Romanian workers, with ostensibly very good results in the treatment of 30 burn cases. Says Dewing: "They reported thirty cases of second or third degree (or mixed) burns. One third experienced pain relief after the first treatment; an additional fifteen were relieved after the second one; and the remainder after the third. They also felt that healing was hastened, and observed no keloids in this (rather small) group."

Dewing suggests this technic is certainly interesting and deserving of further study. The logic is not so far-fetched. Dewing states: "On the one hand there was the long-established anti-inflammatory action to recommend radiation. On the other, they [the Romanian investigators] suggested that if x-ray is useful to control keloids arising in burn scars, then it might be useful at other stages of the evolution of body response to the burn --- both immediately, and as prophylaxis against keloid formation."

We do not know how far this idea got, but it is an indication that the radiologists of the day had a great deal of belief and confidence in the anti-inflammatory action of ionizing radiation.

● - Neuritis

Dewing at p.61: "Neuritis is a subject which ought, perhaps, to be subject to clear definition. In practice, however, it has been obfuscated by more or less careless overlap with other (and more ill-defined) painful conditions of the fibrositis-bursitis-tendonitis group ... Nevertheless, there is a sizable body of experience in treating neuritis or neuropathy, however empiric it may be. The technic of therapy is quite comparable to that employed for tendonitis. Results were considered good (i.e., complete or substantial relief of pain) in about 90 percent of cases."

Dewing cites the work of Heidelman who described 139 patients (with adequate follow up) treated for brachialgia paraesthesia nocturna. "This condition was characterized by numbness, paraesthesia and pain in the hands and arms, typically occurring in middle aged females, and awakening them from sleep. Treatment was administered to the cervical and upper thoracic vertebral column, 100-150 R (air) to a 10 x 15 cm field, using conventional deep therapy." The treatment was repeated in a week, and a third dose was used if no response had occurred. Overall, Heidelman reported 37 percent completely well, and 56 percent more or less improved.

Dewing adds: "All of his [Heidelman's] patients had had the diagnosis of brachialgia made by excluding other etiologies, had not been relieved by other therapy, and were treated with x-ray alone."

Such cases would certainly have experienced breast irradiation, whether AP or PA beams were used in therapy. This is a situation where many women could have been treated, and where irradiation of the breasts was never even considered. (Dewing also mentions a few other varieties of neuritis, treated by radiation to the vertebral levels corresponding to the location of the reported pain.)

● - Pancreatitis

We suspect that some eyebrows will be lifted to have to consider pancreatitis as an inflammatory condition to be treated with radiation. But it clearly was regarded as a subject for consideration. The rationale is provided by Dewing at pp.62-63:

"Pancreatitis is a condition without specific therapy, in which pain is a conspicuous feature. Reasoning by analogy from the known sensitivity of the inflamed parotid gland to radiation, many investigators have speculated on what might be done with radiotherapy for inflammation of the somewhat similar tissue of the pancreas. Treatment is uniformly with conventional deep technic, 200 Kv, 1.0 mm.Cu HVL." Three series are cited by Dewing:

(1) Morton and Widger (1940) gave individual doses in the 50-100 R range to the pancreas, every one to two days for four to five exposures. "They [Morton and Widger] felt response to this therapy was quite encouraging."

(2) "Levi and Engle (1950) cited 28 cases treated rather 'lightly' with 75 R (air) to a 15 x 15 cm. anterior epigastric field twice, with a twenty-four hour interval. They reported definite clinical improvement which lasted hours to days, but did not appear to alter the overall course of the disease."

(3) "Heacock and Cara (1954) described fifty-three cases given a regular course of 200 R (air) daily for three doses to an anterior abdominal 15 x 15 cm. field. Of their cases, seven required a second course some weeks later, four were given a third, and one received a fourth course. They claimed a good result in thirty-three patients, fair response in an additional fifteen, and poor or no benefit in the remaining five. Their conclusion was that radiation therapy given early enough was effective in counteracting the inflammatory process, and would abort abscess formation and other complications, as well as the chronic state of the disease."

Pancreatitis is a serious disease. It took some bravery to suggest treating it with x-ray. Our concern is for the scattered radiation from those anterior abdominal fields. How much of that radiation dose got to breasts depends upon how well collimated the beam was and how much external scatter was present. From some of what we have seen in the pre-1960 period, we would have to wonder seriously about how well that beam was controlled.

● - Peptic Ulcer

Again, those only recently familiar with medicine may find it incredible that peptic ulcer should be treated by a regimen which aimed at shutting down the acid-producing mechanism of the stomach. But that is exactly what was done. We have personally reviewed many of the major papers on this subject, and can vouch for Dewing's description of the seriousness with which this approach was taken.

We do not know, from phantom studies or other studies, what the dose was to BREASTS of treated women, but considering the dose delivered to the stomach, we would have to worry a great deal about that problem.

Dewing (at p.63) claims a place for radiation: "The primary treatment of peptic ulcer is medical (and perhaps psychiatric). There are also definite indications for surgery, of course. Between these, however, radiation has a definite place as an adjunct." And:

"The rationale of radiotherapy in peptic ulcer is happily simple and clear-cut: suppression of hydrochloric acid secretion by the gastric glands. That this effect IS produced by a tissue dose of the order of 2000 R has been thoroughly documented experimentally. Thus one can dismiss the older literature which aimed very light doses at the sympathetic ganglion chains, and critical articles by persons who gave excessive doses of 4000-6000 R, and ran into complications."

Alerted by Dewing to this use of radiation therapy, we examined several other sources directly. In order not to interrupt the selections from Dewing, we will return to peptic ulcer in Part 5.

● - Thyroiditis

Dewing refers to two varieties of thyroiditis for which radiation therapy has a role: Subacute Thyroiditis and Hashimoto's Struma.

Dewing on Subacute Thyroiditis (p.69)

"Quite a few authors have reported very encouraging results from radiotherapy in recent years, and Crile even lauds radiation as the method of choice." (The name of George Crile, Jr. is akin to magic in the field of thyroid disease.)

Several regimens are cited by Dewing:

Osmond and Portmann (1949) reported on 55 cases. The course consisted of 100-150 Roentgens (air), directed to a single 10 x 10 cm field encompassing the thyroid gland, and repeated every two days for four to six exposures, depending on the response of the inflammation.

Crile and Rumsey (1950) gave daily doses of 100-150 Roentgens (air) to 35 patients, and used a single field. They fixed upon 800 Roentgens as an optimal average total dose, and felt that above 1,500 Roentgens, there was some danger of impairing thyroid gland function. Fourteen of their cases had a complete remission in one week, most of them within two weeks. Five cases required a second course of treatment after evaluation at six to eight weeks.

Our Comments

We are concerned about there being a dose to some breast tissue, from external scatter, from lack of coning. We would feel much more comfortable about dismissing the possibility of appreciable breast-dose if some phantom data were available.

Dewing on Hashimoto's Struma (p.70)

Dewing suggests that Hashimoto's Struma recommends itself to radiation therapy because of the predominance of lymphocytic infiltration, and the known sensitivity of the lymphocyte. He lists several regimens:

Means (1948) used right and left fields, and gave 100 Roentgens (air) to each on alternate days until a total of 400 R to each field was reached. Allen and Reeves (1951) used 100-150 R (air) every two days to a single field up to a total of about 1,000 R to the gland. Bromley (1955) cited Crile (1948) suggesting a maximum total dose of 1,500

Roentgens for this disorder. Bromley used a dose of 2,000 Roentgens (tissue) in two weeks and was enthusiastic about this therapy.

We retain our skepticism that the dose to the breasts was really negligible.

Part 5. Radiation Treatment of Peptic Ulcer: Additional Authors

We return to the issue of radiation therapy for peptic ulcer, because of the high doses employed and the probability that the breasts received some exposure. Below, we present data and comments from three sources supplemental to Dewing.

● - The 1951 Report by Ricketts and Palmer

William E. Ricketts and Walter L. Palmer wrote "Radiation Therapy in Peptic Ulcer," which was Chapter 34 in a book devoted to the clinical aspects of peptic ulcer. At page 381:

"The result depends in part upon the technic used, the amounts of irradiation given, and the individual susceptibility of the organism. The portals selected are opposite each other, one located in the left hypochondrium and the other in the left costolumbar region. The size of the irradiated area should be the smallest possible to include the body and the fundus of the stomach, 13 by 13 cm. is adequate. The location, size, and configuration of the stomach should be determined fluoroscopically and the portals altered accordingly. The treatments are given daily; the portals are treated alternately. The total depth dose, as calculated in a plane one third of the distance from the anterior wall to the posterior wall, varies from 1600 to 2400 roentgens in a period of twelve days; this has been found to be perfectly safe."

We note both the claim that the therapeutic dose was "perfectly safe," and the use of fluoroscopy in order to position the portals. At page 385, Ricketts and Palmer state:

"In a series of approximately 1000 patients treated during the past twelve years, the development of malignant degeneration of the stomach or skin has not been seen; in fact, aside from the transitory and usually moderate nausea with dislike for milk and antacid especially, the side effects have been negligible. There has been no clinical evidence of injury of adjacent organs such as the liver and pancreas, except for one initial case in which the radiation was given at too rapid a rate. In a series of twelve patients subjected to electrocardiograms for periods of six weeks, no evidence of myocardial injury was detected." And:

"The incidence of healing [of the peptic ulcer] following adequate amounts of irradiation together with standard antacid medical management is usually above 90 percent. The length of time required for healing varies, but in most patients it occurs within ninety days. There is evidence of a direct correlation between depression of acidity and the healing of the ulcer." And:

"There is no correlation between the age or sex of the patients and the effect of irradiation, nor among these factors, the duration of symptoms, and healing."

Our Comments on the Ricketts-Palmer Statements

We note that their claim of no side-effects covers a maximum follow-up time of only 12 years, and an even shorter average follow-up time.

Our concern here is about breast irradiation. In 1951, that was not their concern at all. So of course they provide no phantom study to establish what dose an average female breast would get from the beam during such treatments. We wonder, for the period before 1951, whether the coning, the collimation, the aiming of the beam were really so accurate as to mean that breast-dose from such therapy would have been negligible. The claim is made of an irradiated area 13 by 13 cm (about 5 x 5 inches). How well was this really achieved? A phantom study would have helped a great deal.

● – The 1956 Paper by Carpender and Co-Workers

In 1956, the American Journal of Roentgenology and Radium Therapy published "Radiation in the Therapy of Peptic Ulcer," by J.W.J. Carpender and colleagues. Data cited below are from pages 374 and 375:

This study of gastric ulcer included 116 patients observed during the period of 1937 to 1954. The patients with duodenal ulcer were the 113 treated in 1945 and 1946. In the gastric ulcer patients, the total depth dose varied from 1,100 to 2,930 Roentgens. Most of the patients received 1,600 to 1,700 R. The patients with duodenal ulcer all received 1,600 to 1,700 Roentgens depth dose to the body and fundus of the stomach.

The two-portal technic was used, as was the case in the Ricketts-Palmer series. Carpender et al report (p.378):

"A reduction in gastric acidity in most patients for varying periods of time has been demonstrated with achlorhydria also for variable periods of time in a small number of patients. In no instance did an ulcer fail to heal when achlorhydria was produced for three months or longer, nor was there recurrence during such a period of achlorhydria."

So this study of 229 additional patients with peptic ulcer confirms the broad finding of the Ricketts and Palmer study.

● – The 1957 Study by Levin and Co-Workers

In 1957, the journal Gastroenterology published the results of a large study by Erwin Levin and colleagues entitled "Observations on the Value of Gastric Irradiation in the Treatment of Duodenal Ulcer." Their paper presented the results in 723 patients with duodenal ulcer treated with radiation and observed for 5 to 18 years. The dose used in the most recent period (1948-1950) was 1,600 to 1,700 Roentgens to the gastric fundus, with the use of 13 by 13 cm portals (p.43). Their conclusion (p.48):

"Roentgen irradiation in moderate amounts to the acid-secreting areas of the stomach constitutes a safe and valuable adjunct in the treatment of duodenal ulcer."

Another optimistic assertion about safety, of course.

Our Comments on the Combined Studies

It appears that hypochlorhydria and achlorhydria were achieved in all the studies, and that ulcer healing accompanied reduction in acid production.

Perhaps the aiming of the x-ray beam and its restriction were very good. We certainly hope so. Before MacKenzie's 1965 paper, it is not surprising that none of the studies did measurements of actual breast-dose with phantoms. So the breast-dose is an open question. And it is potentially consequential.

Large and favorable studies were coming out of several institutions. The treatment was declared "safe." Even "perfectly safe." If radiation therapy for peptic ulcer was widely used for a while, it would make quite a difference if it delivered an associated breast-dose per patient more like 100 milli-rads, or more like 100 rads. Could it have been 50 or 100 rads?

At this time, we do not know. There is no entry whatsoever in our Master Table for annual average breast-dose from this source.

Part 6. The Combined Frequency of Many Treated Disorders

This chapter presents a spectacular array of benign diseases treated with radiation therapy. All or almost all of them may have contributed breast-doses NOT evaluated in our Master Table.

We were startled by a statement in the Introduction to Dr. Dewing's book (p.ix):

"The experience of many of us is that benign treatments may account for as much as 50 per cent of the volume of clinical radiotherapeutic practice. This proportion is very apt to reflect the interest of the radiologist. He can build a practice, or let it run down, by the energy (or the lack of it) with which he sets his talents at the disposal of his referring colleagues."

If radiotherapy of BENIGN diseases could account for half of the "volume" of clinical radiotherapy practice in 1965, such a high fraction --- though apparently not common in 1965 --- suggests that breast-irradiation due to such treatments in the 1920-1960 period may have produced an annual average breast-dose APPRECIABLY greater than what we were able to evaluate in our Master Table.

This concern is fortified by the widespread and very careless use of x-ray equipment by non-radiologists (see Chapters 31 and 32, for example) and by the so-called "wasted radiation" from unnecessarily large areas of exposure (Chapter 23, Part 2), and by the fact that even some beauty-shop operators were using radiation for non-diagnostic purposes (Chapter 26).

Moreover, the combined frequency of the disorders reviewed in Parts 3, 4 and 5 must have been quite high. Even individually, some of them may not have been negligible, as contributors to breast irradiation. Is anyone in a position to rule out radiation treatment just of sore shoulders, for example, as a significant but unevaluated source of breast-irradiation? Until such possibilities can be ruled out, one by one, on the basis of some real evidence, they should not be dismissed too promptly on the basis of wishful thinking.

Even though our Master Table presently excludes breast-dose from the therapies reviewed in this chapter, we already know this:

Past radiotherapy of benign diseases has had an unintended consequence: It is a cause of radiation-induced breast-cancers. We state this again, not as a criticism, but as a sobering reminder about unintended long-term consequences from actions which superficially may appear sensible.

CHAPTER 37

Recent Concerns: Intensive Care Units, Insurance Cases

Part 1. Identification of Current Radiation Sources of Especial Concern

Perhaps the most unintelligent response to this book, and what it teaches us about the most dreaded cancer feared by women, would be, "But many of the sources of breast irradiation no longer exist. So why should we concern ourselves about a problem of the past?"

A problem of the past? Hardly! It is the irradiation in the past and the present, but largely in the past, which is causing the largest share of the breast-cancers of today, of the recent past decades, and which will be causing large numbers of breast-cancers in decades to come.

If ever there were a memorable statement about forgetting the lessons of past follies in the exposure to radiation sources, it is that of George Santayana:

"Those who cannot remember the past are condemned to repeat it."

Radiation Exposures Which Are No Longer Present

We no longer irradiate the thymus gland of newborn infants.

We no longer test for enlarged thymus gland before permitting pediatric surgery.

We do not treat infectious diseases, such as pneumonia, with x-rays.

We do not treat peptic ulcer with massive, ablation doses to the stomach.

We do not treat bronchial asthma with x-rays to the chest.

The dermatologists, who once claimed 80 separate benign diseases as best treated with roentgen rays or radium gamma rays, no longer treat any of those diseases with ionizing radiation.

The fluoroscopic "shoe-fitters" have left the shoe stores.

We are not aware of any pediatricians who still routinely fluoroscope babies and children at their monthly, semi-annual, and annual health checkups.

The beauty shops are not likely to be treating freckles or excess hair with x-rays.

Pertussis (whooping cough) is now quite well under control with immunization, but in any case we do not hear of x-ray treatment of this disease.

Hopefully the management of tuberculosis does not deteriorate to a point where collapse therapy, with extensive fluoroscopy, is again needed. Tuberculosis bears serious watching.

Acute and chronic mastitis are managed without x-ray therapy.

Most of the inflammatory disorders (bursitis, tendinitis, etc. as described by Dr. Dewing), are not likely to be treated with x-rays.

We have learned the lesson of cutting the dose to breasts to 1/20 of what they were in spine examinations by putting the x-rays into the back instead of into the front of the body.

Mammography doses have been reduced by a very large factor.

We no longer test nuclear weapons in the atmosphere.

Radiation Exposures Which May Be As Prevalent or More Prevalent TodayRadionuclides in Nuclear Medicine Diagnostic Procedures

The use of radionuclides in nuclear medical diagnostic procedures has increased appreciably. NCRP 100 (Table 4.1) gives data from Mettler (1985) showing the trend in diagnostic radionuclide examinations in the United States over a 10 year period, 1972 to 1982.

Exams (in thousands)	Year							
	1972	1973	1975	1978	1980 Source 1	1980 Source 2	1981	1982
Total	3,300	3,500	4,800	6,400	5,800	6,400	7,000	7,400

Frequency of Exams Number per 1000 of Population	16	17	22	29	26	28	31	32
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The actual absorbed population dose to organs such as the breast will still need evaluation.

General Diagnostic Radiology Examinations

We are particularly interested in what has been occurring in the post-1960 period, after our 1920-1960 period of data accumulation.

Examination	Year		
	1964	1970	1980
Total (in thousands)	58,500	81,700	132,400
(Rate per 1000 population)	310	410	580

The increase in rate of exams, 1970 to 1980, using totals, is $132,400 / 81,700$, or 1.62. This 62 % increment, NCRP 100 points out, occurred during a period of population increase of only 11 % (at p.15). The increment in rate per 1000 of population also confirms that the rise between 1970 and 1980 is a real increase since it is PER 1000 of population.

It will require serious investigation to ascertain the extent to which this large increase in PER CAPITA "Hospital x-ray examinations" offsets x-ray exposures which are no longer used. It is not possible to state this quantitatively now, but it is an important agenda item for the near future, if we are to sustain or increase the annual incidence of breast-cancers or to see some decline in the future.

Fluoroscopic Examinations in General Diagnostic Radiology and in Newer Sophisticated Invasive Procedures.

It is a difficult problem to evaluate the radiation doses from all the fluoroscopies. Certainly (see Chapter 29) the high-dose fluoroscopic examinations which worry the FDA appear characterized as showing an astounding dose-increment per procedure in comparison with the fluoroscopies associated with past "usual" hospital diagnostic procedures. Also, much will depend upon the age-distribution of such high-dose fluoroscopic procedures.

We regard an evaluation of the newer fluoroscopic procedures and the more "usual" ones for the post-1960 period, and especially for the recent period in the 1980s and 1990s, as another essential priority evaluation. Such evaluation is essential for making an assessment of future breast-cancer prospects --- in the decades to follow. We must remember that breast-exposures in the recent several DECADES will be the major determinants for breast cancer-incidence in the first quarter of the 21st century.

We note the American Cancer Society's advice in 1992:

"Fluoroscopy delivers larger doses of x-ray than that used in standard films. If there is an alternative means of making a diagnosis, fluoroscopy should be avoided."

Part 2. Special Situations of Major Concern

The Intensive Care Units for Babies and Children

The remarkable accomplishments in the saving of the premature infant in the past several decades is well known. And the remarkable surgical accomplishments in the diagnosis and surgical therapy of congenital heart, vessel, and other abnormalities is equally well-known. We have encountered concern over the number of radiographic procedures which are utilized in the care of the premature neonates and other neonates requiring intensive care in the hospitals.

NCRP 100 (at pp.31-32) has stated the following: "The dose incurred in pediatric x-ray examinations is of interest since, in many circumstances, a large portion of the child's body is included in the primary beam ... Radiation doses to neonates requiring intensive care were examined in Great Britain by Robinson and Dellagrammaticas (1983). These babies are of particular concern since they may receive relatively large numbers of radiographs compared to adults, and such studies often include fluoroscopic examinations and CT scans. The mean active marrow dose from all examinations was found to vary inversely with the birth weight. Overall, children with lower birth weight received more examinations ... "

We are quite surprised at the paucity of sources of information concerning the very small neonates under intensive care, in the 1989 version of NCRP 100. It will be important to seek out more recent information on a much larger body of data in order to assess carefully the quantitative significance of extensive radiologic examinations in the neonatal intensive care unit.

Study of Doses in a Single Intensive Care Unit in a United Kingdom Hospital

The Robinson-Dellagrammaticas study (1983) consists of a series of 84 total subjects admitted to the Neonatal Intensive Care Unit at the Jessop Hospital for Women (Sheffield, U.K.). These authors state:

"Radiological investigations remain one of the most important sources of information for the clinician in his evaluation of the severely ill newborn baby. Relatively large numbers of diagnostic X-ray examinations are given to some neonates requiring intensive care over the first few weeks of life. In some instances, we have noted up to 40 chest or abdominal films being taken, with, possibly, barium studies and CT scans also performed."

This series of cases includes 50 neonates with gestation periods up through 33 weeks. The data characterizing the findings are as follows:

Gestation Weeks	Number of Babies	Survivors	Mean Birth Weight Kg.	Mean No. of Films	Mean Number of CT Scans
26, 27	8	3	0.83	6.75	0.5
28, 29	15	11	1.15	10.5	0.33
30, 31	9	7	1.49	11.3	0.55
32, 33	18	16	1.80	3.67	0.28

The number of CT scans quoted is the average number of "cuts" (i.e., 2 slices)

The typical skin exposure in these neonatal X-ray examinations were:

Exam	Dose in milli-Roentgens
Chest Films	5.8
Abdomen Films	6.2
CT scans	1550
Barium Enema	2310

The authors indicate that the Barium Enema estimate could be off a factor of two in either direction.

They also point out the enormous variation in exams per infant --- from those having a single chest radiograph to one having 43 films (15 chest radiographs, 24 abdominal films, a barium enema, and a CT scan).

Robinson and his colleague suggest that the cases requiring intensive care must be fewer than 3 % of the total number of births in the hospital during the period when these cases were collected. Since the hospital in question is a specialized maternity unit, it is expected to have a higher-than-average number of "high risk" cases. Therefore, overall, the radiation exposure in neonates requiring intensive care might not impose a large population dose for all births. Since this seems at variance with opinions we have heard, carefully-evaluated additional sources of information are definitely needed. One can wonder whether the financial arrangements for care of neonates can influence the results. Some United States experience will be sought out for recent decades.

Criteria for the Care of the Neonates

Some of the neonates requiring the most radiation exposure will carry an appreciable excess rate of development of breast-cancer beyond the age of 30 years. That is no reason for withholding necessary radiation exposures in the intensive care unit. Thirty, forty, fifty, or sixty years of good life surely are worthwhile, even if a later cancer is a result in some cases. Robinson and Dellagrammaticas indicate their concern that some of the radiation exposure may be unnecessary, as they state (p.397):

"The highest doses are received in CT scans and barium examinations and it is recommended that the need for these should be carefully considered and requests for such examinations only made by experienced staff." We would agree.

Persons Involved in Accidents, Occupational and Other

It has come to our attention that there is what has been described as "massive" use of x-ray films in the resolution of compensation claims for industrial and non-industrial injury in accidents. It has been pointed out that the various groups and individuals involved in litigation have quite differing opinions concerning the number and type of x-ray films needed. The result in some cases is that a stack of films "inches thick" results before a settlement is reached. Some of those films are the result of follow-up examinations in the therapy of accidental injuries.

A large number of these accidental injuries involve the back and the neck. Cervical, dorsal, and lumbar spine films can all be sources of radiation to the breasts. We know that orthopedic and chiropractic examinations (and repeat examinations) are involved in many such cases, so the increment in breast-doses from these sources may not be negligible. Some of the individuals involved in such cases have suggested that the unnecessary radiation in such cases is far from negligible. Our only comment is that radiation received in settlement of such compensation claims can be enough to have a major effect on radiation-dose to the breast, with ensuing breast-cancers several decades later. Some serious study of this issue would be worthwhile.

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• – The Difference between X-Rays and Diagnostic "Nuclear Medicine"

Diagnostic nuclear medicine usually involves putting radioactive substances into a patient's body, and then interpreting the radiation which reaches the outside of the patient from those sources inside. The patient "remains radioactive" until the radio-nuclide either decays or is excreted from the body.

By contrast, x-rays do not make a patient radioactive at all. The radiation exposure from x-rays (including x-rays from a fluoroscopy machine) lasts only as long as the x-ray beam is "on." X-rays (like gamma rays) are a type of "light" --- some of which passes right through the body and is then recorded by a film or other image-receiver on the opposite side. The DOSE to internal organs comes from the x-rays which do NOT pass all the way through the patient.

An essay by Dr. George E. Pfahler at his 80th birthday
in 1955:

MORE GOOD THAN EVIL

A half century ago Pierre Curie said, that "in criminal hands, radium might become dangerous ... is humanity ripe enough to profit by learning the secrets of nature, or might not that knowledge prove harmful? I believe that humanity will obtain MORE GOOD THAN EVIL from future discoveries."

The discovery of radioactivity by Becquerel and the Curies has been an incalculable blessing, and radium has eased pain, parried death, and given life to numberless cancer sufferers. And yet Pierre Curie was a greater prophet than he knew, for this same discovery was the seed from which was developed the most potent agent for suffering, death and mass destruction the world has ever known. Radioactivity, the bane and blessing of modern man, is an example of the utter impartiality of science in ministering to the best and the worst that is in us. Science is not to blame, for it is the servant of man. The fault lies in man himself, who wills to put science to such paradoxical uses.

On the credit side of the ledger of man's stewardship of radioactivity is the application of the many forms of radiation to the treatment of cancer --- first Roentgen's "new kind of rays," then radium and radon with the numerous refinements and techniques, followed by the radioactive isotopes resulting from nuclear fission. Advances in supervoltage therapy, particle-accelerating beams, precision targeting, rotation therapy, and induction of greater tumor susceptibility to radiation have made radiotherapy a worthy partner to surgery --- previously the sole cure for cancer.

Of greatest importance in the long-term control of cancer are the rapidly accumulating data concerning the effects of ionizing radiations on normal and cancer cells, particularly the effects on genes and chromosomes and the effects in nucleic acid synthesis.

Thus radiant energy from the many sources now available has become a valuable factor not only in the immediate therapy of cancer but also in research by revealing more and more of the intimate physiology of the cell in which the cause of cancer still lies hidden.

Surely, from the discoveries of Roentgen, of the Curies, and of those following them has come MORE GOOD THAN EVIL.

From CA: A BULLETIN OF CANCER PROGRESS
Vol.5, No.1: 2. January 1955.

CHAPTER 38

Summary on Underestimation of Dose in Our Study

Part 1. Why We Need to Know about the Exposures We Have NOT Measured

The entire principle of this study of causation of breast-cancer is based upon the identification and measurement of sources of annual breast-irradiation over the period from 1920 to 1960. If our goal is to identify how large a fraction of breast-cancer causation ionizing radiation is responsible for, we need to identify ALL the sources, with measurement of the dose received annually from each source.

For every source we cannot quantify, we are "losing" some part of the causation. And we will, therefore, be underestimating the radiation causation of breast-cancer as the result.

We realized at the outset of these investigations that there were undoubtedly going to be some major sources which we would not be able to quantify. But we also realized that for every source we could identify and quantify, we could be sure of at least the minimum extent to which ionizing radiation was a cause of breast-cancer. That ionizing radiation is a cause of breast-cancer was without any doubt at the outset, no matter how poorly that appears to have been recognized by the uninformed or mis-informed.

The Effort Went Better Than We Expected

We have been surprised and amazed at what it was possible to accomplish in this quest. The fact that we have identified ionizing radiation as the major causal factor in breast-cancer and have identified much about the time periods which are involved in breast-cancer development, spurs us on to try to evaluate QUANTITATIVELY any remaining radiation factors. The problem is NOT that we do not know the remaining radiation factors. Rather, the nature of the scientific literature is such that it is simply not easy to get reliable information to quantify them. Part 2 discusses three major areas of concern.

Part 2. The Major Remaining Radiation Factors: How Large a Role?

● - First: Fluoroscopy (or Roentgenoscopy)

Fluoroscopy was very popular, and was used by even more non-radiologists than radiologists (Chapter 31, Part 5). There is simply no doubt that fluoroscopy was used in multitudinous ways which irradiated breast tissue, but which were not covered by our method in Chapter 23. A prime example, separately and independently revealed by Blatz, Pifer, and Buschke/Parker, was inclusion of pediatric fluoroscopy in well-baby and well-child examinations (Chapter 31, Parts 2 and 3). Yet our Master Table completely excludes such use.

We have described the papers from Metropolitan Life Insurance Company, where nearly 5,000 consecutive applicants were fluoroscoped to screen out tuberculosis (Chapter 30). After the initial publications, how many additional applicants nationally were

processed by this same company? How many additional companies and industries did this too, and did not write a paper on it? Yet our Master Table excludes such pre-employment uses of fluoroscopy.

And these examples are not the only uses of fluoroscopy for which there is no permanent record of dose received by female breasts. This is one of the big problems about fluoroscopy; it was (and is) widely used, and there is almost never a record of WHAT dose was given to HOW MANY persons.

Numerous pieces of evidence point to fluoroscopy as likely to be the dominant source of radiation breast-exposure. We contemplate with amazement Braestrup's comment that New York City passed an ordinance forbidding fluoroscopic exposures higher than 100 Roentgens per exam. By itself, the unevaluated use of fluoroscopy in the 1920-1960 period might account for an annual average breast-dose larger than the combined sources in the Master Table.

● - Second: Dermatologic Use of Radium Gamma Rays and X-Rays in Therapy

There can simply be no doubt that dermatological use of radium gamma rays and x-rays up through 1960 can only be described as massive. The perusal of Chapters 33 and 34 makes that quite clear.

We know that the dermatologists prided themselves on the therapy of some 80 different dermatological disorders, wholly aside from any therapy of superficial or deep cancers. We know that this continued unabated over many decades. We know that the radiation doses to tissues would undoubtedly have been high in those dermatological applications which were in the physical neighborhood of breast-tissue, or where breast-skin was in fact the organ being treated. But we do not generally have any way to measure just what fraction of the breast-tissue was irradiated in the dermatological applications.

Skin disorders are common. Doses were high. It is possible that, by itself, the unevaluated dermatologic uses of radiation in the 1920-1960 period also might account for an annual average breast-dose larger than the combined sources in the Master Table.

● - Third: The Array of Inflammatory Disorders Reviewed in Chapter 36

A vast number of inflammatory disorders --- from tuberculous lymphadenitis to sore shoulder --- used to be treated with radiation therapy. Chapter 36 lists many disorders for which radiation therapy must have caused breast-irradiation, sometimes or often. Even if therapy of one disorder by itself did NOT add a great deal to the annual average breast-dose, the COMBINED uses may have made an appreciable contribution to dose --- not evaluated in our Master Table.

Part 3. Review of the Probable Underestimates from Chapters 8-25

The major omissions, discussed above, are not the only issue. Even the entries in the Master Table represent a credible LOWER limit of breast-dose from the sources to which they apply. We will just review the probable underestimates incorporated in the Master Table, by chapter.

● - Chapter 8, Thymus Irradiation before Age 1. In Part 2, Item 10, we assumed that for every infant who received therapeutic doses, only 2.5 infants received diagnostic doses. And in Item 11, we assumed a very low dose from the use of fluoroscopy in such diagnosis. And in Part 3, Item 12, we assumed that no diagnosis or therapy at all occurred in 1957, 1958, or 1959.

● - Chapter 9, Thymus Irradiation to Reduce Sudden Death, Ages 1-9. In Part 5, Item 2, we assumed that only ONE hospital in the entire city of Boston and the entire Suffolk County, did this. In Item 8, we assumed that the dosage was no higher than in Chapter 8, even though it was probably higher. In Item 10, we assumed there was never any use of fluoroscopy in pre-therapy screening, and we assigned no dose at all from diagnostic screening.

● - Chapter 10, Pre-Surgical Thymus Irradiation. In Part 4, Item 12, we subtracted about 25 % from the breast-dose in Chapter 8.

● - Chapter 12, Pre-Birth Irradiation. In Part 2, we reduced the frequency reported in our source by 25 %. In Part 4, Item 5, we used only the lowest dose in the range reported by our source --- a dose 2-fold lower than the highest level reported.

● - Chapter 13, Treatment of Acute Postpartum Mastitis. In Part 3, Item 2, we assumed that one report covered ALL cases treated in Monroe County.

● - Chapter 14, Chronic Mastitis. In Part 5, we assumed that there was no "silent" use of radiation therapy going on, and also that Dr. Pfahler was the only physician in all of Philadelphia who ever used radiation therapy for chronic mastitis.

● - Chapter 15, Fluoroscopic Exposure in Management of Pneumothorax Treatment of Tuberculosis. In Part 3, we assumed 1.5 rads as breast-dose per fluoroscopy, using the Massachusetts studies. Yet we know that the Nova Scotia studies considered 7.5 rads as the proper dose, based upon the direction of the radiation introduction to patients. We chose the lower dose, conservatively, to avoid any possibility of overestimate of radiation dose.

● - Chapter 16, Mass-Screening for Tuberculosis. There was some uncertainty of the years of duration of this program. We arbitrarily cut the duration to one-half of the period of concern, thus possibly underestimating the radiation dose.

● - Chapter 18, Treatment of Pneumococcal Pneumonia with X-Rays. We assumed that no institution other than Bowman Gray School of Medicine did therapy of pneumonia cases in Forsyth County. This may have led us to a large underestimate of radiation dose. Also, we eliminated all cases other than those with pneumococcus as the etiologic agent, when it is highly likely that pneumonias caused by other organisms were also treated with x-rays.

● - Chapter 19, Treatment of Whooping Cough with X-Rays. We assumed that only the Boston Floating Hospital treated pertussis with x-rays, but other hospitals in Boston may have done so. Our assumption may have led to an underestimate of radiation dose (person-rads) to breasts.

● - Chapter 20, Treatment of Hyper-Thyroidism and Breast Irradiation. We made the assumption that when radium gamma-rays were used in therapy of this disease, there was no direct gamma-ray exposure to the breasts. The conditions of radium use did not

permit any estimate of this source of breast-dose, so for our effort to provide the Credible Lower Limit, we assigned Zero as the dose to the breast from this source.

• – Chapter 21, X-Rays in the Management of Adolescent Scoliosis. Even though we suspected a larger radiation dose in 1920–1930 than in the later periods for which records were available, we made the decision simply to assign Zero as the x-ray dose in 1920–1930 to avoid any possible overestimate of dose.

• – Chapter 22, Chiropractic Examinations and Breast Irradiation. Some of our colleagues in disability evaluation have indicated to us that both chiropractors and physicians commonly take many, many films of the back in cases of disability claims and in evaluation of ameliorative therapy. We would judge that a share of those films, not taken in hospitals, may not be counted in any total assessment of chiropractic use of x-rays.

• – Chapter 23, Major Diagnostic Radiological Contributions to Breast-Tissue Dose. For the fluoroscopic part of several diagnostic procedures, we have assumed an entrance dose of 3 Roentgens per exposure --- probably a great underestimate at a time when some machines were putting out 100 Roentgens per minute and when New York City had to post a limit of 100 Roentgens per fluoroscopic exam. Diagnostic doses from fluoroscopy in office practice are simply not trackable.

• – Chapter 24, Occupational Sources of Breast Irradiation. There are reasons to doubt official evaluations of occupational radiation doses in the 1920–1960 period. First, the 1941 Cowie–Scheele Study indicates how the good low-dose behavior by most technicians can be undone by a few high-dose exceptions. Second, the way that radium was really handled in many hospitals was shocking (Chapter 35). Third, much x-ray work was done outside hospitals (Chapters 31–34, 36).

• – Omission of person–rads received at ages above 64. This, too, is a source of dose underestimation.

Part 4. Our View of the Evidence at Hand

The evidence already solid is far more than enough to point the path to a very great deal of breast–cancer prevention --- EFFECTIVE cancer prevention. It is not necessary to account for 100% of causation or to await impossible exactitude about the radiation–induced percentage, before initiating preventive ACTION based upon the finding from this study.

The estimate that 75% of all breast–cancers have a radiation etiology is based on the Master Table and the numerous instances of our underestimation of doses in the effort to produce a Credible Lower Limit. In view of all the ancillary evidence from fluoroscopy and dermatology and treatment of inflammatory conditions, the issue is hardly one of defending a 75% etiology; rather the question may well be how much HIGHER than 75% this might be.

There may be some valuable resources in the literature which have not yet come to our attention. We intend to continue upgrading our estimates in an on-going fashion, and to report new findings as appropriate. We hope and expect that others will inquire into this topic too.

CHAPTER 39
Bottom Line: The Master Table

Part 1. A Few Reminders about the Master Table

The description for each alphabetical column of the Master Table is provided in Part 2 of this chapter, and the three pages of numerical entries follow.

The rows of the Master Table represent 65 age-years, for breast-irradiation during a SINGLE typical calendar-year of the 1920-1960 period. 65 ages, one year. Dose-estimates are provided in "medical rads," a term explained in Chapter 3, Part 1. The numerical entries for estimated breast-doses are added sideways by age-year, to obtain their SUM for a typical calendar-year in Column T.

What about Irradiation Which Occurred after 1959?

Readers who were born after 1959 may be the first to wonder: Does the Master Table, based on a 1920-1960 study-period, apply to annual production of breast-cancer cases NOW? Yes, to a good "first approximation," as we noted in Chapter 5. This is discussed further in Part 2, in the section describing Column W.

Why Are the Doses in Column T So Low?

Why are the doses in Column T so low, despite some of the very high doses described in the text? One reason: Not all of the female population received the various exposures (natural background radiation excepted). To obtain the average annual breast-dose applicable to the WHOLE female population, we made DOWNWARD adjustments to the breast-doses actually received by those who were irradiated (Chapter 5, Part 2). This was first demonstrated in Chapter 8, Part 2, Item 9. Another reason: We adjusted the actual breast-doses DOWNWARD, as appropriate, so that our low-dose conversion-factors would not overestimate the consequences from higher doses (Chapter 5, Part 5). This was first demonstrated in Chapter 8, Part 2, Item 8.

The Relationship of Annual Production and Annual Incidence

The dose-estimates in Column T allow us (and others) to estimate the annual PRODUCTION of radiation-induced breast-cancers from a single year of irradiation. The DELIVERY of the single year's production happens gradually over many decades, due to variable latency periods (Chapter 2). If a female population of constant size receives a constant level of breast-irradiation year after year, finally the ANNUAL delivery rate of radiation-induced breast-cancer equals the annual production-rate (Chapter 4). As we said at the end of Chapter 4:

If we can figure out the annual production-rate for a specific period of exposure, then we already know the annual incidence-rate which will occur decades later related to that exposure --- and thus we can compare that to the total incidence and learn what fraction of the existing breast-cancer problem was caused by that ionizing radiation.

The sum of entries in Column W is a remarkable number, to be discussed in subsequent chapters.

Part 2. Description of Every Column, Followed by Numerical Entries

● - Age-Years: This column refers to age when irradiation occurs, NOT to age when cancer may occur. Age 0 means irradiation between birth and the first birthday.

● - Column A, No. of Persons: The number of female persons alive in each age-year, for an average calendar-year of the 1920-1960 study-period. The origin of these entries is shown in Chapter 8, Part 2, Item 6. By using the AVERAGE population-size for the period 1920-1960, we can keep the population at a constant size --- which is a requirement for the "Law of Equality" (Chapter 4).

The sequence of the next columns, through S, is arbitrary.

● - Column B, Irradiation from Natural Sources: Typical whole-body annual dose (exclusive of radon and its daughters), adjusted to less energetic medical rads (Chapter 3, Part 1; and Chapter 8, near the end).

● - Column C, Enlarged Thymus Gland: X-ray breast-dose, during first year of life (usually during first few months), in diagnosis and therapy of "enlarged thymus" and "status lymphaticus." Chapter 8.

● - Column D, Enlarged Thymus Gland: X-ray breast-dose, mainly during age-years 2 through 15, in screening and therapy for "enlarged thymus," prior to tonsillectomy, adenoidectomy, and other childhood surgeries. Chapter 10.

● - Column E, Acute Mastitis: X-ray breast-dose in therapy of acute mastitis (inflammation of the mammary gland). Chapter 13.

● - Column F, Chronic Mastitis: X-ray breast-dose in therapy of chronic mastitis, a disorder which has many names (including fibroadenosis, chronic cystic mastitis, benign fibroadenoma, or adenofibrosis), and is characterized by lumpy, tender breasts. Chapter 14.

● - Column G, Management of Tuberculosis: X-ray breast-dose in the fluoroscopic monitoring of artificial pneumothorax therapy, for patients having tuberculosis (the Detroit experience). Chapter 15.

● - Column H, Management of Adolescent Scoliosis: X-ray breast-dose from spinal x-rays in the monitoring of adolescent scoliosis (curvature of the spine). Chapter 21.

● - Column I, Mass Screening for Tuberculosis: X-ray breast-dose in mass screening-programs to detect tuberculosis (unlike Column G). Chapter 16.

● - Column J, Bronchial Asthma: X-ray breast-dose in the therapy of bronchial asthma (the Mayo Clinic experiences). Chapter 17.

● - Column K, Pre-Birth Breast-Irradiation: X-ray breast-dose to the fetus as a result of the mother's pelvic and abdominal x-ray examination while pregnant. Chapter 12. Due to a shortage of vertical space, we use the top row (age=0) for this entry rather than adding a "prenatal" row.

● - Column L, Hyper-Thyroidism: X-ray and gamma-ray (from radium and iodine-131) breast-dose in the radiation therapy of exophthalmic thyroid disease (hyper-thyroidism). Chapter 20.

- - Column M, Enlarged Thymus Gland: X-ray breast-dose, mainly during age-years 1 through 9, in prophylactic therapy of "enlarged thymus" (the experience of the Massachusetts Eye and Ear Infirmary). Chapter 9.
- - Column N, Whooping Cough: X-ray breast-dose in the therapeutic management of pertussis (whooping cough). Chapter 19.
- - Column O, Fission-Product Fallout: Equivalent medical rads to breasts from radioactive fallout in the 1945-1960 period of weapons-testing. Chapter 25.
- - Column P, General Diagnostic X-ray Exams: X-ray breast-dose from general diagnostic exams, roentgenograms plus fluoroscopic examination. Chapter 23.
- - Column Q, Occupational Exposures: X-ray breast-dose, occupationally incurred. Chapter 24.
- - Column R, Chiropractic Exams: X-ray breast-dose in chiropractic applications, largely from full-spine x-rays used in diagnosis and follow-up. Chapter 22.
- - Column S, Pneumonia: X-ray breast-dose in the roentgen therapy of pneumococcal pneumonia. Chapter 18.
- - Column T, Sum of Annual Breast-Doses: The horizontal sums of the entries in Columns B through S. For each age-year, the dose represents the average breast-dose for EVERY female in the age-group in an average year for the period 1920-1960. Moreover, each dose represents an average annual dose for persons of each age which recurs at the same level year after year, for the "new" people moving through that age-year. This constant level of exposure meets the requirement of the "Law of Equality" (Chapter 4). If the average annual doses were unchanged for a sixty-five year period, the average female breast-dose accumulated between birth and age 65 would be the sum of the dose-estimates in Column T: 27.88 medical rads.
- - Column U, Person-Rads: The product of multiplying Column A (total persons irradiated) times Column T (the rads received by each, on the average). Persons x Rads = Person-Rads (Chapter 8, Part 2, Item 9). Of course, in this table, person-rads refers to female BREAST-rads, not whole-body rads.
- - Column V, Cancers per 10,000 Person-Rads: The conversion-factors which convert annual dose (in breast-rads) into annual breast-cancer production. There are five different conversion-factors in Column V --- for five different groups of ages at the time of irradiation. The number of breast-cancers produced per 10,000 person-rads declines as age at irradiation increases. This reflects the observation that the young are more vulnerable to induction of cancer by radiation. Chapter 40 explains the origin of these conversion-factors.
- - Column W, Radiation-Induced Breast-Cancers: For each row, the entry is the product of (Person-Rads, from Column U) times (Breast-Cancers per 10,000 Person-Rads, from Column V). Each entry represents the production from a SINGLE year's exposure.

Delivery of the breast-cancers from a single year's exposure occurs gradually, during the subsequent lifespan of the women in each age-group. After decades of such exposures occurring each year, the delivery of radiation-induced breast-cancer each year is equal to the production of radiation-induced cases per year (Chapter 4).

It is our thesis that the sum of the entries in Column W approximates BOTH the past production of cases per year AND the current delivery of new cases per year.

How Column W Applies to Breast-Cancer Production 1960–1995

In Part 1, we said that the Master Table extends to years beyond the 1920–1960 study-period, as a "first approximation." Suppose we assume that the average per-person annual dose-level to female breasts after 1960 fell appreciably below the average level of 1920–1960 (Column T). Even if it did, we have to recognize the large and undeniable increase in the average population of women (Column A) who are receiving the average annual per-person dose.

The entries in Column A of the Master Table are based on a female population of 69 million, for all ages combined (Chapter 8, Part 2, Item 6). By contrast, if we consider the midpoint of the 1960–1995 period as 1977, the female population was about 112 million (estimated from Table 2, located after the final chapter). And by 1993, the female population of the United States was about 132 million, for all ages combined.

An increase in the irradiated population (Column A), and a decrease in average dose received by each (Column T), tend to balance each other out in terms of person-rads (in Column U), since Column U = Column A times Column T.

Person-rads convert to radiation-induced cancers by applying conversion-factors (Column V) which are assumed to be independent of time. If they are independent, then as long as the value for person-rads maintains an approximately steady level beyond 1960, the annual production-rate of radiation-induced breast-cancer (Column W) will also maintain a steady level. At this time, it seems reasonable to think that the value for person-rads in Column U, and for radiation-induced cancers in Column W, are acceptable "first approximations" of the values for 1960–1995 too.

The Numerical Entries of the Master Table

The next three pages provide the numerical entries of the Master Table. The retention of many digits does not indicate that they are "significant figures" in the formal sense. We avoid "rounding off" merely to facilitate the tracing of computations.

The "bottom line" is the SUM of Column-W entries: An annual incidence-rate of radiation-induced breast-cancer equal to an unrounded value of 114,336 new cases per year in the USA --- prior to any upward adjustment for the many doses NOT yet evaluated (Chapter 38).

The five numbers to the right of Column W (which is shaded) show how many of the total radiation-induced breast-cancers arise from the following ages (ages at the time of irradiation):

Age-years 0–9 :	Cases = 34,857; percent of 114,336 = 30.5%
Age-years 10–19:	Cases = 24,935; percent of 114,336 = 21.8%
Age-years 20–34:	Cases = 26,185; percent of 114,336 = 22.9%
Age-years 35–49:	Cases = 15,458; percent of 114,336 = 13.5%
Age-years 50–64:	Cases = 13,265; percent of 114,336 = 11.6%

Age-Years	No. of Persons	Med. Rads Col. A	Med. Rads Col. B	Med. Rads Col. C	Med. Rads Col. D	Med. Rads Col. E	Med. Rads Col. F	Med. Rads Col. G	Med. Rads Col. H	Med. Rads Col. I	Med. Rads Col. J
0	905213	0.05	0.633							0.0021	
1	892820	0.05								0.0021	
2	892097	0.05		0.1577						0.0021	
3	891518	0.05		0.1577						0.0021	
4	891047	0.05		0.1579						0.0021	
5	890657	0.05		0.1579						0.0021	
6	890332	0.05		0.1579						0.0021	
7	890051	0.05		0.1580						0.0021	
8	889806	0.05		0.1581						0.0021	
9	889589	0.05		0.1581				0.0112		0.0021	
10	889390	0.05		0.1581			0.0604	0.0112		0.0021	
11	889209	0.05		0.1581			0.0604	0.0112		0.0021	
12	889028	0.05		0.1582			0.0604	0.0112		0.0021	
13	888829	0.05		0.1582			0.0604	0.0112		0.0021	
14	888585	0.05		0.1583	0.0045		0.0604	0.0112		0.0021	
15	888277	0.05		0.1583	0.0045		0.0604	0.0112		0.0021	
16	887906	0.05			0.0045		0.0604			0.0021	
17	887462	0.05			0.0045		0.0604			0.0021	
18	886973	0.05			0.0045		0.0604			0.0021	
19	886449	0.05			0.0045		0.0604			0.0021	
20	885914	0.05			0.0368	0.0013	0.0604			0.0021	
21	885371	0.05			0.0368	0.0013	0.0604			0.0021	
22	884810	0.05			0.0368	0.0013	0.0604			0.0021	
23	884231	0.05			0.0368	0.0013	0.0604			0.0021	
24	883642	0.05			0.0368	0.0013	0.0604			0.0021	
25	883045	0.05			0.0533	0.0013	0.0604			0.0021	
26	882438	0.05			0.0533	0.0013	0.0604			0.0021	
27	881823	0.05			0.0533	0.0013	0.0604			0.0021	
28	881189	0.05			0.0533	0.0013	0.0604			0.0021	
29	880528	0.05			0.0533	0.0013	0.0604			0.0021	
30	879840	0.05			0.0274	0.0013	0.0604			0.0021	0.00190
31	879107	0.05			0.0274	0.0013	0.0604			0.0021	0.00190
32	878329	0.05			0.0274	0.0013	0.0604			0.0021	0.00190
33	877496	0.05			0.0274	0.0013	0.0604			0.0021	0.00190
34	876618	0.05			0.0274	0.0013	0.0604			0.0021	0.00190
35	875677	0.05			0.0110	0.0013	0.0604			0.0021	0.00190
36	874662	0.05			0.0110	0.0013	0.0604			0.0021	0.00190
37	873567	0.05			0.0110	0.0013	0.0604			0.0021	0.00190
38	872381	0.05			0.0110	0.0013	0.0604			0.0021	0.00190
39	871077	0.05			0.0110	0.0013	0.0604			0.0021	0.00190
40	869638	0.05			0.0028	0.0013	0.0604			0.0021	0.00190
41	868045	0.05			0.0028	0.0013	0.0604			0.0021	0.00190
42	866289	0.05			0.0028	0.0013	0.0604			0.0021	0.00190
43	864361	0.05			0.0028	0.0013	0.0604			0.0021	0.00190
44	862243	0.05			0.0028	0.0013	0.0604			0.0021	0.00190
45	859917	0.05				0.0013	0.0604			0.0021	0.00190
46	857373	0.05				0.0013	0.0604			0.0021	0.00190
47	854585	0.05				0.0013	0.0604			0.0021	0.00190
48	851552	0.05				0.0013	0.0604			0.0021	0.00190
49	848266	0.05				0.0013	0.0604			0.0021	0.00190
50	844718	0.05				0.0013	0.0604			0.0021	0.00190
51	840889	0.05				0.0013	0.0604			0.0021	0.00190
52	836752	0.05				0.0013	0.0604			0.0021	0.00190
53	832289	0.05				0.0013	0.0604			0.0021	0.00190
54	827473	0.05				0.0013	0.0604			0.0021	0.00190
55	822286	0.05					0.0604			0.0021	
56	816719	0.05					0.0604			0.0021	
57	810736	0.05					0.0604			0.0021	
58	804282	0.05					0.0604			0.0021	
59	797275	0.05					0.0604			0.0021	
60	790469	0.05					0.0604			0.0021	
61	781353	0.05					0.0604			0.0021	
62	772364	0.05					0.0604			0.0021	
63	762779	0.05					0.0604			0.0021	
64	752739	0.05					0.0604			0.0021	

MASTER TABLE, Columns K through S

Age-Years	Med. Rads Col. K	Med. Rads Col. L	Med. Rads Col. M	Med. Rads Col. N	Med. Rads Col. O	Med. Rads Col. P	Med. Rads Col. Q	Med. Rads Col. R	Med. Rads Col. S
0	0.16			0.154	0.00029	0.055			
1			0.0184	0.134	0.00029	0.055			
2			0.0184	0.145	0.00029	0.055			
3			0.0184	0.100	0.00029	0.055			
4			0.0184	0.115	0.00029	0.055			
5			0.0184	0.108	0.00029	0.055			
6			0.0184	0.077	0.00029	0.055			
7			0.0184	0.039	0.00029	0.055			
8			0.0184	0.017	0.00029	0.055			
9			0.0184	0.006	0.00029	0.055			
10				0.006	0.00029	0.055			
11				0.006	0.00029	0.055			
12				0.006	0.00029	0.055			
13				0.004	0.00029	0.055			
14				0.004	0.00029	0.055			
15				0.004	0.00029	0.145	0.0720	0.0216	
16				0.004	0.00029	0.145	0.0720	0.0216	
17				0.004	0.00029	0.145	0.0720	0.0216	
18				0.004	0.00029	0.145	0.0721	0.0216	
19				0.004	0.00029	0.145	0.0721	0.0216	
20	0.00131		0.004	0.00029	0.145	0.00797	0.0721	0.0216	
21	0.00131			0.00029	0.145	0.00797	0.0722	0.0217	
22	0.00131			0.00029	0.145	0.00798	0.0722	0.0217	
23	0.00131			0.00029	0.145	0.00798	0.0723	0.0217	
24	0.00131			0.00029	0.145	0.00799	0.0723	0.0217	
25	0.00131			0.00029	0.194	0.00799	0.0724	0.0217	
26	0.00131			0.00029	0.194	0.00800	0.0724	0.0217	
27	0.00131			0.00029	0.194	0.00800	0.0725	0.0217	
28	0.00131			0.00029	0.194	0.00801	0.0725	0.0218	
29	0.00131			0.00029	0.194	0.00802	0.0726	0.0218	
30	0.00094			0.00029	0.194	0.00802	0.0726	0.0218	
31	0.00094			0.00029	0.194	0.00803	0.0727	0.0218	
32	0.00094			0.00029	0.194	0.00804	0.0728	0.0218	
33	0.00094			0.00029	0.194	0.00804	0.0728	0.0218	
34	0.00094			0.00029	0.194	0.00805	0.0729	0.0219	
35	0.00094			0.00029	0.225	0.00806	0.0730	0.0219	
36	0.00094			0.00029	0.225	0.00807	0.0731	0.0219	
37	0.00094			0.00029	0.225	0.00808	0.0732	0.0219	
38	0.00094			0.00029	0.225	0.00809	0.0733	0.0220	
39	0.00094			0.00029	0.225	0.00810	0.0734	0.0220	
40	0.00094			0.00029	0.225	0.00812	0.0735	0.0220	
41	0.00094			0.00029	0.225	0.00813	0.0736	0.0221	
42	0.00094			0.00029	0.225	0.00815	0.0738	0.0221	
43	0.00094			0.00029	0.225	0.00817	0.0739	0.0222	
44	0.00094			0.00029	0.225	0.00819	0.0741	0.0222	
45	0.00094			0.00029	0.250		0.0743	0.0223	
46	0.00094			0.00029	0.250		0.0745		
47	0.00094			0.00029	0.250		0.0748		
48	0.00094			0.00029	0.250		0.0751		
49	0.00094			0.00029	0.250		0.0753		
50	0.00094			0.00029	0.250		0.0757		
51	0.00094			0.00029	0.250		0.0760		
52	0.00094			0.00029	0.250		0.0764		
53	0.00094			0.00029	0.250		0.0768		
54	0.00094			0.00029	0.250		0.0772		
55	0.00094			0.00029	0.255		0.0777		
56	0.00094			0.00029	0.255		0.0783		
57	0.00094			0.00029	0.255		0.0788		
58	0.00094			0.00029	0.255		0.0795		
59	0.00094			0.00029	0.255		0.0802		
60				0.00029	0.255		0.0809		
61				0.00029	0.255		0.0818		
62				0.00029	0.255		0.0827		
63				0.00029	0.255		0.0838		
64				0.00029	0.255		0.0849		

Age-Years	Sum, Medical Rads	Person-Rads	Cancers per 10000 Pers-Rads	Radiation-Induced Cancers Col. W
0	1.054	954448	92.74	8851.5
1	0.260	231901	92.74	2150.7
2	0.428	382210	92.74	3544.6
3	0.383	341844	92.74	3170.3
4	0.399	355252	92.74	3294.6
5	0.392	348861	92.74	3235.3
6	0.361	321134	92.74	2978.2
7	0.323	287300	92.74	2664.4
8	0.301	267734	92.74	2483.0
9	0.301	267846	92.74	2484.0
10	0.343	305141	76.13	2323.0
11	0.343	305079	76.13	2322.6
12	0.343	305106	76.13	2322.8
13	0.341	303260	76.13	2308.7
14	0.346	307264	76.13	2339.2
15	0.529	470185	76.13	3579.5
16	0.360	319523	76.13	2432.5
17	0.360	319405	76.13	2431.6
18	0.360	319275	76.13	2430.6
19	0.360	319135	76.13	2429.6
20	0.403	356978	44.95	1604.6
21	0.399	353273	44.95	1588.0
22	0.399	353106	44.95	1587.2
23	0.399	352934	44.95	1586.4
24	0.399	352759	44.95	1585.7
25	0.465	410421	44.95	1844.8
26	0.465	410201	44.95	1843.9
27	0.465	409978	44.95	1842.9
28	0.465	409748	44.95	1841.8
29	0.465	409508	44.95	1840.7
30	0.441	387817	44.95	1743.2
31	0.441	387569	44.95	1742.1
32	0.441	387306	44.95	1740.9
33	0.441	387024	44.95	1739.7
34	0.441	386727	44.95	1738.3
35	0.456	399194	26.38	1053.1
36	0.456	398835	26.38	1052.1
37	0.456	398449	26.38	1051.1
38	0.456	398030	26.38	1050.0
39	0.456	397570	26.38	1048.8
40	0.448	389931	26.38	1028.6
41	0.449	389382	26.38	1027.2
42	0.449	388777	26.38	1025.6
43	0.449	388112	26.38	1023.8
44	0.449	387382	26.38	1021.9
45	0.464	398612	26.38	1051.5
46	0.441	378508	26.38	998.5
47	0.442	377485	26.38	995.8
48	0.442	376372	26.38	992.9
49	0.442	375166	26.38	989.7
50	0.443	373864	24.56	918.2
51	0.443	372459	24.56	914.8
52	0.443	370941	24.56	911.0
53	0.444	369304	24.56	907.0
54	0.444	367537	24.56	902.7
55	0.446	367114	24.56	901.6
56	0.447	365061	24.56	896.6
57	0.448	362855	24.56	891.2
58	0.448	360475	24.56	885.3
59	0.449	357891	24.56	879.0
60	0.449	354639	24.56	871.0
61	0.450	351286	24.56	862.8
62	0.451	347980	24.56	854.6
63	0.452	344454	24.56	846.0
64	0.453	340762	24.56	836.9
Predicted Radiation-Induced Cancers —>				13278.7 Age-years 50-64
Observed Incidence 1993 —>				114336.4 114336.42
				182000

"I use not only all the brains I have, but all I can borrow."

● – T. Woodrow Wilson, 1856–1924,
28th President of the USA.

CHAPTER 40

Conversion Factors: The Basis of Column "V"

Part 1. Introduction

By the term "conversion-factor" in this book, we mean any formula which estimates how MANY radiation-induced breast-cancers result from a specified amount of population-exposure --- for example, from 10,000 person-rads of exposure. In this book, the term person-rads refers to BREAST-rads.

The conversion-factors developed in this chapter differ slightly from the conversion-factors published in our preliminary work for this book. We continue to study the problem of conversion-factors; many other analysts continue to study the problem, too; and relevant new evidence continues to accumulate. So we expect the conversion-factors to keep improving in the future. Meanwhile, this chapter presents one of several ways to arrive at conversion-factors, in view of what is presently known, and what is presently unknowable.

Part 2 of this chapter begins where Chapter 15 of our 1990 book ended. Otherwise, we would have to repeat most of the earlier book. Readers who are not familiar with the previous book can, nonetheless, follow what we do HERE with the "starting point" from the earlier work (Gofman 1990).

Part 2. Step-by-Step Development of Our Conversion Factors

Our starting point for developing conversion-factors is the study of atomic-bomb survivors. Why don't we use evidence based in the United States, since this book focuses on the breast-cancer problem in the USA? The answer is simple: Only the A-Bomb Study provides observations for women irradiated at every age, and then followed-up for decades. No comparable study exists for American women.

We have analyzed both the 1950-1982 and the 1950-1985 follow-up evidence from Japan on radiation-induced cancer mortality. The more recent data are not yet available to us from RERF (as of January 1995). Here, we will use the 1950-1982 data, because readers can refer to Gofman 1990 to check exactly how we handled those data in reaching our starting point for this chapter.

We begin (on the next page) by presenting a series of six boxes, which are subsequently explained in the text.

BOX 1, "Starting Point." All cancer-types, excluding leukemia.

A Age when exposed (years)	B Cancer-deaths per 10,000 initial females as of 1982, in high-dose group	C Cancer-deaths per 10,000 initial females as of 1982, in low-dose group	D Difference per 10,000 initial females as of 1982 (B minus C)
0-9	150.94	55.41	95.53
10-19	295.23	153.32	141.91
20-34	637.48	451.57	185.91
35-49	1318.68	1077.37	241.31
50+	1246.33	1040.42	205.91

BOX 2, Lifetime Factors. All cancer-types, excluding leukemia.

A Age when exposed (years)	B Age when exposed (avg.) (years)	D Difference per 10,000 initial females as of 1982 (B minus C)	E Lifetime factor of increase (1059/Col C)	F Lifetime excess cancer-deaths per 10,000 initial females (D times E)
0-9	4.1	95.53	19.11207	1825.776
10-19	14.9	141.91	6.90712	980.190
20-34	26.6	185.91	2.34515	435.987
35-49	41.7	241.31	none	241.31
50+	58.9	205.91	none	205.91

BOX 3, Supra-Linearity Adjustment. All cancer-types, excluding leukemia.

A Age when exposed (years)	F Lifetime excess cancer-deaths per 10,000 initial females (D times E)	G Supra- linearity factor (see text)	H Lifetime excess cancer-deaths (per 10K females) adjusted for supra-linearity (F times G)
0-9	1825.776	2.40	4381.863
10-19	980.190	2.24	2195.625
20-34	435.987	2.18	950.452
35-49	241.31	2.13	513.990
50+	205.91	2.06	424.175

BOX 4, Division by Dose-Difference. All cancer-types, excluding leukemia.

A Age when exposed (years)	H Lifetime excess cancer-deaths (per 10,000 females) adjusted for supra-linearity	I High-dose group: Average dose in rads	J Low-dose group: Average dose in rads	K Dose-difference in rads (I minus J)	L Lifetime excess cancer-deaths per 10K females with avg dose = 1 A-bomb rad (H / K)
0-9	4381.863	97.61	2.91	94.70	46.271
10-19	2195.625	89.20	2.50	86.70	25.324
20-34	950.452	87.38	2.63	84.75	11.215
35-49	513.990	80.87	2.76	78.11	6.580
50+	424.175	71.73	2.51	69.22	6.128

BOX 5, Adjustment for Medical Rads. All cancer-types, excluding leukemia.

A Age when exposed (years)	L Lifetime excess cancer-deaths per 10K females with avg dose = 1 A-bomb rad (H / K)	M Factor of increase for medical rads	N Lifetime excess cancer-deaths per 10K females with avg dose = 1 medical rad (L times M)
0-9	46.271	2	92.542
10-19	25.324	2	50.649
20-34	11.215	2	22.430
35-49	6.580	2	13.161
50+	6.128	2	12.256

BOX 6, Final Adjustments to Reach Conversion-Factors.

A Age when exposed (years)	N Lifetime excess cancer-deaths per 10K females with avg dose = 1 medical rad (L times M)	"O" Lifetime excess breast-cancer deaths per 10K fem with avg dose = 1 medical rad (see text)	P Incidence/mortality ratio for breast-cancer (see text)	Q US/Japan ratio of breast-cancer vulnerability (see text)	R "Lift-off" reduction factor (see text)	S Conversion factors for Master Table. Described below *.
0-9	92.542	8.8315	3.704	5.67	0.50	92.74
10-19	50.649	4.8335	3.704	5.67	0.75	76.13
20-34	22.430	2.1405	3.704	5.67	1	44.95
35-49	13.161	1.2560	3.704	5.67	1	26.38
50+	12.256	1.1696	3.704	5.67	1	24.56

* Each conversion factor is the estimated number of radiation-induced excess breast-cancer cases (lifetime incidence) per 10,000 females (USA) from an average breast-dose of one medical rad. Each entry in Column S is the product of Columns "O" x P x Q x R.

● - BOX 1, Starting Point

In Box 1 are the findings for cancer mortality for ALL types of cancer (leukemia excluded) in the female population, divided into low-dose and high-dose groups for five separate age-groups (age in 1945, at the time of the bombings). The observed differences between high-dose and low-dose groups (Column D, Box 1) are the radiation-induced cancer-deaths.

The boxed data come from Tables 15-G, 15-H, 15-I, 15-J, and 15-K of Gofman 1990. We are using the entries from those tables in the T65DR dosimetry. Those very same tables show that the results are negligibly different when the revised DS86 dosimetry is used properly. By "properly," we mean that the cohorts remain constant (no shuffling of cases) while receiving a revised estimate of average dose from the DS86 system.

Our protest against the retroactive shuffling of cohorts, and against the constant retroactive alteration of the DS86 database, is fully presented in Gofman 1990 (especially Chapters 5 and 6). In our opinion, use of the unstable DS86 database (which already has many versions) is scientifically acceptable only as part of a "constant-cohort, dual-dosimetry" analysis in which the T65DR system remains the stable anchor for the follow-up studies.

● - BOX 2, Adjustment for Lifetime Follow-Up

The values in Box 1 cover only the period through 1982. We (and others) have to estimate what the observations may be when ALL the initial participants have been followed for their full lifespans. In 1945, the average age of the 50+ age-group was 58.9 years for females, and average age was 41.7 years for the age-group 35-49 years (Gofman 1990, Table 26-G). In 1982, both of these age-groups have essentially told their lifetime "story," so we can use those results without adjustment. But we must make estimates for the other three age-groups.

How? Tables 15-G through 15-K of Gofman 1990 show that the whole-body dose in the low-dose groups was very similar in all five age-bands (range = 2.50 rems to 2.91 rems). So we will use the approximation that the low-dose women in the three youngest age-groups will "behave" like the two oldest age-groups, with respect to LIFETIME rate of cancer mortality. When we average the lifetime rates of the two oldest age-groups, we obtain 1,059 cancer deaths per 10,000 initial women.

For the age-group 0-9 years, the value 1,059 represents a 19.112-fold multiplication of the 55.41 rate observed in 1982 (Box 1, Column C). For the age-group 10-19 years, 1,059 represents a 6.907-fold multiplication of the 153.32 rate observed in 1982. And for the age-group 20-34 years, 1,059 represents a 2.345-fold multiplication of the 451.57 rate observed in 1982. These "lifetime factors" are shown in Box 2, Column E. (As usual, we retain all the digits without endowing them with the formal status of "significant figures.")

And what about the lifetime DIFFERENCE between the high-dose and low-dose groups --- the lifetime radiation-induced EXCESS for the three youngest age-groups? For now, we temporarily use the assumption that the difference will also increase by the same "lifetime factors." Later, in Box 6, we make downward adjustments for the two youngest age-groups. Meanwhile, Box 2 applies the "lifetime factors" to obtain the estimated lifetime excess of cancer-deaths (all sites) per 10,000 initial females (Column F).

• - BOX 3, Adjustment for Supra-Linear Dose-Response

The differences in Box 1 (Column D) come from assuming a linear dose-response. In reality, supra-linearity describes the dose-response among the A-bomb survivors significantly better than linearity, both in T65DR and DS86 constant-cohort analyses (Gofman 1990, Chapters 14 and 29). The shape of the dose-response for 1950–1982, with all ages and both sexes combined, is reproduced below from Figure 14-E of Gofman 1990. The curve has the same shape in the DS86 dosimetry, properly handled with "constant-cohorts."

We notice with interest that the excess relative risk specifically for breast-cancer incidence also shows a supra-linear shape in Thompson 1994 (Figure 3, p.S26, which is a DS86 analysis not anchored to T65DR cohorts).

If it were not for the bend of supra-linearity, the differences between high-dose groups and low-dose groups would have been approximately twice as high as the values presented in Box 1, Column D. Indeed, we evaluated how much higher for each female age-group separately in Gofman 1990 (Chapter 15, Part 6, tabulation of factors). Now we must use those supra-linearity factors to adjust the differences in Column F. This is done in Box 3.

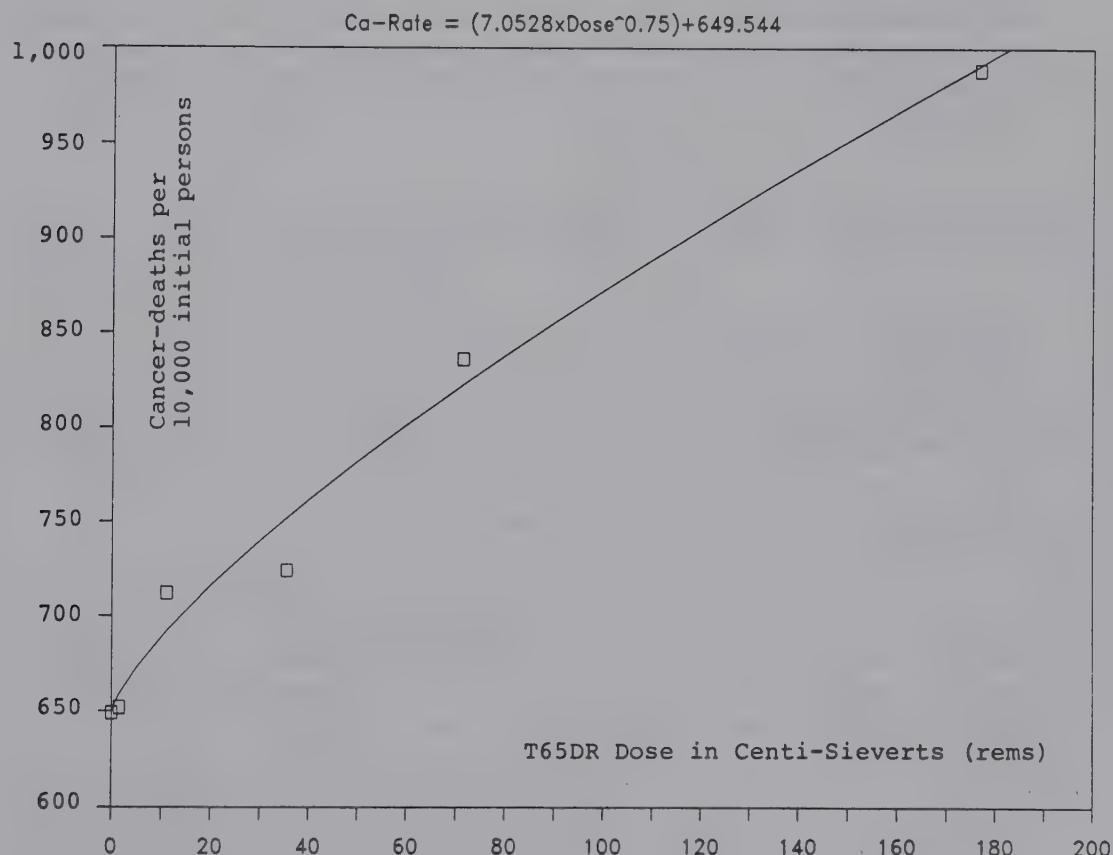


Figure 14-E, from Gofman 1990.

The supra-linearity adjustment explains why we refer to our conversion-factors as "low-dose conversion-factors" (Chapter 39, Part 1). The supra-linearity adjustment bases the difference between high-dose and low-dose groups on the STEEPER slope which characterizes dose-response in the LOW-DOSE region (approximately zero to five rads). Readers have seen (initially in Chapter 8) how we maintain the applicability of these low-dose conversion-factors to exposures which occurred at higher doses, too. We do it by adjusting DOSES downward, whenever appropriate, by factors derived from the supra-linear curve itself.

● - BOX 4, Division by Dose-Difference

So far, we have not considered the difference in dose which produced the difference in cancer-rates. In order to obtain the lifetime excess per rad, we use Box 4 to divide the values in Column H by the dose-differences, for which the data are provided by age-group in Gofman 1990, Tables 15-G through 15-K. This provides lifetime excess cancer-deaths per 10,000 females, from an average dose of one A-bomb rad.

● - BOX 5, Adjustment for Medical Rads

It is widely agreed that the carcinogenic potency of high-energy gamma-rays is less than the potency of lower-energy x-rays, as mentioned in Chapter 3, Part 1. The "ballpark" estimate is that medical x-rays are about two-fold more carcinogenic, per rad, than high-energy gamma-rays (references in Gofman 1990, Chapter 13, Part 4). Thus, if the Hiroshima-Nagasaki exposure had been to x-rays instead of A-bomb gamma-rays, the number of excess cancers per 10,000 women, from an average dose of one medical rad, would have been about twice as great. Box 5 converts Column L from A-bomb rads to medical rads.

Part 3. Explanation of BOX 6: Transition to Breast-Cancer Incidence, USA

Every step to reach the entries in Column N has an anchor in various real-world observations. And what we have, so far, are the numbers of radiation-induced cancer-deaths (all sites) per 10,000 females, from an average dose of one medical rad, for five different age-groups. What we want are the estimated numbers of radiation-induced BREAST-cancer cases per 10,000 females, per medical rad, for each age-group. So, we continue to look for anchors in real-world observations to make the next transitions.

● - Transition to Breast-Cancer - Column "O"

We know the relationship of the all-cancer death-rate to the breast-cancer death-rate in Japanese females for 1964-1965 (American Cancer Society 1970, pp.22-23). These rates for the entire country are barely influenced by the atomic bombings. The years 1964-1965 are chosen by us because they are approximately the midpoint of the 1950-1982 follow-up study from which we obtain our knowledge of RADIATION-induced rates. The all-cancer deaths per 100,000 Japanese females were 94.7 deaths per year. The breast-cancer deaths per 100,000 Japanese women were 3.8 deaths per year. The fraction of cancer-deaths which came from breast-cancer was 3.8 / 94.7, or 0.040127 --- four percent. If all cancers were equally radiation-inducible, then we could assume that approximately four percent of the radiation-induced excess cancer-deaths in Column N would be from breast-cancer. But it is not so simple.

We also have the observation that breast-cancer is MORE inducible by radiation than other cancers. This observation comes from the 1994 Thompson Study of cancer

incidence in the A-bomb survivors, 1958–1987. Although the Thompson Study is a DS86 analysis which is not anchored to the T65DR cohorts, it is unlikely that this shortcoming distorts the ratio of relevance here: The ratio of observed Excess Relative Risk (per sievert) for breast-cancer, over the observed Excess Relative Risk (per sievert) for cancers at all sites --- including breast-cancer. That ratio is 1.59 / 0.63, or 2.524 (from Thompson 1994, pages S26, S49, S61). Breast-cancer has by far the highest Excess Relative Risk of any cancer reported at page S26.

In the ratio above, the denominator of 0.63 for all sites includes breast-cancer. The all-site value would be lower than 0.63 if it were not elevated by breast-cancer. This means that the radiation-inducibility of breast-cancer must be somewhat more than 2.524-fold higher than the radiation-inducibility of NON-breast-cancers. However, the available data do not allow us to adjust the ratio for females alone.

(a) So, we use the 2.524-factor without adjustment, as a reasonable "first approximation" for the relative inducibility of breast-cancer versus non-breast-cancer by ionizing radiation.

(b) Also, we use the vital statistics from above to estimate the ratio of cancer mortality from breast-cancer to cancer mortality from non-breast-sites. The breast-rate (per 100,000 women per year) is 3.8 when all-site-rate is 94.7, so the non-breast-rate is (94.7 minus 3.8), or 90.9. So the ratio of breast-cancer mortality to non-breast-cancer mortality is (3.8 / 90.9), or 0.041804.

Then, for each radiation-induced entry in Column N, what is the estimated number from BREAST-cancer?

The first entry, 92.542 excess cancer-deaths = (the radiation-induced number from non-breast sites) + (the radiation-induced number from the breast).

Let n = the number of NON-breast cancer-deaths produced per 10,000 women from an average dose of one medical rad.

The number of BREAST-cancer deaths produced per 10,000 per rad will be (n) x (0.041804, which is the breast to non-breast ratio) x (2.524, which is the radiation-inducibility factor). The product = 0.1055n = breast-cancer cases. This term for breast-cancer cases will be used for all five age-groups. Hence, for the age-years 0–9, we treat the all-site value of 92.542 cases (from Column N) as follows:

92.542 radiation-induced cancers = non-breast cases + breast cases = (n) + (0.1055n) = 1.1055n. Therefore:

$$n = 83.71 = \text{non-breast cases. And:}$$

$$\text{Breast cases} = 0.1055n = 8.83 \text{ radiation-induced cases.}$$

Using the same procedure, we obtain values in Column "O" for all five age-groups.

● – Transition to Incidence – Column P

How shall we convert the estimates for radiation-induced breast-cancer mortality to INCIDENCE? Again, we have real-world observations from the study of A-bomb survivors. For the 1958–1987 period, the reported ratio of breast-cancer mortality to incidence is 0.27 (Mabuchi 1994, Table 4, page S10). This is, of course, an incidence to mortality ratio of (1 / 0.27), or 3.704. We do not think this ratio is likely to be distorted by a DS86 analysis, even though the Mabuchi analysis is not anchored to the constant

T65DR cohorts. (Our comments about T65DR and DS86 occur with Box 1, above.) Mabuchi et al also report that the mortality/incidence relationship for solid tumors is observed to be very nearly the same for exposed and non-exposed participants in the study (Mabuchi 1994, Table 5, p.S10).

We will use the assumption that if radiation-induced cancer-mortality (at any site) goes up by 5 cases (for example), the radiation-induced incidence at the same site goes up by (5 cases) times (the ratio of incidence over mortality). Thus, to convert Column "O" to breast-cancer incidence, we multiply its entries by 3.704 (displayed in Column P).

● – Transition to the USA – Column Q

For reasons which are not yet understood --- and which badly NEED to be understood --- the rates of specific cancers often vary enormously from country to country. In Japan, the so-called spontaneous rate of breast-cancer is very much lower than in the United States. We will evaluate the reported US/Japan rates for 1964–1965, approximately the midpoint of the A-Bomb Study follow-up. For the USA, breast-cancer deaths per 100,000 females per year were 21.55; for Japan, they were 3.80 (from American Cancer Society 1970, p.23). The vulnerability to breast-cancer for women in the United States was 5.67-fold greater than for women in Japan. In view of this difference, we are making the assumption, tentatively, that the number of radiation-induced cases per 10,000 females, from an average dose of one medical rad, is about 5.67-fold higher in the USA than among A-bomb survivors. So, 5.67 is entered into Column Q as the US/Japan ratio.

Up until this point, our conversion-factors are based on the number of excess cases per rad derived from the Japanese experience. Use of the ratio of 5.67 in Column Q acknowledges the real-world difference in "background" rates of breast-cancer in the USA versus Japan. Use of this factor with our method is equivalent to saying that the PERCENT increase in the background rate, per rad of radiation exposure --- the Excess Relative Risk --- is approximately the same from one population to another, regardless of DIFFERENCES in their background rates. If the percent increase per rad is the same in the USA and Japan, then one rad of breast-exposure induces more cases of breast-cancer in the USA than in Japan.

The concept that ionizing radiation induces DIFFERENT numbers of cancers per rad, in one country versus another, is consistent with the concepts that --- within a SINGLE country and a SINGLE study, such as the A-Bomb Study --- the lifetime number of cancers induced per rad DIFFERS by site (for example, breast versus bone) and DIFFERS by age at the time of exposure. In other words: The number of radiation-induced cases per rad is not fixed by the number of genetic lesions induced. The number of radiation-induced cancers per rad DIFFERS with the circumstances.

Circumstances can differ within a population, and also from one country to another. If ionizing radiation acts in concert with some other factors (internal or external), present in the USA but less present in Japan, the interaction could well cause a six-fold disparity in the vulnerability for breast-cancer per medical rad. We do not suggest that a rad in the USA induces six times as many genetic lesions as it causes in Japan. We (and others) suggest only that the impact of carcinogenic lesions is affected by co-factors --- and vice versa. Whatever combined factors cause the breast-cancer mortality rate in the mid-1960s to be 5.67 times higher in the USA than in Japan, these

combined factors also cause radiation-induced genetic lesions from medical irradiation to have a greater effect in the USA than in Japan.

At this time, we think the 5.67 ratio of background breast-cancer mortality-rates (USA / Japan, in the mid-1960s) is the most reasonable approximation to use in our conversion-factors. As additional evidence develops, it may point to other ways to handle country-to-country "transport" of observations. Meanwhile, we keep an open mind toward a variety of old and new hypotheses about the actual process of radiation carcinogenesis, including interaction between radiation and other factors.

A Closer Look at Recent Cancer-Rates, USA vs. Japan

It is interesting to compare cancer rates between the USA and Japan. By no means is the far higher U.S. rate for breast-cancer a general phenomenon, as shown by the female and male tabulations below. For stomach cancer, the Japanese rate is far higher than that for the United States. And overall, the Japan cancer rates are not very different from those in the United States (see "All" in the tabulations).

All data are death rates, 1988-1991 per 100,000 population, age adjusted to the WHO world standard population. (From ACS 1994, at page 28.)

Cancer	Japan	U.S.	Ratio	Cancer	Japan	U.S.	Ratio
Site	Females	Females	U.S./Japan	Site	Males	Males	U.S./Japan
Breast	6.3	22.4	3.6	Prostate	3.8	16.8	4.4
Lung	8.0	24.7	3.1	Lung	30.1	57.1	1.9
Oral	0.6	1.3	2.2	Oral	2.3	3.7	1.6
All	76.7	110.6	1.4	Leukemia	4.3	6.3	1.5
Uterine				Colon &			
Cervix	1.8	2.6	1.4	Rectum	15.1	16.7	1.1
Leukemia	2.8	3.8	1.4	All	150.0	164.0	1.1
Colon &				Stomach	34.9	5.2	0.1
Rectum	9.7	11.4	1.2				
Uterine							
Other	2.4	2.6	1.1				
Stomach	15.5	2.3	0.1				

Comparison of the Extremes

Cancer Sites Compared	Females	Cancer Sites Compared	Males
Breast USA/Japan	3.56	Prostate USA/Japan	4.42
Stomach USA/Japan	0.15	Stomach USA/Japan	0.15
Ratio: A Factor of	23.73	Ratio: A Factor of	29.47
Quite A Range of Relative Rates		Quite A Range of Relative Rates	

We do not think any single carcinogen, acting alone, explains these vastly different relative rates.

A Suggestion That Will Not Compute

In the effort to deny the idea of a much greater U.S. vulnerability to breast-cancer induction per medical rad (Column Q), it has been suggested that the observed relative rate in the mid-1960s of 5.67 is explained by a possible difference in x-ray dose. If there was a dose-difference (with higher annual average dose in the USA), then it would HELP explain the relative rate in the mid-1960s --- and it would have an additional implication worth exploring. We will explore the suggestion, below, that a dose-difference FULLY explains the 5.67 relative rate for breast-cancer mortality.

The proposal is thus entertained, that female persons in the United States had been getting much more x-radiation than female persons in Japan and that this accounts for the relative rate of 5.67 in the mid-1960s. The relative rate of 5.67 means, of course, an excess relative rate of $(5.67 - 1.00)$, or 4.67. If we were to blame the USA-Japan difference in rates totally upon the difference in radiation dosage up to that time, we would be saying that about 4.67 out of 5.67 breast-cancer deaths in the United States at that time must have been x-radiation-induced --- that is 82 % of all breast-cancers were radiation-induced. So, the suggestion leads to the absurdity of trying to disprove the hypothesis of radiation-causation with a proposition which would confirm it.

A Suggestion of an Opposite Nature: Denial of Co-Action

We must consider another possible explanation for the 5.67 relative rate of breast-cancer mortality. We can suppose that non-radiation causes of breast-cancer exist in the USA which do not exist in Japan, and that they are NOT co-active with each other or with radiation. They cause breast-cancer without involving radiation-induced lesions at all. When radiation is added to such a "scenario," we would suppose that the effect per rad would be the SAME in the USA and Japan.

For simplification, we can assume that the amount of radiation exposure was the same in the USA and Japan before the mid-1960s. So, the relative rate of RADIATION-induced breast-cancer mortality would be 1.0. Then the EXCESS relative rate, from all other causes combined, would be 4.67 in the mid-1960s. This would mean that $(4.67 / 5.67)$, or 82.4 % of all breast-cancer mortality in the USA was due to non-radiation causes (internal and external) --- each acting alone, and present in the USA but less present in Japan. This is a possibility, neither provable nor disprovable by current knowledge.

We think (but can not prove) that it would be a mistake to deny the impact of co-action between cancer-causing agents. We are very comfortable with the concept that a rad of medical radiation has a greater impact in the USA than in Japan, due to interaction with other factors.

● - "Lift-Off" Reduction-Factor - Column R

For the two youngest age-groups in the A-Bomb Study, the lifespan follow-up is far from complete. In 1995, the 0-9 year-olds reach an average age of about 54 years; the 10-19 year-olds reach about 64.5 years of age, on the average (calculated from Gofman 1990, Table 26-E). We and others necessarily have to make assumptions about what the full lifetime follow-up will show, as already noted with respect to Box 2.

We KNOW that the observed number of cancers in the low-dose column (Box 1, Column C) will increase after 1982, as the two youngest age-groups advance in age. We

used the observations of their older colleagues to estimate what would happen to the number of cases in the youngest low-dose groups. And then we applied the SAME factor of increase (Box 2, Column E) to the radiation-induced difference between high-dose and low-dose groups (Column D). This was equivalent to assuming that the total number of cases in the high-dose group (Box 1, Column B) and the low-dose group (Box 1, Column C) would increase by the same factor. For example: $(150.94 \times 19.11207) - (55.41 \times 19.11207) = (2884.7758) - (1059) = 1825.776$, which is the first value shown in Box 2, Column F, for "Lifetime excess."

However, we have shown in Chapter 3, Part 4, why this treatment may overestimate the lifetime difference for the youngest age-group, and possibly for the 10-19 year-olds too.

Chapter 3 explored the "lift-off" phenomenon! By this, we mean the temporary inflation of a disparity between two curves, if they "lift off" at different years or at different slopes from a baseline rate which was NEAR ZERO. The inflated difference is temporary, and becomes diluted by subsequent observations at older ages.

Because there are more "subsequent observations" to come in the 0-9 age-group than in the 10-19 age-group, we adjust the lifetime difference in Column N more severely downward for the 0-9 age-group than for the 10-19 age-group. In Column R, we are going to slash the lifetime excess in HALF for the 0-9 year-olds, with a reduction-factor of 0.5; for the 10-19 year-olds, we use a reduction-factor of 0.75; we make no adjustment for the 20-34 year-olds. Only additional follow-up data will tell whether these "lift-off" factors are too high or too low. Meanwhile, in view of the "lift-off" phenomenon, we feel that a correction of some sort is indicated.

● – Conversion Factors – Column S

In Box 6, Column S provides the conversion-factors used in our Master Table. Each entry is the estimated number of radiation-induced excess breast-cancer cases (lifetime incidence) per 10,000 females (USA) from an average breast-dose of one medical rad. The entries are the product of Columns "O" x P x Q x R.

#

• - *"Doesn't Everything Cause Cancer If the Dose Is High Enough?"*

This question is asked at page 8 of the National Cancer Institute's 1990 booklet, and answered as follows:

"No. High doses of many chemicals are toxic, but they will not cause tumors. Other forms of toxicity, such as loss of hair or weight, various organ malfunctions, or even death, should not be confused with carcinogenesis." And:

"In one study, 120 pesticides and industrial chemicals were tested at the highest doses the mice could tolerate and survive. The mice were exposed for two years. These chemicals were not randomly selected, but were chosen because they were suspected of carcinogenicity. However, only 11 of these chemicals caused cancer in the test animals."

• - *"What Happens When People Are Exposed to Several Carcinogens at the Same Time?"*

This question is asked at page 10 of the National Cancer Institute's 1990 booklet, and answered as follows:

"The resulting cancer rate may be higher than would be predicted by adding the risks from each carcinogen alone. Cigarette smoking and asbestos exposure, for example, each cause cancer. But asbestos workers who smoke are subject to a cancer risk that is far higher than would be expected by adding the risk from smoking to the risk from asbestos." And:

"Animal studies have shown similar jumps in cancer rates from multiple exposures. This effect does not occur in animals with all carcinogens, and sometimes two carcinogens will somehow interact to give reduced rates of cancer. Although it is conceivable that this type of reduction could occur with human exposures, it is not something people can count on."

Source: National Cancer Institute (USA), "Everything Doesn't Cause Cancer," 12-page booklet, March 1990 (NIH Publication 90-2039).

CHAPTER 41

Some of the Uncertainties and Certainties of Our Finding

Part 1. The Estimate of 75 %

The number of radiation-induced breast-cancer cases per year in the USA is estimated as 114,336 cases in the Master Table (sum of Column-W entries), not rounded-off. This number is (114,336 / 182,000), or 63 percent of the annual total incidence, if yearly production = yearly delivery.

In showing every step of the estimate's derivation, we have pointed out several unavoidable uncertainties. The uncertainties in the conversion-factors (Master Table, Column V) may operate in either direction --- either to make 63 % an underestimate or an overestimate. On the other hand, Chapter 38 summarizes the many reasons, shown in both Sections 2 and 3 of this study, for saying that the average annual doses for the 1920-1960 period are seriously underestimated in the Master Table. Among the reasons: Complete OMISSION of some very important sources of breast-irradiation from the Master Table. These omissions operate with certainty in the direction of making 63% an underestimate.

In offering the most reasonable estimate that we can, we are not entitled just to ignore a certainty. So we must adjust 63 % upward. We choose to make only a very modest increment, to 75 %. This is the midpoint of the range from 50 % to 100 % --- a credible range in view of the evidence currently at hand.

The "Law of Equality" (Chapters 4 and 5) does not tell us how many decades are required for build-up to equilibrium --- the situation when annual production of radiation-induced breast-cancer cases equals annual delivery in a population of all ages, due to a steady rate of person-rads per year. No one can know, until the lifetime observation of infants and children is complete in the A-Bomb Study.

But we can make a "first cut" estimate without knowing the exact number of years because we took the long view --- 1920 to about the year 2000 --- and because we have probably have a fairly constant annual rate of person-rads before and after 1960 (see Chapter 5, Part 1). This is why we are confident that equilibrium (with respect to radiation) must be approaching soon.

What If the Dose Was Really Twice What Is Evaluated in the Master Table?

We believe that our Master Table seriously underestimates the annual average breast-dose in the 1920-1960 period. We believe that the true dose was probably at least twice the estimate in the Master Table from all sources combined, for the reasons discussed in Chapter 38 --- especially the omitted doses from fluoroscopy and from treatment of both skin and inflammatory conditions.

Despite its probably large underestimate, the Master Table indicates that past radiation is responsible for about 63 % of the recent, current, and future breast-cancer problem in the USA. If the annual average breast-dose, in person-rads, were really at least twice what we estimated, are we saying something absurd: That MORE than 100 % of the breast-cancer problem is radiation-induced?

Of course not. 100 % of a problem is "the max."

If the annual average dose was at least twice what was estimated in the Master Table, would it mean that the estimated conversion-factors need reduction? It might mean that. And it might not. It might mean that the number of new breast-cancer cases "delivered" per year is going to rise ABOVE 182,000, and that additional cases are going to be radiation-induced. Even the inherited "destiny" cases may require help from radiation and other non-inherited factors, as discussed in Chapter 1, Part 5.

This comment on the underestimation of dose, however, does not mean that we are "married" to any particular set of conversion-factors. No matter who proposes conversion-factors, such factors necessarily combine real-world evidence with some assumptions. If future evidence invalidates some of those assumptions, objective analysts will discard the assumptions without hesitation.

This study uses a current set of reasonable conversion-factors --- and they are appropriate for the initial inquiry. Still, we would like to point out (A) that these conversion-factors take no account of individuals who develop MORE than one radiation-induced breast-cancer, and (B) that the conversion-factors are lifetime factors which take no account of WHEN breast cancer occurs --- even though it makes a big difference to breast-cancer patients whether it occurs at age 30 or at age 80. We regard this study as the beginning, not the end, of such inquiries.

Part 2. Some Intriguing Questions for Future Resolution

An underlying assumption in the Master Table is that conversion-factors remain valid in a population, decade after decade. That is a reasonable assumption if all other carcinogenic forces remain constant. With respect to breast-cancer, many of these other forces are not yet identified with certainty.

No matter how high is the percentage for breast-cancer's radiation etiology, it is important to learn how other agents and events (e.g., childbirth) ALSO participate in breast-cancer development, as emphasized in Chapter 1, Part 5. For instance, interaction of other agents and events with ionizing radiation may make matters worse, by permitting radiation-induced breast-cancers to appear earlier than they otherwise would. Such information would be of great interest.

The world is a long way from knowing how to quantify the net interaction of ionizing radiation with other carcinogens. Indeed, we do not even know yet whether some of the non-radiation risk-factors for breast-cancer operate by inducing permanent genetic lesions, or by inappropriately turning critical genes off-or-on (without inflicting any permanent molecular injury), or by some other mechanism. We do not know whether the non-radiation risk-factors require the presence of permanent radiation-induced lesions in order to have their effect --- or vice versa, with radiation-induced lesions requiring the presence of non-radiation factors --- or whether all these factors are independent of each other. These are important and intriguing questions.

Disappearance of the Excess Relative Risk

Even if the factors act independently at the cellular level, there is the potential for severe confounding of studies by chronic exposure to a SINGLE agent, like ionizing radiation. For example, suppose (for the sake of simplification) that ionizing radiation is the ONLY cause of breast-cancer. And suppose that we do a study in which we carefully

observe the A-bomb survivors (or female nuclear workers, etc.) to compute the percent increase in the apparent "spontaneous rate" of breast-cancer per rad over full lifespans.

If we fail to take into account that the apparent "spontaneous" rate is rising equally both in the comparison-groups AND in the matched control-groups, due to equal amounts of MEDICAL irradiation, we are going to underestimate the Excess Relative Risk per rad (Chapter 3, Part 3). In fact, one implication of the "Law of Equality" is that exposure of a stable population to a constant level of ionizing radiation would --- at equilibrium --- cause no INCREASE per rad in the apparent "spontaneous" rate, even if radiation were causing 100 % of the problem.

Another Potential Pitfall in Studies of Cancer-Causation

It is well worth noting that, among risk-factors for breast-cancer, not all have been studied with respect to the full lifespan of women. We do not doubt the validity of observations which correlate the presence of various non-radiation risk-factors with elevated rates of breast-cancer, and conversely, correlate their absence with reduced rates of breast-cancer. But we regard the "lift-off" phenomenon described in Chapter 3 (Part 4) as a potential pitfall in non-lifespan studies.

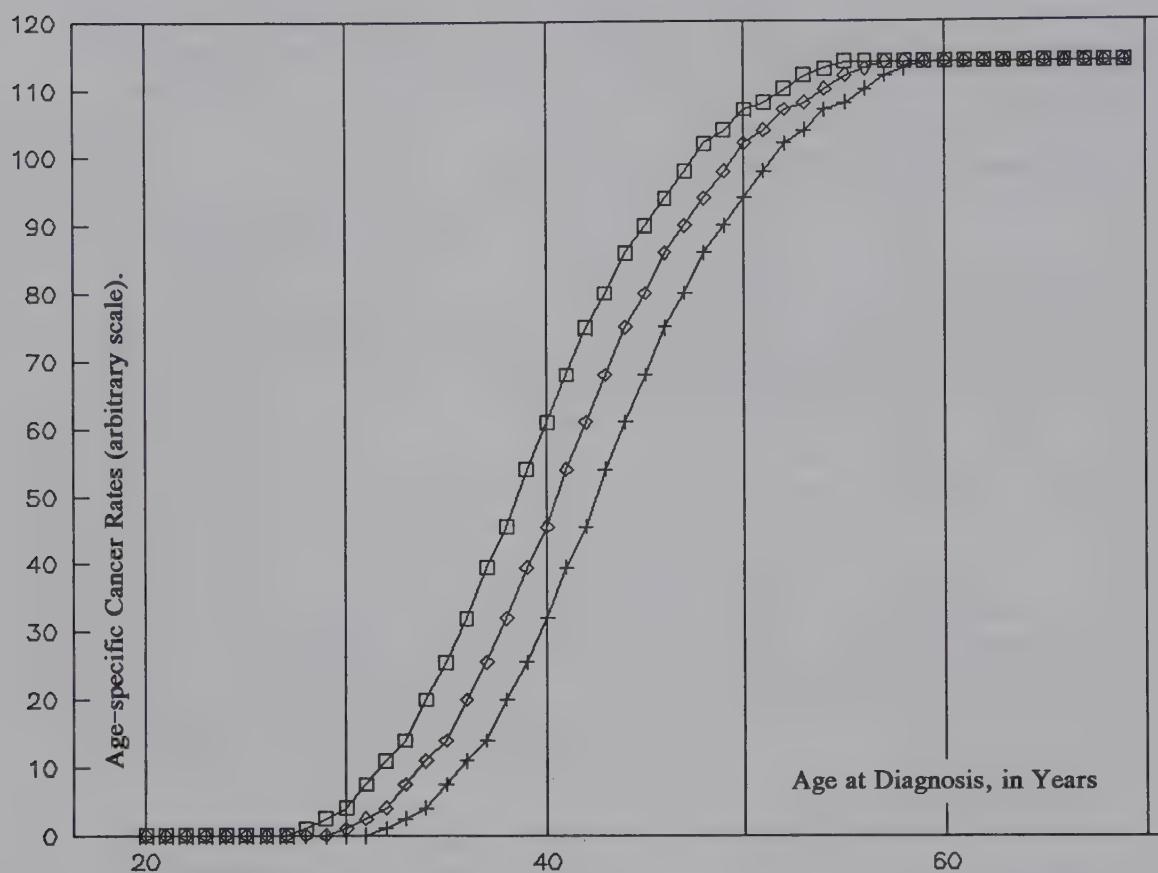
The figure on the next page depicts three curves under which the lifetime area is NOT very different. Suppose the middle curve depicts the age-specific breast-cancer rate, for which we use an arbitrary scale. Suppose (for simplification) that the middle curve is due exclusively to ionizing radiation.

Next, let us suppose that presence of some additional factor shifts the middle curve just SLIGHTLY to the left (to earlier ages, so we can call it the "lead" curve). Investigators will observe some BIG differences in rates as the two curves "lift-off" at slightly different ages from the baseline of zero. It is easy to observe 10-fold, 4-fold, and 100 % increases over several years of study. Nonetheless, the factor causing the big increases does not have much more area under its lifetime "lead" curve than the area under the middle curve, due to radiation alone. In this illustration, a failure to have lifetime data on the non-radiation factor could result in erroneous assumptions about its real, lifetime impact.

Lastly, let us suppose that presence of some additional factor shifts the middle curve just SLIGHTLY to the right (to older ages, so we can call it the "lag" curve). Investigators will observe some BIG differences in rates as the two curves "lift-off" at slightly different ages from the baseline of zero. Nonetheless, the factor causing the big "protection" does not have much less area under its lifetime "lag" curve than the area under the middle curve, due to radiation alone. In this illustration, a failure to have lifetime data on the non-radiation factor could lead to erroneous assumptions about its real, lifetime impact.

For ionizing radiation, the Atomic Bomb Study evaluates the LIFETIME carcinogenic effect of exposure upon its participants, with completion approaching even for the youngest ages at exposure. We can not overemphasize the unique value of the A-Bomb Study, and the importance of maintaining a single continuous set of cohorts until the study is complete.

Cancer Rate: Generic "Lead-Lag" Curves.



Importance of Exact Age-Matching in Epidemiologic Cancer-Studies

The "Lead-Lag" Curves illustrate another potential pitfall in epidemiologic cancer-studies. Suppose we are doing a prospective study to learn if an X-type-diet (or pharmaceutical, or whatever) has any effect on the rate of breast-cancer. And suppose that the experimental group on an X-type-diet and the control group are quite well matched --- except that the Diet-X group is older by just a few years. All three curves in the figure reflect the fact that, after "lift-off," a few additional YEARS mean an appreciable increase in cancer-rate, when the curves are steep. A difference of two years in age can mean a difference in rates which is NOT negligible.

So the figure illustrates why epidemiologic studies simply can not ignore small differences in age. In the Diet-X Study, if we observe a higher rate of breast-cancer in the Diet-X women, we had better pay close attention to the small difference in AGE. It might explain everything.

Part 3. The Key Certainties about Our Finding

In this chapter and in earlier ones, we have pointed to various approximations and uncertainties in our study. Now, it is time to summarize some of the underlying certainties.

• – (a) Radiation is a proven cause of breast-cancer.

We stated at the outset (Chapter 1) that causation of extra breast-cancer by ionizing radiation is proven --- it is not a speculation. And in this book's Reference list, we flag (with #) some of the papers which present the evidence of causation and quantify the risk from various studies. With respect to irradiated groups, "risk" does not mean "maybe" --- it means the observed RATE of radiation-induced breast-cancer.

• – (b) Latency varies by decades for people irradiated at the same age.

This is another observation which is not in doubt (Chapter 2). In order to evaluate the contribution of radiation to recent, current, and future breast-cancer incidence, we must include radiation exposures which occurred decades earlier.

• – (c) Breast-irradiation received by females during infancy and childhood increases their rate of breast-cancer in adulthood.

The evidence for this is clear, now (Chapter 3). The increase shows up first in extra cases of EARLY-onset breast-cancer, and the increased rate continues for at LEAST 40 years after the exposure.

• – (d) The radiation response per rad is the most severe for irradiation at the youngest ages.

Comparisons between different ages at irradiation are made meaningful on the basis of the LIFETIME response. The comparisons necessarily incorporate approximations for the younger age-groups, because their lifetime follow-up is not yet complete in the A-Bomb Study. Over the past twenty years, comparisons have become increasingly reliable, as observations of the younger groups gradually replace approximations.

Is it reasonable to regard the elevated sensitivity of the young as a certainty?

In the Tokunaga Study --- specifically of BREAST-cancer incidence in the A-Bomb Study for 1950–1985 --- the analysts have presented Excess Relative Risks per sievert for six age-groups (age at the time of the bombings). At 40 years post-bombing, they report that the Excess Relative Risk is 10-fold higher for age-years 0–9 than for age-years 50+ (Tokunaga 1994, Table 6, p.215).

What is the estimated LIFETIME ratio in our independent conversion-factors? It is $(92.74 / 24.56)$, or only 3.78. The ratio would have been 7.55-fold if we had not slashed the conversion-factor in HALF for the 0–9 year-olds (see Chapter 40, Box 6, Column R). We made this downward adjustment because we know that the interim observations are affected by the "lift-off" factor. Therefore, the interim observations must decline somewhat by the end of the LIFETIME follow-up.

With the difference in age-sensitivity still as large as 10-fold or 7.5-fold, it is extremely unlikely that the sensitivity will completely disappear. We can classify the special sensitivity of the young as a certainty, with respect to radiation-induced breast-cancer.

• – (e) Breast-cancer is more easily induced by ionizing radiation than cancer at other sites.

This observation is discussed in Chapter 40, in the text for Box 6. The observation comes from the 1994 Thompson Study of cancer incidence (all sites) in the A-Bomb Study, 1958–1987. Breast-cancer shows by far the highest Excess Relative Risk per sievert in the study. By comparison with all cancer-sites combined, breast-cancer is 2.524-fold more inducible per unit of radiation.

• – (f) There is no safe dose (risk-free dose) of ionizing radiation.

This observation was mentioned in Chapter 5, Part 5, and will be further discussed in Chapter 42.

• – We make a recommendation.

We recommend that readers keep this short list of certainties in their minds. The list will keep some responses to this book in perspective.

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CHAPTER 42

Prevention of Breast-Cancer, Starting NOW

Part 1. The Key Action

The news from this book is good news. Knowing that the major cause of a serious disease is preventable represents an enormous step toward controlling the number of cases of the disease.

There is simply no doubt that past irradiation of breasts accounts for a large share of recent, current, and future breast-cancer in the USA (and almost certainly, in Europe). Some people will prefer to debate the exact size of the share (when exactitude is impossible), rather than to help eliminate unnecessary amounts of CURRENT AND FUTURE breast-irradiation.

The exact share for which ionizing radiation is responsible will be irrelevant to people who care about preventing this disease. Can people really argue that preventive action is worthwhile if radiation's share is 75%, but not worthwhile if the share is 50%? Indeed, could people argue against action if radiation's share were 25%?

The list of certainties at the end of Chapter 41 means that every action which reduces unnecessary breast-irradiation is GUARANTEED to prevent a share of future breast-cancers which would otherwise occur. We doubt very much that the same statement can be made today about any OTHER focus of action.

Part 2. Target: Unnecessarily High Frequencies and Doses

The target of eliminating unnecessarily high frequencies and doses in breast-irradiation is very different from eliminating or refusing the medical procedures themselves. Dr. Joel Gray (of the Mayo Clinic), who is certainly no "enemy" of radiology and nuclear medicine, acknowledged the difference in 1984 when he described offices which won't tell patients the expected radiation dose:

"My feeling is that if they won't tell you, they don't know, and if they don't know, they could be among the facilities delivering a hundred times the necessary dose" (Gray 1984, p.96 --- also cited in Chapter 28).

Do such horrible practices really occur in the post-1960 period? Indeed they do. The U.S. Bureau of Radiological Health did a survey, published in 1977, of x-ray doses for extremely common diagnostic procedures at hundreds of medical institutions. The variation in doses is confirmed by the data in the box on the next page.

We are not currently knowledgeable about the situation in radionuclide usage.

The Fallacy Which Promotes Careless Over-Dosing

What accounts for the use at some places of radiation doses which are 5, 10, 20, or even 100 times higher than necessary? It is not difficult to measure entrance doses. And it is not difficult to eliminate unnecessarily high doses (see below). We believe the principal cause of unnecessarily high doses is the mistaken belief that there is a "safe" dose. The mistaken claim that low doses are harmless is usually followed by the mistaken

● - VARIATION IN DOSE FROM ONE FACILITY TO ANOTHER.
(1972-1974 DATA)

Number of Institutions	Examination	Entrance Dose in Milli-Roentgens (mR)			
		Mean Value	Standard Deviation	Highest Dose	Lowest Dose *
1,433	Chest PA	23	29	2,300	3
126	Skull LAT	270	343	2,700	13
491	K.U.B. or Abdomen AP	562	341	2,900	22
95	Retrograde Pyelogram AP	594	282	1,400	93
52	Thoracic Spine AP	690	585	3,200	64
210	Cervical Spine AP	228	299	2,600	7
634	Lumbo-Sacral Spine AP	792	545	5,500	11
31	Full-Spine	291	150	700	50
70	Feet	210	306	2,000	29
1,408	Dental Bitewing	650	727	6,800	68
759	Dental Periapical	644	696	7,500	75

Source: J.F. Wochos + J.R. Cameron "Patient Exposure from Diagnostic X-Rays:
An Analysis of 1972-1974 NEXT DATA" (April 1977).

* Entries in this column may not always produce useful images.

claim that "repair" takes care of injury from low doses. Reporters in the major media tell us that, even today, they continue to hear these twin claims from some very influential people.

Repair of DNA damage, including single-strand breaks, most certainly does occur. Every day, more than 10,000 DNA-repairs are made in every cell. The cell copes quite well with DNA damage induced by the free radicals which, due to normal cellular activities, are chronically present. However, ionizing radiation does more to cells than producing some routine free radicals.

The particle-tracks of ionizing radiation can do what no toxic chemical agent can do: Each track can deposit abnormally LARGE amounts of energy in very concentrated areas near or within the genetic molecules. This is not speculation --- this is fact. And because of this special property, each track can inflict complex (non-routine) lesions which the cell is unable to repair, no matter how much time is available. Such unrepaired and misrepaired genetic lesions are not speculative --- they include well-observed radiation-induced double-strand breaks, "locally multiply damaged sites," and enduring chromosome lesions of a great variety.

Observations of enduring, radiation-induced chromosome lesions are not limited to human cells irradiated in vitro. Such observations include human cells irradiated in vivo --- for instance, in living A-bomb survivors (Kodama and colleagues 1993) and in living nuclear dockyard workers exposed very slowly to less than 5 extra rems per year (Evans 1979). Moreover, persistence of a convincing chromosome dose-response for 40 years in the A-bomb survivors (Kodama 1993) shows that not all cells, genetically damaged by radiation, are removed by failure to reproduce. Definitely not. The combined teams of RERF scientists and Lawrence Livermore National Lab scientists were quite elated to be able to demonstrate the dose-response in A-bomb survivors 40 years after the bombing.

We and others (such as John Ward and Keith Baverstock) are not saying that all radiation-induced lesions are unrepairable and misrepaired. Far from it. But we and Ward and Baverstock are saying that the FRACTION which is unrepairable and misrepaired accounts for the OBSERVED effects of exposure to ionizing radiation. And no matter how low the radiation dose, or how slowly it is delivered, a fraction of the radiation-induced lesions will be unrepairable or misrepaired.

This is a powerful basis for saying that "repair" can not and does not provide any safe dose (Gofman 1990, p.18-2; Ward 1991, p.385-386; Baverstock 1991, p.384). Moreover, we have shown how mainstream human evidence confirms the logic and provides PROOF that there is no safe dose or dose-rate with respect to radiation-induced cancer (Gofman 1990, Chapters 18-21, 32, 33).

This book reports many of the mistaken assurances, given in the past to medical patients and professionals alike, that HIGH doses of radiation were harmless. Now, everyone agrees those assurances were mistaken. Yet today, the same sort of ignorance and wishful thinking produce the same mistaken assurances --- about LOW doses. Reality: There is no safe dose or dose-rate. All doses matter --- roughly in proportion to their magnitude.

Real-World Cooperation between Radiologists and Physicists

Spectacular dose-reduction in medical irradiation has been achieved --- whenever people stop buying the safe-dose fallacy and make up their minds to get medical procedures done with the LEAST amount of radiation. This book has already described some examples:

- - More than a 50-fold reduction in breast-dose, demonstrated as achievable in management of curvature of the spine (Chapter 21, Part 2).
- - More than a 30-fold reduction in breast-dose from mammography, when 1970 doses are compared with current doses (Chapter 28, Part 2).
- - Substantial reduction in doses from fluoroscopy, with no loss of quality in diagnostic images (Chapter 32, Part 4).

The Canadian team of radiation physicists, discussed in Chapter 32 with regard to fluoroscopy, also worked with radiologists in Ontario to reduce unnecessarily high doses from making x-ray FILMS. The remarkable results are reported in Taylor 1979, Johns and Cunningham 1983, and Gofman/O'Connor 1985. The box on the next page shows

some of the results. Johns and Cunningham state the following, in the fourth edition of their classic book, "The Physics of Radiology" (1983, p.557):

"We have evidence (Taylor, 1979) that the dose from diagnostic radiology can be reduced by a factor of at least 3 with a little work and by a factor of 10 or more if all conditions are optimized."

● - REAL-WORLD DOSE-REDUCTIONS ACHIEVED IN BUSY X-RAY FACILITIES.

Examination	Minimum Exposure Used (mR)	Average Dose Used (mR) in 1979
Skull Lateral	100	265
Cervical Spine AP	90	140
Thoracic Spine AP	260	460
Chest PA	8	25
Lumbar Spine AP	180	620
Lumbar Spine Lateral	500	2,445
Abdomen AP (K.U.B.)	190	530
Intravenous Pyelogram	150	600

Source: Table 16-6 in Johns and Cunningham (1983, p. 650).

Kenneth Taylor and colleagues achieved their results in busy x-ray facilities with whatever equipment the facility already had. No major purchases of new equipment were involved. For example, some facilities were using an entrance-dose three times higher than necessary because of poor PROCESSING of the exposed films. In such cases, Taylor and colleagues proved that a three-fold reduction in radiation dose was achievable just by paying attention to the correct chemistry and conditions to PROCESS the exposed films. Taylor and colleagues also showed that different combinations of screen and film led to a variation in the required exposure by a factor of 6. Attention to the proper choices was another route to big reductions in dose. Most importantly, the radiologists did not perceive any decrease in the quality of the diagnostic information at lower doses.

It is a credit to the Ontario radiologists that they invited Taylor's teams into their facilities. The result is a beautiful demonstration of what co-operating physicians and physicists CAN achieve, when motivated.

How Much Attention to Dose Is Given by NON-Radiologic Offices?

The evidence in the boxes indicates that unnecessarily high radiation doses occur even in some offices SPECIALIZING in radiology. If some of THEM are using doses much higher than needed, then what is happening in the offices of NON-radiologists? We have shown that there is widespread use --- today --- of both x-ray and fluoroscopy machines outside of radiology offices:

- - In chiropractic (Chapter 22).
- - In surgery, especially cardiac procedures. Because of high radiation doses, the FDA's Center for Devices and Radiological Health issued a Public Health Advisory in September 1994 (Chapter 29).
- - In offices of cardiology, urology, neurology, and other specialties (Chapter 32, Part 5).
- - In intensive care units (Chapter 37, Part 2). And in hospital rooms, with use of bedside fluoroscopes.
- - In offices of unspecified type. On December 9, 1990, the Associated Press reported: "In recent years, many doctors have purchased x-ray and ultrasound machines so that they can take diagnostic images in their offices" (Assoc. Press, Dec. 9, 1990). The report was based on a study by Dr. Bruce J. Hillman at the University of Arizona.

The Issue of Unnecessary Frequency

Wherever the fallacy of "safe-dose" exists, there will be a tendency to take x-rays more often than needed. And the tendency is certainly fortified by legal wrangles over insurance claims and disability claims and malpractice claims.

Part 3. Two Approaches NOT Recommended by Us

The thesis of this book is that breast-irradiation is a major, proven, preventable cause of breast-cancer. The evidence is overwhelming, and can not be denied even by those who will challenge the size of the share.

Therefore, we recommend AGAINST excessive deference to those who say that action on the thesis ought to be postponed --- while everyone waits for some "blue ribbon commission" to bless such action, or waits for "more studies."

The studies which establish the role of ionizing radiation in breast-cancer causation have been DONE. Many of them are flagged by " #" in our Reference section. If the response to paying for those studies (almost entirely with hard-earned tax-dollars) is to throw away the results and start all over again, preventable breast-cancers will surely blossom forth for many more decades. Why did anyone do the studies in the first place, if we plan NOT to use the information gleaned?

Many citizens will say, "Elimination of unnecessary breast-irradiation is a government function --- not something WE should attempt." To such citizens, we say "Think again." There are segments of the U.S. government which continue to press hard for lenient limits on the radiation doses which may be imposed on the public by nuclear pollution. They are the main sponsors of the safe-dose fallacy. And they are far more

powerful than some individuals in the FDA's Center for Devices and Radiological Health, who seem really to have protection of public health at heart.

Counting on government to do the right thing is very, very risky. Pressing the government in the right direction consumes a lot of effort --- effort which is likely to be far more effective if it is directed at the media, at the medical schools, and at the physicians who "order" breast-irradiating procedures when they do not even know the dose.

Part 4. Several "Do-able" Steps, Starting Now

Whenever the topics of radiation and breast-cancer are mentioned in one breath, we find that most people expect to hear about mammography. But mammography is certainly not the focus of THIS book. Mammography does nothing at all to PREVENT breast-cancer.

Prevention is our focus. The finding of our study points directly to a key preventive action: Eliminating unnecessarily high frequencies and doses in breast-irradiation. How can readers achieve that goal?

● - Suggestion One: Informing the Media

Some medical journals and most of the mass media have been perpetrating a major fallacy about the breast-cancer problem. Most commonly, they list "risk-factors" for breast-cancer without even mentioning ionizing radiation. Or sometimes they assert that there is no proven cause of breast-cancer. For example, an article on breast-cancer in Parade Magazine (September 11, 1994, at page 27) said:

"Can we find the cause? One theory on the cause of breast cancer holds that environmental toxins --- both man-made and natural poisons --- are, in part, to blame. However, the proof eludes scientists. A high fat diet has been pointed to as another possible cause. Some believe that pesticides or chemicals that may be stored in the fatty tissue of meat or fish or that are otherwise ingested may be associated with increased risk. Again, no real proof."

How does it happen that a PROVEN cause --- ionizing radiation --- is not even mentioned?

People who are organizing to prevent breast-cancer surely recognize that misinformation can kill, and that ignorant commentary on this major health problem must be challenged. For starters, we suggest that breast-cancer activists (including any who are within the medical system) adopt the goal of PREVENTING more of such ignorant commentary, by systematically acquainting editors at all the major media with the list of certainties at the end of Chapter 41.

● - Suggestion Two: Validating the Expectation of Information

Many people, men and women, have told us: "I don't feel I can challenge the doctor who pooh-poohs the hazards of radiation. Most of them tell me that x-ray exams are comparable to taking a plane trip or a sun-bath. Some physicians even seem angry about my raising the question. I'm afraid to ask whether they are sending me and my children to an x-ray place which measures the doses, or if they know the doses when they

do the x-rays themselves. They get defensive. Very defensive. And so I don't know how to do the right thing for myself and my family."

The frequency of such comments tells us two things:

(a) There are some physicians who were never exposed to real education on ionizing radiation. In terms of radiation risk, airplane comparisons are valid only for a few types of x-ray exams, and sun-bath comparisons are wrong because ultra-violet radiation does not reach internal organs. Diagnostic x-rays do.

(b) There are some physicians who were never trained to recognize their obligation to serve as "ombudsperson" for patients in the medical system. We adapt the term "ombudsperson" to mean physicians who inform themselves about perils for their patients ELSEWHERE in the medical system, before they send their patients off to learn about such perils on their own --- the hard way.

In general, patients do not refer THEMSELVES to laboratories or to radiologic facilities. Who makes the decision that Radiology Office XYZ really is the one to which patients should be referred? Who should take the responsibility for ensuring that the patients do NOT receive 2-fold, or even 5-to-50-fold, more than the necessary radiation dose (see Part 2, above)?

Since family physicians, internists, surgeons, pediatricians, gynecologists, orthopedists, sports and occupational medical specialists, and others, are the ones who "order" the patients to have radiation exposures (including exposures from nuclear medicine), THEY are the ones who have the responsibility, as a minimum duty to their patients, to boycott facilities which can not at least tell them the expected radiation dose. We remind them of Dr. Joel Gray's warning (Part 2 of this chapter):

"My feeling is that if they won't tell you, they don't know, and if they don't know, they could be among the facilities delivering a hundred times the necessary dose."

In medicine, failure to know and to record the dose of every agent administered to a patient is remarkable. And recording is not done only for the purpose of billing. It is done for better care of the patients, for better operation of the facility, and for a better chance of useful research.

It is patently unfair to expect the PATIENTS to find out if the radiology facility is one which makes a marvelous effort to measure its doses and to keep them to the minimum required for obtaining useful medical information --- or whether it is NOT one of those. Patients are entitled to expect that the REFERRING physicians can tell them just what they (the physicians) have done to ensure that unnecessary radiation doses are not occurring in the radiology facilities which they recommend.

Risk from One Exam vs. Aggregate Cancer-Toll from Millions of Exams

Why do the referring physicians NOT take the responsibility to find out? The answer can probably be traced to their medical education --- where this responsibility was probably never brought up. Some medical deans themselves may suffer from the "safe-dose" fallacy or the "same-as-an-airplane-trip" fallacy.

In reality, allowing unnecessary amounts of irradiation is harmful. The extra cancer-risk need not be high PER EXAM in order for referring physicians to induce a

very serious cancer-consequence from ordering millions of exams every year. We can believe that medical schools are doing their job on cancer-prevention when every graduate accepts the "ombudsperson" role with respect to seriously considering and minimizing doses when ordering exposures to radiation. After all, a prime rule for physicians is: "First, do no harm."

Meanwhile, advocates of breast-cancer prevention need to help patients resist intimidation when they ask about the expected breast-dose from procedures causing irradiation. Patients are not obliged to prove to the physician that they can interpret the information "correctly." In reality, the first step for patients is just to ascertain whether anyone in the MEDICAL system has bothered to know the dose, before the patients or their children are told to go take it.

Measurement of radiation entrance doses is neither difficult nor expensive, and referring physicians could even supply their patients with little self-stick "TLDs" (Thermo-Luminescent Dosimeters) as a reality-check on pre-exam dose-estimates. Indeed, about ten years ago, two radiologists in New York State tried to start a commercial service which would have enabled patients nationwide to measure their OWN doses during x-ray exams. They met with immense resistance from medical colleagues, and the idea collapsed.

● - Suggestion Three: Meeting with Deans of Medical Schools

If women find that their physicians know virtually nothing about ionizing radiation and its role in breast-cancer causation, we would not suggest running away from them. Instead, it would be enormously more helpful if women would seek out the deans of our medical schools to discuss why training of physicians has been deficient in at least two ways:

Many graduates of medical school appear not to appreciate the proper role of physicians in preventing cancer (instead of just treating it).

Many graduates appear not to recognize their duty as "ombudsperson" for their patients within the medical system.

And the women must persevere until they achieve some meaningful action on the part of medical educators to remedy those deficiencies with regard to physicians-to-be. With regard to physicians-in-practice, they are generally required to take courses each year for "CME credits" (Continuing Medical Education). They are highly educable.

● - Suggestion Four: A Cash Prize for Dose-Reduction

We are extremely impressed by the opportunities for reducing unnecessarily high levels of breast-irradiation (Part 2, above). With the exception of mammography, there is no reason to believe "It's already been achieved."

On the contrary.

● - First, achievements of this nature tend to be temporary. An expert office which was a very low-dose place in 1985 can be a very high-dose place in 1995 --- if the personnel change. Keeping doses down requires continuous commitment and continuous checking by measurements.

● - Second, many users of x-ray equipment operate OUTSIDE of expert radiologic offices.

● - Third, Kenneth Taylor and his colleagues did not think that a 3-fold reduction in typical diagnostic doses in radiologic offices was the maximum achievable. They thought that a 10-fold reduction could be achieved.

People concerned about preventing breast-cancer might think about how to establish a prize. Why not award a cash-prize to the radiologic office which develops and demonstrates exactly how to achieve a 3-fold reduction in average dose for the five procedures which presently cause the most breast-irradiation? A follow-on could be distribution of the "recipes" to every place where such procedures occur. The American College of Radiology, the Radiological Society of North America, the American Society of Radiologic Technologists, or all of them, might be approached for their ideas about this.

● - Suggestion Five: Organizing Community Watchdog Groups

One of the most useful tasks, for people concerned about breast-cancer prevention, would be to form an on-going watchdog group in every community to "see to it" that radiation doses are measured (in radiologic and non-radiologic offices), that facilities can document their measurements, and that medical schools do a better job in educating past and future graduates about ionizing radiation and about their obligation to serve as "ombudspersons" for their patients with regard to radiation.

If the citizens who are concerned about breast-cancer prevention do not accept the task of watchdogs, then who will do it effectively? Not the government. Not business. Not the press.

This book has told the story of how past medical irradiation (with small contributions from natural radiation and from fall-out) has been responsible for hundreds of thousands of breast-cancers, with many more to be delivered in the future. A high priority of watchdog groups, in our opinion, should be to identify all of TODAY's radiation exposure of breasts, and to see that every source of exposure is reduced as much as possible.

Watchdog groups can find ways to "get the job done" without imposing great costs on everyone. Taylor and co-workers have shown that large decrements in dose can be achieved (see Part 2) without large investments --- when people are motivated to do it. Watchdog groups can specialize in the motivation.

And in the friendly vigilance required.

The wisdom and virtues acquired by one generation never pass automatically to the next generation. The transfer requires "tender, loving attention." Problems, once fixed, seldom stay fixed. We are humans, after all, and it is so easy to become careless.

The Expanding Use of Radiation in Medicine

We have noted that the rates of x-ray examinations and nuclear medicine examinations, per thousand people, both have INCREASED (Chapter 37). Is this cause for concern? In Chapter 28, Table 28-B illustrated a fundamental principle: If nearly

everyone receives extra radiation, even low doses will induce a huge amount of cancer, in the aggregate. The menace is never just the size of an individual dose (in rads). It matters enormously how many people receive it (in person-rads). And the related principle is this: When large numbers of people are receiving extra radiation, very large aggregate benefits in health accrue even from small reductions in dose per exposure. So friendly vigilance can make a big difference.

Watchdogs need to think very seriously about proposed new uses of radiation (medical and other). Technology enthusiasts tend to assume that the benefits of their technology will vastly exceed their price (in health). Chapter 27, for example, shows how lucky we were that female children were getting shoes instead of SWEATERS fitted with the "help" of those very popular fluoroscopes. Chapter 28 shows how excessive use of mammography, WITHOUT reducing the 1970 dose-levels, would have caused a breast-cancer disaster. And Chapter 31 shows how UNIVERSAL use of fluoroscopy in monthly "well-baby check-ups" also would have caused a breast-cancer disaster.

These "new uses" of radiation did not get fully adopted, but enough "new uses" DID get adopted that we DO have a breast-cancer problem today. Women and their families can depend on luck to prevent the problem from continuing in the future, or they can depend on "authorities" to provide the "tender, loving attention" --- or they can depend largely on their own watchdog abilities.

• - Breast-Cancer Prevention: A Reality

In cancer-prevention, the latency period makes it impossible to equate preventive action TODAY with observable benefits the day after TOMORROW.

Nonetheless, the watchdog groups have a certainty to sustain their efforts. They can be CERTAIN that each reduction they achieve in breast-irradiation will prevent some of the future breast-cancers which would otherwise occur.

We urge all the citizens who are trying to prevent breast-cancer to make use of the knowledge that radiation is a major, proven, preventable cause of this disease.

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CHAPTER 43

The Process of Genuine Peer-Review

- Part 1. The Initial List for Stimulating Peer-Review**
- Part 2. Why Consume This Valuable Space?**
- Part 3. Comments Which Speak for Themselves**
- Part 4. Not Taken Seriously?**

We begin this chapter with a reminder from one of the two brothers who invented the airplane, Orville Wright: "If we all worked on the assumption that what is accepted as true really is true, there would be little hope of advance."

Research, like most human activities, is necessarily a co-operative effort. Neither the Wright brothers nor any single individual begins "de novo." We all start with knowledge of the accumulated evidence, techniques, and insights of our predecessors and colleagues (peers). And whenever anyone launches a proposed new insight, the subsequent corrections, modifications, and additions from colleagues constitute the "peer review" which may really improve the initial work.

We welcome genuine peer-review of our work. Indeed, we actively sought it for this book --- not from two or three anonymous "referees" of a single journal, but from countless peers in the fields of cancer causation and cancer prevention. It would be ill-informed to imagine that peer-review is limited just to comments in journals.

Part 1. The Initial List for Stimulating Peer-Review

Our initial list of book recipients (below) was designed to stimulate peer-review. With each book went a personal note inviting critiques or comments on the work. The list included some people who have a conflict of interest with respect to physician-causation and radiation-causation of cancer. Why did we not limit the list to colleagues who are free from a personal or a grant-related conflict? Because bias does not always interfere with valid scientific criticism. Everyone on the list below received the book from us in April, May, or June of 1995:

• – American Cancer Society:

Twenty-two individual physicians, of the American Cancer Society's Medical Affairs Committee and Editorial Advisory Board, received books.

Ahmann, David L., Prof. Oncology, Mayo Clinic, Rochester, MN.
Averette, Hervy, Prof. Gyn. Onc., Sylvester Cancer Ctr., Miami.
Bal, Dileep G., Chief, Chronic Diseases, Calif. State Health Dept.
Beerline, Donald, Pathology, Mt. Diablo Medical Ctr., Concord CA.
Cunningham, Myles P., Univ. of Illinois College of Medicine.

List continues, next page

DeMare, Paul A., Queen's Medical Ctr. Radiation Oncology, Honolulu.
 Dodd, Gerald D., Chair, Diagnostic Imaging, M.D. Anderson Ca.Ctr.
 Donegan, Wm. L., Chair, Surgery, Sinai Sam. Med. Ctr., Milwaukee.
 Foley, John F., Prof. of Med., Univ. Nebraska Med. Ctr., Omaha.
 Haase, Gerald M., Prof. Pediatric Surg., Children's Hosp., Denver.
 Hanke, C. Wm., Dir., Mohs Micrographic Surgery Unit, Indianapolis.
 Harper, A. Patricia, Med. Dir., Indianapolis Breast Center.
 Joseph, Rosaline R., Dept. Med., Med. College of PA, Philadelphia.
 Klatt, Gordon R., M.D., Tacoma, Washington.
 Lang, Nicholas P., Dept. Surgery, Univ. Arkansas, Little Rock.
 Lange, Richard H., Mohawk Val. Physicians Health Plan, Schenectady.
 Leitch, A. Marilyn, Prof. Surg., Univ. Texas SW Med. Ctr., Dallas.
 Levitt, Seymour H., Chair, Ther. Radiol., Univ. Minnesota, Minneap.
 Mansour, Ed. G., Dir. Surg. Onc., MetroHealth Med. Ctr., Cleveland.
 Murphy, Gerald P., Dir., Pacific NW Research Inst., Seattle.
 Simmons, Jerry L., Prof. Clin. Med., So. Dakota Sch. of Medicine.
 Woolam, Gerald L., Surg., St. Mary of Plains Hosp., Lubbock, TX.

Of the above group, not one acknowledged receipt of the book.

● – American Medical Association (see Chapter 44):

Three individual editors of the Journal received books:
 Lundberg, George D., M.D., Editor of JAMA
 Flanagan, Annette, R.N., M.A., Associate Senior Editor
 Meyer, Harriet S., M.D., Book Editor

● – British radiation establishment (see Chapter 46):

National Radiological Protection Board, in Didcot.
 Dr. Colin R. Muirhead, Chief of Epidemiology.
 Health and Safety Executive, in Sheffield.

● – California Breast Cancer Research Council (see Part 3, below)

Claymon, Susan, Breast Cancer Action, San Francisco.
 Hopper, Cornelius, M.D., Univ. Calif. V.P. Health Affairs, Oakland.
 Shinagawa, Susan M., M.D., Univ. Calif. Cancer Ctr., San Diego.

Not one acknowledged receipt of the book.

● – Canadian National Cancer Institute, Breast Cancer Initiative

Dr. Elizabeth Kaegi, NCI Breast Cancer Initiative, Toronto.
 Louise Liao, NCI Breast Cancer Initiative, Toronto.

Neither one acknowledged receipt of the book.

● - National Action Plan on Breast Cancer (USA)

This is a government-private "partnership" formed in December 1993, with initial co-chairs from the U.S. Dept. of Health and the National Breast Cancer Coalition: 19 members of the leadership roster received books from us in May 1995.

Apantaku, Funmi, Dept. Epidem. & Biostat., Univ. Illinois, Chicago.
 Blumenthal, Susan J., M.D., Dep. Asst. Secy. for Health, USDHHS.
 Brinton, Dr. Louise A., Env. Epidem., National Cancer Inst.
 Brogan, Dr. Donna, Etiology, Env. Epidem., National Cancer Inst.
 Browne, Doris, M.D., Ph.D., Office Asst. Secy. Defense, Health Aff.
 Burhansstipanov, Dr. Linda, Native Am. Ca. Research Ctr., Denver.
 Crisp, Dr. Tom, Office Research & Biol., U.S. Envir. Prot. Agency.
 Evans, Nancy, ex-president of Breast Cancer Action, San Francisco.
 Fenner-Crisp, Dr. Penelope, Pesticide Programs, US EPA.
 Haynes, Dr. Suzanne, Senior Advisor, Women's Health, US Dept. HHS.
 Liburdy, Dr. Robt. P., Lawrence Berk. Lab Life Sciences, Univ. CA.
 Malins, Dr. Donald C., Pacific NW Research Foundation, Seattle.
 McLachlan, Dr. John A., Ctr. Envir. Research, Tulane Univ. Med.Ctr.
 Robert-Guroff, Dr. Marjorie, Cancer Etiology, Natl. Cancer Inst.
 Saslow, Dr. Deborah, Off. on Women's Health, US Dept. Health & HS.
 Sieber, Dr. Susan M., Dep. Dir. for Ca. Etiology, Natl. Canc. Inst.
 Soto, Ana M., M.D., Tufts Med. Sch. Reproductive Research, Boston.
 Visco, Frances M., President of the Natl. Breast Cancer Coalition.
 Zahm, Dr. Sheila Hoar, Ca. Etiology, National Cancer Institute.

Of this group, Nancy Evans acknowledged receipt.

● - Radiation Effects Research Foundation, in Hiroshima

Mendelsohn, Mortimer, M.D., Ph.D., Associate Director.
 Preston, Dr. Dale L.

● - Additional Early Recipients

Bailar, John C. III, M.D., PhD.; Chair Epid., McGill Univ., Montreal.
 Benson, Allen B., PhD.; Prof.Chem.; author Radioactive Fallout 1989.
 Bertell, Dr. Rosalie; rad'n analyst; Internat'l. Institute, Toronto.
 Bradley, David J., M.D.; author books, incl. No Place to Hide 1984.
 Clapp, Dr. Richard W.; Envir. Health, Boston U. Sch. Public Health.
 Cobb, John Candler, M.D., MPH; Prof. Emer. Epid., Univ. Colorado.
 Davis, Devra Lee, Ph.D.; Office of Asst. Secy. for Health, USDHHS.
 Elkind, Mortimer L., M.D.; Radiol. Health Sci., Colorado State U.
 Epstein, Samuel, M.D.; Univ. Illinois Sch. Public Health, Chicago.
 Fredrickson, Donald S., M.D.; former head, Natl. Inst. of Health.
 Good, Robert A., M.D.; All Children's Hospital, St. Petersburg FL.
 Gould, Dr. Jay M.; Radiation & Public Health Project, NYC.
 Grundy, Scott, M.D., Ph.D.; Univ. TX. SW Med. Ctr., Dallas.

List continues, next page

Henderson, I. Craig, M.D.; Chair, Med. Onc., UCSF Cancer Ctr.

Hoffman, Dr. Daniel A.; Geo. Washington Univ. Medical Sch, Wash DC.

Kirsch, Jan, M.D.; onc; Mt. Diablo Reg. Cancer Ctr., Concord CA.

Kohnlein, Dr. Wolfgang; Inst. Strahlenbiol., W-W Univ., Munster.

Kradjian, Robert M., M.D.; onc., author, Save Yourself from Br.Ca.

Land, Charles E., Ph.D.; radiation epid., Natl. Cancer Inst.

Landrigan, Phillip, M.D.; Community Med., Mt. Sinai Med. Ctr., NYC.

Love, Susan M., M.D.; author; Dir. Revlon/UCLA Breast Center.

Montague, Dr. Peter; dir., Envir. Research Foundation, Annapolis.

Moore, Francis, M.D.; New England Journal of Medicine, Boston.

Morgan, Karl Z., Ph.D.; "father" of health physics; ICRP emeritus.

Morton, Wm. E., M.D., Ph.D.; Sch. of Medicine, Oregon Health Sci.

Moses, Marion, M.D.; author; founder, Pesticide Education Ctr.

Moss, Ralph W., Ph.D.; author; NIH Advisory Counc. Alternative Med.

Nussbaum, Rudi H., Ph.D.; radiation analyst; Portland State U., OR.

O'Toole, Dr. Tara; Deputy Secretary of Energy, US Dept. of Energy.

Peters, John M., M.D.; Preventive Med., Univ.So.Calif. Sch. of Med.

Pilgrim, Ira H., Ph.D.; retired cancer biologist, Laytonville, CA.

Radford, Edward P., M.D.; Chair of the BEIR-3 Com'tee; Surrey, UK.

Ragovin, Cathie, M.D.; Exec. Bd. Member, Mass. Br. Ca. Coalition.

Read, Cathy; Brit. physician; author, Prev. Br. Ca.: Politics.

Richter, Dr. Elihu; Occ. Med., Hebrew Univ. Med. Sch, Jerusalem.

Rush, David, M.D.; epidem. Tufts Univ.; author 1992 Dead Reckoning.

Slesin, Louis, Ph.D.; founder and editor, Microwave News, NYC.

Sloan-Kettering Cancer Ctr.; Mortimer Chute, Senior Vice President.

Steingraber, Sandra, Ph.D.; biologist; author; cancer activist.

Sternglass, Ernest, Ph.D.; physicist; author of radiation studies.

Stewart, Alice, M.D.; pioneer, Oxford Survey Childhood Canc., UK.

Strauss, Harlee, Ph.D.; Dir., Silent Spring Institute, Newton, MA.

Warf, James C., Ph.D.; USC chem.; author 1990 All Things Nuclear.

Whelan, Dr. Wm.J.; Editor Journal Fed. Amer. Soc. Experimental Biol.

Wilkinson, Dr. Gregg; Epid.& Prev. Med., U.TX. Med. Ctr., Galveston.

Wing, Steve, Ph.D; Epid., Univ. of No. Caro. Sch. of Public Health.

Zippin, Calvin, Sc.D.; Prof.Emeritus Epid.& Biostat., UCSF Med.Sch.

Part 2. Why Consume This Valuable Space?

The reason we consume valuable space on the issue of peer-review is because people who want to imply the work is worthless (whether or not they have ever read it) often say nothing more than, "Well, you know the book is not peer-reviewed!"

These ostensible fans of independent peer-review are often the people who treat as "gospel wisdom" any book, report, or monograph self-published and self-reviewed by the national and international "radiation committees" (BEIR, ICRP, NCRP, NRPB, RERF, UNSCEAR; respectively, Biological Effects of Ionizing Radiations, USA-NAS; International Commission on Radiological Protection; National Council on Radiation

Protection, USA; National Radiological Protection Board, Britain; Radiation Effects Research Foundation, USA-Japan; United Nations Scientific Committee on the Effects of Atomic Radiation).

The radiation committees do not submit their self-published books and reports for pre-publication review by independent peer-reviewers like myself. Independent review begins AFTER publication.

So, many of the people who say "Gofman's book is not peer-reviewed!" are just using a double-standard. Unless they can offer a critique of some substance, they contribute obstacles rather than insights to the scientific effort.

Now this book is in a genuine peer-review process, as the following chapters will amply demonstrate. The book may already be one of the most peer-reviewed books in the field.

Readers of the next chapters may wonder, "Weren't there any favorable comments?" Yes, there were many (even a few from the fiercest critics), but the positive comments are not in our text because they require no response from us.

Part 3. Comments Which Speak for Themselves

Not every comment by a colleague qualifies as peer-review. Comments about a 300-page study fail to qualify whenever their makers have not even seen the work, much less studied it! A rush to judgment speaks for itself.

No advance-copies of the First Edition were issued to anyone, although we talked freely about the work with interested peers, activists, and reporters. The printer produced the first copies on March 28, 1995. Examples of comments issued BEFORE that date include:

● - Charles L. Gruder, Ph.D., Director of the Breast Cancer Research Program, a program of research and education grants funded by a special California tax on cigarettes, and administered for the California Legislature by the University of California, wrote:

"I regret to inform you that the Breast Cancer Research Program has decided not to invite you to submit a grant application based on the project proposed in the above-referenced Letter of Intent (LOI). [Our Letter of Intent to Submit a Grant Application described, in three double-spaced sheets, the findings set forth in this book, and it promised that a copy of the book would accompany the Grant Application.] All LOIs were reviewed by screening committees comprised of peer reviewers and members of the BCRP's Breast Cancer Research Council; screening committee rosters will be released when grants are announced." I had intended to request a one-year grant of \$35,000.

The refusal, even to receive a grant application based on the thesis of this book, was dated February 1, 1995 --- eight weeks before the book was available for peer-review examination.

You do the peer-review first, and then you don't even have to look at the work itself? We call this peer-preview, not peer-review.

The mandate of California's Breast Cancer Research Program is to support "innovative research to enhance: understanding of the causes of breast cancer; access to early detection services... ; and the development of more effective interventions for preventing the incidence and progression of breast cancer." The only comment from the peer-review committee on its LOI evaluation-form was that my work would be "not responsive" to these goals. With an "x" in the correct box, the committee did acknowledge that I am an "established investigator."

● - Gerald Dodd, M.D., a former president of the American Cancer Society and emeritus professor of radiology at the University of Texas M.D. Anderson Cancer Center: "I see absolutely no way that he [Gofman] can make his determinations with any degree of accuracy ... What can be said is that even if you assume the worst, the number of cancers that are produced by radiation are far outnumbered by the number that occur spontaneously, and at least half of those can be arrested by timely treatment." From an interview by Dr. Peter Radetsky, quoted in the February 1995 issue of Longevity Magazine (p.88, 90).

Criticism: January 1995.

First availability of the work criticized: April 1995.

● - Stephen A. Feig, M.D., professor of radiology at the Thomas Jefferson University Hospital in Philadelphia: "Respected people disagree with Gofman. They don't take him seriously ... He doesn't make any sense. If there is a risk from very low doses [of radiation], it's so small you can't even measure it." From an interview by Dr. Peter Radetsky, quoted in the February 1995 issue of Longevity Magazine (p.90).

Criticism: January 1995.

First availability of the work criticized: April 1995.

Part 4. Not Taken Seriously?

Flimsy personal attacks, such as the one by Dr. Feig above, should be put into perspective by just a few statements from other sources.

● - Devra Lee Davis, Ph.D., MPH, senior advisor to the Asst. Secretary for Health, U.S. Department of Health and Human Services: "I think Gofman is making a very important contribution. There's growing evidence to show that past uses of radiation may explain some part of the increase in breast cancer." Quoted in Your Health, Vol.34, No.12, June 13, 1995.

● - Mortimer Mendelsohn, M.D., Ph.D., Associate Director of the Radiation Effects Research Foundation in Hiroshima, and former Associate Director of the Livermore National Laboratory: "John Gofman is a superb analyst and has always been at the cutting edge of medical science, particularly when it comes to protecting people." A 1995 on-camera statement in the half-hour program "The X-Ray Effect" (based on this book), produced by London's 20/20 Television and broadcast over Britain's Carlton TV network on August 3, 1995.

• - Edward P. Radford, M.D., epidemiologist and Chairman of the BEIR-3 Committee (Biological Effects of Ionizing Radiations) of the National Academy of Sciences, USA: "Dr. Gofman is owed a debt of gratitude by the scientific community because he was one of the first people to raise the issue of cancer risks from radiation exposure." A 1995 on-camera statement in the half-hour program "The X-Ray Effect" (based on this book), produced by London's 20/20 Television and broadcast over Britain's Carlton TV network on August 3, 1995.

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"A dwarf standing on the shoulders of a giant may see farther than the giant himself."

• — *Didacus Stella, A.D. 39–65.*

CHAPTER 44

Criticisms in the Journal of the American Medical Assn.

- Part 1. My Suggestion, in Reply to JAMA's Invitation**
- Part 2. The Subsequent Sequence of Events at JAMA**
- Part 3. Our Response to Skolnick 1995**
- Part 4. Our Response to Heath 1995**
- Part 5. A Headline Which Merits Dispute**

In early 1995, I received an invitation from Annette Flanagin, R.N., M.A., Associate Senior Editor of the Journal of the American Medical Association (JAMA). The letter invited me to submit a paper for review and possible publication in JAMA's radiation issue of August 1995 --- the 50th anniversary of the Hiroshima-Nagasaki atomic bombings.

Part 1. My Suggestion, in Reply to JAMA's Invitation

In response to this invitation, I talked with Ms. Flanagin and Dr. Harriet Meyer by telephone, and followed-up with a letter sent simultaneously to Ms. Flanagin, to JAMA's book editor (Harriet S. Meyer, M.D.), and to the chief editor (George D. Lundberg, M.D.). Text of the letter:

March 14, 1995

Dear Colleagues:

As all of you will recall, in answer to your invitation to me to submit an article to be considered for the "Hiroshima" issue of JAMA, we mutually agreed that Dr. Meyer could get an unbiased review of my new book, "Preventing Breast Cancer: The Story of a Major, Proven, Preventable Cause of This Disease," as a contribution to this issue. I not only think this decision is appropriate; I think this is an excellent forum for presenting the issues I have to address.

I am pleased to say that I shall be able to provide finished books, rather than manuscript xeroxes, to you for the Symposium. The printing establishment has informed me that we shall have books before the end of March, and I will forward copies to all of you just the moment we have books in hand. I know the Dr. Meyer needs several copies. These shall be provided, plus any additional copies which would be helpful to any of you.

Meanwhile, I urge you all to examine the several [enclosed] pages from the book, especially the BACK COVER which conveys important messages of the book.

I have a few things to say about medicine, about fairness, and about bias. Medicine and medical research have suffered greatly as a result of charges of conflict-of-interest, and I would hope that medicine will not add fuel to this controversy. My experience, which may not be familiar to you, is very relevant on this issue.

One rarely has an opportunity to do something in medical research that really makes a difference. In 1948-1954, my colleagues and I introduced the discovery of the various classes of low-density lipoproteins and the various classes of high-density lipoproteins, through our work with the ultracentrifuge. And very soon after the initial discoveries, we related the low-density lipoproteins to coronary heart disease. [Insert of January 1996: See Gofman 1996 in the Reference List.]

The resistance to those discoveries was fierce, and there is no doubt that such resistance unnecessarily wasted a decade or more in moving the heart disease field along. Ask Dr. Donald Fredrickson about this as a fact. [Insert of January 1996: See Fredrickson 1993 in the Reference List.]

Today, none of the young scholars even know about that era, or that there was fierce resistance to new ideas. And, after the resistance phase, my work was widely accepted, and I have received several major awards in heart disease research, including the Lyman Duff Lectureship, the Stouffer Prize, and the commendation of the American College of Cardiology. In 1993, the American Heart Association invited me to be the Guest Lecturer at the Annual Arteriosclerosis Section Dinner Meeting in Atlanta. [Insert of January 1996: See Gofman 1993 in the Reference List.]

I am happy that all turned out well, but there was little reason to be happy about the personal attacks during the height of the resistance.

So the issues of bias, resistance, are not novel events in my life. I shall not be surprised that my recent work on the origin of breast cancer will receive a fierce "going over." I WELCOME honest criticism. There is a monumental difference between honest criticism and exercise of conflict-of-interest. Medicine is the big loser in those instances where eventually it turns out that conflict-of-interest, rather than merit, is at work in an assessment of a piece of work.

Dr. Meyer, you and I have discussed this issue by phone. I would consider choice of a radiologist, or a nuclear medicine specialist, or a radiologic physicist to review my book to be an obvious conflict-of-interest. What one needs is an honest scientist-physician who does not have a conflict-of-interest. I could name many, if asked.

I look to you, Dr. Lundberg, to assess this problem, when the review comes in. I would trust you to decide whether some editorial comment from you might be in order in the Hiroshima JAMA issue. The matter of breast cancer is a monumental issue in our society, and we will all be judged, in our profession, by how we handle the issue of causation. There are some who think the problem will go away if we shut our eyes, ears, and brains to evidence that is as close to a smoking gun as we shall ever see.

I have never taken the position of being "anti-medical x-rays." The enclosure here of the BACK cover of the new book proves beyond doubt that I do NOT fall in that category. The text of my book is laden with compliments to the contributions of famous roentgenoscopists in the era of pneumo-thorax management of tuberculosis. They gave many women decades of good life after recovery from pulmonary tuberculosis. Yes, some [women] later developed breast cancer as a result. I applaud those roentgenoscopists for making it possible for those patients to live many decades, even if some paid a price in breast cancer for that gift of decades of good life, after recovery from tuberculosis.

My suggestions will lead to BETTER roentgenology, not to less roentgenology. Just look at the evidence. Mammography was CORRECTLY criticized in the early 1970s for being a dose-related health hazard. Mammography today is performed with vastly lower doses and with much wider application. Criticism had the opposite effect from that of destroying mammography.

So, if medicine cannot look back on the FIRST HUNDRED YEARS OF ROENTGEN'S DISCOVERY, and assess honestly the good and the bad, that will be a very sad day for medicine. I believe I have made a constructive effort in this book to see that the second hundred years of application of Roentgen's discovery is an era where we achieve the benefits of his discovery, with a drastic reduction in the health costs. That is possible and desirable. That will earn the appreciation of the public. Any conflict-of-interest denial of the undeniable will only earn well-deserved scorn for our profession.

I noted with great interest that you, Annette Flanagin, and you, George Lundberg, specifically mention receiving [inviting] reports of ORIGINAL research. The methods I have used for this research ARE indeed original, and they were not in existence when I started. I feel that this is my best research since my work 47 years ago on the discovery and significance of the low-density lipoprotein classes. And these [1995] research methods can undoubtedly be applied to other cancer research efforts.

The issue is not minor. I look forward to working with all of you toward a constructive approach. This is an opportunity, not a burden for any of us. Think of it --- the findings mean that many, possibly most, breast cancers are avoidable.

Sincerely yours,
John W. Gofman, M.D.

P.S. If you, Dr. Lundberg, do not feel an editorial by you is warranted, you might wish to consider publishing this letter, as a Letter to the Editor, in the Hiroshima issue.

Part 2. The Subsequent Sequence of Events at JAMA

In very early April of 1995, we sent books to JAMA, as promised (above): Copies to Annette Flanagin, George Lundberg, and three to Harriet Meyer.

Who was chosen by JAMA to review the book? Clark W. Heath, Jr., M.D., vice president for epidemiology and surveillance research at the American Cancer Society (ACS). The ACS is a strong advocate of irradiating people, both for diagnostic and therapeutic purposes with respect to cancer. Indeed, the ACS is a leading advocate of mammography --- and was advocating widespread mammography even when the radiation doses were 10 times higher per exam than they are now (Chapter 28 of this book, Part 5).

Dr. Heath's review of the book was published in JAMA on August 23, 1995 (Heath 1995). Meanwhile, JAMA's associate editor for the Medical News and Perspectives section, Andrew Skolnick, wrote two pages about the book in the JAMA "Hiroshima" issue of August 2, 1995 (Skolnick 1995). So JAMA really did its job in contributing to peer-review, although almost all of the substance comes from a single person, Dr. Heath.

We responded to both Skolnick 1995 and Heath 1995 (see Parts 3 and 4, below).

Our response to Skolnick 1995 focused largely on Heath's claim (used by Skolnick) that our calculations are "based on two serious errors." Our response to Heath 1995 focused on his assertion (for which Heath cites Evans 1986) that medical uses of radiation probably account for "less than one percent" of breast cancer in the USA.

Following the instruction of Annette Flanagin, we submitted two 500-word Letters to the Editor, for consideration. The response to Skolnick 1995 was sent by us on August 21, and the response to Heath 1995 was sent by us on September 19.

On October 10, 1995, JAMA notified us that JAMA would publish our response to Skolnick 1995. This occurred in the December 13, 1995 issue of JAMA. Our published letter is followed by the notation: "This letter was shown to Dr. Heath, who declined to reply. -- ED."

On October 11, 1995, JAMA notified us that JAMA would not publish our response to Heath 1995: "After considering the opinions of our editorial staff, we determined that your letter did not receive a high enough priority rating for publication in JAMA ... However, we are forwarding a copy of your letter to the author of the article [Heath]. The author may or may not reply to you personally." The letter says: "cc: Clark W. Heath, Jr., MD" at the bottom. We have not heard from Dr. Heath yet (January 1996).

Both of our responses, to the critiques in JAMA, are presented below. New references cited in the letters have been added to our Reference List.

Part 3. Our Response to Skolnick 1995

Our response to Skolnick 1995 was entitled (by us) "X-Rays Not Exonerated As the Major Cause of Current Breast Cancer." The title's beginning and end were still present when it appeared in the December 13, 1995 issue of JAMA (Gofman 1995-b):

"X-Rays and Breast Cancer."

To the Editor. --- My estimate, that at least 75% of current breast-cancer in the USA is due to earlier medical irradiation of breasts (Gofman 1995), was called a 12-fold overestimate in the article by Skolnick 1995. He is quoting Clark Heath of the American Cancer Society, who asserts that I made "two serious errors."

First, an alleged 2-fold overestimate comes from my "assumption" that dose-response is supralinear. This is no assumption. The human evidence from the atomic-bomb survivors for all cancers combined shows supralinearity fitting the observations provably better than linearity (Gofman 1990). Supralinearity specifically for breast-cancer is visible to anyone who inspects the figure at page S26 of Thompson 1994, although Land's analysis raises questions (Land 1995).

Second, an alleged 6-fold overestimate comes from transport of Japanese evidence to the USA. Why did I not use North American data? Because (a) North American data on risk are inconsistent by a factor of six from one study to another, and (b) such studies exclude infants and children. For these and other reasons, the A-Bomb Study is more informative.

How to transport observations internationally is an unsettled issue, with the uncertainties fully discussed in my book (Gofman 1995). Although Heath asserts he knows which way of transport is a "serious error" and which way is correct, no one today can possibly be sure.

Nonetheless, Heath claims the correct way would be to make no adjustment of the Japanese observations for application here. His unstated assumption is that radiation and other causes of breast-cancer each act alone, without co-action, and therefore, a unit of radiation produces the same number of breast-cancers in all countries. My clearly stated assumption is that radiation and other causes co-act, and therefore, adjustment is required for transport of evidence from one milieu of co-actors to another.

Land 1995 presents evidence on both sides of this wide-open issue. Although he takes a position like Heath's at first, Land quickly allows for radiation co-action with breast-cancer risk-factors like benign breast disease, reproductive history, and inherited lesions.

Skolnick's report (Skolnick 1995) raises the safe-dose issue twice, by quoting Dr. Feig and alluding to "many radiation physicists" who believe DNA damage is fully repaired at doses which do not "overwhelm" the repair-system. Their speculation is refuted by mainstream human evidence from serial breast-irradiation at doses below 0.1

Sv --- in fact, at doses close to the lowest conceivable radiation dose and dose-rate, namely one ionization track per cell-nucleus per exposure (Gofman 1990). [Additional information in Chapter 45.]

Thanks to rejection of the safe-dose fallacy, radiation dosage from mammography is now 30-fold lower than in 1970. Don't we owe it to women also to achieve much lower doses for millions of other useful exams which irradiate the breasts, including upper spine, upper GI tract, and heart procedures, plus neonatal x-rays? In the medically relevant dose-range of 0.1 to 0.5 Sv of accumulated dose, Land's table for Japan (Land 1995) estimates that 10.5 percent to 38.0 percent of all breast-cancers were radiation-induced.

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Part 4. Our Response to Heath 1995

Our response to Heath 1995 was entitled "Relevant and Irrelevant Approaches to Explaining the Breast Cancer Problem." The response was not published at all by JAMA, as related in Part 2.

To the Editor. --- An interesting error merits correction. Clark Heath (Heath 1995) features a 1986 estimate by Evans et al that less than one percent of all breast cancer in the USA results "from diagnostic radiography" (Evans 1986). Then Heath asserts my new book (Gofman 1995) "disputes these facts" because I estimate that 75 percent of cases are due to earlier exposure to medical irradiation (including therapeutic radiation for numerous non-malignant conditions).

Evans' estimate and Heath's use of it fail to take account of the long latency periods of radiation-induced breast cancer. The A-Bomb Study now shows that excess breast cancers are gradually "delivered" over at least 45 years, when a female population (all ages) is irradiated on the same day. Prudent analysts must assume radiation-induced cases will continue for 60-75 years among females irradiated in infancy and childhood.

Because of long latencies, anyone who wants to uncover the radiation-contribution to our contemporaneous incidence of breast cancer must evaluate average breast doses received during many decades beforehand, by females of all ages. My study did it for 1920-1960, whereas Evans et al considered the single year of 1977.

How much does the choice matter? For children up to age ten, the Evans' per capita estimate of average annual breast-dose in 1977 (from diagnostic x-rays) is 35 times lower than my estimate per year during 1920-1960 (from diagnosis plus noncancer therapies). The difference is really bigger, because my dose estimate excluded any contribution by fluoroscopy, despite the documented practice of doing fluoroscopic exams

as part of routine well-baby and pediatric check-ups. So proper attention to latency introduces more than a 35-fold disparity between Evans and me in the RELEVANT per capita dose-estimate for children --- the most vulnerable group.

For everyone above age ten, the Evans' estimate is about 10-fold lower for 1977 than my estimate for the earlier time-period. Again, the disparity is really bigger, because my analysis excluded all uses of radiation in dermatology, all radiation therapies for other inflammatory conditions (from tuberculosis of the lymph glands to peptic ulcer), and almost all uses of fluoroscopy.

An undeniable, major flaw in the Evans' analysis is its exclusion of doses from the RELEVANT period. When Heath presents its conclusion as a "fact" which contradicts my conclusion, he is just wrong.

My 75-percent estimate is the product of two factors: (Dose in 1920-1960) times (Cancers per Unit Dose). For the second factor, all analysts including Evans have to incorporate important assumptions, pending future evidence. If some JAMA readers accept Heath's opinion (Heath 1995) that my second factor is too high, they must also recognize the first factor: Past dosage. My book shows repeatedly why my dose estimates are probably many-fold too low --- a point not mentioned by Heath.

Thus the bottom line is that my critics and I must already be much closer than Heath indicates, in recognizing that past medical irradiation explains a large fraction of the current breast cancer problem.

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Part 5. A Headline Which Merits Dispute

JAMA is one of the leading medical journals of the world. Such journals are meant to be an important vehicle for exchange of well-informed opinion --- rational dialog --- about the causes, prevention, and treatment of illness. Both Skolnick and Heath acknowledge our standing for such a dialog. Skolnick characterizes Gofman as "a respected authority on the biological effects of ionizing radiation" (Skolnick 1995, p.367), and he quotes Heath as saying that Gofman is "a very good radiation physicist who has had a remarkable career" (p.368).

One of the major diseases of our time is breast cancer. Countless papers are published about it. Along comes an experienced researcher who produces evidence that the main cause of breast cancer is a preventable one: Irradiation of the breasts. In response, someone at JAMA creates a three-column headline:

"Claim That Medical X-rays Caused Most US Breast Cancers Found Incredible"
(Skolnick 1995, p.367).

"Found incredible?" Who at JAMA selected and permitted two words which indicate that the work had flunked peer-review, when peer-review was just in its very first step? It had to be people who were not even interested in whether or not our response would invalidate the criticism. This is NOT the way a leading medical journal serves as a neutral vehicle in a debate of singular importance for women and their families. But every institution has failures from time to time! [And it's easy for editors to miss the boat. E. O'Connor, Editor.]

By contrast, Skolnick's text --- for any readers remaining after its headline --- was an excellent introduction to the issue. Skolnick even included some of our position on peer-review: We want it to occur widely and in the open, not "behind closed doors."

Both JAMA items (Skolnick and Heath) relied almost entirely on Heath for peer-review --- one peer. And one peer can make numerous claims in a short space. Everyone knows that it takes more space to refute a claim than just to state one. Although JAMA allowed us a response of only 500 words (with a limit of five references), it is likely that JAMA will return to our work in the future.

JAMA-readers have a right to expect a series of in-depth exchanges until there is some RESOLUTION of an issue which actually addresses prevention of future breast cancer. Meanwhile, JAMA's headline is sure to stick in many memories, but our 75-percent thesis has certainly not been shown by ANYONE to be "incredible" --- as readers of this book's Section 5 will see for themselves. Above, we have shown why "incredible" is the appropriate adjective for Heath's one-percent claim. JAMA got it wrong this time.

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CHAPTER 45

Three Remarkably Similar Reports on the Safe-Dose Fallacy

Part 1. Demolition of a Dream

Part 2. Gofman 1990: Proof There Is No Threshold Dose or Dose-Rate

Part 3. UNSCEAR 1993: "Highly Unlikely That a Dose-Threshold Exists"

Part 4. NRPB 1995: Evidence "Falls Decisively" against a Threshold

Part 1. Demolition of a Dream

In one critique of the First Edition (Skolnick 1995, p.367), the radiologist Dr. Stephen Feig suggests that low-dose diagnostic x-rays may be incapable of inducing any breast cancer. Feig asserts that any risk at all from mammography is "hypothetical" and, "With such low levels of radiation, there may be much less or even no risk."

If Dr. Feig were the only remaining distributor of the no-risk dream about low-dose radiation, we would not devote a chapter to it. But even some medical schools are still teaching radiologists that cancer-induction by diagnostic radiation is uncertain and just assumed. For example, the following statements come from the 1996 Radiology Syllabus for students at the University of California San Francisco Medical School (Goldberg 1996, p.129):

"High doses of ionizing radiation can produce breast cancer, but this has been demonstrated only at doses above 90 rads." (This claim, invalidated by several studies including the A-Bomb Study, also slipped into *The Lancet*, in Hulka 1995, p.885). The Syllabus adds: "There is absolutely no evidence ... that breast cancer is caused by mammography."

The no-risk, safe-dose dream about ionizing radiation has been powerfully demolished by three major analyses: NRPB 1995, UNSCEAR 1993, and Gofman 1990. (NRPB is Britain's National Radiological Protection Board; UNSCEAR is the United Nations Scientific Committee on the Effects of Atomic Radiation.) This chapter provides excerpts from all three. Because UNSCEAR and NRPB embrace much of the analysis in Gofman 1990, we will begin in Part 2 with Gofman 1990.

Does It Really Matter?

What makes it so important to settle the threshold (safe-dose) issue for ionizing radiation? The widespread exposure.

Low-dose ionizing radiation is not an exotic carcinogen and mutagen which exposes just a SMALL segment of the population. There is universal exposure from natural sources and from nuclear pollution, and there is voluntary exposure, occupationally and medically. Speaking about exposures from diagnostic medical x-rays, UNSCEAR warns (1993, p.228):

"Although the doses from diagnostic x-ray examinations are generally relatively low, the magnitude of the practice makes for a significant radiological impact."

UNSCEAR has appropriately acknowledged the AGGREGATE impact of millions upon millions of low-dose exposures, year after year, in medical practice. And not just in the USA. (Details in Chapter 48.)

Part 2. Gofman 1990: Proof There Is No Threshold Dose or Dose-Rate

The no-risk speculation about low-dose radiation, illustrated at the outset of this chapter, has been tied for a long time to the fact that cell-nuclei have massive capacity to repair DNA damage (Chapter 42, Part 2). Once upon a time, nearly everyone (myself included) hoped that carcinogenic lesions might invariably be repaired --- correctly --- whenever the repair-system was not overwhelmed by "too much" radiation-induced damage all at once.

In the 1970s, however, it was already clear that perfect repair of injured human chromosomes did NOT occur, even when low total doses of radiation were received very slowly from weapons-testing fallout or chronic occupational exposures. And some evidence was already solid that radiation-induced human CANCER is associated with very low doses and dose-rates. But might there be a safe dose (no-risk dose) at even lower levels?

Between 1970 and 1990, it was frequently asserted that the safe-dose issue could never be settled, because of the limits of epidemiology. In Gofman 1990, however, we were able to prove, by any reasonable standard of biomedical proof, that no safe dose or dose-rate exists with respect to radiation carcinogenesis.

The key breakthrough lies in recognizing that the relevant way to define the lowest possible dose and dose-rate of radiation is NOT in fractions of a rad. The RELEVANT definition occurs in "tracks" per cell (Gofman 1971, pp.275-276; Gofman 1981, pp.405-411; Gofman 1986, pp.6-14). We will show why, by explaining "tracks" in Section 2a, below.

2a. The Least Possible Amount of Damage to Repair

- - (1) "The dose from low-LET ionizing radiation is delivered by high-speed electrons, traveling through human cells and creating primary ionization tracks" (Gofman 1990, p.18-2).

- - (2) When genetic molecules are damaged by ionizing radiation, each cell-nucleus attempts to un-do the damage by repair. The damage done by a single primary ionization track is the LEAST POSSIBLE damage which the repair-system ever can face. "Fractional tracks do not exist. Either a track traverses a nucleus somewhere (one nuclear track) or it does not (zero nuclear track)" (1990, p.19-2).

- - (3) "For disproof of any safe dose or dose-rate, it is more important to establish the dose in terms of the average number of tracks per nucleus, than to establish it in terms of rads. The reason is that the lowest conceivable dose or dose-rate with respect to repair is not a millionth or any other tiny fraction of a rad or centi-gray. The lowest conceivable dose or dose-rate is one track per nucleus plus sufficient time to repair it" (1990, p.18-3,4).

• - (4) "Because the minimal event in dose-delivery of ionizing radiation is a single track, we can define the least possible disturbance to a single cell-nucleus: It is the traversal of the nucleus by just one primary ionization track" (1990, p.19-1). The traversal is complete in a tiny fraction of one second.

• - (5) "Single, primary ionization-tracks, acting independently of each other, are never innocuous with respect to creating carcinogenic injuries in the cells which they traverse. Every track --- without help from any other track --- has a chance of inducing cancer by creating such injuries" (1990, p.18-2).

• - (6) "... Any lesion which can be inflicted in a nucleus by a PAIR of tracks, can also be inflicted by a single track acting ALONE ... The earlier parts of this chapter leave no doubt that events [injuries] at multiple, separate sites are certainly producible by a single track, acting alone" (1990, p.19-8).

2b. What Dose in Rads Delivers an Average of ONE Track / Nucleus?

• - (7) Because a single primary track represents the least POSSIBLE challenge to the repair-system in a cell-nucleus, we wanted to find out if there is solid human evidence of radiation-induced CANCER as a result of doses which deliver just one track or a few tracks per nucleus. If such evidence exists, it indicates that repair is NOT ALWAYS PERFECT even when the challenge is about as low as it can ever get. In other words, it would be DIRECT evidence that the hypothesis of a no-risk dose is false, with respect to radiation-induced cancer.

• - (8) So a necessary step in our analysis was figuring out what dose in rads (cGy) delivers an average of ONE primary track per cell-nucleus. Chapters 20, 32, and 33 in Gofman 1990 show how such doses were derived, step-by-step. The doses vary with the diameter of the cell-nucleus and with the energy of the radiation.

• - (9) The values in the box apply to cell-nuclei with an average diameter of 7.1 micrometers (p.20-3). The heading "Medical X-rays" refers to diagnostic x-rays with an average energy of 30 KeV, generated when the peak kilovoltage across the x-ray tube is 90 KeV. The heading "596 KeV Gammas" refers to gamma rays from radium-226 and daughters. Several additional sources of radiation are evaluated in Tables 20-M and 20-"0" of Gofman 1990.

Radiation	Average number of tracks per nucleus	Tissue-dose in rads (centi-grays)
Medical X-rays	1 track	0.75 rad
	10 tracks	7.48 rads
	134 tracks	100.00 rads
596 KeV Gammas	1 track	0.34 rad
	10 tracks	3.40 rads
	294 tracks	100.00 rads

From Gofman 1990, Table 20-M.

- - (10) When the AVERAGE number of primary tracks per nucleus is one, then:

37 percent of cell-nuclei experience no primary track at all;
 37 percent of cell-nuclei experience one primary track;
 18 percent of cell-nuclei experience two primary tracks;
 6 percent of cell-nuclei experience three primary tracks;
 1.5 percent of cell-nuclei experience four primary tracks;
 Half-percent of cell-nuclei experience more than four primary tracks.
 (From Table 20-N of Gofman 1990).

2c. How Many Tracks at Once Can Overwhelm the Repair System?

- - (11) In our 1990 analysis, we reviewed the existing experimental evidence on what radiation doses are required to overwhelm the repair-system for genetic molecules. In Gofman 1990, p.18-4, we quote Albrecht Kellerer, one of the leading experts on the issue:

"There is, at present, no experimental evidence for a reduction of the repair capacity or the rate of repair at doses of a few gray [a few hundred rads] which are relevant to cellular radiation effects" (Kellerer 1987, p.346). And: "There is little or no evidence for an impairment of enzymatic repair processes at doses of a few gray. Studies, for example by Virsik et al on chromosome aberrations, have established characteristic repair times that are substantially constant up to 10 Gy [1,000 rads], that is, up to the highest doses investigated" (Kellerer 1987, p.358).

- - (12) We also reviewed the existing evidence on the time required to finish repair (Gofman 1990, Chapter 18). Numerous studies indicate that cell-nuclei finish whatever repair they can perform on genetic molecules within 3 to 6 hours, even after doses of 100 to 400 rads.

- - (13) "The dazzling speed of repair has an extremely important implication for settling the threshold issue. It means that certain HIGH-dose evidence can reveal a great deal, as we will explain" (Gofman 1990, p.18-5).

2d. Existing Human Evidence of Cancer from Minimal Doses

- - (14) The relevant high-dose evidence comes from studies of breast-cancer rates among women who received serial fluoroscopies in the course of pneumo-thorax treatment for tuberculosis (see Chapter 15 of this book, and see entries in the Reference list for Boice 1977, Boice 1978, Boice 1981, Boice 1991, Howe 1984, Hrubec 1989, MacKenzie 1965, Miller 1989, Myrden + Hiltz 1969).

Because the women had so many fluoroscopic exams over months and years of treatment, their breasts accumulated radiation doses ranging from about 150 rads to over 1,000 rads (Gofman 1990, Chapter 21). But each exposure delivered single doses of 1.5 to 7.5 rads at a time. Such doses deliver, respectively, an average of just 2 or 10 tracks per cell-nucleus, as we see from paragraph 9 above.

• - (15) These are very nearly the lowest POSSIBLE doses and dose-rates, with respect to challenging the repair-system in a cell-nucleus. If the repair-capacity of cell-nuclei is not overwhelmed by the tracks from hundreds of simultaneous rads (paragraphs 11 and 12, above), we can regard 10 tracks per nucleus, on the average, as nearly minimal.

• - (16) Referring to the Nova Scotia Fluoroscopy Study of female tuberculosis patients, we wrote (1990, p.21-2):

"If carcinogenic injury was produced in the irradiated women at their first fluoroscopy exposure-session, but if repair-systems were able to perform flawless repair afterwards, then that particular exposure-session would have left no residual harm, in terms of any increased risk of future breast-cancer." And:

"Similar carcinogenic injury inflicted at EVERY subsequent fluoroscopy session would also have been without residual harm, if a flawless repair-system operated at a total dose per exposure-session of 7.5 rads. And thus, after accumulating 850 rads in this fashion, the irradiated women would have had NO radiation-induced breast-cancer."

And:

"The Nova Scotia Study is certainly not a high-dose study; at every critical step along the way, it is a test of how perfectly the repair-system can un-do carcinogenic injury produced by 7.5 rads, or 10 nuclear tracks on the average --- a LOW dose and dose-rate." Between exposures, ample time elapsed for completion of repair-work (paragraph 12).

• - (17) The repair-system FAILED the test, conclusively, not only in the Nova Scotia series of women, but also in additional pneumo-thorax series in Canada and in Massachusetts. The evidence of excess breast-cancer in the fluoroscoped women is very solid, and shows a positive dose-response. This evidence of radiation-induced human cancer is widely acknowledged and cited, but not many people recognize that it shows REPAIR-FAILURE even after a challenge which was MINIMAL.

• - (18) Our disproof of any threshold dose or dose-rate includes six additional studies from the mainstream literature which show radiation-induced cancer when the average number of tracks per cell-nucleus ranged from 0.3 track to 12 tracks (Gofman 1990, Table 21-A). They are the Israeli Scalp-Irradiation Study (Modan 1977, 1989); the Stewart In-Utero Studies (1956, 1958, 1970); MacMahon's In-Utero Study (1962); the British Luminizer Study (Baverstock 1981, 1983, 1987); Harvey's In-Utero Study of Twins (1985); Modan's Study of Breast-Cancer in the Scalp Irradiation Study (1989). The evidence against any threshold embraces infants in-utero, children, adolescents, young women, high-energy gamma rays, medical x-rays, acute single doses, acute serial doses, and chronic occupational doses.

• - (19) "In recent years, it has been fashionable to suggest that epidemiologic investigations can not usefully address the low-dose radiation question. The epidemiologic studies described here make it apparent that this is incorrect ... When the effort is made to evaluate the doses in such studies, in terms of tracks-per-nucleus, then it becomes evident that studies whose doses are not 'next-to-zero' are nonetheless studies of truly minimal doses and dose-rates" (Gofman 1990, p.21-19).

2e. Failure of Repair: "The Troublesome Trio"

● - (20) It is the COMBINATION of epidemiology with track-analysis which reveals that we already know that (a) repair has failures even when the repair-system has the least possible challenge, and (b) the failure has CANCER consequences. We do not need impossible-to-obtain studies at doses like 10 milli-rads or 10 micro-rads --- because the least possible challenge to the repair-system occurs at much higher doses.

● - (21) "One can look with awe, humility, and gratitude at a system of repair with the capacities demonstrated by the DNA repair-system. But an independent analyst, or a realist of any stripe, does not casually dismiss the troublesome trio: Unrepaired lesions. Unrepairable lesions. Misrepaired lesions" (1990, p.18-6). And:

"One cannot fault the repair-system in cell-nuclei for leaving a relatively small number of injuries unrepaired, or misrepaired, or for having some inherent inability to repair every conceivable type of injury inflicted at random by the tracks of high-speed electrons ..." (1990, p.18-6)

● - (22) "... the human epidemiological evidence on dose versus cancer-response provides no support for the speculation that repair makes each rad less carcinogenic as dose falls. If that were the net result of repair, the shape of dose-response would be concave-UPWARD. But what is seen in the A-Bomb Study and in others is NOT concavity-upward. The finding is either supra-linearity or linearity --- both of which are inconsistent with the speculation that repair processes make each rad less carcinogenic as dose and dose-rate fall" (1990, p.18-6, 18-7).

● - (23) "Our entire experience with human radiation carcinogenesis should have made it evident that the problem we might be facing is that --- regardless of dose-level --- some fraction of radiation injury to nuclei is unrepaired ... some fraction is unrepairable ... and some fraction is misrepaired" (1990, p.18-7).

2f. Not "Hypothetical": Fatal Cancers from Minimal Doses

● - (24) "The radiation-induced cancers arising from the unrepaired lesions at low doses do not wear a little flag identifying them as any different from cancers induced by higher doses of radiation, or induced by causes entirely unrelated to radiation. Therefore, threshold proponents cannot argue that the cancers arising from the lowest conceivable doses of radiation will somehow be eliminated by the immune system or any other bodily defenses against cancer. Such an argument would require the elimination of cancer in general by such defenses. Instead, we observe that cancer is a major killer ... So the proposition would lead to a non-credible consequence, and must be rejected" (Gofman 1990, p.18-2).

● - (25) What about the speculation that low radiation doses may induce a net health benefit, by stimulating DNA repair or by stimulating the immune system? "When excess fatal cancer is observed in humans after such exposures [minimal doses and dose-rates], the excess has occurred DESPITE any possible stimulation of the repair- and immune-responses by low-doses. The NET result is injury, not benefit. I wish it were otherwise" (1990, p.18-2).

• - (26) "By reasonable standards of proof, the safe-dose hypothesis is not merely implausible --- it is disproven ... We conclude with a warning: Disproof of any safe dose or dose-rate means that fatal cancers from minimal doses and dose-rates of ionizing radiation are not imaginary. They are really occurring in exposed populations. Proposals, to declare that they need not be considered, have health implications extending far beyond the radiation issue ..." (1990, p.18-18).

Part 3. UNSCEAR 1993: "Highly Unlikely That a Dose-Threshold Exists"

UNSCEAR 1993, written by the United Nations Scientific Committee on the Effects of Atomic Radiation, is a 922-page report (with no index) which presents a lot of valuable information and analysis.

Although authors of its nine big sections (called "annexes") are not identified, the total international membership of the Committee is identified on page 29. The biggest delegations are from Canada (9), China (7), France (9), Germany (7), Japan (11), Russian Federation (12), United States (11). Staff and consultants are identified on page 30.

Pagination in the report is consecutive from beginning to end, but paragraph numbers start over with each annex. Below, we will separate the page number and the paragraph number by a slash.

• - (27) In its introduction, the report states: "The combination of epidemiology and radiobiology, particularly at the molecular and cellular levels, is a useful tool for elucidating the consequences of low doses of radiation" (1993, p.27/184). That very combination is the essence of our proof, above, that there is no threshold dose with respect to radiation carcinogenesis.

• - (28) UNSCEAR also affirms our premise in paragraph 24, when it states: "Epidemiological studies of human groups exposed to low-LET radiation show that a range of neoplasms are represented in excess and, broadly, that these do not differ markedly from those arising spontaneously in the population ... no unique neoplastic signature of human radiation exposure is, as yet, apparent" (p.578/153).

3a. The Smallest Possible "Insult" at the Cellular Level

• - (29) UNSCEAR 1993, like Gofman, recognizes the importance of using an APPROPRIATE definition of the lowest possible radiation dose or dose-rate. And it embraces our "microdosimetric approach to defining low doses and low dose rates" (p.680/321):

"Photons deposit energy in cells in the form of tracks, comprising ionizations and excitations from energetic electrons, and the smallest insult each cell can receive is the energy deposited from one electron entering or being set in motion within a cell." See paragraphs 1-4 above.

• - (30) The only conversion offered by UNSCEAR between tracks and dose in rads (centi-grays) is for cobalt-60, which produces a far more energetic gamma ray than the 596 KeV gammas presented above in our paragraph 9. Says UNSCEAR (p.680/321):

"For cobalt-60 gamma rays and a spherical cell (or nucleus) assumed to be 8 micrometers in diameter, there is an average of one track per cell (or nucleus) when the

absorbed dose is about 1 mGy [0.1 cGy or rad]. The dose, corresponding to one track per cell, on average, varies inversely with volume and is also dependent on radiation quality, being much larger for high-LET radiation."

- - (31) At page 696, UNSCEAR supplies Table 17, "Proportion of a cell population traversed by tracks at various levels of track density." It is like Table 20-N in Gofman 1990. For instance, it shows what percentage of cells experience 0, 1, 2, 3, 4, and more tracks per cell-nucleus, when the average track density is ONE track per cell-nucleus. The percentages are the same as we show in paragraph 10, above.

- - (32) The UNSCEAR authors define the region of "definite" single-track action as the dose-region where not more than TWO PERCENT of the cell-nuclei experience more than a single track. "In this dose-region, there are so few radiation tracks that a single cell (or nucleus) is very unlikely to be traversed by more than one track" (p.628/42). For cobalt-60, the two-percent criterion means a tissue-dose of 0.2 mGy. Two percent is an arbitrary choice which seems completely unrelated to the repair-issue --- even though UNSCEAR agrees with us that the repair-issue is a critical part of the threshold-issue, as we will show. However, after choosing cobalt-60 and a dose of only 0.2 mGy (20 milli-rads), the UN authors are correct in saying that there are no corresponding human or animal data (p.628/42).

3b. UNSCEAR: The Carcinogenic Potency of a Single Track

- - (33) "The most basic, although not sufficient, condition for a true dose threshold is that any single track of the radiation should be totally unable to produce the effect" (p.630/54).

- - (34) "Radiation is able to induce a diversity of genomic lesions, ranging from damage to single bases to gross DNA deletions and rearrangements" (p.578/153).

And: "Biophysical analyses based on Monte Carlo simulations of track structure show clearly that all types of ionizing radiation should be capable of producing, by single-track action, a variety of damage to DNA, including double-strand breaks alone or in combination with associated damage to the DNA and adjacent proteins" (p.632/63).

And: "In all these mechanistic models, a single radiation track from any radiation is capable of producing the full damage and hence the cellular effect" (p.632/64).

- - (35) "There is compelling evidence that most, if not all, cancers originate from damage to single cells ... Point mutations and chromosomal damage play roles in the initiation of neoplasia" (p.8/37).

And: "Single changes in the cell genetic code are usually insufficient to result in a fully transformed cell capable of leading to cancer; a series of several mutations (perhaps two to seven) is required ... The whole process is called multi-stage carcinogenesis" (p.8/38). And: "It is possible that radiation acts at several stages in multi-stage carcinogenesis, but its principal role seems to be in the initial conversion of normal stem cells to an initiated, pre-neoplastic state" (p.8/39).

• - (36) "... the majority of neoplasms originate from damage to single cells. In principle, therefore, the traversal of a single target cell by one ionizing track from radiation has a finite probability, albeit low, of initiating neoplastic change" (p.556/26).

• - (37) Our topic here is real-world human evidence relating to the threshold-issue for radiation-induced cancer. We omit unrelated references by UNSCEAR to dose-response curves induced in various experiments, although we are interested in such experiments (see Gofman 1990, Chapter 23). With respect to the threshold-issue, we quote UNSCEAR:

"Multi-stage models of carcinogenesis could lead to expectations of a dose threshold, or a response with no linear term, under particular, highly restricted sets of assumptions" (p.636/84). But, "it would be difficult to conclude on theoretical grounds that a true threshold should be expected even from multi-stage mechanisms of carcinogenesis, unless there were clear evidence that it was necessary for more than one time-separated change to be caused by radiation alone" (p.633/69).

3c. UNSCEAR: Does "Repair" Deliver a Threshold Dose?

A threshold-dose for radiation-induced cancer is a dose below which there is NO risk of radiation-induced cancer. A safe dose.

• - (38) As long as there are any primary tracks at all occurring in a biological tissue, a radiation dose is occurring. UNSCEAR acknowledges that "the dose and dose-rate region of main practical relevance in radiation protection (0-50 mSv per year) [0-5 rems per year] is characterized by small average numbers of tracks per cell with long intervals of time between them. Effects are, therefore, likely to be dominated by individual tracks, acting alone" (p.628/43). This is precisely the point made in Gofman 1990, p.20-7 .

• - (39) "Cells are able to repair both single- and double-strand breaks in DNA over a period of a few hours, but sometimes misrepair can occur" (p.625/28).

• - (40) "The extent to which radiation-induced DNA damage may be correctly repaired at very low doses and very low dose rates is beyond the resolution of current experimental techniques. If DNA double-strand breaks are critical lesions determining a range of cellular responses, including perhaps neoplastic transformation, then it may be that wholly accurate cellular repair is unlikely even at the very low lesion abundance expected after low dose and low-dose-rate irradiation" (p.634/74).

• - (41) "It is highly unlikely that a dose threshold exists for the initial molecular damage to DNA, because a single track from any ionizing radiation has a finite probability of producing a sizable cluster of atomic damage directly in, or near, the DNA. Only if the resulting molecular damage, plus any additional associated damage from the same track, were always repaired with total efficiency could there be any possibility of a dose threshold for consequent cellular effects" (p.636/84).

• - (42) "Biological effects are believed to arise predominantly from residual DNA changes that originate from radiation damage to chromosomal DNA. It is the repair response of the cell that determines its fate. The majority of damage is repaired, but it is

the remaining unrepaired or misrepaired damage that is then considered responsible for cell killing, chromosomal aberrations, mutations, transformations and cancerous changes" (p.680-681/323).

Part 4. NRPB 1995: Evidence "Falls Decisively" against a Threshold

In October 1995, Britain's National Radiological Protection Board released a 77-page report entitled "Risk of Radiation-Induced Cancer at Low Doses and Dose Rates for Radiation Protection Purposes" (NRPB 1995). Its five authors are Cox, Muirhead, Stather, Edwards, and Little.

- - (43) Chapter 2 of NRPB 1995 reviews the existing human epidemiologic evidence and concludes (p.25/61): "It is important to note that the studies of low-LET exposure considered in this chapter are consistent with a linear trend in cancer risks at low doses without threshold." This statement embraces the pneumothorax-fluoroscopy studies (p.13/23).

- - (44) Chapter 5 of NRPB 1995 reviews "Cellular and molecular mechanisms of radiation tumorigenesis." There, the authors also state the now-familiar definition of the lowest possible dose and dose-rate from ionizing radiation:

"It may be argued ... that a single radiation track (the lowest dose and dose rate possible) traversing the nucleus of an appropriate target cell, has a finite probability, albeit low, of generating the specific damage that will result in tumour-initiating mutation" (p.58/27).

- - (45) The authors consider existing evidence relating to the reduction of radiation risk by so-called cellular "adaptive" responses and immune-system responses. In particular, they discuss issues raised in UNSCEAR 1993 and in UNSCEAR 1994 (Annex B). The authors reach the same conclusion that we do: Such cellular responses do not provide any threshold dose with respect to post-repair genetic damage. NRPB concludes (p.75/21):

"Whilst adaptive responses or other protective mechanisms may influence the risk of tumour development, they do not provide a sound basis for judgement that tumorigenic response at low doses and low dose rates of radiation is likely to have a non-linear component which might result in a dose threshold below which the risk may approach zero."

4a. NRPB on Special Difficulties in Repairing Radiation Damage

The NRPB authors understand very well that failure of repair is the key to the absence of any threshold dose. The following excerpts from their 1995 report show they understand that ionizing radiation has the power to induce some UNREPAIRABLE damage to chromosomes and DNA, and that a difference exists between action by primary ionization tracks, and action by the free radicals which are produced by normal cellular metabolism (see p.292 of this book).

- - (46) "Radiation-induced damage to DNA nucleotide bases and to the sugar-phosphate backbone on one strand of the DNA duplex closely resembles the cellular damage that occurs through normal endogenous metabolic processes" (p.59/28).

"It is generally accepted that, in the absence of exogenous agents, each cell in the human body sustains 5,000 to 10,000 DNA damage events per hour [they cite Ames 1989 and Billen 1990], principally as a consequence of thermodynamic instability and attack by chemical radicals produced via endogenous biochemical reactions; this damage is believed to contribute to natural cancer risk" (p.59/29).

- - (47) "On this basis, arguments have been made [they cite Billen 1990 and Abelson 1994] that the small increment of additional cellular DNA damage resulting from low dose radiation exposure will have an insignificant effect on the frequency of gene and chromosomal mutations, and by implication, on cancer risk. This would be a valid hypothesis if the DNA damage resulting from spontaneous endogenous processes were to be IDENTICAL with that induced by ionising radiation. There is, however, strong evidence that this is not the case and, consequently, that the hypothesis lacks credibility" (p.59/30).

- - (48) "The vast majority of endogenous DNA lesions takes the form of DNA base damage, base losses, and breaks to one of the sugar-phosphate backbone strands of the duplex. Such single-strand DNA damage may be reconstituted rapidly in an error-free fashion by cellular repair processes ..." (p.59/31).

- - (49) "In contrast, although a single ionising track of radiation will also induce single-strand damage when an energy-loss event takes place in close proximity to one DNA strand, a cluster of such loss events within the diameter of the DNA duplex, of about 2 nanometers, has a significant probability of simultaneously inducing coincident damage to both strands. In support of this, an approximately linear dose-response for double-strand break induction by low-LET radiation is observed, confirming that breakage of BOTH STRANDS of the duplex may be achieved by the traversal of a SINGLE IONISING TRACK and does not demand multiple-track action ..." (p.59/32).

And:

"There is also evidence that a proportion of radiation-induced double-strand breaks are complex and involve local multiply damaged sites --- LMDS [they cite Ward 1991-a] ..." (p.59/32).

- - (49) "A given fraction of radiation-inducible double-strand damage will be repaired efficiently and correctly, but error-free repair of all such damage even at the low abundance expected after low dose exposure should not be anticipated" (p.60/33). And:

"Unlike damage to a SINGLE-strand of the DNA duplex, a proportion of double-strand lesions --- perhaps that component represented by LMDS --- will result in loss of DNA coding from BOTH strands. Such losses are inherently difficult to repair correctly, and it is believed that misrepair of such DNA double-strand lesions is the crucial factor underlying the induction of chromosomal aberrations and gene deletions that represent the principal hallmarks of stable mutations induced by ionising radiation of various qualities" (p.60/33). And:

"Double-strand DNA losses may in principle be repaired correctly by DNA recombination, but there is evidence that radiation-induced DNA damage may be subject to error-prone illegitimate DNA recombination which can result in the forms of gene and chromosomal mutations that are known to characterise malignant development" (p.60/33).

● - (50) "The importance of DNA double-strand damage and its repair for the radiation response of cells is further supported by studies indicating, firstly, that the repair of such damage is the principal determinant of dose and dose-rate effects after low-LET radiation and, secondly, that genetically determined cellular radiosensitivity is predominantly associated with deficiencies in DNA double-strand break repair. Finally, there is evidence that it is the difference in the QUALITY and not the QUANTITY of induced DNA double-strand lesions that principally provide for the increased biological effectiveness of high-LET radiation such as alpha particles compared with low-LET radiation such as x-rays and gamma rays; these observations are best explained by experimental and computational data indicating that, overall, DNA double-strand lesions in cells induced by high-LET radiation are more complex and less likely to be repaired correctly than those induced by low-LET radiation ..." (p.60/34).

● - (51) "In summary, a coherent argument may be assembled that at low doses and low dose rates of low-LET radiation, DNA single-strand damage either is repaired in an error-free fashion or is an insignificant component of tumour risk. For double-strand DNA damage, there is good reason to believe that repair has an error-prone mutagenic component irrespective of damage-abundance and, by implication, will, even at very low doses, contribute to tumour risk" (p.60/36).

● - (52) "It may be concluded ... that existing data from both in vitro and in vivo [radiation] studies support a linear rather than a threshold-type response for neoplasia-initiating gene mutations" (p.61/38).

4b. NRPB's Conclusion on a Threshold Dose

● - (53) "It is concluded ... that data relating to the role of gene mutations in tumorigenesis, the monoclonal origin of tumours, and the relationship between DNA damage repair, gene/chromosomal mutation and neoplasia are well established and broadly consistent with the thesis that, at low doses and low dose rates, the risk of induced neoplasia rises as a simple function of dose and does not have a DNA damage or DNA repair related threshold-like component" (p.75/21). And:

● - (54) The following statement by the NRPB authors is remarkably similar to paragraph 26 above:

"In consideration of a broad body of relevant cellular and molecular data, it is concluded that the weight of the evidence, in respect of the induction of the majority of common human tumours, falls decisively in favor of the thesis that, at low doses and low dose rates, tumorigenic risk rises as a simple function of dose without a low dose interval within which risk may be discounted" (p.68/80).

Comment:

In view of parts 2, 3, and 4 of this chapter, we hope that editors at JAMA, Lancet, and elsewhere will stop helping to distribute the deadly safe-dose fallacy.

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CHAPTER 46

"War in Britain": The Natl. Radiological Protection Board

- Part 1.** The NRPB's Effort to Protect Women from This Book
- Part 2.** NRPB's Extensive Consultation for Its Critique
- Part 3.** NRPB on Known Breast-Cancer Causes: What's on the List?
- Part 4.** Claim: Gofman Did Not Use the Latest Data
- Part 5.** Claim: Gofman Used Assumptions "Not Accepted" by Most
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- Part 7.** Claim: Gofman's Dose-Estimates for 1920-1960 Are Unreliable
- Part 8.** "If Gofman Were Right" We Should See Far More BC Than We Do
- Part 9.** NRPB Preference: Better to Use American Data
- Part 10.** NRPB on "Optimising" Doses: Talk vs. Action
- Part 11.** Claim: The Book Offers a "False Hope"

Part 1. The NRPB's Effort to Protect Women from This Book

How It All Began

In mid-April 1995, Mark Lewis and Julian Bellamy of 20/20 Television in Britain began to investigate the thesis of this book. They had received a copy carried from San Francisco to London by one of their colleagues. Mark (producer) and Julian (correspondent) prepare 28-minute investigative reports for the well-watched British television program called "The Big Story."

Mark and Julian accepted NONE of the book "on faith," for they are hard-nosed skeptics whose first rule is never to be manipulated or fooled by anyone who might appear in one of their reports. I began getting questions from them in late April, after experts at the NRPB told them that I was "wrong by 100-fold." My impression, by telephone, was that Mark and Julian were highly suspicious of both me and NRPB.

The decision actually to build a report around the book was not made until later. During the intervening weeks, I was providing Mark and Julian with scientific papers and answers to every objection they heard on three continents. They were transmitting to me many scientific assertions which the makers declined to put into writing. They seemed exceedingly suspicious of experts who would not stand behind their claims.

Meanwhile, we were shipping books for peer-review. NRPB received one from us by Express Mail on May 25th.

1a. Should This Program Be Banned?

After a tentative decision to do a program, Mark and Julian asked the NRPB to participate and to present its own position. The NRPB declined in writing, with the following statement which was included prominently in the final program: "We feel Dr. Gofman's work is so poor that we do not want to be associated with it by appearing on the program. His track record has no impact on other professionals."

But Mark and Julian had independently checked on my "impact" (for example, see Chapter 43, Part 4). They were not deterred. They just continued to read the scientific literature, to interview experts everywhere, and to bombard me with scientific questions. After a while, they displayed an amazing grasp of the topic --- far, far better than most radiologists and greater even than many epidemiologists. The broadcast was planned for late July or early August. Mark and Julian continued to urge the NRPB to participate in the program.

But the NRPB had other plans. It tried to stop the broadcast, according to a news story in the London Express by Paul Crosbie, on August 3. The program was scheduled for broadcast at 7:30 pm on August 3. The huge headline on Crosbie's report is, "Doctors' outcry over X-ray link to breast cancer; Call for ban on TV show." According to Crosbie:

"The decision to show the programme has been condemned by scientists and doctors in Britain." And:

"The national radiation watchdog, the National Radiological Protection Board, urged ITV chiefs to halt the broadcast. It called the professor's claims 'alarming, unsound, and misleading.' The NRPB said showing the programme could cause women unnecessary anxiety and disrupt screening for the early detection of breast cancer."

1b. An "Unprecedented Step" by the NRPB

All the "outcry" was set in motion by the Head of NRPB's Medical Department, Dr. Chris Sharp. On July 11, 1995, Dr. Sharp signed a "Dear Colleague" memo on NRPB letterhead. It begins:

PREVENTING BREAST CANCER – JOHN W. GOFMAN

"The Royal College of Radiologists has agreed, in principle, to join with the NRPB in briefing media journalists prior to transmission of the 20/20 TV programme on the risks of medical radiology relating to breast cancer and, if necessary, to arrange a Press Conference on the day after transmission – in which the Department of Health would participate." And:

"I attach the draft material on which NRPB would wish to base oral briefings to individual newspaper journalists. The material is in 2 parts: the first two pages are a fairly simple statement of the main points with the important sections bolded for the journalists to use as quotes. The remaining three pages are a more detailed brief to give background should they want it." The five pages for the press are in single-spaced rows. NRPB's draft press handout winds up as follows:

"The Board wishes to reassure women, in particular, that Professor Gofman's claims are unsound, inaccurate, misleading and unnecessarily alarmist and should not dissuade them from accepting X-ray procedures to detect or assist in the treatment of serious or significant disease. However, NRPB continues to encourage all medical practitioners to only use diagnostic X-ray procedures when justified and to keep exposures as low as reasonably practicable, even though the risks are small."

The NRPB's pre-broadcast campaign was acknowledged by Dr. Sharp and his assistant, Dr. John Harrison, in a joint letter published by the British Medical Journal, November 11, 1995. Defending NRPB's failure to participate in the 20/20 program, they wrote: "The board [NRPB] distributed a detailed scientific critique of Gofman's work to the media." (See Part 1c, below.)

Stories began appearing in the newspapers on July 27: "Cancer link with X-rays 'alarmist'" by the science editor of the Daily Telegraph. "X-ray link to breast cancer 'misleading'" by Liz Hunt, the medical correspondent of the Independent. Ms. Hunt wrote:

"In an unprecedented step, the National Radiological Protection Board took action to discredit the claims by Professor John Gofman of the University of California, Berkeley, who features in a television programme to be broadcast next week." On August 3, there were many additional stories, including "Doctors' outcry" about the attempted ban.

In the end, the NRPB's "war" to protect women from our work had one very educational effect: Often for the FIRST TIME, many science and medical reporters, as well as the women who do not watch "The Big Story," heard a well-established fact --- medical x-rays are a proven cause of breast cancer. In addition, millions watched the program. (Its title: The X-Ray Effect).

1c. The Official NRPB Critique, and Our Request to Dr. Sharp

The NRPB publishes the Radiological Protection Bulletin. Its August 1995 issue devotes 2.5 pages to a critique of this book. The Bulletin critique is almost identical to the critique prepared for the press. The Bulletin critique is authored by Dr. Colin Muirhead, head of epidemiology at NRPB, and Dr. Chris Sharp, head of the medical department at NRPB, so their critique is Muirhead 1995 in our Reference list.

On August 23, 1995, I faxed Dr. Sharp to make arrangements for my response in the Bulletin. I reminded him that "It is customary for any Journal to provide a reasonable space for response to an article such as yours, which is an attack on many points in my book."

On August 23, 1995, Dr. Sharp faxed his reply: "The Bulletin is not a peer-reviewed publication, but primarily the means to express to a wider audience NRPB's interpretation of developments in the science of radiological protection. It is therefore not our normal practice to publish letters in discussion of our articles."

Our attitude is this: Women and their families deserve experts who care enough to push toward a RESOLUTION of this issue. When the issue is the main cause of breast cancer and its consequent prevention, attempts to suppress exchange among peers are especially appalling.

Some Very Consequential Errors by Muirhead and Sharp

Muirhead and Sharp offer one argument in their critique which CONFIRMS our estimate (see Part 8b, below). When they try to use the argument AGAINST our estimate, it's a surprise. And we think they make additional errors, three of which will be easier for readers to comprehend than the others (Parts 5b, 5c, and 7). Muirhead and

Sharp present no information which was not already considered by us when we did the First Edition. We explained, especially in Chapter 40, our considerations and judgments on the points which are unknowable by anyone.

We take up the NRPB's points in their printed order, for the remainder of this chapter. Page-references to our First Edition are the same in the Second Edition.

Part 2. NRPB's Extensive Consultation for Its Critique

The introductory paragraph of the NRPB critique asserts that "Gofman's claims could cause widespread anxiety among women if publicised widely in the media and could dissuade them from accepting procedures beneficial to their continuing good health. The potential effects of the book are significant and it is felt that an article rather than the normal book review is appropriate." And:

"The purpose of this article is therefore to discuss the basis of Gofman's claims and highlight where his calculations of risk differ from those published by NRPB and others for female populations exposed to medical x-rays. In writing this article, we have conferred with colleagues in the Radiation Effects Research Foundation and the US National Cancer Institute and with members of the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR)."

Comment on Female Anxiety

We too, like the NRPB, are eager to make it clear to women that our findings do NOT mean that they should reject all uses of medical x-rays. So, we made the point clear even on the rear cover of the First Edition! We quote from the rear cover:

We have often been asked the question: "Have Medical X-Rays Done More Harm Than Good?" That is the WRONG question. The appropriate question is, "Can we have all the good things in medicine which x-rays can do with vastly less harm?" The answer is unequivocally, "Yes" ... We hope that all physicians will join with health scientists in a determination to reduce unnecessary x-radiation. As discussed in this book, this effort can succeed without ever interfering with a single essential x-ray examination. (End of quotation from the rear cover.) Also, we made the same points in Chapter 1 (on its first page) and in Chapter 42 (on its first page, followed by details).

Was it accurate for the NRPB to tell medical and science reporters (and thus the public) that our work was "unnecessarily alarmist?" Obviously not. We note that this phrase (see Part 1b, above) was edited out of the Bulletin version of NRPB's critique.

Comment about Worldwide Consultation

Muirhead and Sharp state that they conferred with various peers at RERF, NCI, and UNSCEAR in preparing their critique. In other words, they confirm our statement in Chapter 43 that this work is in the process of very wide peer-review indeed --- just as we intended.

Part 3. NRPB on Known Breast-Cancer Causes: What's on the List?

NRPB's introduction is followed by a section which names known causes of breast cancer. "Breast cancers occur more frequently with increasing age, being relatively rare below the age of 35 years and increasingly common over 50 years. A range of

epidemiologic studies has positively established that the occurrence of breast cancer is related to [and here, for clarity, we will subdivide NRPB's single paragraph]

- reproductive factors: the age of the woman at the time of birth of her first child and the age at which her periods start (menarche) and her age at menopause;
- a family history of breast cancer;
- the occurrence of previous benign breast disease;
- exposure to ionising radiations (x-rays and gamma rays)."

Comment about Non-Radiation Causes of Breast Cancer

We have no disagreement with NRPB about this list. It may be too short, however.

Many people who only hear of our 75-percent estimate for radiation (but who have not seen the book) assume that we have ruled out important roles for any other cause. Not so. Our finding is fully compatible with important roles for other factors --- as we emphasized in Chapter One (Part 5), Chapter 40 (Part 3), and Chapter 41 (Part 2) of the First Edition. Also, now, in Chapter 47 (Part 7).

Comment on Inclusion of Radiation

NRPB's inclusion of ionizing radiation, in a very short list of known causes of breast cancer, affirms our statements that radiation-causation is an undisputed fact among experts in the field.

Another 1995 affirmation, more readily available to readers in the USA, is the giant medical text entitled "Cancer of the Breast: 4th Edition," edited by William L. Donegan, M.D., and John S. Spratt, M.D. (Donegan 1995). In Chapter 8, which they wrote themselves, Spratt and Donegan state:

"The capacity of ionizing radiation to produce breast cancer has been repeatedly confirmed" (p.131). After this statement, they cite much of the same evidence flagged in our Reference list.

Part 4. NRPB Claim: Gofman Did Not Use the Latest Data

Now we arrive at NRPB's first science-based complaint about the First Edition of this book. The complaint comes with three parts, which we will label "a, b, c" (not so labeled in the original). Muirhead and Sharp say (p.12):

"Significantly, he [Gofman] (a) has not used the latest breast cancer incidence data from the A-bomb survivors. Instead he uses older mortality data for all solid cancers and (b) [he uses] the T65D radiation dose estimates, which have now been superseded. In transferring risks from the Japanese to the American population, (c) Gofman has also apparently not relied upon recent data on baseline breast cancer rates in the two countries, but upon data from some 30 years ago. This is particularly inappropriate as many of the breast cancers in the A-bomb study have occurred only in recent years."

Response to (a): Old data not specific to breast cancer

This claim would sound very different if Muirhead and Sharp had told the correct story. In addition to using mortality data for all cancers combined, we did employ the

newest breast-cancer data from the A-Bomb Study in arriving at our risk-estimates. In fact, we used TWO separate reports. In Chapter 3, p.14, we cited both Thompson et al 1994, and Tokunaga and Land 1994, and we used information from both studies in our Chapter 40 (pp.278-279, and 282-283). Our decision to start our analysis with the all-cancer mortality data is related to part (b) of NRPB's complaint.

Response to (b): "Superseded" T65D Dose-Estimates

The comment by Muirhead and Sharp, about the "superseded T65D radiation dose estimates," identifies a fundamental difference between myself and NRPB about how properly to handle proposed revisions of dosimetric estimates. A large part of my 1990 book showed why the T65D dose-estimates for the A-Bomb Study can not just be jettisoned and superseded by an illegitimate, shuffled set of data.

With perpetual reshuffling of the A-bomb database, after results are in, "researchers" could find just about ANY answers which would please them or their sponsors --- which are the Japanese and United States governments. That is why a fundamental anti-bias rule in prospective biomedical research is that you can SUPPLEMENT your original study as it progresses, but you must also reveal what the follow-up shows in the unaltered, legitimate database. If researchers could conceal unwelcome results just by labeling them "superseded," we would really have reached Orwellian, non-credible, worthless science.

No one (myself included) wants to "ban" corrections and improvements in any study --- indeed, we warned about dosimetry errors in the A-Bomb Study (Gofman 1981). New dose-estimates were released by Japan and the United States in 1986 (so they are called "DS86" estimates). And in 1990, our book demonstrated the scientifically proper way to use them, in parallel analysis with the T65D estimates. Our method, called "constant-cohort, dual-dosimetry," rules out bias but includes the revised dose-estimates.

We demonstrated in Gofman 1990 that PROPER use of the new DS86 dose-estimates, without retroactive shuffling of the cases, gives virtually the SAME answer as the original T65D database. It is the unnecessary and improper case-shuffling, done by the radiation establishment, which has the effect of REDUCING risk-estimates from the database (and helping the sponsors).

The A-Bomb Study has been a unique biomedical treasure for all humanity, but the Orwellian handling of its "superseded" past is threatening to ruin its credibility. It is high time for analysts at the NRPB and other bodies to "stick their necks out" just a little to assure that the A-Bomb Study retains a permanent anchor in the T65D cohorts, with parallel analyses using both the T65D and the contemporaneous dose-estimates for direct comparison.

Response to (c): Baseline Data from 30 Years Ago

At issue is the DIFFERENCE in observed vulnerability of American women and Japanese women to breast cancer (see p.280). The gap has been decreasing over time (see p.281). By vulnerability, we mean the integrated tendency to develop breast cancer from any and all causes, as reflected in breast-cancer rates.

It is an amazing phenomenon for Muirhead and Sharp to discuss what we "apparently" did about the date of our baseline rates for breast-cancer in the USA vs.

Japan. On page 280, we explicitly provided the date (1964–1965), the sources, and the reason: 1964–1965 is approximately the midpoint of the follow-up period of the A-Bomb Study.

Our choice of 1964–1965 ("30 years ago") is called "particularly inappropriate" by Muirhead and Sharp, and they hint that breast-cancer rates from "recent years" would be the appropriate choice. Did they back up either idea with any references to evidence? No.

Here is everyone's problem. The A-bomb survivors received their bomb-exposure in 1945. That is the year in which their radiation-induced cases of breast cancer were "put on the shelf for delivery later" (see Chapter 4). For women of equal age in 1945, is the delivery-response per rad of exposure likely to depend more heavily on the existing vulnerability to breast cancer at the time of their IRRADIATION, or more heavily on their vulnerability at the time of DIAGNOSIS, or most of all on their vulnerability during their various latency periods? We can not answer the question. No one can.

We chose to apply the "midpoint" 1964–1965 ratio, as an approximation of the relative vulnerability to breast-cancer in the USA versus Japan, and we make the assumption that this relative vulnerability affects the response to radiation received in the 1920–1960 period of our analysis.

Muirhead and Sharp claim that they know better, when they denounce our choice of the 1964–1965 ratio as "particularly inappropriate." They hint that use of a "recent" ratio of USA/Japan breast-cancer death-rates would be appropriate. Later, they use the 1990 ratio. The Muirhead-Sharp assumption gives a lower risk-estimate than our assumption (see Part 6b).

In contrast to their inappropriate certainty about our assumption, we feel some humility about biomedical mysteries which remain to be solved, so we wrote in the First Edition, at page 281):

"At this time, we think the 5.67 ratio of background breast-cancer mortality-rates (USA / Japan, in the mid-1960s) is the most reasonable approximation to use in our conversion-factors. As additional evidence develops, it may point to other ways to handle country-to-country 'transport' of observations. Meanwhile, we keep an open mind toward a variety of old and new hypotheses about the actual process of radiation carcinogenesis, including interaction between radiation and other factors."

Part 5. Claim: Gofman Used Assumptions "Not Accepted" by Most

"A number of assumptions are made in the book to calculate risk which are not accepted by most of the scientific community" (Muirhead 1995, p.12). This claim also comes in three parts. No part is based on assumption. We go with the existing EVIDENCE, whereas the radiation establishment makes some non-protective assumptions. A non-protective assumption is one which can operate to increase cancer in the population.

5a. The Shape of the Dose-Response

According to Muirhead and Sharp (p.12), our first "assumption" is that "low doses are twice as effective at inducing cancer when compared with high doses --- this is not

consistent with analyses of the A-bomb data which show a linear trend in the risk of solid cancers with dose ..."

Response:

The meaning of a linear dose-response is that one rad has a fixed, unchanging carcinogenicity regardless of dose-level. By contrast, supra-linearity means that each incremental rad is less carcinogenic as dose rises; low-dose rads are more potent than high-dose rads.

The evidence from the A-Bomb Study for all cancer-sites combined, both in the legitimate T65D dosimetry AND in the supplemental DS86 dosimetry, fits a supra-linear dose-response provably better than it fits a linear dose-response --- if the DS86 dose-estimates are properly used (without retroactive shuffling of the cancer cases). See Part 4b. Our claim, above, is demonstrated step-by-step in Gofman 1990, from raw-data to conclusion, with no mystery-gaps.

How do the NRPB and other government committees manage to miss the supra-linearity? They embrace the retroactive shuffling of the cancer mortality cases.

There is something additional for NRPB to explain, when it attacks supra-linearity as an "assumption" at variance with the evidence. In the A-Bomb Study, the latest INCIDENCE data specifically on BREAST cancer are depicting SUPRA-LINEARITY at page S26 of the 1994 Thompson study --- as we noted on page 277 of the First Edition. Muirhead and Sharp are silent on this.

The North American Studies

Muirhead and Sharp assert (p.12) that "women irradiated for medical reasons in North America" show a linear (not a supra-linear) dose-response. Fortunately, it is impossible to obscure the important contribution of those North American studies in helping to settle the threshold issue, as shown in Chapter 45, Part 2d. Beyond that function, however, the utility of those studies is very limited, for the reasons given in Part 9 of this chapter.

5b. The Issue of Low Dose-Rate

According to Muirhead and Sharp (p.12), our second "assumption" is shown when we use "no reduction in stochastic [cancer] risk for low dose rates – both NRPB and ICRP calculate the risks at both low doses and low dose rates to be half of that at high doses and high dose rates." Muirhead and Sharp want us to assume that each rad received from medical x-rays is only HALF as carcinogenic as each rad received by the A-bomb survivors, because of a low dose RATE.

This is a really bizarre comment, since the medical patients in our study and the A-bomb survivors both received their rads at ACUTE rates, not low rates. Why on earth would a reduction in risk "for low dose rates" even occur to Muirhead and Sharp when medical radiation overwhelmingly dominates our Master Table? We wondered if this allusion to RATE was just an editorial error at NRPB. Apparently not. We find the same substance in the NRPB pre-broadcast memo where NRPB says Gofman makes the "assumption" that "radiation given at low dose rates is equally capable of inducing cancer as those [sic] given at high dose rates."

A Non-Protective Assumption by NRPB and Other Protective Bodies

We need to add a comment about "assumption" here. There is no human

EVIDENCE to support any reduction in risk-values for low doses, delivered EITHER fast or slow in the circumstances at issue here. Moreover, there is no need to extrapolate from high doses to low doses, when the A-Bomb Study provides statistically significant evidence of excess cancer all the way down to about 11-15 rads of exposure. All this is extensively shown, including the raw data themselves, in Gofman 1990.

NRPB claims repeatedly that the human evidence fits a LINEAR dose-response (in NRPB 1993, NRPB 1995, Muirhead 1995).

By DEFINITION, linearity means that the risk per rad is identical at low doses and at high doses. Yet Muirhead and Sharp admit (p.12) that NRPB calculates risk "at both low doses and low dose rates to be half of that at high doses and high dose rates." Then overriding the NRPB's claim that the human evidence shows linearity, the NRPB and ICRP substitute an ASSUMPTION --- an assumption which produces lower risk-estimates and thus POORER protection of the public, by a factor of two here. The BEIR-5 Committee does it too.

5c. The Potency of X-Rays vs. Gamma Rays

According to Muirhead and Sharp (p.12), our second "assumption" is that "x-rays are twice as effective as gamma radiation at inducing cancer - this is not supported by comparisons between North American studies (x-ray exposures) and the A-bomb study (mainly gamma)."

Response:

Muirhead and Sharp do not reveal that the North American studies differ among themselves too much to elucidate the issue at all. For example, the Nova Scotia study shows a risk per rad SIX TIMES what the other North American studies show. Against such variation, no one can rationally try to settle the gamma / x-ray difference.

However, we did not just "assume" the two-fold difference. We used the existing EVIDENCE from very mainstream sources, listed below in chronological order. (The usual details are in our main list of References.)

- - 1978, Bond et al, in Health Physics.
- - 1985, Sinclair in Radiation Protection and Dosimetry.
- - 1986, ICRU (International Commission on Radiation Units and Measurements), in its Report 40.
- - 1988, Kerr in Health Physics.
- - 1990, BEIR-5 Report from the National Academy of Sciences, USA.

And new, since the First Edition of this book went to press:

- - 1995, Lucas et al, in Health Physics (see Figure 3).

Surely, the explicit, easily readable statements in BEIR-5 (which NRPB quotes often in its own reports) cannot have escaped Muirhead and Sharp. We quote the statements on this issue from BEIR-5, p.218:

"The general applicability of the experience of the Japanese A-bomb survivors is uncertain on additional grounds. Most human exposures to low-LET ionizing radiation are to x rays, while the A-bomb survivors received low-LET radiation in the form of high energy gamma rays. These are reported to be only about half as effective as ortho-voltage x rays (ICRU 1986). While that is not a conclusion of this Committee,

which did not consider the question in detail, it could be argued that since the risk estimates that are presented in this report are derived chiefly (or exclusively) from the Japanese experience, they should be doubled as they may be applied to medical, industrial, or other x ray exposures."

Another Non-Protective Assumption by the NRPB

The apparent scandal is that the NRPB makes NO USE of the listed evidence. The NRPB appears to assume that all the evidence cited above is inferior to the non-appropriate evidence on which it relies. By invoking this assumption, the NRPB arrives at lower risk-estimates and thus POORER protection of the public, by another factor of two here. While the NRPB proclaims its desire to prevent public anxiety, we are seeing in the same article how it actually arrives at soothing reassurances. The public might be fascinated by this amazing new facet of protection from radiation.

Part 6. Claim: Gofman's Risk-Factors Too High by at Least 10-Fold

"Overall, Gofman's risk estimates are at least 10 times higher than those calculated by NRPB for a UK population ..." (Muirhead and Sharp, p.12). We agree that our estimates per rad are indeed at least ten times higher than those of the NRPB and similar radiation bodies. They use retroactively shuffled data, they invoke non-protective assumptions (see also Part 9), and they indulge in scientifically questionable practices which are fully detailed in Gofman 1990.

Muirhead and Sharp try to QUANTIFY how our per-rad breast-cancer risk becomes higher than theirs: "The reasons, and scale of attributable difference, appear to be [and now we subdivide their paragraph, and we add letters to facilitate discussion]

- (a) – older Japanese data, not specific for breast cancer --- risk increased 1.35 times;
- (b) – old baseline rates for breast cancer in the USA and Japan --- risk increased by 1.6 times;
- (c) – higher values for the effects of x-rays compared with gamma radiation --- risk increased 2 times;
- (d) – higher values for the effects of low doses, low dose rates and fractionation – risk increased about 4 times." End of quotation.

Response to (a): Older data

Our reduction of the mortality data for all solid cancers, into the component for breast-cancer, was perfectly appropriate. Although the data are a few years older, they are valid forever, because dead people do not come back to life. Our decision to use the slightly older data allowed us to use the legitimate, unshuffled cohorts --- not the illegitimate, retroactively shuffled data used by NRPB and the other radiation committees. Properly handled, the old and new dose-estimates yield almost identical risk-estimates (see Part 4b). So NRPB's risk-estimates SHOULD rise by this factor of 1.35.

Response to (b): Transport Factor from Japan to USA

Where does this factor of 1.6 come from? Muirhead and Sharp derived it from our Chapter 40, as follows.

• - On page 280, readers will see that in 1964–1965, the breast-cancer death-rate per 100,000 females was 21.55 in the USA versus 3.80 in Japan. That ratio is (21.55 / 3.80), or 5.67.

• - On page 281, in the box, readers will see that in 1988–1991, those rates had changed to 22.4 in the USA and 6.3 in Japan. That ratio is (22.4 / 6.3), or 3.55.

• - Muirhead and Sharp claim that I should have used the smaller ratio (see Part 4c). Our use of the higher ratio yields a risk-value which is (5.67 / 3.55), or 1.6 times higher than use of the lower ratio. That is where the factor of 1.6 originates for Muirhead and Sharp.

Unlike Clark Heath (Chapter 44, Part 3), Muirhead and Sharp do not challenge the use of SOME ratio, for transport of results between these two countries. Heath claims that our factor of 5.67 introduces a 6-fold error, and that the right factor would be 1. Muirhead and Sharp clearly indicate, with their 1.6 factor, that they would have used 3.55. We used 5.67. We discussed the basis for our choice in Part 4c above. We would make the same choice again if we were starting today. But this is a point on which NO ONE can be certain. Therefore, we would not claim that NRPB's preference for 3.55 is wrong. Conversely, NRPB would not be entitled to suggest that our choice of 5.67 is wrong.

Response to (c): X-Rays vs. Gamma Rays

NRPB should be embarrassed to have raised this issue, as explained in Part 5c. NRPB's risk-estimates for medical x-rays SHOULD rise by this factor of 2. Clark Heath (Heath 1995) did not make this error.

Response to (d): Low Doses and Low Dose-Rates

The factor of 4 consists of two factors of 2 each.

The first factor of 2 for low-doses represents (correctly) the difference in per-rad risk at low doses between the supra-linear dose-response demonstrated from the legitimate, unshuffled cohorts of the A-bomb survivors, versus the linear dose-response derived from the illegitimate, retroactively shuffled database of the A-bomb survivors. So NRPB's risk-estimates SHOULD rise by this factor of two.

What about the additional factor of 2 for low-dose RATES? Again, the NRPB should be embarrassed to have raised this issue, as explained in Part 5b. Clark Heath (Heath 1995) did not make this error. The NRPB's own risk-estimates SHOULD be raised by this factor of 2.

Part 7. Claim: Gofman's Dose-Estimates for 1920–1960 Are Unreliable

Muirhead and Sharp say (p.12): "Gofman also makes his own estimates of medical doses to the female population of the USA in the period 1920 to 1960. These doses are based on extrapolations from local surveys in the USA to medical practices throughout the country. Such calculations will inevitably contain large uncertainties which make the calculated collective doses to patients unreliable. This considerably undermines the assessment of the total number of breast cancers induced by medical exposures ..."

Response:

Yes, we emphasize repeatedly in the book --- with a summary in Chapter 38 --- that the uncertainties are so large that the TRUE past average annual doses may well have been two to four times HIGHER than the estimates we used. BUT THEY CAN NOT HAVE BEEN LOWER! And we show amply why. Why did Muirhead and Sharp fail to mention that our calculations do not even include breast exposures from most of the diagnostic and interventional fluoroscopy, from mammography, from treatment of skin disorders, and from the treatment of dozens of inflammatory diseases?

Is it just an oversight for them to raise the dose-issue --- and then NOT to reveal that the uncertainties work very strongly in FAVOR of our 75-percent estimate?

Part 8. "If Gofman Were Right" We Should See Far More BC Than We Do

Muirhead and Sharp allege (p.13): "As well as being inconsistent with current knowledge, Gofman's risk estimates are inconsistent with the actual occurrence of breast cancer in the American and A-bomb study groups ... In essence, if Gofman was right, then far more women who were exposed to high medical doses in the USA would have developed breast cancer than actually have." In support of that assertion, Muirhead and Sharp (p.13) cite three pairs of figures and make two comparisons.

8a. Every Word of the Faulty NRPB Assertion

We will show below that one of their two comparisons would CONFIRM our estimate, and that the second comparison obviously fails to meet a passing grade in basic epidemiology. At the outset, we set forth their three pairs of figures (doses and percentages), which they presented where we used three dots above.

(a) Fluoroscoped TB patients, USA:

Dose = ~ 79 rems. Share of Breast-Cancer due to radiation = 30 percent.

(b) A-Bomb Survivors, Japan:

Dose = ~ 25 rems. Share of Breast-Cancer due to radiation = 30 percent.

(c) Gofman Analysis (see p.267, Column T, and p.285 at the top):

Dose = ~ 28 rems. Share of Breast-Cancer due to radiation = 63 percent.

Now we will fill in the exact words of Muirhead and Sharp, where we had the dots above: "In the study of women who received high medical doses during fluoroscopic procedures for TB in the USA, the proportion of breast cancers attributable to radiation is about 30% (average radiation dose of about 0.79 Sv) and in the A-bomb survivors study also about 30% (average dose of about 0.25 Sv). However, Gofman attributes 75% of breast cancers in the American population to radiation, based on his calculated average dose of about 0.28 Sv." Then follows "In essence," as quoted above. We have omitted not a single word.

8b. NRPB's Unintended Confirmation of Our Result

We begin by explaining NRPB's third dose figure. The average dose of 28 rems (0.28 Sv) refers to this book at page 267, where we add up the annual breast doses in Column T of the Master Table --- in medical rads. This total is 28 medical rads for

someone who received the listed exposures for 64 years, starting at newborn-age. It is the average dose accumulated in 64 years of life by ALL women which would produce 114,300 breast-cancers per year at equilibrium (p.268).

NRPB's second dose figure of 25 rems (0.25 Sv) is presented as the average dose in the A-bomb survivors --- the study which DOES cover all ages at exposure. Without endorsing that dose-value, we can say that it is not converted to medical rads --- because NRPB rejects that factor of 2, as discussed in Part 5c. And NRPB is mistaken on that.

Because medical x-rays are twice as injurious as bomb-radiation, it means that HALF the dose from medical x-rays would have produced the SAME results cited by Muirhead and Sharp. So, NRPB's average Japanese dose must be corrected to just 12.5 MEDICAL rads before it can be compared with the results of our analysis.

And NRPB says that this dose accounts for 30% of the breast cancers. If those cancers have been estimated for a full lifetime follow-up of all ages at bombing, then it is appropriate for Muirhead and Sharp to make a comparison with our estimate (c). Indeed, it would be absurd for them to offer the comparison at all, unless it includes a lifetime projection --- as ours clearly does.

The claim by Muirhead and Sharp is that our work is "inconsistent" with the "b" figures. Hardly! One could barely imagine a better match:

If a dose of 12.5 medical rads accounts for 30% of breast cancer in the A-Bomb Study, and if the radiation dose is 28 medical rads in our analysis, then this type of comparison means we would expect our dose to account for $(28 \text{ rads} / 12.5 \text{ rads}) \times 30\%$ percent, or 67.2 percent of breast cancer. We estimate 63 percent (p.285, top). This is a fabulously close match. And without our APPROPRIATE adjustment for medical rads, the difference would be two-fold, not "at least ten-fold" --- as Muirhead and Sharp claim elsewhere (Part 6).

With the appropriate adjustment for medical rads, the NRPB's comparison SUPPORTS our finding.

8c. NRPB's Second Comparison

We wonder how our peers at the NRPB could have imagined that the "a" figures above, from the fluoroscopy study, could possibly be compared with the "c" figures from this book, to back up their charge that this book is "inconsistent" with existing evidence. The comparison would be scientifically invalid and meaningless, even though both dose-estimates are in MEDICAL rads. Why?

It's a comparison of "apples with oranges," as we say. The first rule of epidemiology is that groups compared for radiation-response must be COMPARABLE --- most especially in follow-up time and age-distribution.

We do not know if Muirhead and Sharp adjusted the observations in the fluoroscopy study (USA) for the full lifespan. In any case, the bigger problem in this particular comparison is the age-distribution.

The "women who received high doses" did NOT INCLUDE ANY INFANTS OR CHILDREN, who make a large contribution to the total of our estimate (see p.268). Even for the limited age-band of fluoroscoped females, the frequencies of ages would have to be adjusted to be like the general population, before comparison with any PART of our

Master Table --- much less with the sum of the entire Master Table. How could peers at the NRPB offer such an inappropriate comparison?

Part 9. NRPB Preference: Better to Use American Data

"Risks of radiation-induced breast cancer calculated for the UK population by NRPB are based on studies in the American women with x-ray exposures for medical reasons, specifically those who underwent multiple fluoroscopies for TB and therapeutic irradiation for acute postpartum mastitis. These data were used by NRPB, not because of any doubts about the credibility of the data on the Japanese A-bomb survivors, but rather because there is uncertainty about how to transfer breast-cancer risks from a Japanese to a western population" (Muirhead 1995, p.13).

We agree that there is uncertainty on this point --- as we made amply clear in the First Edition (Chapter 40, Part 3).

Why do Muirhead and Sharp not admit that there is at least equal uncertainty inherent in using the studies which NRPB used?

The two biggest uncertainties inherent in the American studies come from the fact that (a) they lack information on many age-groups, including the young, and (b) they differ in risk-values among themselves by six-fold. This revelation requires just a single sentence, but none is present in the Muirhead-Sharp critique. Considering both (a) and (b), we do not agree with NRPB's preference for the American data over the Japanese data on breast cancer.

A Very Non-Protective Use of the North American Data

When Muirhead and Sharp refer to NRPB's use of "American" studies, they mean North American (see NRPB 1993, p.66/61). In the USA, the BEIR-5 Report (1990) also makes use of the North American studies --- selectively. The BEIR-5 Committee just discards the studies which show the six-fold higher risk. We quote from BEIR-5, p.255:

"Within the Canada-TB cohort, the estimated risk per Gray for women treated in Nova Scotia was about six times that for women treated in other provinces. This difference is highly significant ($p < 0.001$) ... the higher risk observed among Nova Scotia women is not attributable to non-linearities in the dose response. Since there is currently no explanation for the difference within the Canadian-TB cohort and since the Committee was generally interested in low dose effects, it was decided to use the data on the Canadian-TB cohort without the Nova Scotia women, as the basis for risk estimates in the parallel analysis."

The excuse about "low dose effects" is unconvincing, to say the least, since the Nova Scotia Study was itself a low-dose study. The average dose per exposure was 7.5 rads (cGy) --- as discussed in our Chapter 45, Part 2d, paragraphs 14-17.

A Warning for the General Public

The effect of discarding the Nova Scotia Study is to UNDERESTIMATE the risk of breast cancer, per rad of radiation exposure, by a lot. Although NRPB 1993 does not reveal if it, too, discarded the Nova Scotia Study, it appears to embrace the same exclusion by not rejecting it (NRPB 1993, p.58/31). But we can not be absolutely sure what NRPB did. Our warning, therefore, may apply more to American than British people.

And our warning is this: Remember the Nova Scotia Study. Do not assume that the BEIR-5 committee --- or any other radiation committee or institute --- invariably puts protection of your health ahead of the needs of the radiation community from which its members so often come.

Part 10. NRPB on "Optimising" Doses: Talk vs. Action

Near the end of their critique, Muirhead and Sharp write (1995, p.13): "Professor Gofman's book is ingenuously written, persuasive, and easily readable by the non-expert. His main message, that all clinicians must justify exposures and optimise the doses, are those firmly held and preached by all in medical radiological protection."

We note that Muirhead and Sharp claim only that people in radiological protection PREACH the policy of preventing unnecessary radiation exposure of patients today. Muirhead and Sharp evade any claim about execution of the policy. They probably knew (they should have known) what Mark Lewis and Julian Bellamy learned as they prepared the 20/20 broadcast:

The radiation dose, for the same x-ray exam, varies from one British facility to another by up to 50-fold, according to an NRPB source. Yes, some variation is unavoidable. For instance, patients vary in their thickness. But such factors do not justify a variation as large as 50-fold. Such a great variation for the same common exam indicates that some patients are receiving higher radiation doses than necessary to obtain the medical information.

Any radiation above the amount necessary for a good x-ray picture is simply radiation going into unnecessary cancer-production. A RISK of unnecessary radiation-induced cancer per patient, times millions of patients, is a RATE of real and unnecessary cancers for a nation. We have already written about this deadly carelessness in Chapter 42. And in Chapter 48, we are adding even more information (from UNSCEAR 1993).

The PB in NRPB stands for "Protection Board." If the NRPB would replace its PREACHING with a verifiable PROGRAM to eliminate unnecessarily high medical exposures, we would be happy to join publicly with NRPB in relieving any unwarranted anxiety about x-ray overdoses in Britain. But let's not issue pseudo-assurances at a time when some anxiety about overdosing would be a healthy phenomenon.

Part 11. Claim: The Book Offers a "False Hope"

Muirhead and Sharp wind up their critique (1995, p.13) as follows: "It is ... particularly lamentable that he [Gofman] should claim that medical radiology is the dominant cause of breast cancer, based on unjustifiable calculations, in order to promote these aims [optimised doses]. The most likely effects will be to discourage women from accepting clinically necessary exposures, increase anxiety in an already uncertain world, and hold out a false hope that cumulative dose reduction will dramatically reduce the incidence of breast cancer in the future."

Muirhead and Sharp claim that our 75-percent estimate is based on "unjustifiable calculations," and yet they have failed to discredit even one ingredient in those calculations. While trying, they revealed NRPB's use of clearly non-cautious assumptions

for radiation protection (especially Part 5c), they revealed what looks like bias (Part 7), and they even managed to produce an argument which CONFIRMS our calculation (Part 8).

If this critique represents the expertise of Britain's National Radiological Protection Board, plus some input from the RERF, NCI, and UNSCEAR, then this peer-review should INCREASE everyone's confidence that our First Edition is very reasonable --- which means that the dramatic hope offered by this work is also very reasonable.

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CHAPTER 47

Seven Short Objections from Other Sources

- Part 1. There Was Breast Cancer before the Discovery of X-Rays**
- Part 2. Complaint: We Did Not Discuss Nuclear Power Plants**
- Part 3. Complaint: We Omitted Breast-Dose from Past Dental X-Rays**
- Part 4. "There Are No Data to Show that BC is Caused by Mammograms"**
- Part 5. "Not Plausible" Because X-Ray Dose Falling without BC Decline**
- Part 6. "Can't Be 75%" When Only 5-10% of My Patients Had Radiation**
- Part 7. "Can't Be 75%" Because Leaves Too Little Room for OTHER Causes**

All of the following comments, except those in Parts 1, 2, and 3, were made by people who could not have even seen the book at the time. They express preconceptions. These preconceptions are common, and interesting, and need responses. The preconception examined in Part 7 seems to dominate all others. If a comment comes from a newspaper, we omit the name of the maker because, when newspapers abbreviate, the residual quotations may not be exactly what the maker really said.

Part 1. There Was Breast Cancer before the Discovery of X-Rays

In the London Herald of August 3, 1995, one of the authorities at the National Radiological Protection Board is quoted as follows:

"He [Gofman] is holding out the prospect to women that if they never have an X-ray in their life, they will not get breast cancer, and that's absolutely not true. Breast cancer did not start when X-rays began to be used."

"Absolutely not true" is the claim that we have EVER held out the prospect of making breast cancer disappear, if women would refuse all x-rays for themselves and their female children. Again and again, we discuss the role of additional causes of breast cancer (pp. 6, 280, 281, 282, 284, 286 --- always the same in both editions, through page 300).

The occurrence of breast cancer PRIOR to the discovery of x-rays is totally consistent with our thesis, that medical x-rays have become the DOMINANT cause of breast cancer. Moreover, some of the pre-x-ray cases were RADIATION-induced, because natural background radiation irradiates every female in-utero and, thereafter, every year of her life. Surely the NRPB's expert knew that.

It is important to note, too, that no one should glibly dismiss the role of natural background radiation in the INHERITED predisposition to breast cancer. Our hypothesis (Gofman 1994) is that humanity's aggregate burden of inherited afflictions is very largely the consequence of exposure to natural background radiation over the centuries and millenia --- and the consequent build-up of radiation-induced genetic lesions in the population.

Part 2. Complaint: We Did Not Discuss Nuclear Power Plants

Drs. Ernest Sternglass and Jay Gould have suggested that radioactive releases from civilian nuclear power plants may explain above-average rates of breast cancer in various counties of the USA. We have been scolded for not dealing, one way or the other, with their suggestion.

The main reason for not dealing in this book with the Sternglass-Gould hypothesis is that our Master Table in Chapter 39 covers doses received in the 1920-1960 period. Civilian nuclear power plants in the USA got underway later, during the 1960s. Regarding the post-1960 period, we are unaware of any dose-estimates associated with the Sternglass-Gould hypothesis. The number of curies of various radionuclides released, per plant, is not an estimate of DOSE at all.

Our guiding principle in this work is to direct attention first to the DOMINANT sources of radiation, and we believe that the dominant source of controllable radiation exposure in this country is still medical irradiation (see Chapter 48). On the other hand, nuclear pollution could BECOME the dominant source one day, if citizens don't watch out.

Part 3. Complaint: We Omitted Breast-Dose from Past Dental X-Rays

One of our most intelligent critics over many years has been Miriam Goodman, of Long Island. We learn a lot from her. And she raised an interesting question about the First Edition, when she asked: Why didn't you discuss breast-dose from past dental x-rays received during the 1920-1960 period?

We should have mentioned dental x-rays in Chapter 38, as a POTENTIAL source of underestimation of breast-dose. Mrs. Goodman suggests that the x-ray beam was probably NOT well focused on just part of the jaw. "Even TODAY, the technicians shield themselves behind a wall when they take dental x-rays. What was going on in the 1920-1960 period? Did they ever shield the patient's chest with a leaded apron?" We do not know how to answer such questions.

Part 4. "There Are No Data to Show that BC is Caused by Mammograms"

"As far as we're concerned, there are no data to show that breast cancer is caused by mammograms," commented the Medical Director of a major Comprehensive Breast Center in California, when asked by a newspaper to comment (May 5, 1995) on the 75-percent estimate of this book. The response reflects two common and mistaken assumptions, occurring in high places.

The First Mistake

The safe-dose fallacy is showing in this statement. Unless the Medical Director assumes a safe threshold-dose, the Medical Director has overwhelming evidence that the x-rays from mammograms are capable of inducing breast cancer. The evidence for radiation-induction of breast-cancer is not in dispute (see flagged # entries in our Reference list). The evidence against any threshold dose is also overwhelming (Chapter

45). Nonetheless, this "authority" --- Medical Director of a Comprehensive Breast Center --- is assuring women that there is NO risk of mammogram-induced breast cancer "as far as we're concerned."

The Second Mistake

The second mistake is the assumption that this book blames a lot of breast cancer on mammography. Reality: The 75-percent estimate of this book does not include a single case caused by mammography. Mammography is not included at all in our Master Table, which covers 1920-1960. But is this book hostile to mammography nonetheless?

We have taken no position on mammography. On page 173, we draw the distinction between wanting to estimate the cancer-consequences of modern mammography, versus wanting to obstruct use of mammography. On pages 180-181, where we show women how to estimate their personal risks from mammography, we emphasize three separate times that the chance of NOT developing mammogram-induced breast cancer far exceeds the chance that a mammogram-induced cancer will ever develop.

Hostile? The First Edition pointed to mammography as a shining MODEL of how much has been achieved in reducing unnecessarily high radiation dosage, whenever the medical world got serious about doing so (p.293). And we emphasized the point again (bottom, p.298).

Part 5. "Not Plausible" Because X-Ray Dose Falling without BC Decline

On May 7, 1995, the London Sunday Telegraph carried "X-ray link to breast cancer," a front-page news story about this book. The reporters (Robert Matthews and Victoria Macdonald) asked for a comment from a cancer specialist at Hammersmith Hospital in London. The professor said:

"There has been increasing awareness of the use of X-rays, and over the past 30 years, there has been a reduction in radiation doses, so one would have expected to see a decline in breast cancers if these claims were correct. Instead, breast cancer cases have dramatically increased across the world in 50 years." Several additional experts have voiced the same assumptions and the same mistaken conclusion: If x-rays were important in breast-cancer causation, then the breast-cancer problem would be declining today.

Not so.

Such critiques fail to take into account the long and variable latent period which follows breast-irradiation (Chapter 2), and the radiation-sensitivity of the women whose x-ray-induced breast-cancers are delivered AFTER 1965. Because of these factors, it is easily possible for x-ray-induced breast-cancer to be flat, or even to increase, during a period when breast-irradiation is gradually declining.

5a. The "Breast-Cancer Years"

Except for the early-onset cases (Chapter 3), the x-ray-induced cases wait until the breast-cancer years --- ages 35 to 85, and beyond. What we mean by "the breast-cancer years" can be illustrated by the rates of breast-cancer deaths, per 100,000 white women in the USA, for 1980 (from USDHHS 1993, Table 39, p.71). For incidence, the climb has to begin at younger ages than for deaths.

Ages 25-34	3.0
Ages 35-44	17.3
Ages 45-54	48.1
Ages 55-64	81.3
Ages 65-74	103.7
Ages 75-84	128.4
Ages > 85	171.7

What Happens between 1945 and 1980?

We can use the year 1980 also to illustrate the role of latency in correct expectations for X-RAY-induced breast-cancers. We will use the year 1945 as a typical year of irradiation from our analysis. The interval = 35 years, from 1945 to 1980.

In the year 1945, some infants were receiving thymus irradiation and "well-baby" fluoroscopic check-ups. Some children were receiving pre-tonsillectomy irradiation. Some women in their 20s were receiving artificial pneumothorax therapy for tuberculosis. In diagnostic radiology, the x-ray beam was poorly collimated, and breasts were in the beam when they did not need to be. Films were slow, and exposures higher than today. Fluoroscopy was popular. We need not review the entire book here.

Now the year 1980 arrives 35 years later. Delivery of the x-ray-induced breast-cancers, produced during 1945, is NOT YET FINISHED. Far from it. Because most diagnosis occurs during "the breast-cancer (mortality) years," some delivery from 1945 is just beginning in 1980. The infants irradiated in 1945 are age 35, and are just barely arriving at their passage through the breast-cancer years. The age-10 children irradiated in 1945 are only age 45 in 1980 --- with most of their breast-cancer years still ahead of them. The age-25 women irradiated in 1945 are age 60 in 1980, with many breast-cancer years still ahead. The age-40 women irradiated in 1945 are age 75 in 1980, and even at that age, discovery of new cases continues.

5b. Bottom Line: Not Only Possible, but Also Plausible

And our analysis did not stop in 1945. It considers x-ray practices out to 1960. So in 1980, the delivery of x-ray-induced cases produced in 1960 is even FAR LESS COMPLETE than the illustrations above from exposure in 1945. The illustrations above used a 35-year interval between irradiation and observation. For irradiation in 1960, a comparable interval would bring the observer to 1995.

During the past 30 years, delivery of radiation-induced breast-cancers just began to include cases from the MOST SENSITIVE age-groups in our analysis (the younger ones in the 1920-1960 period). Their radiation sensitivity is greater than that of women who were older in 1920-1960, and who were already passing through the "breast-cancer years" BEFORE 1965. The greater sensitivity to x-rays, of the groups starting to "deliver" AFTER 1965, could easily offset a gradual decline in dosage.

So it is not only possible, but also plausible, that a radiation-induced cancer problem can be flat or increase while, simultaneously, the x-ray dosage is gradually declining. The long and variable "delivery" period, for cases produced by earlier x-rays, must be kept in mind.

Breast-Cancer Rates per 100,000 Women

It should be noted that the estimates of this book are based on absolute numbers of cases per year: 114,336 and 182,000 (p.285). Our method (a) estimated that 114,336 was the absolute number of radiation-induced breast-cancers "put on the shelf" (produced) each year during the 1920-1960 period, and (b) approximated that the absolute number of cases "delivered" later, per year, would approach equality with the absolute number produced earlier, per year (Chapters 4 and 5). One of the stated approximations was stability of the conversion-factors over decades (p.286).

Our absolute number for (a) and (b) above was 114,336 cases per year. It was compared with 182,000 total cases in 1994, not with trends in breast-cancer rates per 100,000 women. The interesting topic of rates is examined in the forthcoming HEIR-3 Report from this Committee (1996, ISBN 0-932682-97-9).

Part 6. "Can't Be 75%" When Only 5-10% of My Patients Had Radiation

The Oakland (California) Tribune published a story (May 3, 1995, p.A-1) about this book, in which the reporter quoted an assistant clinical professor at UCSF Medical School responding to the 75-percent estimate: "I think it seems implausible." Reason: He said only 5 percent to 10 percent of his patients have a history of radiation exposure. Presumably he meant his patients with breast cancer.

Response:

The comment indicates that the professor asks his breast-cancer patients about radiation exposures in the 1920-1960 period --- which is the source of our 75-percent estimate. We have yet to meet a breast-cancer patient who was ever asked. But we are sure there must be SOME physicians asking.

For the physicians who do ask about the 1920-1960 period, how can the percentage in the response be meaningful? It is not realistic, for example, to think that many women --- say, age 60 at diagnosis in 1990 --- will know that they received irradiation for "enlarged thymus" as a newborn in 1930, or monthly fluoroscopy from birth to age 2, or pre-tonsillectomy thymus irradiation, etc.

How many parents would have thought to tell their children, when such practices were just routine? By contrast, women who were found in childhood to have a congenital problem (say, a heart murmur) would be more likely to have learned something about their childhood radiation history. But why would parents ever mention diagnostic x-rays and fluoroscopy to the even greater number of children whose exams RULED OUT such a diagnosis?

Even though positive response is bound to be falsely low, to questions about a patient's radiation history in the 1920-1960 period, we strongly encourage physicians to ask. If a physician REALIZES that the response is falsely low, then a positive response of just 5 percent or 10 percent ought to put a crack in the existing "mental concrete" surrounding the topic of x-ray-induced breast cancer.

Part 7. "Can't Be 75%" Because Leaves Too Little Room for OTHER Causes

During the past eight months, we have learned that the dominant preconception

about this work is that the 75-percent estimate "can't be right, because it leaves too little room for OTHER causes." This prejudice is so powerful, that people with this belief NEVER read the work! If they did, they would learn how the 75-percent estimate is based on synergism and how it already incorporates other causes.

7a. Synergistic and Additive Co-Action with Radiation

The 75-percent estimate arises out of conversion factors (number of breast-cancer cases per dose-unit of radiation). These conversion factors start with the A-Bomb Study, which already INCLUDES radiation's co-action with the other causes. This is no different from studies which may find a dose-response between, say, pesticide-exposure and breast cancer. The response to pesticides would INCLUDE the co-action with medical x-rays and with the other causes.

What is measured in such studies is the DIFFERENCE in breast-cancer rate when one co-actor is increased and other co-actors are presumed to be constant in all the dose-groups. Then it is correct to say that the INCREASED agent accounted for the difference in breast-cancer response. But also, the observed breast-cancer rate in every dose-group INCLUDES the contribution from all the co-actors.

Synergistic co-action and additive co-action are different. Synergism, defined, is "the simultaneous action of separate agencies which, together, have greater total effect than the sum of their individual effects."

To illustrate the distinction between additive co-action and synergistic co-action, we can imagine that there are only two types of agents which cause breast cancer: Radiation and non-radiation. And we can suppose that these two agents co-act to produce 180,000 new cases per year in the USA. We might suppose that the co-action is exclusively additive --- say 70,000 cases caused by radiation acting independently of non-radiation agents, and say 110,000 cases caused by non-radiation agents acting independently of radiation.

Or, we might suppose that the 180,000 cases are caused exclusively by synergistic co-action between the two types of causes. We have ruled out independent action by either agent in this illustration. So radiation ALONE, in the absence of non-radiation agents, causes NO breast cancer ... and non-radiation agents ALONE, in the absence of radiation, cause NO breast cancer. Without the other, each type of agent is impotent, and "the sum of their individual effects" is zero. But together, their total effect would become very much larger than zero --- some 180,000 new cases per year. That would be synergistic action, with each agent amplifying the effect of the other.

Although we illustrated either one type of co-action exclusively, or the other type exclusively, some carcinogens may act in both additive and synergistic (multiplicative) ways --- and thus have some independent power as well as synergistic power. The issue of co-action is also discussed at pages 280-282, 286, and Chapter 44, Part 3.

7b. "Equal Opportunity" for Non-Radiation Factors

In human experience, radiation as a co-actor is never fully absent, due to natural background sources. Thus, measurements of every other cause of cancer always include radiation co-action (either synergistic, or additive). And we know of no radiation study where all non-radiation co-actors were absent.

We who study radiation are well aware of the uncertainties about co-action (see pages 280-282, 286, and Chapter 44, Part 3). We must consider endogenous and exogenous non-radiation carcinogens (including promoters). Does their presence make the carcinogenicity of ionizing radiation MUCH WORSE than it is in their absence? If so, how much worse? Indeed, does ionizing radiation alone, in the absence of other carcinogens, produce any cancer at all?

With these questions unanswered today, it is clearly a mistake --- a correctable one --- for anyone to assume that our 75-percent estimate "leaves too little room for OTHER causes!"

- - We have said explicitly (pp.280-282) that the 75-percent estimate incorporates the assumption of synergism between radiation and co-factors (other causes). So other causes are already present in the 75-percent estimate. By definition, synergism means that radiation is multiplying the power of the other causes (co-factors), and the other causes are multiplying the power of the radiation. Does this sound as if there is "too little room for other causes?"

- - We have said that without co-factors, the radiation-effect might even be zero (p.286). And we assume that analysts who explore the carcinogenicity of pesticides, estrogens and xeno-estrogens, nutrients, or other exogenous and endogenous substances, sometimes ask themselves:

- (a) Does the carcinogenic potency of these substances DEPEND UPON the presence of radiation-induced genetic lesions, either acquired or inherited? (See Chapter 1, Part 5): (b) Do radiation-induced genetic lesions make the carcinogenicity of the substances MANY TIMES WORSE than they are in the absence of such lesions? (c) Do these substances cause any cancer at all in the absence of radiation-induced lesions?

- - In terms of preventing breast-cancer, we have said (p.5) that "a very large part of the cancer problem can be eliminated, if people CORRECTLY identify and eliminate the non-inherited forces which act alone or act in concert with inherited genetic lesions, in producing malignancy." Ionizing radiation is one of the proven causes which can be reduced VERY EASILY, and if synergism occurs between cancer-causes, reduction of radiation will also reduce the carcinogenic potency of the co-factors. This would be very good news.

- - "There is no inherent conflict or competition between carcinogens. The multi-step genetic model of cancer development 'permits' contributions even to a SINGLE CASE of cancer, from heredity, ionizing radiation, viruses, and chemicals (for example). It is correct to say that each contributor CAUSED the cancer, if the case would not have occurred when it did without that contributor" (p.6). Does this sound like "too little room for other causes?"

There are a lot of reasons to "bet" that synergism occurs among cancer-causes. There is certainly no scientific basis to rule out synergism at this time. And yet that is what people do, whether or not they realize it, when they shut their minds to our 75-percent estimate "because it leaves too little room for OTHER causes." Our 75-percent estimate leaves all the room in the world for other causes to be full partners, as extremely important or probably ESSENTIAL co-factors.

"Every truth passes through three stages before it is recognized. In the first, it is ridiculed. In the second, it is opposed. In the third, it is regarded as self-evident."

● – Arthur Schopenhauer, 1788–1860.
German philosopher.

CHAPTER 48

Susan M. Love, M.D.: Is Radiation Overdosing a PAST Problem?

- Part 1. Dr. Love: Looking Behind and Ahead**
- Part 2. Reality-Check: Some GROWING Aspects of Medical Radiation**
- Part 3. Reality-Check: Some Major Examples of Current OVERDOSING**
- Part 4: WIXMEASE: A Potential Way to Stop Much Careless Overdosing**
- Part 5: Inappropriate Time in History to Assume the Problem Is "Past"**

Susan M. Love, M.D. (surgeon), is Director of the Revlon/UCLA Breast Center at the University of California in Los Angeles, and is the author of the well-known book, "Dr. Susan Love's Breast Book" (Love 1995). We sent her a copy of this book's First Edition, with a personal note, on March 30, 1995. She was in San Francisco on May 19, 1995, to hold a press conference and to give a talk. At each occasion, people asked her about this book. Because both occasions were videotaped by people making a program about breast cancer, we learned of her comments.

Part 1. Dr. Love: Looking Behind and Ahead

Dr. Love stressed two themes, which we will flag as # and ## below. The first comments are from the press conference:

"There is no question that radiation, especially in children, is dangerous, and we ought to avoid it as much as possible. But a lot of that stuff was unique to the period [1920-1960]. #, There is no question that it may be the cause of a lot of the cancer we are seeing right NOW. A significant amount, but not quite that high [75-percent]. ##, We can't do anything about the past. But we can do something about the pesticides and hormones that are being pooh-poohed now. There is not much we can DO about the past." And then at the evening talk (Herbst Hall), Dr. Love said:

#, "I'm not sure that it's QUITE that high [our 75-percent estimate], but I'm sure that a lot of the breast cancer we are seeing now can be explained by that. Back when we were kids, they were using radiation for all kinds of things, and people were not aware of the risk ... We used radiation for everything ... We were shrinking thymus glands with radiation ... People with TB were getting checked with x-rays all the time ... Even mastitis [was treated with radiation]. ALL of those people have a higher risk of breast cancer later on. So there is no question that it does explain some of the increase. I'm not sure I'd go as far as saying 75 percent." She continued:

##, "And we're NOT using radiation quite as liberally now as we did. We still could probably be more cautious, but I think that we DON'T do those things anymore, and what we need to focus on even more are the things that our daughters are being exposed to that will be causing breast cancer 20 or 30 years from NOW."

From the doubly-flagged "##" comments, it seems that Dr. Love considers overdosing by x-rays to be a PAST problem, not worth attention from her or from other breast-cancer activists. This is consistent with her 1993 "Commentary" in JAMA --- a

"Commentary" in which she repeatedly and admirably stressed the need to focus on PREVENTION of breast-cancer. She reported (Love 1993) that:

"Women around the country want breast cancer eradicated. They want research into the causes of breast cancer and they want to know how to prevent this killer. How can we achieve this goal?" Dr. Love suggested various actions (e.g., more research into the possible causal role of pesticides and chlorinated compounds). She neither mentioned radiation as a cause, nor reduction of radiation exposure as a guaranteed way to prevent a share of the future cases.

The assumption is very common, that CURRENT medical uses of radiation will make no significant contribution to the future incidence of breast cancer. Such a CONSEQUENTIAL assumption deserves a reality-check (Parts 2, 3, and 5, below).

Part 2. Reality-Check: Some GROWING Aspects of Medical Radiation

Although we will show, below, that some aspects of medical radiation have been growing since 1960, the average breast-dose per female (which is not the same as person-rads) has surely decreased since its peak, especially for children. That is very good.

But it certainly does not follow automatically that x-ray overdosing has become a problem too trivial for solution by women "who want breast cancer eradicated" and who "want to know how to prevent this killer."

2a. The New, the Old, and the Opportunity

The hasty assumption, that radiation overdosing is a PAST problem, may be partly our fault. We provided a list in Chapter 37 of many past uses of the x-ray which no longer occur. And we pointed out that, per diagnostic radiograph, risk has been reduced by irradiating smaller areas (p.146). Faster films and better equipment have also helped to reduce dose per examination (pp.145-146).

BUT, at the same time, there are many more examinations per 1,000 people ... and there are several new types of breast-irradiating examinations which did not occur in the 1920-1960 "past" ... and most of the "old" breast-irradiating exams continue.

THE NET EFFECT is very probably an average breast-dose lower now than it was during the 1920-1960 period (especially for children), and so what? Large ADDITIONAL dose-reductions are not only readily feasible (as we will show in Part 3), but such additional dose-reductions are also GUARANTEED to prevent a share of future breast-cancers (as we have shown in Chapter 45). The title of this book is no mistake. Our message is that, collectively, women and their families have the opportunity to have LESS radiation-induced breast-cancer in the future, if they make that choice.

2b. Some New Breast-Irradiating Uses of Radiation in Medicine

- - MAMMOGRAPHY. Mammography used to be rare. It is not even included in Chapter 39's Master Table. Now women are urged to have a mammographic exam every year, after they reach age 50, and many women want to have them at much younger ages, too. A controversy rages over such screening below age 50. In the affluent countries, the average annual number of mammographic exams per unit of population approximately tripled between the 1970-1979 and 1985-1990 periods (UNSCEAR 1993,

Table 8, p.283). In 1990, the U.S. Congress instructed Medicare coverage to include a mammogram every two years for women age 65 and beyond (ACS 1994, p.21).

How many women today (USA) have screening mammograms per year? We have two rather different estimates. The higher estimate: Approximately 18.6 million screening mammograms per year --- or 39 percent of women ages 40 to 79 (from UCSF 1995, p.3). The lower estimate: Approximately 12 million women (USA) have a screening mammogram each year --- allegedly 25 percent of the symptom-free women who are "currently eligible" (Khalkhali 1995, p.38).

Presently, "about 5 percent of screening mammograms are positive or suspicious, and of these, 80 to 93 percent are false positives ..." (Wright 1995, p.29, 31).

If the average absorbed dose per mammographic exam is about 0.2 rad (see page 172), and if all women decide to have annual mammograms, the annual average breast-dose from this source alone would become almost half what it was in "the past," from all sources combined, for those ages (Master Table). If the average absorbed dose per exam were to fall to 0.1 rad, it would still amount to an appreciable fraction of total dose from all sources in "the past."

- - X-RAY-GUIDED BREAST BIOPSIES (stereotactic needle biopsies). This non-surgical technique uses x-rays from different angles and a computer to plot the exact location of the suspicious area, before the needle is inserted. Several x-rays must be taken (a minimum of five, for one popular system), but only part of the breast is irradiated. One women whose biopsy required eleven x-rays told us that, when she inquired about the total radiation dose, she was told 1.3 rads. She added, "I was also told that I was the first patient who ever asked them!"

We do not know how many breast biopsies per year are done this way, or the typical x-ray dose. By contrast, the number of surgical excisional breast-biopsies each year (USA) is estimated as follows. "In this country, we perform 750,000 and possibly a million open surgical biopsies, removing an abnormality found on the physical exam and/or mammography. Clearly, the majority of people who do have that procedure do not have cancer," says Joseph P. Crowé, Jr., M.D., director of breast services at the Cleveland Clinic Foundation (Crowe 1995, p.5). Referring to all breast biopsies combined, Dr. Iraj Khalkhali, chief of breast imaging at the Harbor-UCLA Medical Center, asserts that "only one out of four to six breast biopsies is positive for breast cancer" (Khalkhali 1995, p.38).

- - SCINTI-MAMMOGRAPHY. This is a diagnostic technique used experimentally by the Nuclear Medicine Division of the Harbor-UCLA Medical Center in Torrance, California; it is now in clinical trials at various institutions. Dr. Iraj Khalkhali, chief of breast imaging at the Harbor-UCLA Medical Center, is an enthusiast for it. With its further testing and evolution, he hopes that scinti-mammography may reliably distinguish dangerous from benign situations in non-biopsied women, and that "a large number of breast biopsies can be safely reduced" (Khalkhali 1995, p.38).

Patients are injected in the arm with 20 milli-curies of the radioisotope Technetium (Tc) 99m, SestaMIBI. The radiological half-life is a little over 6 hours. Breast images are taken 5 and 60 minutes after the injection (Khalkhali p.35). "There is no significant risk or discomfort to the patient. Compression of the breast is not required and the

radiation risk is minuscule," according to Khalkhali (quoted in Harbor 1995).

The average dose to the WHOLE BODY (including both breasts) per scinti-mammogram is 0.3 rad, with a dose of 3.0 rads to the large intestine (Khalkhali 1995, p.34-35). Since Tc-99m emits a gamma of about 140 KeV, the corresponding doses in our "medical rads" would be somewhat lower than 0.3 rad and 3.0 rads. Reduced or not, any dose to the whole body is very much more serious than the same dose to the breasts alone. Nonetheless, women have every right to choose an option like this, if they prefer it to the alternatives.

Potential alternatives also under development include BBE: Breast Biophysical Examination. BBE is a non-invasive, electrical method of examination, which distinguishes cancerous tissue from non-cancerous tissue after a suspicious area has been detected by mammography or physical examination. BBE, which itself involves no ionizing radiation, is being evaluated at multiple institutions, under the leadership of Joseph P. Crowe, Jr., M.D., director of breast services at the Cleveland Clinic Foundation. Crowe's opinion is that initial breast screening by BBE may become possible someday, but not soon (Crowe 1995, p.5, p.17).

• - BREAST IRRADIATION FROM COMPUTED TOMOGRAPHY, or CT Scans. In the affluent nations, the increasing use of CT scans is remarkable. The average annual rate per 1,000 population rose from 6.1 to 44, in the periods 1970-1979 vs. 1985-1990 (UNSCEAR 1993, p.283, Table 8). For 1985-1990, the annual rate in the USA was about 14.5 CT exams per 1,000 population; in Australia, 30 per 1,000; West Germany, 35 per 1,000; Belgium, 50 per 1,000; and Japan, 97 per 1,000 (UNSCEAR, p.280-281, Table 7).

What share of CT exams irradiate the breasts? UNSCEAR (1993, Table 14, p.297) provides one clue: In Britain (UK) in 1989, about 12 percent (because 0.7 % are thoracic spine exams; 7.9 % are routine chest exams; 4.0 % are mediastinum exams).

And what about doses to the breasts? An indication comes from Table 15 of the same source (p.297). In Japan, CT scans of the chest deliver an average absorbed dose to the breasts of 1.6 rads (15.9 mGy), with a range of 0.87 rad to 4 rads.

Doses to patients from CT scans are typically about 10 times higher than from "conventional" diagnostic examination by x-ray, according to UNSCEAR, p.235/81. However, there are special situations when CT scans give much lower doses than conventional x-ray techniques --- and UNSCEAR mentions myelography of the lumbar spine (p.235/81), and fetal doses from pelvimetry (p.237/95).

The trend in doses from CT scans is upward. Why? "The number of slices imaged on each patient has risen as the time required to perform scans and reconstruct images has decreased. However, since little change has occurred in the dose required per slice, the dose per examination is likely to have increased substantially" (UNSCEAR p.244/141, citing a report from Britain's National Radiological Protection Board: NRPB 1990). UNSCEAR continues:

"Indeed the average effective dose equivalent due to a body scan at the Mayo Clinic in the United States was 15.6 mSv (range: 9-60 mSv) in 1988 (Vetter 1991); in 1980, the comparable figure for the United States was 1.1 mSv (NCRP 1989)." We think this factor of 14 may need further documentation. (15.6 mSv is the same as 1,560

milli-rems. The term "effective dose equivalent" is explained in Part 2c, below.)

For those who assume that the x-ray problem keeps diminishing, we will describe the more complex situation in UNSCEAR's words: "Some examinations with higher doses, such as computed tomography, are becoming more frequent. At the same time, however, better equipment and techniques are allowing doses in other examinations to be reduced" (1993, p.267/302). And the net effect? "The total dose for all x-ray examinations per examined patient may be unchanged or only slightly decreased," with reference to the last decade or so (1993, p.242/130).

• - BREAST IRRADIATION FROM INTERVENTIONAL CARDIAC

RADIOLOGY. Interventional radiology refers mainly to the use of fluoroscopy to guide the passage of needles, wires, and catheters, or to localize renal stones in lithotripsy, or to infuse pharmaceuticals in specific locations. Such uses, which are not purely diagnostic or directly therapeutic, are called "interventional."

In discussing fluoroscopy, UNSCEAR confirms that "The greatest radiation dose to individual patients in fluoroscopy is associated with imaging of the heart (interventional or otherwise)" (1993, p.233/71). Such imaging of the heart almost inevitably irradiates parts of the breasts.

Although cardiac catheterization was developed and used well before 1960, even on children, its use has INCREASED (not decreased) since "the past" 1920-1960 period. The increase accompanies some spectacular developments in surgical repair of congenital heart defects and in repair or supplementation of clogged coronary arteries --- already mentioned at pages 183-185, and 213-214. The duration of fluoroscopy can be very long --- 22 minutes on the average for heart catheterization (p.214), and sometimes lasting long enough to cause serious skin injury (p.184 and p.216)

"Potentially very high doses" are associated with the dilation of cardiac vessels by percutaneous transluminal cardio-angioplasty (PTCA). In an Australian study of this procedure, skin doses ranged from 100 to 500 rads (UNSCEAR 1993, p.233/71). "The number of PTCA procedures in the United States increased to an estimated 400,000 in 1990" (p.232/69). That's just ONE cardiac procedure.

Although modern fluoroscopy equipment does not put out the highest doses per minute listed in our Index (see Fluoroscopy: output), the maximum rate has been reduced to 20 rads per minute only recently (p.185). UNSCEAR remarks, realistically, that "modern equipment may also have a potential for high doses ... For instance, high-level fluoroscopic boost options for image enhancement can contribute to high doses and may be easily activated, e.g. by a simple foot pedal" (1993, p.232/67). Anecdotally, we have heard various physicians characterized as "heavy on the pedal."

• - X-RAY EXAMINATIONS IN NEONATAL INTENSIVE CARE UNITS. By and large, the diagnostic x-ray examinations given to infants are not new. What is new is the larger number of premature and congenitally challenged infants who are now surviving and receiving such x-rays.

• - NUCLEAR MEDICINE (the injection or ingestion of radio-nuclides for diagnostic and therapeutic purposes). As already illustrated by the discussion of scinti-mammography above, a radio-nuclide let loose in the body, because of a problem

or suspected problem in a single area, is going to irradiate additional organs even if it ultimately concentrates in just one.

Thus, the breasts receive irradiation from uses of nuclear medicine which are totally unrelated to breast disorders. In the affluent countries, about 30 percent of nuclear medicine exams are of bone, 20 percent of lung, 15 percent of the cardiovascular system, and 15 percent of the thyroid (UNSCEAR 1993, p.324, Table 32).

The practice of nuclear medicine is a "new" use of radiation in medicine. Except for a few naturally occurring radio-isotopes and some produced on cyclotrons, there were virtually none available to medicine until after World War Two. The practice of nuclear medicine is one which has INCREASED, not decreased, since "the past." Indeed, the number of such exams per thousand people DOUBLED in the USA between 1972 and 1982 (p.256). The annual rate is about 28 diagnostic nuclear medicine exams per 1,000 population (about 7 million annual exams per 250 million people, USA).

New uses for nuclear medicine (including pediatric uses) and new techniques in nuclear medicine continue to develop. For example, "Single photon emission computed tomography has evolved rapidly since the early 1980s, when it was still rare. Not only is it now a standard method for tumour localization, but it is also used in a variety of applications, such as functional brain studies, cardiac studies, bone imaging and abdominal imaging. It can also be used in conjunction with labeled monoclonal antibodies" (UNSCEAR 1993, p.255/216).

2c. A Warning about "Effective Dose Equivalents"

UNSCEAR offers a very rough estimate that diagnostic nuclear medicine already ADDS about 10 percent to the population dose from diagnostic medical x-rays, worldwide (1993, p.257/229). For this estimate, and for many others, UNSCEAR relies on a dosimetric calculation called the "effective dose equivalent." Beware.

The word "effective" associated with any dose-estimate should grab the close attention of readers, regardless of their level of prior knowledge. Whenever that word is present, what follows is not a simple statement of dose (energy delivered per gram of tissue). Instead, the "effective dose equivalent" is a calculation which incorporates not only the quality of the radiation (for instance, high-LET vs. low-LET), but also a string of assumptions. UNSCEAR explains it as follows:

"The various organs and tissues in the body differ in their response to radiation. To allow for this, a further quantity, effective dose, is used. The equivalent dose [in rems or sieverts] in each tissue or organ is multiplied by a tissue weighting factor, and the sum of these products over the whole body is called the effective dose. The effective dose is an indicator of the total detriment due to stochastic effects in the exposed individual and his or her descendants" (p.12/69). And what is the input for those "tissue weighting factors"?

The International Commission on Radiological Protection "takes account of the attributable probability of fatal cancer in different organs, of the additional detriment from non-fatal cancer and hereditary disorders, and of the different latency periods for cancers of different kinds. All these features are included in the selection of weighting factors for converting equivalent dose into effective dose" (p.13/77).

The concept of evaluating "total detriment" is attractive. The big problem is the current quality of the evidence required to do it. Because the existing evidence for such tissue weighting factors is thin to really non-existent, we regard the "effective dose equivalents" as a step very likely to introduce large and needless ERRORS into this field at this time. In our opinion, whenever a table or piece of text provides ONLY "effective dose equivalents" and no actual doses, it is useless --- no matter how well intentioned.

2d. Reminder about Some "Old" but Enduring Breast-Irradiators

By 1960, almost all of the therapeutic uses of radiation, for treatment of NON-malignant conditions, had been discontinued --- but the "old" DIAGNOSTIC uses of x-rays (including fluoroscopy) had certainly not stopped. Conditions and diagnostic examinations, fully or partially irradiating the breasts, include (alphabetical order):

- - **BARIUM SWALLOW.** The patient swallows a barium contrast medium, which shows up as white on films or on a fluoroscopic screen, as it moves from lips to stomach. This exam necessarily exposes part of the breasts --- and almost all of the breasts, when a wide field is used without shielding.

- - **CARDIAC PROBLEMS WHICH ARE "WATCHED" WITH REPEATED X-RAY IMAGES OR FLUOROSCOPY.** Patients who are born with a congenital heart problem are not always fixed by surgery. Sometimes they are "watched" with repeated x-rays or fluoroscopies throughout their childhoods. Of course, we are not critical of such uses. We simply point out that they necessarily irradiate some lower parts of the breasts.

- - **CARDIO-ANGIOGRAPHY** (or Angiocardiography). This diagnostic exam of the heart shows its blood circulation, with the aid of a contrast medium administered by catheter, intra-arterially (or administered intravenously, for digital subtraction angiography). Fluoroscopy is used for 20-30 minutes, typically with the beam traveling from back to front, and about 20 still-pictures are made from front to back (Gofman 1985, pp.199-202). Inevitably, some lower parts of the breasts are irradiated too. UNSCEAR 1993 (p.233/71) confirms, that "Skin doses in cardiac angiography often approach 1 gray" (100 rads, or 100 centi-grays).

- - **CERVICAL SPINE** (neck region). X-ray pictures of the cervical spine have typically extended 6 centimeters (over 2 inches) below the sternal notch, and thus they irradiate upper portions of both breasts, unless measures are taken to exclude them.

- - **CHEST X-RAYS, ROUTINE.** When newborn babies need such exams, the pictures are usually taken with the x-ray beam traveling from front to back. Thus, the breasts receive almost the full force of the beam. However, front-to-back views are generally NOT used for examining older infants, children, and adults. The common chest exam includes one back-to-front view and one side-to-side view. Entrance surface doses today are in the range of about 0.015 to 0.030 rad; only a small fraction of the entrance dose reaches the breasts.

- - **CHIROPRACTIC FULL-SPINE EXAMS.** Such exams necessarily irradiate at least parts of the breasts.

- - **FLUOROSCOPY.** Because fluoroscopy provides immediate information, and also entails no expensive film and film-processing, it is attractive to use. Just press the

pedal. UNSCEAR acknowledges that fluoroscopy "results in much higher doses than those from radiography, and its prevalence is both uncertain and changing with time" (1993, p.19/129). Fluoroscopy is not a problem belonging just to "the past." Even in 1994, the United States Government was urging physicians to keep some records and to use basic precautions to prevent SEVERE over-use (see pp.184-187; also pp.216-217). See also Upper Gastro-Intestinal Exams, below.

- - LUMBAR SPINE EXAMS. Unless precautions are taken, lower parts of the breasts are irradiated during such exams.

- - PELVIMETRY. This exam irradiates the breasts of the female fetus in the womb. Is this exam just part of "the past"? UNSCEAR 1993 (p.246/155) cites one source (MacMahon 1985) to the effect that abdominal irradiation of women during pregnancy has been virtually replaced by other techniques. Replacement may be technically feasible, but in Britain, during the 1976-1981 period, at least 4 percent of all pregnant women were examined by x-rays, and maybe 12 percent --- according to UNSCEAR citing papers by Kendall 1989 and Gilman 1989.

- - RIB EXAMS. Unless precautions are taken, more breast-area than necessary may be irradiated.

- - SCAPULA EXAMS (Shoulder Blade). This exam irradiates only one breast, but the beam is usually front-to-back.

- - SCOLIOSIS (Curvature of the Spine) WHICH IS MONITORED WITH REPEATED X-RAYS (Chapter 21). We will return to this topic in Part 3e, below.

- - SHOULDER EXAMS. This examination irradiates much of one breast, but not all of it.

- - UPPER ARM (Humerus). X-rays of the upper arm expose the outer breast, unless precautions are taken.

- - UPPER GASTRO-INTESTINAL SERIES ("Upper G.I."). Patients swallow a barium contrast medium, as they do for the Barium Swallow Exam. The Upper G.I. Series usually involves an appreciable amount of fluoroscopy, which varies from examiner to examiner, and from patient to patient. The examination usually irradiates lower parts of the breasts, unless precautions are taken. The annual rate of Upper G.I. Series in the United States is estimated at about 33 exams per 1,000 population (UNSCEAR 1993, p.281, Table 7). Since few of these exams are given to children, the annual rate for adults seems extremely high. Nonetheless, the annual rate is even higher in Canada (72 per 1,000) and in Japan (156 per 1,000).

- - UPPER SPINE EXAMS (Thoracic Spine) --- ESPECIALLY POST-INJURY MANAGEMENT. Upper spine examinations necessarily irradiate parts of the breasts. Unless precautions are taken, MUCH of the breast-area is irradiated. After bad accidents and certain occupational injuries, such exams can go on for years and years, as noted in Chapter 37, Part 2. Like scoliosis patients, female children and adults who have had a serious back injury, followed by numerous x-rays, are at elevated risk of breast cancer.

Three Forces in One Direction

Three forces have been operating to RAISE the absolute number of radiation-induced breast-cancers "put on the shelf" each year since 1960, for delivery later.

1. The annual number of x-ray examinations per thousand people has been rising in the USA (p.256, for hospitals). Such examinations are done mostly in hospitals (NCRP 1989, p.12). The annual total estimate for the USA (in-hospital + non-hospital), during the years 1985-1990, is 800 diagnostic x-ray examinations per 1,000 persons, excluding dental x-rays and nuclear medicine (UNSCEAR 1993, Table 6, p.279). And with reference specifically to the United States, UNSCEAR notes: "Some information indicates that the estimate could be an underestimate by up to 60 %" (p.229/46). The growth in exams per 1,000 people is not deep in "the past." We speculate that such growth may be causally linked with growing insurance coverage.

2. At the same time that the number of radiological examinations per 1,000 population has been rising (Point 1), the total population itself has continued to rise. Population (USA) has doubled since 1940, the midpoint of our 1920-1960 study-period; see our Table 2. When both the total population and the annual exams per 1,000 people double, the absolute number of examinations per year increases by a factor of 4.

3. Several new uses of radiation in medicine have been widely introduced.

Three in the Opposite Direction

On the other hand, there are three forces operating to REDUCE the absolute number of radiation-induced breast-cancers produced each year (and delivered later):

- (1) Most therapeutic uses of radiation for treatment of non-malignant conditions have been abandoned.

- (2) Most of the "old" diagnostic exams which are still useful are given with lower doses now.

- (3) Fluoroscopy is used less commonly, especially for children.

Is there anyone who can quantify the net effect of these six forces? We don't think so. Even the total number of exams given today seems very uncertain, and the collective BREAST-dose from CT Scans, fluoroscopy, nuclear medicine, plus all the other x-ray examinations, is simply unknown right now.

Like others, we ASSUME that the annual person-rads of breast-dose, across all age-groups, has been falling in the USA for quite a while. But just a foggy notion about a probable "fall" is no basis for dismissing the opportunity to prevent a real share of future breast cancer by causing a BIG ADDITIONAL "FALL" in breast-dosage --- a provable fall. So in Part 3, we will present evidence to show that this goal is highly realistic.

Part 3. Reality-Check: Some Major Examples of Current OVERDOSING

The more that medical x-rays are used in a nation, the greater is the aggregate impact of even small overdoses per use. The number of diagnostic medical x-ray examinations given annually in the USA is impressive. The approximate number each year is at least 200 million (perhaps 60 percent higher) --- an estimate which excludes

100 million diagnostic dental x-ray examinations per year and 7 million diagnostic nuclear medicine examinations per year (UNSCEAR 1993, p.275, Table 3; also p.229/46; for the years 1985–1990).

3a. What We Mean by "Overdose"

If needed medical information can be obtained with a LOWER total dose of radiation, then an overdose has been given. Overdoses should be separated into two distinct classes. One might be called "careless" and the other "evolutionary."

"Careless" overdoses are those which occur because of failures to maintain the existing equipment well, to process film correctly, to position patients carefully, to avoid unnecessary repeats, to avoid exposure of unnecessary areas, to use the dose-reducing techniques in the literature, to insist on careful training, etc. Several of these failures were mentioned already in connection with current fluoroscopy (p.186, pp.214–216) and with common radiography (pp.292–294). Additional evidence will be provided below.

Carelessness results in doses to patients 3 times, 6 times, 10 times higher than needed from specific offices and users --- but patients and referring physicians presently have no way of knowing from WHICH offices and users.

"Evolutionary" overdoses are those which occur because no one has yet DEVELOPED the techniques and equipment which could achieve even bigger reductions of routine breast dose. Such techniques HAVE been willfully developed into a 30-fold reduction for mammography (Chapter 28, Part 2) and a potential 50-fold reduction for scoliosis examinations (Chapter 21, Part 2). These are models for what might be achieved in other examinations, if the effort were made.

"Where there is a will, there is a way." Unless a comparably serious effort is made for other examinations, it is probably fair to say that nearly 100 percent of x-ray exams (excluding mammography) are done today at doses higher than needed --- in short, are delivering overdoses of the evolutionary class.

3b. Role of Digital Computed Radiography in Dose-Reduction

First the good news, then the bad.

Technical developments like digital computed radiography have the potential to reduce dose. "The rapid development of more powerful yet cheaper computers is revolutionizing all imaging methods ... The transition to digital systems in industrialized countries is likely to continue" (UNSCEAR 1993, p.242/131+132). And:

"At present, 15%–30% of examinations are digital. Digital radiography uses large image intensifiers or photosensitive phosphor imaging plates. Chest examinations using digital techniques can produce substantial savings of time and money for film, chemicals and archiving. While the quality of the image with a large image intensifier is not as good as with full-size images on film, the difference can be small enough to be clinically negligible" (UNSCEAR p.242/132). And:

"If fluoroscopy is not used, an image intensifier can reduce patient exposure to one third that of full-size images on film or, in situations like peripheral angiography, to one tenth" (UNSCEAR, p.242/132; also p.238/100). However:

"Persistent anecdotal evidence indicates that some of the dose reduction per image

in computed radiography may be offset by a tendency of radiologists to obtain more images per patient than they would have done with conventional film/screen systems. Also, while over- or under-exposure shows up in conventional radiology as incorrect blackening of the film, considerable over-exposure can go undetected in a digital system unless exposure is specifically monitored" (UNSCEAR p.243/134). No matter how elegant the machine, it can be carelessly used with respect to overdosing.

3c. Dose-Variation for the Same Exam --- Not Just in "the Past"

Large variation of dose for the same x-ray exam is an indicator that overdoses are occurring. But one must not assume that the minimum dose in a range of doses is the best dose. If a dose is too low to provide useful information, then all of that dose is an OVERDOSE. Moreover, some variation in dose is unavoidable (for instance, due to the different size of patients). Of course, one can be quite confident that the AVERAGE dose is providing useful information (or it would not be so frequent). Thus, doses far above the average are likely to be overdoses. And all doses below the average are much preferable, until they approach a useless extreme.

Situation in the USA

Very large dose-variations for the same x-ray examination have been recorded in the USA and are displayed on page 292, which includes the average doses. Although the table is not from 1995, it is not from deep in "the past" either. The data are from 1972-1974, and were acquired under the NEXT program. NEXT stands for Nationwide Evaluation of X-Ray Trends, now a co-operative program conducted by the federal Food and Drug Administration, Center for Devices and Radiological Health (Telephone: 301-594-3533) and the Conference of Radiation Control Program Directors (Telephone: 502-227-4543).

When we attempted to acquire a current version of the same survey, we learned that such surveys were discontinued long ago in the USA, due to "budget cuts" (which may mean "considered unimportant"). For the last decade, about 400 institutions report on only ONE examination per year.

With this reverse-trend in data collection, we are not surprised that UNSCEAR (p.229/46) is very uncertain even about HOW MANY examinations are given per year in the USA since 1985.

Variations Reported in Other "Level One" Countries

The UNSCEAR 1993 report sorts nations into four levels of health care. Nations in Level One are presumed to have the most health care per 1,000 population.

"Doses per examination vary by a factor of 10 or more, even in a single hospital," reports UNSCEAR 1993 (p.243/136), with reference to nations at "Level One." And: "Screen/film speed is the overriding cause of patient dose variation in the United Kingdom, and fluoroscopy time in gastro-intestinal tract examinations is the second biggest cause" (p.243/137).

Big variations also occur in CT Scans. "In computed tomography, the absorbed dose for a given examination varied by a factor of 3 in New Zealand, and a factor of 5 in Sweden and the United Kingdom. In Japan, the effective dose equivalent for the same examination varied by a factor of up to 3.5, depending on the scanner unit ... Panzer et al

[1988] noted even greater variation, by a factor up to 10, with 122 scanners in the Federal Republic of Germany" (UNSCEAR 1993, p.234/80).

Variable dosage from radiography applies to infants, too . "A study covering 11 member States of the European Community (Schneider 1992), which considered typical x-ray examinations performed on infants (abdomen, skull, chest, spine, pelvis), showed large variations in entrance surface doses, far greater than the known and expected variations for corresponding examinations of adults. The maximum entrance surface doses for the abdomen, skull, chest, and spine were almost 50 times higher than the minimum doses, and for the pelvis, a 76-fold difference was found. The study had been standardized on the size of the infant, so that no additional variation was introduced" (UNSCEAR 1993, p.237/98).

"Examination of infants and young children is not infrequent. The per caput effective dose equivalent to children in the Federal Republic of Germany in 1983 was estimated to be 30 percent of the effective dose equivalent to an adult" (UNSCEAR, p.230/58). UNSCEAR's Table 9 for 1985-1990 combines the findings for ages newborn through age 15, and reports that (in the "Level One" nations), children age 15 and younger receive about 6 percent of the CT Scans, 5 percent of the chest fluoroscopies, 7 percent of the chest photofluorography, 8 percent of the chest films; 11 percent of the abdominal exams, 3 percent of the Upper G.I. Series, 19 percent of the skull exams, etc. (pp.284-290, Table 9).

Dose varies also for chiropractic exams. For example, UNSCEAR (p.237/93) cites a 1989 survey in Manitoba, Canada, which found that "the ratio of maximum to minimum dose was as great as 23. This is similar in magnitude to the variations found in medical diagnostic radiology," at which point UNSCEAR cites NRPB 1986.

The existing evidence from the "Level One" nations points overwhelmingly to major variation in dose for the same exam --- an indication of serious overdosing.

Frequency of X-Ray Examinations in Some "Level One" Countries

UNSCEAR 1993 has provided estimates in its Table 6 (p.279) of the annual estimated rate of x-ray examinations per 1,000 population in 27 countries at "Level One." Just to show the range of exams each year per 1,000 population, for the years 1985-1990, we have selected several countries:

Belgium: 1,290 exams each year / 1,000 population.

Japan: 1,160

France: 990

USSR: 990 --- and all past data from the USSR is in doubt.

Czechoslovakia: 920

USA: 800 --- and UNSCEAR says it may be 60 percent higher (1,280).

Kuwait: 720

New Zealand: 640

Cuba: 620

Netherlands: 530

Sweden: 520

Malta: 320

3d. Exams Which Are Repeated, or Have No Medical Basis

Total overdoses come from x-ray or nuclear medical exams which are repeated due to errors, or were originally done for no medical reason. No part of their radiation dose is medically necessary.

How many x-rays are repeated simply because the quality of the first films is unacceptably poor --- or because the first films are lost? According to Caufield (1989, p.230), the United States Bureau of Radiological Health estimated more than 10 percent, and she cited its 1978 estimate (Bureau 1978, p.70) which we have not seen ourselves. According to Laws 1977 (p.112), some earlier estimates suggest only 3 to 6 percent, but she says such estimates do not count repeats ("re-takes") which occur on a later day!

A high rate of retakes reflects a careless attitude toward overdoses --- but not necessarily by the radiologic technologists ("rad techs"). Even when competent and conscientious "rad techs" know how to make all the calculations, adjustments, and judgments to get a good image with the initial exposure, they may be working under TIME pressure. According to Laws (1977, p.118), workloads can be so unreasonable that competent technicians have too little time to set exposures carefully, to adjust the size of the x-ray beam properly ... or even to employ lead shielding to reduce unnecessary exposure, when such shielding would be appropriate.

Where such work-overloads are normal, they reflect a careless attitude by the BOSSes toward overdosing. Another cause of re-takes (and overdoses without re-takes) is a plain lack of adequate teaching. Only a careless attitude toward overdosing allows inadequate teaching on the topic to persist anywhere.

Sometimes even the FIRST set of x-rays done on a patient is not primarily for a medical diagnostic purpose. "Improper purposes include impressing patients, showing insurance companies that the work has been done, obtaining evidence in case of malpractice suits, and justifying investment in x-ray equipment" (Caufield 1989, p.230, citing Dr. Lauriston Taylor, chairman emeritus of the National Council on Radiation Protection).

According to Caufield (p.230, p.231), the United States Bureau of Radiological Health estimated in 1978 that hospitals were giving more than 18 million unnecessary x-rays per year, and altogether, it estimated that one in five x-rays was unnecessary (Bureau 1978, p.69, p.70).

The practice of "defensive medicine" is a "hot topic" now, but even in 1977, Laws was quoting from the 1973 book, "A Practical Medico-Legal Guide for the Physician" (Gordon 1973, pp.66-67): "An excessive number of x-rays may be taken, but they are necessary to support the diagnosis and to protect the physician from a malpractice claim. A lay jury or judge often considers the examination incomplete without pertinent x-rays. The patients themselves frequently share this opinion ..." This opinion is particularly easy for patients to hold, if the cost of such x-ray exams is covered by insurance.

3e. Slow Adoption of Known Dose-Reducing Techniques

The slow adoption, of known ways to reduce dose, is a type of careless overdosing.

Rare Earth Intensifying Screens

UNSCEAR 1993 provides an example when it states (p.243/135) that "The use of rare earth intensifying screens is one of the more important technical developments leading to lower doses per examination. While such screens are by no means new, having been available since the early 1970s, they are not yet fully utilized in all relevant situations. For instance, sample studies indicate that fewer than 50 percent of the radiographic examinations in the United Kingdom were carried out with rare earth screens in 1986 (NRPB 1990)."

How much can use of such screens reduce dose? "Rare earth screen cassettes, which may reduce doses by 50-90 percent, are used in only about half of British hospitals; and only six carbon fibre x-ray table tops, which may reduce doses by a further 10-40 percent to both staff and patients, are currently being used for general radiography in Britain" (Dawood 1988, p.1277).

Dawood and his co-author are in the Department of Pediatric Radiology, Hospital for Sick Children, in London. They comment (p.1277):

"Most people accept the risk from a small dose of ionising radiation in return for the benefits of radiological diagnosis. They trust that the radiation dose will be the smallest possible. Such trust may, however, be misplaced: There is considerable variation in somatic dose for the same procedure among different hospitals. Dose reduction is of greatest concern for children ..."

Specifically Breast-Irradiation

With respect specifically to breast irradiation, Hull 1985 (p.1) provides a disturbing example of careless overdosing in the USA. We quote:

"Scoliosis, a curvature of the spine, is usually monitored with x-rays. The most frequent victims are adolescent females; about 80,000 female scoliosis patients are monitored with x-rays every year. These exams have traditionally been taken from the front, giving the greatest radiation exposure to the breasts ..." (See Chapter 21.) And:

"In 1979, researchers at Case Western Reserve University in Cleveland found that ... by shooting from the back, [they can] significantly reduce radiation exposure to the breasts. Special shields and filters further reduce dose. Yet these simple practices aren't being used. A recent survey by the FDA of 256 x-ray units found just 7 percent using breast shields and only 11 percent shooting from the back. The FDA found more than a 200-fold range in radiation dose."

At the very same time, a senior editor of the Journal of the American Medical Association told Hull, "There aren't people out there giving more radiation than is needed. All the radiation given for diagnostic procedures is the minimum amount that can be given and still get a good picture" (Hull 1985, p.1).

3f. Additional "Instant" Ways to Cut Some Doses a Lot

Pediatric Radiology

Children receive about 6 percent of CT Scans (Part 3c, above). Their dosage can be reduced to half, with "negligible reduction of image quality," when xenon detectors are replaced by ceramic detectors, according to UNSCEAR (p.238/101, citing Parker 1989).

Infants in neonatal intensive care units (or special care baby units) often receive multiple radiographs from a mobile x-ray unit --- most commonly to diagnose and manage respiratory difficulties. A study of one British hospital (John Radcliffe Hospital, Oxford) found that 7.8 percent of all live births went to such a unit (Fletcher 1986, p.165). Skin dose per radiograph of chest and abdomen was measured there at about 0.007 rad (p.165). The average number of such exams per baby was 6.5 (p.167), with half of the babies receiving only one exam, and with an average of 59 exams for babies requiring ventilation (p.169). See also Chapter 37, Part 2.

Faulkner and co-workers investigated two methods to reduce the dose to newborn infants, per x-ray examination from mobile units (Faulkner 1989). They were able achieve a dose-reduction of 37 percent by using a lead rubber adjustable collimator to restrict the area of the x-ray beam, and an additional dose-reduction of 33 percent by using a rare-earth film-screen combination. They say that the latter reduction could have been even larger if the particular mobile unit at hand had allowed more selection of tube current and exposure time, or if they had also used a rare-earth metal filter (p.232). The two tested methods, used together, cut the neonatal dose more than in HALF per x-ray examination.

General Radiology: The Film-Processing Opportunity

A very common cause of overdosing in "Level One" nations is incorrect processing of radiographic films. And it is very common in the USA, as a 1992 paper by Suleiman and co-workers shows. At the outset (p.25), these workers explain: "The consequence of underprocessing is higher radiation exposure and a degradation of film contrast" (p.25). And the higher radiation dose is not small. There is a great deal to learn from their survey, conducted under the auspices of the federal Food and Drug Administration.

Since 1981, the FDA has been monitoring processing speed of over 2,000 automatic film processors in hospitals, private offices, and mammography facilities. This effort is now part of the NEXT program (see Part 3c). The survey "revealed underprocessing at 33 percent of observed hospitals in 1987, 7 percent of mammography facilities in 1988, and 42 percent of private practices in 1989" (p.25). "The quality of processing, in general, may actually have deteriorated during the study period ..." (p.27).

The Situation at Hospitals

"A detailed analysis revealed that ... the underprocessing component [of the data] for hospitals increased from 18 percent in 1984 to 33 percent in 1987" (Suleiman 1992, p.27). "We can only hypothesize that the deterioration in processing quality in hospitals was in part attributable to cost containment efforts. We have been told on several occasions that hospitals frequently eliminated Quality Assurance technicians to reduce costs" (p.27).

At one hospital, "technical experts identified an inaccurate thermometer and incorrect developer temperatures as the reason for underprocessing. The processors were readjusted. Radiographic kilovolt peak values and photo-timers were readjusted, THE AVERAGE EXPOSURE WAS REDUCED BY MORE THAN 50 PERCENT, and image quality improved substantially" (p.28; emphasis added).

On the average, at hospitals which were underprocessing, "patients undergoing diagnostic radiographic examinations ... WOULD HAVE RECEIVED AN ADDITIONAL 45 PERCENT RADIATION DOSE ATTRIBUTABLE TO UNDERPROCESSING" (p.27, emphasis added).

The Situation in Private Practices

The survey indicates that radiologists may do better than non-radiologists (excluding chiropractors), and that non-radiologists may do better than chiropractors. The 1989 survey of abdominal radiography showed that 25 percent of radiologists in private offices (total sample of 4), 33 percent of non-radiologists (total sample of 82), and 48 percent of chiropractors (total sample of 143) were underprocessing (p.27).

The 1986 and 1989 surveys of private practices showed that, where underprocessing occurred, the average radiation exposure was 67 percent higher than necessary (p.27).

The Situation in Mammography Facilities

Meanwhile, mammography centers were performing better and better. In 1985, underprocessing occurred in 18 percent. In 1988, the percentage had decreased to 7 percent (p.27).

The Big Lesson, Thanks to Suleiman and Co-Workers

The big lesson comes from comparing performance at private offices and hospitals with performance at mammography centers. The comparison shows that people are not asking for unrealistic or impossible levels of performance if they demand an end to careless underprocessing, in order to reduce radiation overdosing by a large amount. When facilities make the effort to do processing right, there is proof that it happens.

3g. A Realistic First Step: Cutting Careless Overdoses in Half

The evidence in Part 3, above, explains some comments by UNSCEAR early in its presentation: "From a radiation protection point of view, doses should be maintained as low as reasonably achievable. This means that exposures above clinically acceptable minimum doses, must be avoided. There is much potential for reducing the risks associated with medical radiation exposures for diagnostic or therapeutic purposes" (1993, p.227/34). And:

"Although the doses from diagnostic x-ray examinations are generally relatively low, the magnitude of the practice makes for a significant radiological impact" (1993, p.228/40). And later:

"A United Kingdom report (NRPB 1990) gives detailed recommendations for reducing patient doses ... It estimates that about half of the current collective effective dose to patients from x-rays could be avoided. This conclusion is drawn in spite of the relatively low frequency of examinations (about twice as many examinations per caput are performed in France and the United States) ... Since it has been suggested that in the United Kingdom the collective effective dose from diagnostic x-rays could be halved (NRPB 1990), there is probably a potential for similar dose reductions in many countries" (UNSCEAR 1993, p.243/137+138).

Very gently, UNSCEAR is suggesting that the "significant radiological impact,"

from hundreds of millions of diagnostic x-ray exams occurring every year, could be cut in half by getting rid of careless overdosing. (And half could be just the FIRST step.)

We are "allowed" to ask a question which UNSCEAR can not: If influential people know about this opportunity and do not use it, what does it say about a callous readiness to inflict upon people, at random, unnecessary cases of cancer --- including breast cancer?

Part 4. WIXMEASE: A Potential Way to Stop Much Careless Overdosing

A double-dose of wishful thinking represents a big obstacle to solving the overdose problem.

- - The referring physicians who order the x-ray exams presently know virtually nothing about radiation, so they WISH to believe that risks are just "hypothetical" and that they need not take any responsibility.

- - The patients hate to irritate their physicians, with whom they would like to have a warm relationship, so they too WISH to believe that radiation risks are just "hypothetical" and that there is no need for them to challenge anyone.

These two sets of people comfortably reinforce each other, while the overdose problem persists.

4a. Getting Realistic? The Meaning of WIXMEASE

On the average, an individual's personal risk from a single x-ray exam is small, and is even smaller from the share of radiation which is the OVERDOSE. So, it is not realistic to think that individual physicians or individual patients are going to look beyond their personal stakes and to take responsibility for the AGGREGATE impact from millions and millions of overdoses, occurring year after year --- an impact particularly dangerous for patients who have inherited an extra vulnerability to ionizing radiation (see p.181; also Part 5, below).

Then does anyone care? The women who have committed themselves to preventing as many cases of breast cancer as possible, must surely care about the radiation-induced cases which result from careless overdosing.

It may be in their power to establish a practical service which would solve the careless overdosing problem while NOT disturbing the mutual comfort of the referring physicians and their patients. What about a Women's Independent X-ray Measurement Service? WIXMEASE.

4b. The Effect of Information

The first step in any serious effort to eliminate careless overdosing would seem to be an independent measurement system to find out where the overdoses occur. A lot could be accomplished just by using TLDs, which can measure entrance dose during an examination without interfering with the x-ray image (see p.298).

For years, a Monitoring-by-Mail Service has existed --- BUT NOT FOR THE PUBLIC --- at the University of Wisconsin's Medical Physics Lab in Madison, Wisconsin (Telephone: 608-262-6320). The Mail Service supplies TLDs to physicians

and others who irradiate people, receives the TLDs back by mail, and evaluates the dose on each TLD.

Women of course are perfectly capable of developing their own expertise, or of hiring expertise, to run a similar service --- with one big difference: The TLDs might belong to the patients, and the dose information would become part of a growing database, openly accessible to other patients, referring physicians, and x-ray offices (which could annotate their high-dose entries.) Use of such a database would finally make it possible to AVOID places which typically give unjustifiably higher doses than other places, to patients of similar size. So, careless places would either have to "shape up," or to fail.

If information on comparative doses were readily available (for instance, on the Internet), what physician would refer patients to a high-dose facility, or to one which declined to participate --- and what patient would go? After a while, insurance systems might refuse reimbursement to non-participants in an independent, trustworthy measurement service. WIXMEASE would not need to remain the only service, if others decided to provide similar, accessible services. The more competition, the more protection against carelessness and corruption at any single measurement service.

4c. The Effect of INDEPENDENT Information

We do not underestimate the problems of getting a pilot project funded and successfully underway in one or more metropolitan areas. However, we certainly do not underestimate the talent and tenacity of the women who, in the past few years, collected 2.6 million signatures from U.S. citizens demanding a more intense national effort to reduce the incidence of breast cancer, who managed to increase the federal budget for breast-cancer research by a great deal, and who managed to establish a special tax in California to do something NEW about preventing breast cancer (Chapter 43, Part 3).

Nor do we underestimate the probable resistance from some physicians who will be fearful of patients "having information which they can't understand."

Today, patients who ask x-ray offices about doses often receive answers --- and those answers may sometimes be pure fiction, looked up in a manual of what the dose SHOULD be. Isolated answers, even if true, do nothing to eliminate the undeniable overdose problem. By contrast, independent, credible, systematic, current sources of information, based on actual measured doses, would do a very great deal to eliminate careless overdosing.

Part 5. Inappropriate Time in History to Assume the Problem Is "Past"

It seems to us a particularly inappropriate time in HISTORY to assume that the causal role of medical radiation in the cancer problem is "past" and now small. We put the emphasis on history for the following reasons:

- - The evidence that there is NO safe dose-level of radiation has only recently been acknowledged as decisive (Chapter 45).
- - Very recent technical advances in molecular biology are confirming the multi-step genetic model of carcinogenesis --- with its implication that radiation and non-radiation carcinogens probably make each other worse (see Index: Co-action).

● - Very recent work is expanding our knowledge about rather large subsets of the population who have inherited a defective system for repairing radiation-induced genetic damage. For instance, Scott reports that sensitivity to radiation-induced chromosome damage has already been shown in more than 15 cancer-prone conditions (Scott 1994-a, Scott 1994-b; Sanford 1990; see also Savitsky 1995, p.1749, and Nowak 1995, p.1701).

● - The rapidly expanding world population, aspiring to "Level One" health care, means that a huge INCREASE in person-rads of collective radiation dose is coming. And due to poverty, the temptation to use inexpensive fluoroscopy is strong. UNSCEAR 1993 mentions Tunisia, where over 50 percent of the radiologic equipment is fluoroscopic --- and is said to be used more often to please patients than to obtain diagnostic information (p.243/139). In China, allegedly "98 percent of all x-ray diagnosis is done with fluoroscopy" (Caufield 1989, p.225, citing a 1987 interview with Dr. Fred Mettler). In Belarus and Russia (where the population is not growing), we have been told that fluoroscopy is used "for everything" because film and film processing are not affordable.

● - The longer lifespan in the affluent countries means a shift in their populations' age-distribution toward older ages --- when more (not less) diagnostic and interventional radiology is used.

● - The number of breast cancers treated by surgery plus adjuvant radiation is growing, and this means a growing number of women at risk for a radiation-induced cancer in the other breast. During radiation therapy, the medial (mid-body) side of the OTHER breast receives hundreds of rads of exposure from scattered radiation, for "most patients" (Muller-Runkel 1990, p.874).

● - The common diagnostic x-ray examinations of "the past" are still in use --- and many of them are breast-irradiators (Part 2d, above). In addition, new examinations (CT Scans, for example, and diagnostic nuclear medicine) have been added to the breast-irradiating scene, and their use is growing (Part 2b).

● - An enormous expansion of mammography has occurred and is very likely to continue, and this screening technique means repeated irradiation of many healthy breasts (Part 2b).

● - There is an undeniable overdose problem today in diagnostic and interventional radiology (Part 3), and even small overdoses and small risks become significant, when multiplied by hundreds of millions of occurrences year after year. For people born radio-sensitive, careless radiation overdosing, during a lifetime of medical care, is no small matter.

● - UNSCEAR 1993 estimates that the aggregate annual radiation dose from diagnostic radiation could be cut in half, without interfering with appropriate usage and needed medical information (Part 3g).

This list is a reality-check on the hasty but common assumption that medical radiation is a problem of "the past" with respect to causation of future breast-cancers (and other cancers). Still, no one should be surprised by the attitude of the medical profession. Recently (but in a different context: Lancet 1993, p.344), the editors of The Lancet remarked on "the extraordinary capacity of the profession for self-delusion."

From UNSCEAR 1988 (Annex C: Exposures from Medical Uses of Radiation, p.282).

Table 23

Procedures to Reduce Collective Dose Equivalent in Diagnostic X-Ray Examinations

Area	Procedure	Entrance-Dose Reduction-Factor	Reference
All Types	Elimination of medically unnecessary procedures	1.2	Cohen 1985.
	Introduction of Quality Assurance programme (general)	2*	Cohen 1985.
Radiography	Decrease in rejected films through Quality Assurance programme	1.1	Gallini 1985. Properzio 1985.
	Increase of peak kilovoltage	1.5	Wiatrowski 1983.
	Beam collimation	1 to 3	Johnson 1986. Morris 1984.
	Use of rare-earth screens	2 to 4	Kuhn 1985. Newlin 1978. Segal 1982. Wagner 1976.
	Increase of filtration	1.7	Kuhn 1985. Montanara 1986. Wiatrowski 1983.
	Rare-earth filtration	2 to 4	Tyndall 1987.
	Change from photofluorography to chest radiography	4 to 10	Jankowski 1984. Mustafa 1985. Neamiro 1983.
	Use of carbon fibre materials	2.0	Huda 1984.
	Replacement of CaWO ₄ screens with spot film technique	4.0	Kuhn 1985.
Pelvimetry	Entrance exposure guidelines	1.5	Laws 1980.
	Gonadal shielding	2 to 10 **	Poretti 1985.
Fluoroscopy	Use of CT topogram	5 to 10	Stanton 1983.
Digital radiography	Acoustic signal related to dose rate	1.3	Anderson 1985.
	Use of 105 mm camera	4 to 5	Rowley 1987.
	Radiologist technique	2 to 10	Rowley 1987.
	Variable aperture iris on TV camera	3.0	Leibovic 1983.
	Change from chest fluoroscopy to radiography	20.0	Sun 1985.
	High and low dose switching	1.5	Leibovic 1983.
Computed tomography, head	Decrease in contrast resolution	2 to 3	Rimkus 1984.
	Use of pulsed system	2	Rimkus 1984.
Mammography	Gantry angulation to exclude eye from primary beam	2 to 4 ***	Isherwood 1978.
	Intensifying screens	2 to 5	NCRP 1986. Shrivastava 1980.
	Optimal compression	1.3 - 1.5	NCRP 1986.
	Filtration	3	Hammerstein 1979.

* The role of proper training in radiation protection is extremely important. Dose reduction-factors in this regard may be large; however, they are difficult to quantify. ** Factor for gonads. *** Factor for eyes.

CHAPTER 49 What Happens Next?

There are two independent aspects to the question, "What happens next?" One is the scientific debate on the 75-percent hypothesis. The other is elimination of the overdose problem.

Part 1. The Scientific Issues

Having considered each critique of which we are aware, we see no basis to change the findings of the First Edition.

Inherent uncertainties in the 75-percent estimate were and are pointed out in Chapters 38, 40, and 41. Uncertainties also characterize the competing estimates, because all estimates which use conversion factors (number of breast cancers per unit of radiation dose) must make some assumptions. In Chapter 44, we have shown why a competing estimate of 1 percent is non-credible, and in Chapters 44 and 46, we have shown why low estimates in the region of 6 percent are far less credible than our 75-percent estimate, on the basis of existing knowledge.

In general, a valid hypothesis can correctly predict some future events. However, our 75-percent hypothesis is tied specifically to absolute numbers of women of various ages, and to their breast-doses during the 1920-1960 period, and to the absolute number of new breast-cancers observed in recent years. We would LIKE to predict that the absolute number of new breast-cancers per year would soon start to fall. It may. But failure to fall would certainly not invalidate the 75-percent hypothesis (see Chapter 47, Part 5, and Chapter 48, Part 2e).

On the basis of what is currently knowable about conversion factors, we are confident that the original estimate of 75 percent is extremely reasonable. Such an estimate is fully compatible with important roles for additional breast-cancer causes, either as independent actors or as co-factors with ionizing radiation (see especially Chapter 47, Part 7, and Index: Co-action).

Coming: A Powerful, New Reality-Check

Like every other hypothesis, the 75-percent hypothesis remains credible only as long as it is consistent with "hard reality" --- with relevant facts which are well-established. Having stressed repeatedly that the First Edition was an INITIAL analysis (see Index: Initial analysis), we have been very actively seeking to test the hypothesis with relevant, well-established facts.

We are in now in the middle of an analysis which is completely independent of the method used in this book. Thus, it eliminates the particular set of uncertainties described in Chapters 38, 40, and 41. Of course, it has its own set of different uncertainties, for nature does not yield truth easily.

The preliminary results of this wholly separate method not only appear consistent with the 75-percent hypothesis for breast cancer, but also consistent with a large causal role for medical irradiation in other types of cancer in both women and men.

Presentation of this additional method, for breast and other cancers, constitutes the HEIR-3 Report. The study will go to press as a separate book (ISBN 0-932682-97-9, Committee for Nuclear Responsibility), probably in 1996. Readers who still have trouble believing that medical irradiation causes a very great deal of the cancer problem, may need to "think again" when they take account of this additional analysis.

Part 2. Elimination of the Overdose Problem

We do not see how anyone who reads Chapter 48 can remain in denial about the radiation overdose-problem in the USA and elsewhere ... and about the feasibility of solving that problem.

Failure to give high priority to eliminating radiation overdoses would seem inconsistent with the announced determination of numerous women's groups, research grant-makers, and editorialists in medical journals, to PREVENT as much breast cancer as possible. The previous chapter surely shows why this is an exceedingly strange time in history to ignore radiation's continuing contribution to the production of future breast cancers.

Misinformed physicians who spread the safe-dose fallacy, or the fallacious comparison of x-ray risks with "a day in the sun," have been the chief obstacle to elimination of overdoses. We are realistic about that problem (Chapter 48, Part 4a). But the editors of our "peer-review" medical journals do not need to become accomplices. Why do they ever let the threshold fallacy pass their review? And why don't those editors lead the way in advocating a credible, independent system to stop millions of careless overdoses, and the AGGREGATE consequences thereof?

The duty of true physicians is like the duty of democratic military leaders. Medical or military, we have a duty to do ALL we can to prevent unnecessary deaths and lethal screw-ups, while still achieving the bigger goal. Patients and troops trust us not to be CARELESS with life. They trust us to make reality-checks instead of mere assumptions. And patients should be able to rely on the medical professions to do that. With respect to radiation overdosing, clearly they can't. Not yet.

Cost-Benefit Speculations

We are often asked, "HOW MANY breast cancers could be prevented by getting rid of overdoses?" Of course it is impossible to know, when (thanks to the medical professions) no one even knows the current aggregate breast doses per year from all sources combined. And without knowing the number of preventable cases, it would also be impossible to know the COST per future case prevented. For the sake of argument, let's suppose that the cost of detection and treatment per case of radiation-induced breast cancer, and the cost of PREVENTING one case of radiation-induced breast cancer by eliminating overdoses, would be equal. Which would the reader prefer?

Whenever we speculate about the cost-benefit aspects of eliminating overdoses, we must always remember that elimination of carelessness in x-ray offices will reduce x-ray

dosage to ALL organs, not just breasts, and so there will also be a reduction of radiation-induced cases of cancer arising everywhere in the body, for both females and males.

An excellent general principle was embraced by the American Cancer Society, in an official statement of 1982 (ACS 1982, p.228). Although the statement was offered in the context of mammography ("Mammography 1982: A Statement of the American Cancer Society"), there is no basis for limiting the principle to only one type of x-ray examination. The ACS statement was:

"The American Cancer Society firmly believes that any risk, no matter how small, should be reduced as much as possible and that radiographic equipment should deliver the lowest dose of radiation consistent with producing an optimal diagnostic image."

The Bottom Line

There are not many certainties in the field of cancer prevention. But one of the certainties is this: Whatever number of x-ray-induced cancers are being "put on the shelf" (for delivery later) by today's practice, that number can be drastically reduced just by eliminating careless overdoses --- without interfering with a single useful x-ray procedure. UNSCEAR 1993 suggests that the number could be cut in half. The opportunity to have LESS radiation-induced cancer is staring us in the face.

With what is known today about the important role of DNA-chromosome injuries in cancer development, and about the power of x-rays at any dose-level to induce even the worst such injuries (least repairable), and with what is known from epidemiology about the induction of radiation-induced cancer, why do we continue to TOLERATE x-ray overdoses? In my opinion, we owe it to society to establish independent, trustworthy services which will eliminate such overdoses. And that is what I hope "happens next."

#



"It's no use saying 'we are doing our best.' We have got to succeed in doing what is necessary."

● – Winston Spencer Churchill, 1874–1965,
British wartime leader, and author.

Table 1
Estimated Breast-Cancer Mortalities, Incidence, and I / M Ratios, U.S.A.*

Year	Breast Cancer Mortality	Breast Cancer Incidence	I / M Values
1960	23,755	NA	NA
1965	NA	62,000	NA
1967	26,900	64,000	2.379
1968	28,350	65,000	2.293
1970	30,100	68,000	2.259
1971	30,500	69,000	2.262
1972	32,000	70,000	2.188
1973	32,400	73,000	2.253
1974	32,500	89,000	2.738
1975	32,600	88,000	2.699
1977	33,700	89,000	2.641
1978	33,800	90,000	2.663
1979	34,200	106,000	3.099
1980	35,500	108,000	3.042
1981	36,800	110,000	2.989
1982	37,000	112,000	3.027
1983	37,200	114,000	3.065
1984	37,300	115,000	3.083
1985	38,400	119,000	3.099
1986	39,900	123,000	3.083
1987	41,000	130,000	3.171
1988	42,000	135,000	3.214
1989	43,000	142,000	3.302
1990	44,000	150,000	3.409
1991	44,500	175,000	3.933
1992	46,000	180,000	3.913
1993	46,000	182,000	3.957
1994	46,000	182,000	3.957
1995	46,000	182,000	3.957
1996	44,300	184,300	4.160

(1) Breast-cancer incidence rises from 68,000 to 184,300 between 1970 and 1996. Factor of Rise = $184,300 / 68,000 = 2.71$. Rise = 171 %.

(2) Female Population Rise from 1970 to 1995 = $134,461 / 104,309 = 1.29$. Rise = 29 %. (Table 2)

(3) There is no way that female population increase alone can account for the enormous rise in breast-cancer incidence.

(4) During the same period (1970–1996), the number of breast-cancer deaths rose to 44,300 from 30,100. Factor of Rise = 1.47. Rise = 47%.

(5) Meanwhile, the fraction of all U.S. women over age 60 keeps increasing (longer lifespan), which means more women are in the ages of high breast-cancer mortality. Thus the raw number of breast-cancer deaths per 100,000 women (all ages combined) has risen, while the AGE-ADJUSTED number of breast-cancer deaths per 100,000 females has remained almost constant.

* Source: American Cancer Society, annual January–February issues of CA – A Cancer Journal for Clinicians. Exception: The 1960 figure came from ACS 1994, p.5.

Table 2
Growth of the United States Population: 1850 to 1990
 U.S. Population, in 1000s
 (Statistical Abstract of United States 1993, 113th Edition)

Year	Male	Female	Total	Female Population Relative to 1850
1850	11,838	11,354	23,192	1.000
1860	16,085	15,358	31,443	1.353
1870	19,494	19,065	38,559	1.679
1880	25,519	24,637	50,156	2.170
1890	32,237	30,711	62,948	2.705
1900	38,816	37,178	75,994	3.274
1910	47,332	44,640	91,972	3.932
1920	53,900	51,810	105,710	4.563
1930	62,137	60,638	122,775	5.341
1940	66,062	65,608	131,670	5.778
1950	75,187	76,139	151,326	6.706
1960	88,341	90,992	179,333	8.014
1970	98,926	104,309	203,235	9.187
1980	110,053	116,493	226,546	10.260
1989	120,982	127,258	248,240	11.208
1990	121,239	127,471	248,710	11.227
1991	122,979	129,198	252,177	11.379
1992	124,358	130,564	254,922	11.499
1993	125,699	131,893	257,592	11.616
1994	127,010	133,194	260,204	11.731
1995	128,292	134,461	262,753	11.843
2000	134,338	140,477	274,815	12.372

Data beyond 1995 are projections.

Comments

It is clear that the United States Population has been anything but stable since 1850. Roentgen's discovery of the x-ray occurred in 1895, so our tabulation covers the period from 45 years before the discovery up through the present period.

In all our considerations of breast-cancer, we must keep in mind that an increasing population can be anticipated to have an increasing number of breast-cancers, if all other factors are held constant.

However, there is no way that female population increase alone can account for the enormous rise in breast-cancer incidence, as shown beneath Table 1.

About the Author

John William Gofman is Professor Emeritus of Molecular and Cell Biology in the University of California at Berkeley, and Lecturer at the Department of Medicine, University of California School of Medicine at San Francisco.

He is the author of several books and more than a hundred scientific papers in peer-review journals in the fields of nuclear / physical chemistry, coronary heart disease, ultracentrifugal analysis of the serum lipoproteins, the relationship of human chromosomes to cancer, and the biological effects of radiation, with especial reference to causation of cancer and hereditary injury.

A Narrative Chronology

While a graduate student at Berkeley, Gofman co-discovered protactinium-232, uranium-232, protactinium-233, and uranium-233, and proved the slow and fast neutron fissionability of uranium-233.

Post-doctorally, he continued work related to the chemistry of plutonium and the atomic bomb development. At that early period, less than a quarter of a milligram of plutonium-239 existed, but a half-milligram was urgently needed for physical measurements in the Manhattan Project. At the request of J. Robert Oppenheimer, Gofman and Robert Connick irradiated a ton of uranyl nitrate by placing it around the Berkeley cyclotron (to capture neutrons), for a total exposure period of six weeks, with operation night and day. In 110 Gilman Hall, they scaled up Gofman's previous test-tube-sized sodium uranyl acetate process for the plutonium's chemical extraction. Dissolving 10-pound batches of the "hot" ton in big Pyrex jars, and working around the clock with the help of eight or ten others, they reduced the ton to a half cc of liquid containing 1.2 milligrams of plutonium (twice as much as expected).

After the plutonium work, Gofman completed medical school. In 1947, he began his research on coronary heart disease and, by developing special flotation ultracentrifugal techniques, he and his colleagues demonstrated the existence of diverse low-density lipoproteins (LDL) and high-density lipoproteins (HDL). Their work on lipoprotein chemistry and health consequences included the first prospective studies demonstrating that high LDL levels represent a risk-factor for coronary heart disease and that low HDL levels represent a risk-factor for coronary heart disease. His principal book on the heart disease research is CORONARY HEART DISEASE (1959, Charles C. Thomas, Publisher).

In the early 1960s, the Atomic Energy Commission (AEC) asked him if he would establish a Biomedical Research Division at the Lawrence Livermore National Laboratory, for the purpose of evaluating the health effects of all types of nuclear activities. From 1963-1965, he served as the division's first director, concurrently with service as an Associate Director of the entire Laboratory, for Biomedicine. Later he stepped down from these administrative activities in order to have more time for his own laboratory research in cancer, chromosomes, and radiation, as well as his analytical work on the data from the Japanese atomic-bomb survivors and other irradiated human populations.

In 1965, Dr. Ian MacKenzie published an elegant report entitled "Breast Cancer Following Multiple Fluoroscopies" (British J. of Cancer 19: 1-8) and in 1968, Wanebo and co-workers, stimulated by MacKenzie's work, reported on "Breast Cancer after Exposure to the Atomic Bombings of Hiroshima and Nagasaki" (New England J. of Medicine 279:667-671), but few were willing to concede that breast-cancer could be induced by low-LET radiation.

Gofman and his colleague, Dr. Arthur Tamplin, quantified the breast-cancer risk (1970, *The Lancet* 1:297), looked at the other available evidence, and concluded overall that human exposure to ionizing radiation was much more serious than previously recognized (Gofman 1969; Gofman 1971).

Because of this finding, Gofman and Tamplin spoke out publicly in favor of re-examining two programs which they had previously accepted. One was the AEC's "Project Plowshare," a program to use hundreds or thousands of nuclear explosions to liberate natural gas in the Rocky Mountains and to excavate harbors and canals. Experimental shots had already been done, for example, in Colorado and Nevada. The second program was the AEC's plan to license about 1,000 nuclear power plants as quickly as possible and to build a "plutonium economy" based on breeder reactors. In 1970, Gofman and Tamplin proposed a five-year moratorium on licensing of commercial nuclear power plants.

For Gofman and Tamplin, the public health was the issue of prime importance. The Atomic Energy Commission was not pleased. In 1973, Gofman returned to full-time teaching at the University of California at Berkeley, until choosing an early and active "retirement" --- a retirement to full-time research on radiation health-effects. This research led to publication of four scientific books, and to the current work, "Preventing Breast Cancer." The previous books are:

1. RADIATION AND HUMAN HEALTH, 908 pages (1981).
2. X-RAYS: HEALTH EFFECTS of COMMON EXAMS (with Egan O'Connor), 439 pages (1985).
3. RADIATION-INDUCED CANCER FROM LOW-DOSE EXPOSURE: AN INDEPENDENT ANALYSIS, 480 pages (1990).

4. CHERNOBYL ACCIDENT: RADIATION CONSEQUENCES for THIS and FUTURE GENERATIONS, 574 pages (1994). It is in the Russian language. An English-language edition will be published in the future.

Recent Honors and Awards

December 1992, in Stockholm, Sweden: The Right Livelihood Award of the Right Livelihood Foundation. Dr. Jakob von Uexküll's statement, in presenting the award for John Gofman's "pioneering work in exposing the health effects of low-level radiation," was:

"The Right Livelihood Award for vision and work forming an essential contribution to making life more whole, healing our planet, and uplifting humanity."

November 1993, in Atlanta, Georgia: Selection as Honored Speaker for the 1993 Meeting of the Arteriosclerosis Section of the American Heart Association, in recognition of work described by Donald S. Fredrickson in Circulation (Suppl., Vol.87, No.4: 1-59, April 1993).



Birth: September 21, 1918 in Cleveland, Ohio.

Education:

Grade and high school in Cleveland. A.B. in Chemistry from Oberlin College, 1939.
 Ph.D. in Nuclear/Physical Chemistry from the University of California at Berkeley, 1943. Dissertation:
 Discovery of Pa-232, U-232, Pa-233, and U-233. Proof of the slow and fast neutron fissionability of U-233.
 Discovery of the $4n + 1$ radioactive series.
 M.D. from the School of Medicine, University of California at San Francisco, 1946. Internship in internal medicine
 at the University of California Hospital, San Francisco, 1946-1947.

Positions:

Academic appointment in 1947 in the Division of Medical Physics, Department of Physics, University of California
 at Berkeley. Advancement in 1954 to the full professorship, a position held to the present time, with shift to Emeritus
 status in December, 1973. Under recent University re-organization, the affiliation is now the Division of
 Biochemistry, Department of Molecular and Cell Biology.

Concurrent appointment since 1947 as either Instructor or Lecturer in Medicine in the Department of Medicine,
 University of California, San Francisco.

Additional appointments held:

Associate Director, Lawrence Livermore National Laboratory, 1963-1968. Resigned this post to gain more time for
 research and teaching. Remained as Research Associate at Livermore through February, 1973.

Founder and first Director of the Biomedical Research Division of the Lawrence Livermore Laboratory,
 1963-1964. This work was done at the request of the Atomic Energy Commission.

Member, Advisory Board for NERVA (Nuclear Engine Rocket Vehicle Application), approximately 1963-1966.

Member of the Reactor Safeguard Committee, University of California, Berkeley, approximately 1955-1960.

Group Co-Leader of the Plutonium Project (for the Manhattan Project) at the University of California, Berkeley,
 1941-1943. This work included meetings at Chicago and Oak Ridge to exchange information and to help DuPont
 engineers prepare for the reprocessing operations at Hanford, Washington.

Physician in Radioisotope Therapy, Donner Clinic, University of California, Berkeley, 1947-1951.

Medical Director, Lawrence Radiation Laboratory (Livermore), 1954-1957.

Medical consultant to the Aerojet-General Nucleonics Corporation, with special emphasis on the hazards of ionizing
 radiation, for approximately eight years during the 1960s.

Consultant to the Research Division of the Lederle Laboratories, American Cyanamid, 1952-1955.

Consultant to the Research Division of Riker Laboratories, approximately 1962-1966.

Scientific consultant to Vida Medical Systems, 1970-1974; co-invented the VIDA heart monitor, a pocket-worn
 computer to detect and announce the occurrence of serious cardiac arrhythmias; invented a skin cardiographic electrode
 subsequently used widely throughout the USA.

Appointment in April 1995 to the Breast Cancer Etiology Working Group, National Action Plan on Breast Cancer, a
 co-operative effort of the National Breast Cancer Coalition and the U.S. Dept. of Health and Human Services (Public
 Health Service, Office of Women's Health).

Chairman of the Committee for Nuclear Responsibility, 1971 to the present; pro-bono work; no book-royalties or
 compensation of any type has ever been accepted.

Patents:

3,123,535 (Glenn T. Seaborg, John W. Gofman, Raymond W. Stoughton): The slow and fast neutron fissionability
 of uranium-233, with its application to production of nuclear power or nuclear weapons.

2,671,251 (John W. Gofman, Robert E. Connick, Arthur C. Wahl): The sodium uranyl acetate process for the
 separation of plutonium in irradiated fuel from uranium and fission products.

2,912,302 (Robert E. Connick, John W. Gofman, George C. Pimentel): The columbium oxide process for the
 separation of plutonium in irradiated fuel from uranium and fission products.

Earlier honors and awards:

Gold-Headed Cane Award, University of California Medical School, 1946, presented to the graduating senior who
 most fully personifies the qualities of a "true physician."

Modern Medicine Award, 1954, for outstanding contributions to heart disease research.

The Lyman Duff Lectureship Award of the American Heart Association in 1965, for research in atherosclerosis and
 coronary heart disease; lecture published in 1966 as "Ischemic Heart Disease, Atherosclerosis, and Longevity," in
 CIRCULATION 34: 679-697.

The Stouffer Prize (shared) 1972, for outstanding contributions to research in arteriosclerosis.

American College of Cardiology, 1974; selection as one of twenty-five leading researchers in cardiology of the past
 quarter-century.

University of California, Berkeley, Bancroft Library, 1988; announcement of the "Gofman Papers" established in the
 History of Science and Technology Special Collection (October 1988, BANCROFTIANA, No. 97: 10-11).

*"The strongest human instinct is to impart information,
and the second strongest is to resist it."*

• – Kenneth Graham, author of "The Wind in the Willows."

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INDEX and GLOSSARY

Preventing Breast Cancer

NOTES:

• - As a convenience to readers, both in the USA and abroad, we have tried to define all abbreviations and many terms. We do it either here in the Index-Glossary, or right in the text --- and sometimes in both places.

• - An "e" before a page number (e41, for example) means an explanation is on that page.

• - Many quotations in the book contain medical terms. When the weight of the passage can be felt without defining every term, we made choices.

• - Readers may want to look for Index entries with indented sub-entries. For recurrent topics or key concepts, we try to provide specific reminders, instead of long lists of page numbers. There are a few exceptions.

• - Within this Index, we sometimes abbreviate:

BC = breast cancer (br.canc.)
ca = cancer
irradn = irradiation
J = Journal
radn = radiation
w = with

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• - We have tried to use an alphabetical order which "credits" only LETTERS (not spaces, etc.). A few numerical entries come first:

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 • -- "Do what you can. Start where you are." --
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- -- "You can observe a lot by watching." -- Yogi Berra, famous American baseball player.
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- -- "Everybody is ignorant, only on different
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• -- "Don't be afraid to take a big step if one is indicated. You can't cross a chasm in two small jumps." -- David Lloyd George, 1863-1945, British statesman.

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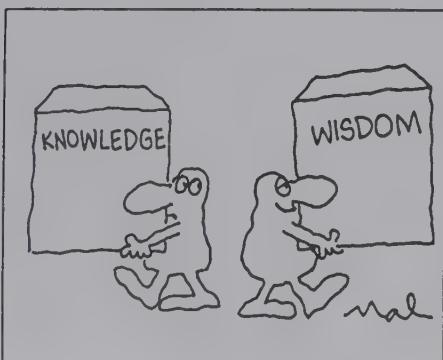
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• -- "Life is what happens to us while we are making other plans." -- Thomas la Mance.

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• -- "I'm in favor of leaving the status quo the way it is!" -- Yogi Berra, famous American baseball player.

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LET = Linear Energy Transfer, the amount of energy transferred from a high-speed particle to the surrounding tissue, per unit of distance traveled along its path. As the particle transfers its energy, bit by bit, it loses speed. When it is slower, the average distance decreases between consecutive energy transfers, and the amount of energy transferred per unit of distance BECOMES HIGHER, on the average. Relative to alpha particles, which are HIGH-LET particles ("densely ionizing," with very short tracks), the high-speed electrons from x-rays and gamma rays are LOW-LET particles. SEE also "Ionizing radiation"

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• -- "The rule on staying alive as a forecaster is to give 'em a number or give 'em a date, but never give 'em both at once." -- Jane Bryant Quinn, contemporary financial analyst.

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• -- "To avoid delay, please have all your symptoms ready." -- Sign in a physician's waiting room.

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• -- "A hundred times every day I remind myself that my inner and outer life depend on the labours of other men, living and dead, and that I must exert myself in order to give, in the same measure as I have received." -- Albert Einstein, 1879-1955, Nobel Laureate in Physics, 1921.

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XYZ

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#

Note:**● – Rads and Grays**

The rad is defined on page 11. Here, we supply two boxes which may be helpful in relating rads to grays. First, ABC:

- (A) There are 100 rads per gray, so there is 1 rad per 0.01 gray.
- (B) 0.01 gray is 1/100 of a gray, or a centi-gray (cGy).
- (C) So 1 rad and 1 centi-gray are doses of the same size.

Since a rad is 100-times smaller than a gray, a milli-rad (0.001 rad) is 100-times smaller than a milli-gray (0.001 Gy).

1.00 rad
0.01 gray (Gy)
1.00 centi-gray (cGy)
10.00 milli-grays (mGy)

are all doses of the
same size.

1.0 milli-gray (mGy)
100.0 milli-rads
0.1 rad
0.1 centi-gray (cGy)

are all doses of the
same size.

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1995, The Hundredth Anniversary of Roentgen's Momentous Discovery of the X-Ray:
Can We Insure a More Fitting Tribute in the Next 100 Years?

We have often been asked the question: "Have Medical X-Rays Done More Harm Than Good?" That is the WRONG question. The appropriate question is, "Can we have all the good things in medicine which x-rays can do with vastly less harm?" The answer is unequivocally, "Yes."

This book relates the evidence which shows that more than 100,000 women are developing breast cancer per year in the United States, due to past overexposure to medical x-rays, mainly from radiotherapy of benign disease in dermatology and other specialties, and over-zealous use of diagnostic x-rays and fluoroscopy by physicians and non-physicians.

Why did this happen in the past, and how can we prevent further accumulation of women destined to develop life-threatening breast cancer?

● - Medical science failed in the past to realize in time that production of cancer can occur 10-20-30-40-50 (and possibly more) years before CLINICAL manifestation of breast cancer and other cancers.

● - As a result of this failure, medicine embarked on a half-century of denial that even exposures as high as 100-500 rems could cause human cancer. That era is over. However, medicine today, in some but not all quarters, is engaged in suggesting that LOW doses of radiation do not produce cancer. This fallacy, if not abandoned, will lead to a century of abusing and insulting the great contribution of Dr. Roentgen to medical science.

If one claims a toxic agent is safe at some level, when that is untrue, the person making the claim is inflicting disease upon other persons, as a result of false information. This is a very serious matter.

If one claims a toxic agent is safe at some level, and one does not know whether or not that is true, the claim leads to human experimentation (a Nuremberg Crime).

Nothing can undo the massive harm caused by past misunderstanding. But that is surely no reason to compound the errors of the past. We would do well to observe Santayana's "law" that those who cannot remember the past are doomed to repeat it.
We do NOT need more cases of breast cancer.

The Essential Messages

Our estimate in this book is that about 75% of breast cancer is caused by earlier irradiation. There is absolutely no doubt that reducing unnecessary x-radiation will prevent vast numbers of future breast cancers.

We hope that all physicians will join with health scientists in a determination to reduce unnecessary x-radiation. As discussed in this book, this effort can succeed without ever interfering with a single essential x-ray examination. That is the main route to prevention of breast cancer. Women will not be willing to forgive ANYONE who stands in the way of this objective.

Who will look out for women's health better than they themselves?