

CHAPTER 2

Pre-1960 and Post-1960 Uses of Medical Radiation, and Its Carcinogenic Action

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● Part 1. Is Hypothesis-1 Long Overdue?

Hypothesis-1 proposes that exposure to medical radiation is a highly important cause (probably the principal cause) of cancer-mortality in the United States during the Twentieth Century --- even though medical radiation is only rarely mentioned in lists of "risk factors" for Cancer.

Then how did we reach the point of deciding that such an idea deserved someone's careful examination? Very slowly, as Part 9 of this chapter relates. Perhaps the conception and testing of Hypothesis-1 is long overdue.

Hypothesis-1 becomes a proposition "demanding" evaluation when two types of knowledge COMBINE: Knowledge about some history of medicine in the United States during the Twentieth Century, and knowledge about the evidence that xrays and other ionizing radiations are proven carcinogens --- indeed, are mutagens with some uniquely potent properties. Many people are versed in one of these fields, but not the other.

On both topics, this chapter provides some basic orientation, with references to ample supporting evidence. Parts 2 and 3 describe a little medical history, and Parts 4, 5, 6, 7, and 8 state some of the key knowledge about radiation carcinogenesis.

This book presents a powerful test of Hypothesis-1 and concludes that the evidence strongly supports the hypothesis. The same evidence is the basis for Hypothesis-2.

● Part 2. 1896-1960: Rapid and Widespread Embrace of Xrays in Medicine

Wilhelm Konrad Roentgen discovered the xray on November 8, 1895 (Roentgen 1895). "The ray," as it was often called, immediately caused a sensation among physicians and the general public. Commemorating the hundredth anniversary of Dr. Roentgen's discovery, Dr. Ronald G. Evens provides some vivid details in his "Roentgen Retrospective," in the Journal of the American Medical Association (Evens 1995). Referring to the USA, Evens writes (1995, p.912):

"By the time of the appearance of the first American clinical diagnostic radiograph [also called roentgenograph and skiagraph], made at Dartmouth College by Dr. Edwin Frost on February 3, 1896, physicians were becoming increasingly aware of the extraordinary potential for the new discovery. By April, 'xray mania' had seized the United States. Xray studios had opened for 'bone portraits,' and countless photographers and electricians had set up shop as 'skiagraphers.'" Thomas Edison became an enthusiast in 1896, and attempted to xray the human brain "at work" (Evens 1995, p.914).

2a. The Xray in Medicine: Diagnostic, Therapeutic and Interventional Uses

In medicine, a journal entitled Archives of Clinical Skiagraphy made its appearance in April/May 1896 (London), and the American Xray Journal began publication in 1897. In 1900, the American Roentgen Ray Society was founded. "Soon, the appearance of xray machines in general practitioners' offices across the United States would underline the notion that a new technology was

available to diagnose any and every ailment. Some physicians even thought it would eliminate the need for laboratory analysis in medicine" (Evens 1995, p.915).

The xray was employed immediately not only for diagnosis of medical problems, but also for treatment. There was hope that xrays would cure Tuberculosis, Cancer and every other affliction. The ten years, up to 1906, were described as follows by Dr. George MacKee, a great figure in dermatology and an enthusiast for reasonable radiation therapies (from MacKee 1938, p.16):

"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 xray operator of the period and in spite of repeated warnings from capable men, the 'radiomaniacs' held the reins."

Although of course the chaos of the first ten years subsided, enthusiasm for diagnostic, therapeutic, and interventional uses of xrays did not subside, as Parts 2c and 2d indicate.

Interventional Radiology

A term is needed, to identify uses of medical radiation which are neither strictly diagnostic nor directly therapeutic. Such a term, loosely used, is "interventional radiology." Examples include xray-use in setting broken bones, locating foreign objects, placing catheters and needles, and helping to guide many types of surgical procedures. In the past, xrays were used also to guide the deliberate collapsing of a lung, in patients who were trying to recover from Pulmonary Tuberculosis.

2b. The Skin as the Initial Dose-Meter (Dosimeter)

Appendix A of this book defines the commonly used dose-units (rad, roentgen, centi-gray, and others), and dose-ranges for what is regarded as low, moderate, and high dosage.

But when xrays were introduced into medicine, it was far from clear how to measure the xray doses given to patients, and what was biologically "too much." Everything was figured out by trial and error. Today, it is regarded as a rare event when the skin of a patient gets damaged by medical xrays. But for many years during the first half of the Twentieth Century, the skin was often the dose-meter. The reddening or burning of skin on enough patients gradually established the fact that excessive dosage could occur. Indeed, the early dose-unit in medicine was the "erythema dose" --- the dose-level which generally provokes a morbid reddening of the skin (estimated today as a dose of about 200 rads for temporary erythema, 600 rads for main erythema, and 1,500 rads for late erythema; FDA 1994, Table 2). In 1926, "erythema dose" was a term still in use in medical journals. For example (Husik 1926, p.859):

"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 [on the diagnostic film] a broad superior mediastinum are considered as suspicious cases, and are given four xray treatments of a third of an erythema dose. The treatments are repeated at intervals of ten days." (The purpose of such "treatments" was to shrink the thymus gland, for it was widely believed that patients with smaller thymus glands had a lower chance of sudden death under anesthesia; Gofman 1995/96, Chapter 10.)

2c. Popularity of Fluoroscopy (Roentgenoscopy)

The fluoroscope is an xray machine which leaves the xray beam "on" while the physician examines the motions of a patient's organs, and/or the motions of various instruments and catheters (during surgical and other procedures). Because the beam stays "on," the fluoroscope has the potential to deliver high xray doses.

During World War One, the Army managed to reduce the size and complexity of fluoroscopes, which were used in field hospitals during bone-setting and removal of bullets and other debris. After the war, in the 1920s, fluoroscopy (also called roentgenoscopy) became an enormously popular procedure not only among radiologists (roentgenologists), but also among many kinds of physicians.

The fluoroscope produces information instantly, without the delay, expense, and training required to develop xray-exposed films.

Routine Use of Fluoroscopes in Office Practice

In 1922, Dr. Louis Bishop made the following prediction before the Medical Society of the Greater City of New York (Bishop 1922): "Fluoroscopy, I venture to assert, will become a routine measure in every physician's office before long." In 1923, Dr. Preston Hickey reported to the American Roentgen Ray Society as follows (Hickey 1923):

"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 xray work, but simply wishing to have conveniently at hand an xray control of their physical findings. Here again, the simplified apparatus which has developed from war-time practice is conspicuous." By 1937, Dr. Eugene Leddy of the Mayo Clinic reported (Leddy 1937, p.924):

"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 [fluoroscopy]. These studies are often 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."

Operation of Fluoroscopes in Pediatric Offices

By 1940 (perhaps much earlier), some pediatricians (not all) included fluoroscopy as part of every "well-baby" visit. In 1942, Dr. Franz Buschke and Herbert M. Parker wrote (Buschke 1942):

"Recently we became aware of the fact that apparently a number of pediatricians include fluoroscopy in the monthly routine examinations of infants in their care during the first and second years of life." This pediatric practice is confirmed in Pifer 1963 and in Blatz 1970. Dr. Hanson Blatz, who was New York City's chief of Radiation Control, reported (Blatz 1970): "When we questioned this practice, pediatricians would say, 'Well, the parents expect it. They think if we don't fluoroscope the patients, they are not getting a complete examination'."

After studying the radiation output of seven fluoroscopes in the offices of "reputable pediatricians selected at random," Buschke and Parker estimated (Buschke 1942, p.527): "If the average rapid fluoroscopy by an experienced and well-adapted examiner takes twenty seconds, about 8.3 roentgens [entrance dose] will be delivered at this rate or 100 roentgens during the first year of life." The roentgen is a dose-unit which is approximately equivalent to a rad (Appendix-A, Part 2).

Of course, not all examiners were well trained with fluoroscopic machines. In the seven pediatric offices visited by Buschke and Parker, "none of them knew the output of their machine" (Buschke 1942, p.525). And (p.527): "In another place under the direction of one of the best radiologists, we found that the output differed with the operator." The dose-rate differed by nearly a factor of 2.

Operation of Fluoroscopes in Hospitals

Fluoroscopy was popular not only in medical offices, but also in hospitals --- for diagnostic and surgical uses. Carl B. Braestrup, of the Physics Laboratory of the New York City Department of Hospitals, was persistent in warning about careless use of fluoroscopes. In an address to the New York Roentgen Society, he reported (Braestrup 1942, p.210):

"During the past years, we have measured the roentgen output of large numbers of fluoroscopes, using the settings at which they are normally operated ... and have found a very wide variation ... Attention is called particularly to test B-116, where the R [roentgen] 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." And (Braestrup 1942, 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." In an attempt to prevent some injuries, a limit of 100 roentgens per fluoroscopic examination was set in New York City hospitals (Braestrup 1969). "Recommended" would be a better word than "set," for even today, radiation doses during fluoroscopy are seldom measured (Part 3d).

Estimated Dose per Fluoroscopic Procedure at Mid-Century

In 1953, Dade W. Moeller (then of the Public Health Service; later, president of the Health Physics Society) published an estimate that the average entrance dose per fluoroscopic examination was about 65 roentgens at mid-century (Moeller 1953, pp.58-59). Our Appendix-K explores the implications of the Moeller estimate.

2d. Diagnostic Films: Slow Film-Speeds and Wide Beams

In addition to fluoroscopy, physicians made use of a vast number of diagnostic xray photographs ("films"). Most of the common diagnostic examinations used today were also used well before mid-century. But in terms of cancer hazard, the hazard caused per film was higher in the past, because dose was higher and because a larger area was exposed. One reason that the dose was higher in the past is that the films were "slower" and exposure required more "light" (more xray photons). A larger area was exposed because few were trained to confine the xray beam to the area of the film, and certainly not to the organs whose picture was needed. In addition to the organs which were irradiated on purpose, most of the torso and neck were often irradiated simultaneously. We surmise (but do not know) that dental xrays also exposed much more area than needed.

Pre-Birth Irradiation

Fetal irradiation was quite common. "Roentgenographic evaluation of the relative size of the fetal head and maternal pelvis has been used clinically almost since the advent of medical radiography" (Kelly 1975). The estimated frequency of xray pelvimetry in the 1947-1970 period was 1 birth out of every 13.5 births in the USA (Gofman 1995/96, pp.88-89, based on MacMahon 1962 and Kelly 1975).

2e. Radiotherapy of Benign Diseases: "Every Disease There Is"

Therapeutic irradiation for non-malignant conditions began soon after the xray's discovery. Radium, which was discovered in 1898, was sometimes used as a source of gamma rays, but unlike xrays, radium was scarce and expensive. A few examples of the ailments treated by high-dose medical radiation can illustrate the range of applications, without implying that radiation was tried on EVERY case:

Acute postpartum mastitis, ankylosing spondylitis, arthritis, asthma, excessive menstrual bleeding, herpes zoster(shingles), hyper-thyroidism, neuritis, pneumonia, pyogenic (pus-forming) infections, skin disorders of numerous variety (see below), sore shoulders (bursitis, tendonitis), stomach ulcers, swollen lymphoid tissues (e.g., "swollen adenoids"), thymus-gland enlargement (widely believed, from about 1915 to 1945, to be associated with sudden death under anesthesia, and with sudden infant death), thyroiditis, tuberculous lesions of practically every organ, and whooping cough. Documentation and references can be found in Gofman 1995/96.

In 1965, Dr. Stephen B. Dewing, a radiologist, authored a fine book in which he wrote (Dewing 1965, p.ix): "It has been said that radiation therapy has been used promiscuously, on every disease there is, and probably so."

Skin disorders deserve a paragraph of their own. By 1922, over 80 skin disorders were being treated with high-dose radiation (MacKee 1922). And this continued (MacKee 1938). Very few of these conditions were malignant. They included acne vulgaris, actinomycosis (a fungus), eczema, incessant itching, lichen planus, psoriasis, neurodermatitis, and ringworm of the scalp. Typical therapeutic doses began at about 85 roentgens per week, and could accumulate up to 1,400 roentgens per regime (Sulzberger 1952, p.639).

"Super-Soft" Xrays and a Mistaken Generalization

In 1925, Dr. Gustav Bucky introduced the use of "grenz rays" (also called "super-soft roentgen rays") for some skin disorders. Super-soft xrays lie on the continuum between xrays and ultraviolet rays, and most of them penetrate only about 2 millimeters of tissue. By contrast, "superficial roentgen rays" (which come from xray machines operated at peak kilovoltages in the 60-100 kilovolt range), penetrate more deeply. As of 1952, "most dermatoses" were treated with "superficial roentgen-ray treatments" --- not by grenz rays, according to New York University's head of Dermatology (Sulzberger 1952, p.639).

Perhaps it is the concept of super-soft non-penetrating xrays which accounts for the mistaken idea, still circulating in some medical circles, that medical xrays in general are "too weak" to cause Cancer. Therefore, a reminder may be appropriate: Whenever a medical xray procedure exposes a film (or other image-maker) on the opposite side of a patient, such exposure is proof that some of the xrays fully penetrated the patient --- not just the top 2 millimeters. Medical xrays are definitely not "too weak" to penetrate and to leave carcinogenic damage in the internal organs.

2f. Were People Too Poor to Visit Physicians?

Today, most medical care in the United States is paid for by a third party --- some variety of private and government insurance. Some readers might assume that in the 1900-1960 period, when such arrangements were absent or less common, few people could afford to visit physicians. The following estimate for the year 1950 may indicate otherwise, although the estimate is not elaborated by income-level or by "service." The estimate is that there were 150,000 practicing physicians, who performed 750,000,000 medical services per year, when the population was 150,000,000 people (Donaldson 1951, p.931). If valid, the figures mean an average of 5 "medical services" in a year for each man, woman, and child.

In addition, in 1949, allegedly 60 million people (40% of the U.S. population) visited a dentist, according to Dr. Dade W. Moeller and colleagues (Moeller 1953, p.59). These authors report that 84 million dental xray films were used in 1949: "The average exposure to the patient per film is about 5 roentgens, most of the exposure being limited to the mouth of the patient" (Moeller 1953, p.59).

2g. Emphatic Assurances of Safety

Since virtually no one keeled over as a result of diagnostic, interventional, and therapeutic xray usage, the xray was repeatedly declared harmless. "Absolutely no danger." "Harmless." "No reports of harmful effects." "So far as we know, harmless both as to immediate and remote effects." Even 2,000 roentgens, delivered to ulcer patients over 12 days, was a dose pronounced "perfectly safe" (Ricketts 1951, p.381). The context of such statements is presented in Gofman 1995/96.

The medical professions did not think about delayed consequences, like Cancer, despite some evidence from experimental animals of xray-induced Cancer. By the 1940s, a few experts were trying to discourage pediatricians from fluoroscoping well-babies every month during check-ups, lest gonadal irradiation cause INHERITED afflictions in the next generation (Buschke 1942, pp.527-532). Concern about xray-induced CANCER was hardly voiced before the late 1950s, and by then, radiation health-science was very deeply entangled with the nuclear aspects of national security.

Meanwhile, during the 1940s and 1950s, the Defense Department and the Atomic Energy Commission had staffed themselves and their numerous research arms with radiation experts transferred from medicine --- the very same people who were confident that even very high doses of xrays did no harm.

2h. A Rather Strong Warning in 1959 to the Medical Profession

Above-ground nuclear bomb-tests in Nevada during the 1950s had deposited radioactive fallout, unevenly, nearly from coast to coast. It caused a furor --- especially because milk was contaminated by strontium-90. Dr. Linus Pauling and others were warning about long-term health effects, particularly radiation-induced inherited afflictions and radiation-induced Cancers. What was their evidence?

By 1927, H.J. Muller had established, in the fruit fly, that ionizing radiation induced heritable mutations. Radiation-induced malformations and radiation-induced Cancer had been demonstrated in

some experimental animals. Human evidence in the 1950s was thin --- because remarkably little epidemiologic inquiry had been undertaken, to find out if there were delayed effects from medical radiation. But evidence was far from absent. For example, human evidence of radiation-induced Cancer already included the following (and more):

- Bomb-induced Leukemia in Hiroshima-Nagasaki.
- Xray-induced Skin Cancers in radiologists.
- Xray-induced childhood Leukemia and childhood Cancer in children irradiated before birth.
- Xray-induced Thyroid Cancer following childhood radiotherapy for "enlarged thymus."
- Thorium-induced Liver Cancer in medical patients who had received thorotrast (used as a "contrast medium" to enhance diagnostic information from certain types of fluoroscopic procedures).
- Radon-and-radon-daughter-induced Lung Cancer in uranium miners.
- Radium-induced Bone Cancer in radium dial-painters and others.

The furor over radioactive fallout resulted in a 1956 report from the National Academy of Sciences entitled "The Biological Effects of Radiation: A Report to the Public," followed by a 1958 report from the United Nations. The evidence already indicated that children are probably more vulnerable than adults to radiation carcinogenesis. In 1959, Dr. Russell Morgan (Chairman of Radiology at Johns Hopkins Medical School) chaired a National Advisory Committee on Radiation for the U.S. Public Health Service. In its 20-page report, to the Surgeon General of the Public Health Service, the Committee began (PHS 1959, p.1):

"During the past several years, a number of scientific bodies, including the National Academy of Sciences of the United States (NAS 1956) and the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR 1958), have reported extensively on the influence of ionizing radiation on biological systems. From these reports it is evident that serious health problems may be created by undue radiation exposure and that every practical means should be adopted to limit such exposure both to the individual and to the population at large." And (PHS 1959, pp.1-2):

"The principal sources of ionizing radiation which have been created or developed by man include xray machines, nuclear reactors and their radioisotopic byproducts, high-energy particle accelerators, a number of concentrated forms of naturally occurring radioactive materials, and the fallout constituents of nuclear weapons ...Most of the ionizing radiation received by the population today, other than that received from natural sources, has been from xray machines employed by the health professions."

While the general public may not have realized that radioactive fallout, nuclear pollution, and medical radiation all deliver ionizing radiation, the authors of the 1959 report were explicit on that fact (above). And so, we have chosen the next year, 1960, as the year in which the medical profession was warned that it should stop issuing emphatic assurances, to itself and to its clients, about the safety of medical radiation.

● Part 3. 1960 to Present: Some Changes in Usage of Medical Radiation

Before our overview begins, of post-1960 practices in medical radiation, a comment belongs here about Hypothesis-1 and the pre-1960 period. What happened in the pre-1960 period has a direct impact not only on the 1900-1960 death rates from radiation-induced cancer, but also on such death-rates from 1960 to the present year --- a fact which is documented by Part 8 of this chapter.

In 1990, over 50% of the age-adjusted cancer death-rate (USA) came from people who died of Cancer at age 65 and older. Over 93% comes from people who died at age 45 and older. Their lifetime exposure to medical radiation was very probably NOT limited to post-1960 practices. This statement will be true even well beyond the year 2000. The age-distribution of the 1990 age-adjusted cancer mortality-rate is shown in Chapter 4, Box 4.

3a. Effect of the 1956, 1958, and 1959 Warnings

After human evidence of radiation carcinogenesis began appearing, did it cause a big reduction in the population's average annual per capita exposure from medical radiation?

Parts 3b and 3c show that, during the past 40 years, some events have operated in the direction

of REDUCING the population's average per capita dose from medical radiation, but during the same years, some other events have operated in the direction of ADDING to the per capita dose. If we assume that the NET effect is a reduction in the population's average per capita dose, we still lack justification for assuming it is a "big reduction." We are unaware of any reliable quantification of the population's average per capita dose from medical radiation, for any period, past or present. If such a statement seems shocking, readers need to consider these points:

- Even today, there is great uncertainty about something as basic as the NUMBER of diagnostic xrays given per year in the USA. The annual number for 1985-1990 was at least 800 diagnostic xray exams per thousand population, excluding dental xrays and nuclear medicine (UNSCEAR 1993, Table 6, p.279). That estimate "could be an underestimate by up to 60%" (UNSCEAR 1993, p.229/46).
- With regard to the average DOSE per diagnostic examination, measurement and recording were not --- and are not --- required. Today, at some facilities, dose-estimates and recording are routine, but this is not the standard practice. Dose-measurements (as distinct from expected doses, calculated by rules in a handbook) are extremely rare, even though measurement of entrance dose is not at all difficult these days.
- The ratio of measured dose over expected dose in the USA was found in a government survey to range from 0.1 to 4.0 (Wochos 1977 + Wochos 1979, p.134). In 1989, the National Council (USA) on Radiation Protection and Measurements (NCRP) warned that there may be very large disparities between true doses and expected internal-organ doses, based on commonly used "Monte Carlo methods." NCRP cites an Italian report showing that actual breast, thyroid, and testicular xray-doses from certain medical procedures "were higher by factors of 4 to 50 than Monte Carlo calculations would suggest" (NCRP 1989, p.35). The NCRP is described in our Reference List.
- Post-1960 sampling, by measurements, repeatedly shows that diagnostic doses differ by many-fold from facility to facility, and even from room to room, for the same xray procedure on patients of the same size (Wochos 1977 + Wochos 1979, p.134 + Suntharalingham 1982, among others). The reason for large variation in diagnostic doses will be clear to anyone who has examined Box 1 of Chapter 1. Facilities which implement the known ways to reduce doses, can give doses which are 10 to 50 times lower than places which do not.
- Because neither the frequency of diagnostic exams nor the average doses from them are known, we warn against believing any of the published estimates of a population's average per capita dose, (e.g. UNSCEAR 1993, p.302). But for anyone who does believe such estimates, we present the following comparison. Calculating from sales of xray film in the USA and some other data, the 1959 PHS report (PHS 1959, p.3) estimated that per capita annual whole-body dose in 1955 was 135 milli-rems from diagnostic xrays. For the 1980s, the most nearly comparable estimate in the NCRP Report Number 100 (NCRP 1989, p.44) is 115 milli-rads --- which is not a "big reduction" from 135 milli-rads.
- Moreover, diagnostic examinations contribute only part of the dosage from medical radiation. In both past and present, interventional fluoroscopy (e.g., during surgery) has made an unmeasured but large contribution to the xray dosage. And until about 1960, radiotherapy for a great variety of NON-malignant disorders also made an unmeasured but large contribution to the xray dosage (details in Gofman 1995/96).
- How little is known about dosage became clear to us recently, when we attempted to make a responsible estimate of medical radiation-dose, accumulated by the average female breasts between 1920-1960. That endeavor began with many months of combing through the magnificent collections of old medical journals in the University of California San Francisco Medical Library, and ended in Gofman 1995/96 with about 150 final pages of cautious assumptions about the frequency and typical dosage of just a few of the breast-irradiating procedures (excluding cancer therapy).
- Neither we nor anyone else is in a position to quantify the effect, of the 1956-1959 warnings, on the population's average per capita dose from medical radiation. Everyone needs to be careful about hasty assumptions.

3b. Five Forces toward Reduction of Average Per Capita Dose

1. Most therapeutic uses of medical radiation, for treatment of non-malignant conditions, have been abandoned.
2. Most of the "old" diagnostic exams (which are still useful) are now administered at lower dose and with less area receiving the dose. According to Johnson and Goetz (Johnson 1986), between 1964 and 1983, operators learned to use more care in collimating the xray beam, with the goal of reducing the area irradiated down to the size of the film. Additional reduction in area would be achieved if xray beams were collimated to the body-part needing examination, rather than to the edges of the film (Rosenstein 1979; Discussion in Gofman 1985, p.358-359).
3. Fluoroscopy is rarely if ever used now for routine check-ups of asymptomatic patients. Of course, fluoroscopy is still used (with contrast media) in common diagnostic exams like the Barium Swallow, Upper Gastrointestinal Series, Small Bowel Series, Barium Enema, Gallbladder (Cholecystogram), Cystogram-Urethrogram, Fallopian Tubes (Hysterosalpingography), Intravenous Pyelogram (I.V.P.), Retrograde Pyelogram, and all the vessel-studies (cardiac angiography, celiac angiography, cerebral angiography, pulmonary angiography, renal angiography, etc.). Additional information on such exams is available in Gofman 1985.
4. Reduced use of pelvimetry has reduced in-utero and maternal irradiation from that source.
5. Widespread population-screening for Tuberculosis became unnecessary in the USA, and this event eliminated the associated medical irradiation from repeated chest xrays (and sometimes chest fluoroscopy). Chest xrays in the past, especially from mobile units, gave doses about 100 times higher than chest xrays today.

3c. Seven Forces toward Increase of Average Per Capita Dose

On the other hand, other forces have been operating since 1960 in the opposite direction:

1. Increasing Number of Exams per Thousand Population.

Between 1964 and 1980, the estimated annual number of diagnostic xray procedures per thousand population (USA) increased from 580/1,000 to 790/1,000, according to NCRP 1980 (p.15, Table 3.7, citing Mettler 1987). This is an upward change by a factor of 1.36 --- partly due to inclusion in 1980 of estimates for chiropractic and podiatry. NCRP 1989 (p.69) also estimates that average per capita dose from diagnostic medical radiation to adult bone marrow (which provides a fair approximation of whole-body dose) increased by about 38% during the 1964-1980 period.

According to the same report (NCRP 1989, p.11, citing Wolfman 1986), the total sheets of medical xray film sold annually in the USA, per capita, rose from 1.38 (in 1963) to 3.79 (in 1980). This is an upward change by a factor of 2.75. Did the number of exams per capita rise by 1.36 fold, while sheets of medical xray film per capita rose by 2.75-fold? The correct way to reconcile the two change-factors is certainly not clear. It does seem reasonable to conclude, however, that a very considerable increase in xray exposures per capita did occur.

2. Introduction of Computed Tomography (the CT Exam).

Xray doses to patients from CT exams are typically, but not always, about 10 times higher than from "conventional" diagnostic xray examinations (UNSCEAR 1993, p.235/81). And the trend for CT doses has been upward. Why? "The number of slices imaged on each patient has risen as the time required to perform scans and reconstruct images has decreased" (UNSCEAR 1993, p.244/141). Currently under debate is expanding the use of "ultra-fast" CT scans, with "stop-motion" capability, to detect calcium deposits in coronary arteries.

3. Introduction of Digital Radiography.

Progressively more powerful and cheaper computers have resulted in great expansion of digital radiography, which accounted for 15%-30% of xray examinations by 1993 (UNSCEAR 1993 p.242/132). Among other benefits, digital radiography saves the time and money associated with films, chemicals, and archiving. Digital computed radiography has the potential to reduce xray dosage and area irradiated (UNSCEAR 1993 p.242/132; also p.238/100), and to enable image-sharing by wire.

On the other hand, "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, compared with conventional radiography] considerable over-exposure can go undetected in a digital system unless exposure is specifically monitored" (UNSCEAR 1993 p.243/134). The 1989 NCRP Report comments that the capability of digital systems, to provide more shades of gray than needed in various diagnostic circumstances, increases the dose by 5 to 10 fold over what it need be (NCRP 1989, p.36).

4. Expansion of Nuclear Medicine.

Nuclear medicine involves placement of radio-nuclides inside the body for diagnostic, interventional, or therapeutic purposes. The estimated number of diagnostic nuclear-medicine exams per thousand population, USA, doubled between 1972 and 1982, and the annual rate was estimated at 26 such exams per thousand population in the 1985-1990 period --- a total of 6.8 million exams per year (UNSCEAR 1993, p.306, p.275).

New uses for nuclear medicine (including pediatric uses) and new techniques in nuclear medicine continue to develop. For example, recently in trial is the placement of radioactive stents into the coronary arteries of patients, immediately after angioplasty, as an attempt to prevent re-stenosis. Also in trial is the use of nuclear medicine to diagnose Breast Cancer.

5. Increased Use of Xrays in NeoNatal Intensive Care.

The diagnostic xray examinations given to infants are generally not new. What is new is the larger number of premature and congenitally challenged infants who are now surviving long enough to receive such xrays.

6. Additional Incentives to Cut Corners.

According to Taylor (1983) and Suleiman (1992), underprocessing of xray films is a frequent cause of higher than necessary radiation doses --- higher by 50% to 300%. Since 1981, the U.S. Food and Drug Administration (FDA) has been monitoring the processing speed of over 2,000 automatic film processors in hospitals, private offices, and mammography facilities. The survey "revealed underprocessing at 33% of observed hospitals in 1987, 7% of mammography facilities in 1988, and 42% of private practices in 1989" (Suleiman 1992, p.25). "... The underprocessing component [of the data] for hospitals increased from 18% in 1984 to 33% in 1987 ... We have been told on several occasions that hospitals frequently eliminated Quality Assurance technicians to reduce costs" (Suleiman 1992, p.27).

Recent pressure on health-care providers --- to reduce referrals to specialists, and to recover some of their own costs in circuitous ways --- also may have the effect of inducing even more primary-care physicians and other non-radiologists to perform their own xray examinations (Krieger 1996). The 1989 NCRP Report comments (p.34): "In many office practices in the United States, xray examinations are performed by persons with little or no formal training in the uses of xrays or xray protection."

Even prior to the newer financial pressures on health-care providers, orthopedists, cardiologists, urologists and other specialists have often performed their own xray work --- including fluoroscopy. Chiropractic offices, too, do their own xray work in general.

7. Expanded Use of Interventional Radiology.

Xrays (including fluoroscopy) are commonly used to guide needles, wires, and catheters, and to localize renal stones in lithotripsy. Xrays are used to guide some common types of biopsies (for example, stereotactic needle biopsies). They are used in many kinds of surgical procedures, involving heart, kidney, liver, gallbladder, pancreas, and vessels (see below).

"Over the past 20 years, there has been a substantial increase in the use of xray fluoroscopy as a visualization tool for a wide range of diagnostic and therapeutic procedures," reports the Public Health Service's Center for Devices and Radiological Health (Shope 1997, p.i).

3d. The Longest Fluoroscopic Procedures

The duration of interventional fluoroscopy can still be long enough to cause serious injury of a patient's skin --- and simultaneously to cause high radiation doses to various internal organs. On September 30, 1994, the U.S. Food and Drug Administration issued a Public Health Advisory entitled, "Avoidance of Serious Xray-Induced Skin Injuries to Patients during Fluoroscopically-Guided Procedures" (FDA 1994). The Advisory provides a listing of the serious skin injuries (which increase in severity with increasing xray dose), as well as the following list of "procedures typically involving extended fluoroscopic time":

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 cholangiography,
transjugular intrahepatic portosystemic shunt,
percutaneous nephrostomy,
biliary drainage,
urinary/biliary stone removal.

Procedures likely to give a patient more than 100 rads of skin-dose include radiofrequency cardiac catheter ablation, vascular embolization, transjugular intrahepatic portosystemic shunt placement, and percutaneous endovascular reconstruction (Shope 1996, p.1199).

Among procedures requiring extended fluoroscopy-time is percutaneous transluminal cardio-angioplasties --- or PTCA. Estimated average skin-dose from PTCA is about 60 rads per procedure if one stenosis is dilated, and 130 rads if two stenoses are dilated (NCRP 1989, p.31). By 1990, in the USA, the rate of PTCA each year reached an estimated 400,000 procedures (UNSCEAR 1993, p.232/69).

About 25% of dose from fluoroscopy can be pure waste, with no informational value whatsoever, because the xray beam generally falls on rectangular areas, while the image intensifier is a circle fitting inside such rectangles (NCRP 1989, p.36). In 1997, the Public Health Service was urging purchase and use of continuously adjustable, circular collimators (beam adjusters) for fluoroscopes (Shope 1997, p.14).

3e. Data Absent for an Assumption that Fluoroscopic Doses Are Falling

In 1997, the Public Health Service was warning that "Recent developments in the technology of fluoroscopic systems have resulted in ... a variety of special modes of operation and methods of recording fluoroscopic images. Some of these modes may significantly increase the entrance exposure rate to the patient " (Shope 1997, p.6). At the same time, many fluoroscopic systems now on the market offer an optional feature which could reduce radiation dose to patients: The "freeze-frame" or "last-image hold" capability. As noted, the feature is optional (Shope 1997, p.21).

Also not yet in wide use is a timing display and audible alarm on fluoroscopy machines, so that the operator could easily know the cumulative time during which the xray beam has been on, and when the usage-time during a procedure is approaching a pre-set alarm level (Shope 1997, p.20).

Recommended for years, but not yet required, is use of commercially available means to display, to the fluoroscopist, real-time DOSE-rates and cumulative DOSE to the patient's skin during a procedure (Shope 1997, p.23).

In the pre-1960 period and in the post-1960 period right up to today, fluoroscopy has been delivering by far the highest doses in non-therapeutic radiology. Yet even in 1997, there was still no system in place to quantify those doses.

3f. The Issue of Age at Exposure

Age at irradiation is another factor which interferes with efforts to compare pre-1960 and post-1960 population doses from medical radiation. Infants and young adults probably are more vulnerable to radiation carcinogenesis than older adults --- although the difference in magnitude is less than once thought (discussion in Gofman 1995/96, Chapter 3, Part 4).

It would be a big mistake to assume that medical radiation, today, is confined mainly to patients over age 65. The NCRP Report of 1989 (p.19) cites the following estimates from the FDA in 1985, for diagnostic medical xrays performed in hospitals:

Upper GastroIntestinal:	35.7% below age 45; 70% below age 65.
Cholecystography:	38.6% below age 45; 73.2% below age 65.
Barium Enema:	27.3% below age 45; 62% below age 65.
Intravenous Urography:	40.3% below age 45; 71.8% below age 65.
LumboSacral Spine:	50.8% below age 45; 79.4% below age 65.
CT Exams:	34.8% below age 45; 66.6% below age 65.
All Xrays:	47.2% below age 45; 74.2% below age 65.

NCRP 1989 (p.44) also cites a 1985 estimate that over 40% of the dose to active bone marrow, from diagnostic radiology, occurs before age 55.

In addition to problems like aching backs, curvature of the spine, and accidents, cardiovascular problems constitute a major reason for xray procedures. The variety of such problems is vast (Chapter 39, Part 4), and they are not limited to the "senior years." Today, for example, an estimated 32,000 babies per year are born with recognized heart defects (AHA 1995, p.14).

Diagnostic cardiac catheterizations were done BELOW age 45 at a rate in 1994 of about 118,000 per year; the rate was 471,000 per year in patients age 45-64, and 532,000 per year in patients over age 65 (AHA 1996, p.27). For all ages combined, the annual number increased about 3.7-fold between 1979 and 1994. Fluoroscopic xrays are used during these procedures.

Radiation doses are much higher from the PTCA (angioplasty) procedure, of course, than from diagnostic cardiac catheterizations. The PCTA procedure was done BELOW age 45 at a rate in 1994 of about 26,000 per year; the rate was about 182,000 per year in patients age 45-64, and 190,000 per year in patients over age 65 (AHA 1996, p.27). For all ages combined, the annual number increased about 4-fold between 1986 and 1994.

Such data indicate (a) that medical radiation is by no means confined to the over-65 set, and (b) that certain uses are increasing faster than the population.

3g. Profound Uncertainty about the Magnitude of Post-1960 Dose-Reduction

Some of the important differences, between the practices of pre-1960 and post-1960 radiology, have been described in Part 3. But the frequency of medical procedures, and the doses delivered (particularly during fluoroscopy), have not been measured in either era. The ubiquitous post-1960 "pie-charts" of total radiation exposure, which include average annual per capita dose from non-therapeutic uses of medical radiation, are necessarily guesstimates with respect to medical radiation.

Several post-1960 changes in radiologic practice clearly operate in the direction of reducing average annual per capita radiation dose. "We don't DO that anymore!" is a familiar refrain among today's physicians, many of whom happily embrace an assumption that today's doses are negligible from medical radiation. Such colleagues may not have realized that several post-1960 changes clearly operate in the direction of increasing average annual per capita dose from medical radiation, as shown above. The current "pie-chart" estimates for medical radiation are very probably too low by quite a bit.

Is the NET effect, of post-1960 changes, really a "big reduction" in dose? Our opinion is that a net post-1960 reduction has occurred in the average annual per capita dose from medical radiation (excluding cancer therapy), but that the magnitude of decrement is FAR from clear. Among informed

people, profound uncertainty about its magnitude is likely to be permanent, given the lack of records.

● Part 4. Ionizing Radiation: A Proven Carcinogen with Some Unique Properties

Along the electromagnetic continuum of photons, from low to progressively higher energy, there are radio waves, microwaves, infra-red heat waves, visible light, ultra-violet light, xrays, and gamma rays. Xrays and gamma rays are ionizing radiations. Ionizing radiations have enough energy not only to "kick" electrons out of their normal atomic orbits, but also to endow these liberated electrons with kinetic energy which sets them into high-speed linear travel. Ultra-violet light, which lacks enough energy to penetrate to the body's internal organs, is not in the same class with medical radiation from xrays and gamma rays. Appendix-A describes alpha and beta ionizing radiations.

4a. The Unique Biological Property of Ionizing Radiation

When an xray or gamma-ray photon interacts with a molecule in living cells, the photon has enough energy not only to "kick" an electron out of its atomic orbit, but also instantly to endow the electron with such energy that it travels like a high-speed bullet through the home-cell and neighboring cells.

The damage from xrays and gamma rays does not come directly from the photon --- it comes from the high-speed high-energy electrons which are set into motion by a photon. When peak voltage across an xray tube is 90,000 electron-volts, the average energy per photon is about 30,000 electron volts. Virtually all 30,000 electron-volts get transferred to a single high-speed electron. The trail of ion pairs and excited molecules, produced by the high-speed high-energy electron along its path, is called the "primary ionization track." (Additional information in Gofman 1990, Chapter 20).

Each high-speed, high-energy electron gradually slows down, as it unloads portions of its biologically unnatural energy onto various biological molecules along its track, at irregular intervals. Such molecules include, of course, water, DNA, proteins --- whatever molecules happen to be in the path when an energy-deposit occurs. Even though each energy-deposit transfers only a portion of the electron's total energy, the single deposits very often have energies which far exceed any energy-transfer which occurs in a natural biochemical reaction. Such energy-deposits are more like grenades and small bombs.

The uniquely violent energy-transfers, caused by ionizing radiation, are simply absent in a cell's natural biochemistry. We know of no one who would dispute this statement.

4b. Repair of Chromosomal and DNA Damage: Complexity Counts

What matters, with respect to gene-based Cancers and other gene-based disorders, is MUTATION: Damage to the genetic molecules which is unreparable, unrepaired, and enduring. By contrast, there are no mutations from damage which a cell repairs correctly.

There are reasons, in both real-world evidence and logic, to say that ionizing radiation is an especially potent mutagen. It clearly belongs to a much more potent class than the free radicals which attack genomic DNA all the time --- as shown in Appendix C.

The special potency of ionizing radiation is almost certainly due to its unique property of delivering so much extra energy, all at once, in very small regions of a cell. Dr. John F. Ward, Research Professor of Radiology at the University of California, San Diego, reports that the average energy-deposit from a high-speed high-energy electron is thought to be about 60 electron-volts, all within an area having a diameter of only 4 nanometers (Ward 1988, p.103). By comparison, the diameter of the DNA double-helix is 2 nanometers.

Double-Strand Chromosome Breakage and Mutation

As a result of such concentrated deposits of energy, a cell can experience a level of mayhem, in a segment of the DNA double helix, which far exceeds what a single free-radical can inflict upon a comparable segment. For decades, ionizing radiation has been recognized to be extremely efficient at causing double-strand chromosome breaks (e.g., Kucerova 1972, + Brewen 1973, + Sasaki 1975, +

Evans 1978, 1979, + Tonomura 1983, + Lloyd 1992). These violent double-strand ruptures, caused by ionizing radiation, are very different from the orderly double-strand breaks initiated and guided, with normal physiological energy-transfers, by enzymes for a cellular purpose. The deliberate breaks, initiated by the cell, need no repair --- whereas the messy breaks at random locations, caused by ionizing radiation, can be very difficult for cells to repair correctly. The result, of imperfect or absent repair of these double-strand breaks, is mutation.

If the pieces of a broken chromosome are re-united incorrectly, but if the break occurred at an inconsequential site, the mutation will have no biological consequences (by definition). But if the break occurred within a gene which is active in that type of cell, the incorrect reunion can cause the matching protein to be dysfunctional or non-functional. The mutated gene could be one of the many genes directly required to prevent the cell from becoming malignant. Or it could be a gene required to distribute the chromosomes correctly during cell division. Or it could be a gene required for making routine DNA repairs. If it is a repair-gene, the mutation can magnify the consequences of the cell's subsequent exposures to all mutagens (radiation and non-radiation), because of the cell's diminished ability to repair damage correctly.

The biological consequences for a cell, of acquiring a structural chromosomal mutation, depend on the site and nature of the mutation, of course. For example, removal (deletion) of just a single nucleotide can result in garbling of the nearby genetic code. A single larger deletion can result in permanent loss of partial genes or entire genes.

Imperfectly repaired chromosome-breaks cause micro-deletions, macro-deletions, terminal deletions, interstitial deletions, reciprocal translocations, dicentric chromosomes, acentric fragments, rings, inversions, insertions, and other structural re-arrangements of the chromosomes. It is a fact that many cells survive (and reproduce themselves) despite having a consequential chromosomal mutation.

Ionizing Radiation: Very Low Doubling-Dose for Chromosomal Mutations

A "doubling dose" of ionizing radiation is the dose which adds a rate (of some effect) equal to the effect's pre-existing rate. Presently, doubling-dose values for structural chromosomal mutations in human cells are reported in the range of 2 to 20 rads for radiation-induced deletions (Brewen 1973) and dicentrics (Kucerova 1972, + Evans 1979 p.523, + Lloyd 1992 Table 8) and translocations (Lucas 1999 Part 4.1 and Table 3). Some common medical procedures which deliver xray doses in the range of 2 to 20 rads, per procedure, are named in Parts 3d and 7e of this chapter.

Although some of the doubling-dose values mentioned above have large error-bands, the values suffice to indicate that very low doses of radiation readily induce structural chromosomal mutations. For example, the doubling-dose for monocentric translocations induced by gamma-rays is roughly 7.5 rads at age 24, and 15 rads at age 49 --- based on Lucas 1999, Table 3 and Figure 1, and on the observation (from Hsieh 1999) that a rad of gamma rays from cobalt-60 induces 0.00024 translocation per human lymphocyte in vitro, or 24 translocations per 100,000 cells. (Part 7a, below, cites evidence that the number of chromosomal mutations induced per rad is about 2-fold higher from xrays than from cobalt-60.) Induction-rates per 100,000 cells can be viewed in the context that, per gram of human tissue, there are roughly 675 million cells (Gofman 1990, Chapter 20, Part 2).

Laboratory techniques for detecting structural chromosomal mutations are rapidly advancing (for instance, see Lucas 1997, 1999). Observations confirm the expectation that the frequency of chromosomal mutations per 1,000 cells rises with age (for instance, see Tonomura 1983, + Tucker 1994, + Lucas 1999) --- an observation which is consistent with progressive lifelong accumulation of such lesions from exposure to ionizing radiation and nonradiation co-actors.

Genomic Instability: Inducible by Xrays and Other Types of Ionizing Radiation

Among the consequences of mutation, one of the most fearsome is genomic instability. If the original mutation involves (for instance) a gene required for repair of gene-damage or required for proper segregation of chromosomes during cell division, the cells which descend from the originally mutated cell, evolve into cells which are increasingly aberrant, genetically.

Damage, to any of the numerous genes which are part of the cell's system for maintaining genomic stability, can result in genomic instability --- a very frequent characteristic of the most

aggressive cancers. Xrays and other classes of ionizing radiation are a proven cause of genomic instability (Appendix D).

The Complex and Unrepairable Injuries

The very nature of ionization tracks means that no part of the genomic DNA is protected, by shape or chemistry, from the violent energy-deposits described above. They can inflict their damage ANYWHERE, along any chromosome. Ionizing radiation can induce every known kind of genetic damage, common and rare, simple and complex.

The complex injuries --- including double-strand chromosome breaks --- are not always correctly repaired or repairable by a cell. The probability, that genetic injury will be complex and unrepairable, is greatly elevated by the unique capability of ionizing radiation to deliver the energy "grenades" and "bombs" described above.

4c. Evidence that Ionizing Radiation Is a Proven Human Carcinogen

Of course, many readers are not familiar with the accumulated epidemiologic evidence which shows that ionizing radiation (including the medical xray) is a proven human carcinogen. The purpose of Parts 4, 5, 6, 7 and 8 is to assure such readers that they can accept the assertion as fact. And not just for a few kinds of Cancer, but for virtually every kind of human Cancer.

In 1969, Dr. Tamplin and I warned that, "Contrary to a widespread notion that only Leukemia plus certain rare Cancers are radiation-induced in man, the evidence now points strongly to the induction of all forms of human Cancer plus Leukemia by ionizing radiation" (Gofman 1969-b, p.1). And we predicted that: "All forms of Cancer, in all probability, can be increased by ionizing radiation ..." (Gofman 1969-b, p.1).

From "Controversial Supposition" to "Accepted Wisdom"

Our warning met resistance by most of the radiation community for over a decade. By 1980, the evidence was acknowledged by the BEIR-3 Committee of the National Research Council (USA). BEIR is the acronym for Biological Effects of Ionizing Radiation. BEIR-3's Subcommittee on Somatic Effects had sixteen members, who wrote as follows (BEIR 1980, Section 5, Summary and Conclusions on "Somatic Effects: Cancer"):

- - "The Committee considers cancer induction to be the most important somatic effect of low-dose ionizing radiation ..." And:

- - "Cancers induced by radiation are indistinguishable from those occurring naturally; hence their existence can be inferred only on the basis of a statistical excess above the natural incidence." And:

- - "Cancer may be induced by radiation in nearly all the tissues of the human body."

The Chairman of the entire BEIR-3 Committee and also of the Somatic Effects Subcommittee was Edward P. Radford, M.D., then professor of epidemiology at the Graduate School of Public Health, University of Pittsburgh. Two years later, as a participant in a "roundtable" on medical irradiation for the New York Times, Dr. Radford stated (Radford 1982):

- - "The point that I feel is important is the consistency with which radiation has proved to be carcinogenic in man. It is far and away the most consistent agent that we know of to cause Cancer of any type." Subsequent human evidence continued to fortify the conclusion.

- - In 1988, UNSCEAR (the United Nations Scientific Committee on the Effects of Atomic Radiation) wrote: "It now appears that most (indeed, probably all) organs are vulnerable to radiation-induced Cancer, given the right conditions of exposure" (UNSCEAR 1988, p.460/para.394).

The power of ionizing radiation to increase virtually all forms of human Cancer is simply not in dispute anymore. For the convenience of readers, our Reference List flags --- with a dot in the margin --- some reports and papers which provide extensive bibliographies from which anyone can

reconstruct the sequence in which the proof developed. Medical xrays are the source of much of the evidence.

National Cancer Institute + American Cancer Society + World Health Organization

- - In 1990, the National Cancer Institute (USA) issued a 12-page booklet entitled "Everything Doesn't Cause Cancer" (NIH publication 90-2039; NCI 1990 in our Reference List). NCI starts its booklet with a statement on page 1: "Cancer-causing agents also include xrays, sunlight, and certain viruses." At page 5, the booklet lists "radiation and radioactive materials" as proven human carcinogens. And at page 12, the booklet advises: "Don't ask for an xray if your doctor or dentist does not recommend it. If you need an xray, be sure xray shields are used if possible to protect other parts of your body."

- - In 1992, the American Cancer Society issued the following advice under the title, "Guidelines for the Wise Use of Medical Xrays" (ACS 1992): "Fluoroscopy delivers larger doses of xray than that used in standard films. If there is an alternative means of making a diagnosis, fluoroscopy should be avoided."

- - In 1996, the World Health Organization issued its 1996 report entitled "The World Health Report 1996." The section on Cancer states (WHO 1996, p.59): "An estimated 6.6 million people died of Cancer [worldwide] in 1995, and 10 million new cases were diagnosed. It is generally believed that environmental and lifestyle factors, as well as common practices such as diagnostic radiographic procedures, are largely responsible for this disease. In addition, the link between infectious diseases and Cancer is becoming increasingly clear, opening up new possibilities for prevention."

What about the IARC Monographs?

We anticipated that some readers might ask, "Why is ionizing radiation missing from the monographs issued by the International Agency for Research on Cancer?"

We put the question directly to IARC in November 1996. IARC (located in Lyon, France) has been trying to classify various carcinogens for decades, and its monographs are well known in biomedical libraries. The two-paragraph reply from IARC, dated November 25, 1996, is signed by Jerry M. Rice, Ph.D., Chief, Unit of Carcinogen Identification and Evaluation. It says, in its entirety:

"In answer to your note of 14 November, addressed to the IARC Librarian, it is true that radon is the only source of ionizing radiation that has been evaluated to date in the IARC Monographs on the Evaluation of Carcinogenic Risks to Humans." And:

"As is stated on page 1 of every volume of the Monographs, as a 'Note to the Reader,' the fact that an agent has not yet been evaluated in a Monograph does not mean that it is not carcinogenic. It is simply a historical fact that the Monographs Programme began in 1971 with chemicals, and has only in recent years begun to broaden its focus to include biological and physical agents. We expect to direct increasing attention to physical agents, including ionizing radiation, during the next several years. Thank you for your interest in IARC Monographs."

● Part 5. Is the Carcinogenic Power, per Rad of Radiation, the Same at All Dose-Levels?

In 1950, a prospective study was initiated in order to find out what would happen to the health of survivors of the 1945 atomic bombings of Hiroshima-Nagasaki. That study, sponsored jointly by the U.S. and Japanese Governments, is on-going --- for about half of the participants are still alive. Updated results are issued every 4 or 5 years. The study is managed by the Radiation Effects Research Foundation (RERF), with headquarters in Hiroshima and a contact point in Washington DC at the National Academy of Sciences.

Several features of the A-Bomb Life-Span Study make the study uniquely informative: (a) Participants of both genders and all ages at the time of the bombings, (b) Radiation exposure ranging from very low to very high doses, (c) Irradiation of all organs (not just some), and (d) Very long follow-up time. Because of its comprehensive nature, the A-Bomb Study continues to be the principal source of information concerning many aspects of radiation-induced cancer --- including the shape of the dose-response at low and moderate dose-levels.

5a. Primarily a Study of LOW Radiation Doses at Hiroshima-Nagasaki

When the study-group is described by the ages, the distribution of its 91,231 participants is as follows (from Gofman 1990, Table 4-A):

Table 4-A):

- - 18,402 persons age 0-9 years old in 1945.
- - 19,224 persons age 10-19 years old in 1945.
- - 17,691 persons age 20-34 years old in 1945.
- - 20,903 persons age 35-49 years old in 1945.
- - 15,011 persons above age 50 in 1945.

Contrary to common assumption, very few of the participants (about 3%) in the A-Bomb Life Span Study received high doses of ionizing radiation from the bombings (Pierce 1996-a, p.632-633). In general, doses at or below 10 rads (centi-grays) are called "low," and doses at or above 100 rads are called "high" (Appendix-A of this book). The rad and the centi-gray are identical dose-units. We and many others regard the simpler name as preferable. For the past decade, the centi-Sievert (cSv) has been treated as closely equivalent to the rad and centi-gray (cGy), with respect to the A-Bomb Study --- an issue discussed in Part 7 of this chapter.

Of the 91,231 participants listed above, average absorbed internal organ-doses were distributed as follows (Gofman 1990, Table 13-A, Column C):

- - 37,173 received 0.1 rad of bomb-radiation.
- - 28,855 received 1.9 rad of bomb-radiation.
- - 14,943 received 14.6 rads of bomb-radiation.
- - 4,225 received 40.6 rads of bomb-radiation.
- - 3,128 received 74.2 rads of bomb-radiation.
- - 2,907 received 197.0 rads of bomb-radiation.

Anyone claiming that the A-Bomb Study can elucidate response only to HIGH doses of ionizing radiation, just can not be familiar with the study. It is primarily a study of response to LOW doses of bomb-radiation.

5b. Shape of the Dose-Response in the A-Bomb Study, and in High-Dose Data

What does the A-Bomb Life-Span Study reveal about the shape of the dose-response for solid Cancers (in other words, excluding Leukemia)? Before the answer, definitions are needed for the relevant terms.

Terms: A positive linear dose-response means, of course, that response is directly proportional to dose, because the carcinogenic power of each incremental dose-unit (e.g., rad) is the same throughout the entire dose-range, from zero dose to very high doses. Positive linear dose-responses are depicted in Figures 1-A and 1-B of Chapter 1; discussion of their shape occurs in Chapter 5, Part 5d. By contrast, a supra-linear dose-response has curvature such that the curve lies ABOVE a straight line drawn between any two points along the curve. When such a connecting line has an upward slope, each rad at the lower dose-point is more carcinogenic on the average than each rad at the higher dose-point. The linear-quadratic dose-response (if the quadratic term is positive rather than negative) means that each rad is less carcinogenic at low total doses than at high total doses.

- 1990. In Gofman 1990, we presented a step-by-step analysis of the A-Bomb Life-Span Study data, 1950-1982, which shows that the dose-response in those data for all types of solid Cancers, combined, has a supra-linear shape at doses above about 5 rads (Gofman 1990, esp. Chapter 14). Analysts at RERF also reported supra-linearity, but they concluded that the supra-linear dose-response was not statistically superior to the linear dose-response in fitting the observations (Shimizu 1987, pp.28-30, + Shimizu 1988, pp.50-51, p.53, Table 19). In reality, the dosimetry in the A-Bomb Survivor Study has been and remains quite uncertain. Therefore, it is impossible for anyone to know whether the supra-linearity therein is based on biology or on mistaken dose-estimates.

- - 1990. The BEIR Committee (Committee on the Biological Effects of Radiation, of the National Research Council) reported its analysis of the 1950-1985 data from the A-Bomb Life-Span Study: "The dose-dependent excess of mortality from all cancer other than leukemia, shows no

departure from linearity in the range below 4 sievert [approximately 400 rads], whereas the mortality data for leukemia are compatible with a linear-quadratic dose response relationship" (BEIR 1990, p.5). For now, we can ignore BEIR's questionable distinction about Leukemia, because Leukemia has accounted for a very small fraction of U.S. cancer mortality. Solid Cancers have accounted for the overwhelming share of cancer deaths. In 1940, Leukemia accounted for 3.2% of the cancer mortality rate (Grove 1968, p.700 & p.676). In 1998, the fraction of cancer deaths (USA) due to Leukemia is estimated at 3.8% (Landis 1998, p.13, Table 4).

- - 1994. The UNSCEAR Committee (United Nations Scientific Committee on the Effects of Atomic Radiation) reached the same conclusion as did the BEIR Committee, from the A-Bomb Life-Span Study: "The life span study data for solid tumours from 1950 to 1987 are consistent with linearity between 0.2 Sv [approximately 20 rads] and 4 Sv [approximately 400 rads] ..." (UNSCEAR 1994, p.89/402). The report presents a graph which depicts linearity in the data down to zero dose (UNSCEAR 1994, p.157). However, in the range between 0 dose and 20 rads, the authors say the findings lack statistical significance (UNSCEAR 1994, p.89/406).

- - 1996. RERF analysts, Donald Pierce and co-workers, report their findings on solid Cancers from a longer follow-up period (1950-1990) in the A-Bomb Life-Span Study. They state (Pierce 1996-b, p.9): "The dose response is quite linear up to about 3 Sv [up to about 300 rads] ... These data do not suggest the existence of a threshold below which there is no excess risk." The RERF analysts also report (Pierce 1996-b, pp.9-10) that the 1950-1990 data, "taken at face value," show supra-linearity and indicate that the cancer rate per cSv (rad) grows progressively more severe as dose DECREASES in the region between about 35 rads and zero dose --- but they reject the finding as statistically inferior to the linear dose-response.

The RERF analysts, working with later data than the analysts in UNSCEAR 1994, find statistically significant excess Cancer even at doses as low as about 5 cSv --- about 5 rads (Pierce 1996-b, p.10). We have not yet independently checked the 5-rad finding from the 1950-1990 raw data.

Findings from Higher Doses: A Path to Underestimating Risk at Low Doses

Although the data in the A-Bomb Study are sparse at high doses (Part 5a), other types of data have led analysts to general agreement that dose-response for radiation carcinogenesis and mutagenesis is curved in a supra-linear fashion when acute high doses are included (NCRP 1980, p.17, p.160, + BEIR 1990, pp.141-142 for carcinogenesis, + UNSCEAR 1993, p.9/42 for carcinogenesis). This means that risk per rad, from xrays received at low doses, will be underestimated whenever such analysis is based on observing medical patients who received acute high doses.

5c. Peril for the A-Bomb Database: Recent Actions

It worries us that recent actions have needlessly placed the credibility of future results from the Atomic-Bomb Survivor Study in great peril (Gofman 1988 + 1990 + 1992 + 1995/96).

Since 1986, both the number of participants in the study and their dose-estimates have been altered several times, after the results of decades of follow-up were already known. Epidemiologists worldwide recognize that retroactive changes in dose-assignments and shuffling of dose-cohorts create the opportunity for bias to enter any study. With enough retroactive changes, the "findings" can become whatever the fiddlers desire. Therefore, in order to prevent suspicion, well-established rules, which create barriers against entry of bias, are normal practice in prospective studies. Unfortunately, during the past decade, several such barriers have been demolished in the A-Bomb Study.

The impending crisis in the A-Bomb Study developed because of over-estimated doses delivered by neutrons --- especially in Hiroshima. Indeed, we discerned that there must have been errors involving neutrons in the pre-1986 dosimetry (Gofman 1981, p.246), and we applaud correction of the neutron-errors by what is called the study's "DS86" dosimetry. What worries us is the way in which use of "the new dosimetry" has unnecessarily become the occasion for removing some significant barriers against potential bias. For instance, many former participants have been discarded and thousands of new ones added from a "reserve." The former dose-estimates and dose-cohorts are

no longer any part of RERF analyses. In short, current practice deprives the A-Bomb Study of its continuity, its anchor, its permanent architecture --- and thus, of its above-suspicion status.

A potential remedy for this problem would be to use "DS86" dosimetry as part of "constant-cohort, dual-dosimetry" analyses, in which the former dose-estimates (1965 vintage) and former dose-cohorts provide the continuity in future follow-up studies, and comparable results are calculated also from "the new dosimetry." This practice would simultaneously eliminate suspicions of bias AND deliver the benefits of improved dosimetry. In the computer age, the extra set of dose-estimates (DS86) is easily handled. Indeed, with the excellent cooperation of Dr. Donald Pierce at RERF, we acquired the data we needed to demonstrate "constant-cohort, dual-dosimetry" analysis of the 1950-1982 cancer-data (in Gofman 1990). We need not claim that "constant-cohort, dual-dosimetry" is the ONLY possible solution to the A-Bomb Study's impending credibility problem, but we do claim that an approach OTHER than current practice is urgently needed, in order to keep this unique and painfully acquired Japanese database forever above suspicion.

● Part 6. Absence of Any Threshold Dose: "Risk" versus Rate

Because ionizing radiation is a proven cause of human Cancer, one might assume that virtually no one would deny that the use of medical radiation has caused and is causing radiation-induced Cancers. But there are some in medicine who try to limit such an admission to "high-dose" medical radiation. Such people continue to hope for a threshold-dose, below which they speculate that REPAIR of radiation-injury may prevent any radiation-induced Cancer. They claim that no one can know for sure about very low doses. They are mistaken. IT IS POSSIBLE TO KNOW.

6a. A Five-Point Summary of the Evidence that No Threshold Exists

The nature of the evidence, that no threshold-dose exists for radiation carcinogenesis, can be summarized by five points (Gofman 1990, Chapter 18):

- Point ONE: The radiation dose from xrays, gamma rays, and beta particles is delivered by high-speed electrons, traveling through human cells and creating primary ionization tracks. Whenever there is ANY radiation dose, it means some cells and cell-nuclei are being traversed by electron-tracks. There are roughly 675 million typical cells in 1 cubic centimeter.
- Point TWO: Every track --- without any help from another track --- has a chance of inflicting chromosomal or gene-damage, if the track traverses a cell-nucleus.
- Point THREE: There are no fractional electrons. This means that the passage of one primary ionization track is the lowest conceivable dose and dose-rate which a cell-nucleus can experience from ionizing radiation.
- Point FOUR: There is solid epidemiologic evidence that extra human Cancer does occur from radiation exposures which deliver just one or a few tracks per cell-nucleus, on the average. Such evidence shows that the cell's repair-system is fallible even when it is confronted only by a minimal challenge.
- Point FIVE: The combination, of real-world evidence from epidemiology and from track-analysis, establishes that there is NO dose or dose-rate low enough to guarantee correct repair of every carcinogenic injury inflicted by ionizing radiation. Some injuries are just unrepaired, unreparable, or misrepaired.

6b. Three Remarkably Similar Reports on the Safe-Dose Fallacy

The threshold hypothesis, with respect to radiation carcinogenesis, has been invalidated in three major reports: Gofman 1990, UNSCEAR 1993, and NRPB 1995. (UNSCEAR is the United Nations Scientific Committee on the Effects of Atomic Radiation. NRPB is Britain's National Radiological Protection Board.)

The key to each report is the insight that the appropriate way to define the lowest possible dose

and dose-rate of ionizing radiation is NOT in fractions of a rad or centi-gray. The relevant definition occurs in tracks per cell-nucleus.

● - Gofman 1990, p.19-1: "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." Traversal occurs in a tiny fraction of a second. To test the threshold hypothesis, no one needs impossible-to-obtain epidemiologic studies, at tissue-doses like 10 milli-rads or 10 micro-rads --- because minimal challenge to a cell's repair system occurs at much higher tissue-doses. From Gofman 1990, Table 20-M:

Radiation	Average number of tracks/nucleus	Tissue-dose in rads (centi-grays)
30 KeV medical xrays	1 track	0.75 rad (750 milli-rads)
	10 tracks	7.48 rad
1608 KeV gamma-rays, as at Hiroshima-Nagasaki	1 track	0.185 rad (185 milli-rads)
	10 tracks	1.85 rad

● - UNSCEAR 1993, 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."

● - NRPB 1995, p.58/27: "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."

For the convenience of readers, Appendix B provides extensive excerpts from all three reports. Here, we will present just the conclusions:

Gofman 1990, p.18-2: "Human epidemiological evidence shows that repair FAILS to prevent radiation-induced Cancer, even at doses where the repair-system has to deal with only one or a few tracks at a time, and even at dose-rates which allow ample time for repair before arrival of additional tracks ... Such evidence is proof, by any reasonable standard, that there is no dose or dose-rate which is safe ..."

UNSCEAR 1993, p.636/84: "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 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." And (p.680-681/323): "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."

NRPB 1995, p.60/36: "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." And (p.61/38): "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." And (p.68/80): "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."

6c. Dr. Dale L. Preston: An Additional View on the Safe-Dose Fallacy

The bottom line is that exposure to ionizing radiation creates violent random events at the cellular level. Repair of the resulting genetic damage is sometimes absent or imperfect. The failure of

correct repair is not due to saturation of a cell's repair system (Gofman 1990, Chapter 18, Parts 2, 3, 4). Failure is due to the exotic nature of the lesions. In studies of radiation-induced human Cancer and of radiation-induced chromosomal mutations in human cells, generally the dose-response is linear. Linearity almost certainly means that the unrepairable fraction of genetic lesions is constant, even when there is an average of just one track per cell-nucleus.

The newest evidence on linearity has led Dr. Dale L. Preston, also, to speak out on the threshold-issue. Dr. Preston is a major analyst at RERF and was also Scientific Advisor to the BEIR-5 Committee of the National Research Council. Referring to the 1950-1990 evidence from Hiroshima-Nagasaki (Part 5b, above), Preston states:

"For solid Cancers, there is simply no way of looking at the RERF data which suggests the existence of a threshold, or even a lower risk per unit dose in the low-dose range. The lack of such evidence is not due to a relative paucity of survivors in the low-dose range, as more than 85% of the survivors have dose estimates <0.2 Sv. In fact, taken at face value, these data are quite inconsistent with the existence of a threshold, or the adequacy of a linear-quadratic dose response for solid cancers" (Preston 1997).

6d. An Important Distinction: Risk versus Rate

The proof exists, by any reasonable standard of biomedical proof, that there is no threshold-dose for radiation carcinogenesis.

Thus, there is no dose-level or dose-rate for a population which is harmless. A radiation dose which gives an individual "just a risk" of radiation-induced Cancer --- say, 1 chance in 1,000 --- is the same dose which gives a RATE of 1,000 radiation-induced Cancers among a million people irradiated at a comparable age. In such a case, all one million irradiated people are "at risk," and later, one thousand of them develop radiation-induced Cancers. Radiation-induced Cancer is "a maybe" for each individual but a certainty for the group.

● Part 7. Xrays: More Carcinogenic than Gamma Rays at Equal Doses

For about two decades, experimental evidence has been accumulating that xrays inflict more chromosomal mutations per 1,000 cells than do gamma rays, at equal tissue-doses. It follows (from more mutations) that xrays are more carcinogenic than gamma rays, at equal tissue-doses. We warned that medical xrays are about twice as carcinogenic as gamma rays, at equal rad-dose, in Gofman 1990 (p.13-4, p.20-5, p.25-15).

7a. Other Publications: Xrays Two-Fold to Four-Fold More Injurious

The BEIR-5 Committee, of the National Research Council, acknowledged a factor of two as follows (BEIR 1990, p.218):

"Most human exposures to low-LET ionizing radiation are to xrays, while the A-bomb survivors survived low-LET radiation in the form of high energy gamma rays. These are reported to be only about half as effective [injurious per rad] 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 [for Cancer] 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 xray exposures." Note: LET and ortho-voltage xrays are defined in Part 7b.

In 1995, Tore Straume's analysis of evidence indicated that xrays may be FOUR TIMES as harmful as Hiroshima-Nagasaki gamma rays, at equal rad-doses (Straume 1995). Dr. Straume, who was then at the Livermore National Laboratory, used experimental evidence produced at the Harwell Lab of Britain's National Radiological Protection Board: Prosser 1983, + Lloyd 1986, + Purrott 1977. The evidence consists of dose-responses for dicentric chromosomes induced by ionizing radiation in human lymphocytes (in vitro), evaluated at the first post-irradiation cell-division (Straume 1995, Figure 2). Dicentric chromosomes (having two centromeres) result from misrepaired double-strand chromosome breakage in two separate chromosomes. The frequency of post-irradiation dicentrics has been one standard measure of radiation mutagenesis for decades. Straume's analysis showed the

following results, relative to the atom-bomb gamma rays and at equal rad-dose (Straume 1995, p.955):

- - Cobalt-60 gammas rays are about 2-fold more injurious than A-bomb gamma rays.
- - 250 kVp xrays (called "orthovoltage xrays," and having an average energy of 83 KeV) are about 4-fold more injurious than A-bomb gamma rays.
- - Tritium beta rays (average energy of 5.7 KeV) are about 5-fold more injurious than A-bomb gamma rays.
- - Using data from almost entirely different studies, Joe Lucas and co-workers find that xrays produce about 2-fold more dicentric per dose-unit than cobalt-60 gamma rays (Lucas 1995, Figure 3).

Straume comments (Straume 1995, p.955): "It is well known that biological effectiveness [damage per dose-unit] decreases as radiation energy increases, i.e., becomes less densely ionizing (Dobson 1976, + Bond 1978, + NCRP 1980, + Borek 1983, + ICRU 1986, + Brenner 1989, + NCRP 1990)."

And, Straume p.955: "The dependence of human Cancer dose-response relationships on radiation energy has not been established and therefore may or may not be equivalent to that for the model endpoint (dicentric) used here. It is, however, established that the energy dependence of dicentric compares well with those of a broad range of other biological endpoints (NCRP 1990), including that for malignant cell transformation (Borek 1983), and is a convenient endpoint that has been well characterized and widely used for similar purposes (e.g., see ICRU 1986)."

Quite explicitly, Straume warns that health consequences from xrays and tritium (radioactive hydrogen) may be larger, by a factor of 4 to 5, than the harm from an equal dose of Hiroshima-Nagasaki gamma rays (Straume 1995, p.956).

7b. An Independent Check on the Four-Fold Estimate

We wondered: Is a four-fold disparity in mutations reasonable? Credible? We were able to make an independent check on the reasonableness, by consulting our own work in Gofman 1990.

As noted by Straume (Part 7a), there is a large body of evidence on ionizing radiation showing that the biological damage per rad rises with the DENSITY of the energy-deposits left by the high-speed particles along their tracks. LET (Linear Energy Transfer) is a common measure of such density, for LET is defined as the average amount of energy lost per unit of track-length. For example, LET can be measured in KeV per micrometer. Xrays, gamma rays, and beta particles are low-LET radiations because the distance between energy-deposits is large, on the scale of a typical cell-nucleus, relative to such distance from alpha-particle radiation (a high-LET radiation).

The relative intensity of low-LET radiations, in interacting with biological soft-tissues, is reflected in the number of cell-nuclei which must be traversed by electrons in order to deposit one rad of energy. The more cell-nuclei required, the less intense is the interaction.

In order to test the threshold hypothesis in Gofman 1990, we calculated the number of traversals of cell-nuclei, by the electrons set in motion by photons of various energies, per rad of tissue-dose delivered. Column C, below, shows the values from Gofman 1990, and Column E shows how many-fold MORE traversals are required for the A-bomb gammas to deliver 1 rad of tissue-dose:

Col.A Type of Photon	Col.B Table in Gofman 1990	Col.C Number of Cell-Nuclei Traversals per Rad (cGy)	Col.D Hiro-Naga Divided by Other	Col.E Factor of Disparity
30 KeV xrays, mean energy.	Table 20-Eye	0.903 billion	3.65/0.903	4.042
83 KeV xrays, mean energy.	Table 20-O	1.54 billion	3.65/1.54	2.370
100 KeV xrays, mean energy.	Table 20-O	1.64 billion	3.65/1.64	2.226
596 KeV gammas (radium-226).	Table 20-Eye	1.98 billion	3.65/1.98	1.843
662 KeV gammas (cesium-137).	Table 20-Eye	2.13 billion	3.65/2.13	1.714
1608 KeV gammas (Hiro-Naga).	Table 20-Eye	3.65 billion	3.65/3.65	1.000

From Column E on the previous page, we note two results in particular:

Medical xrays, of 30 KeV average energy (from a peak kilovoltage of approximately 90), interact with human soft-tissue cells about 4-fold more intensely than do the Hiroshima-Nagasaki gamma rays. Ortho-voltage xrays, of 83 KeV mean energy (from a peak kilovoltage of approximately 250), interact with human cells about 2.4-fold more intensely than A-bomb gamma rays. Therefore, on the basis of both track-analysis (Part 7b) and observed chromosomal mutations (Part 7a), it is realistic to accept the warning that xrays are much more injurious, per rad, than the Hiroshima-Nagasaki gamma rays.

7c. What Do the Epidemiologic Data Reveal?

Readers may wonder why the relative carcinogenic potency per rad, of medical xrays versus gamma rays from Hiroshima-Nagasaki, has not been established directly from epidemiologic studies. The principal problem has been described in Parts 2 and 3 of this chapter: The unreliability or complete absence of records concerning which patients received which doses from medical radiation.

This is not a small obstacle. For example, a SIX-FOLD disparity exists in the rate of radiation-induced Breast Cancers, per rad of medical xrays, among various studies of female tuberculosis patients in North America who received serial fluoroscopies. The most likely explanation is assignment of retroactive dose-estimates to the wrong patients. After years of study, the BEIR Committee admitted defeat in trying to reconcile the different studies (BEIR 1990, p.255). Then WHICH value of xray potency, estimated from such studies, would make a reliable comparison with the results on radiation-induced Breast Cancer from Hiroshima and Nagasaki gamma rays? The uncertainty is very large.

This is just one illustration of why analysts consider experimental data, with well-measured doses, to be more reliable than epidemiology when they try to estimate the relative carcinogenic potency of xrays and gamma rays of various energies.

7d. The A-Bomb Survivors: Bomb-Rads Converted to Medical Rads

There is a large body of experimental evidence (cited and independently tested in Parts 7a and 7b) which indicates that 0.25 to 0.5 rad of tissue-dose, received from medical xrays, has as much mutagenic (therefore carcinogenic) impact as 1 rad received from the Hiroshima-Nagasaki bombs. If we average the two fractions, we have 0.375. Thus, a reasonable conversion-factor, from bomb-dose to xray dose, is 0.375 medical-rad per bomb-rad.

Using the conversion factor of 0.375, we can express the list of bomb-doses from Part 5a in equivalent xray doses, as follows (we use * to denote multiplication):

- - 37,173 survivors: $(0.1 * 0.375) = 0.04$ rad xray-equivalent (40 milli-rads).
- - 28,855 survivors: $(1.9 * 0.375) = 0.71$ rad xray-equivalent.
- - 14,943 survivors: $(14.6 * 0.375) = 5.48$ rads xray-equivalent.
- - 4,225 survivors: $(40.6 * 0.375) = 15.23$ rads xray-equivalent.
- - 3,128 survivors: $(74.2 * 0.375) = 27.83$ rads xray equivalent.
- - 2,907 survivors: $(197.0 * 0.375) = 73.88$ rads xray equivalent.

7e. Some Common Current Medical Procedures, with Approximate Dose-Levels

Irradiation from the Hiroshima-Nagasaki bombings exposed the entire body of the survivors. By contrast, xray exposure from a diagnostic or interventional medical procedure today may irradiate most of the head, or a quarter to three quarters of the torso, but almost never the entire body. However, during a lifespan of various diagnostic and interventional medical procedures, a person today can readily accumulate doses to specific organs which far exceed the comparable organ-doses received by most of the A-bomb survivors. Some common procedures, with approximate dose-levels:

- **CT Scan:** A CT scan (torso) typically delivers an entrance dose of 6 rads from xrays (NCRP 1989, p.33). Within the scanned "slices," the ratio of near-surface organ-dose over body-center organ-dose is approximately 6 to 1 (Gofman 1985, pp.248-249). This ratio would make the range of internal tissue-doses per examination about 1 to 5 rads.

- **Upper GI:** A male adult receives about 1.1 rad of absorbed xray dose to his stomach during a well-conducted Upper Gastro-Intestinal examination (FDA 1992, p.27). During such an exam, many additional organs are also irradiated, including thyroid gland, esophagus, breasts, lung, active bone marrow, large intestine, liver, kidney, and pancreas.

- **Interventional Fluoroscopy:** Any procedure involving "extended fluoroscopy time" (Part 3d) may deliver xray doses to some internal tissues of 15, 25, even 50 medical rads or more.

- **Thallium-201 Injection (a common heart-exam):** Dose from thallium-201 comes from a complex mixture of gamma rays and xrays, so the following doses are not directly comparable to the others above. From administration of 2 milli-Curies to a 70-kilogram adult, approximate dose to the kidneys is 2.5 rads, thyroid 1.3 rad, liver 1.2 rad, heart wall 1.1 rad, testes 1.1 rad, ovaries 0.99 rad, stomach wall 0.84 rad, upper large intestine wall 0.54 rad, lower large intestine wall 0.46 rad, whole-body dose 0.45 rad ("Technical Product Data" from a major supplier).

● **Part 8. Variable Latency-Periods for Radiation-Induced Cancer**

If an exposure to ionizing radiation causes a genetic mutation which is carcinogenic in a cell (certainly NOT all mutations are carcinogenic), then the elapsed time between mutation and manifestation of the radiation-induced Cancer is formally called a "latency period." After its production, the carcinogenic mutation is always present, like an inventory waiting for delivery. Therefore, we like to refer to latency periods as "delivery times." They are extremely variable in duration.

8a. The Variable Delivery Times in Mixed-Age Populations

Participants of all ages in the A-Bomb Study received the bomb-irradiation in August 1945 --- and the radiation-induced Cancers were still being delivered 45 years later in a dose-dependent fashion (Part 5b). Indeed, 22% of ALL the fatal bomb-induced solid Cancers, in the A-Bomb Study, occurred during the 1986-1990 period according to the RERF analysts (Pierce 1996-b, p.1, p.5, and Table 3).

It is highly reasonable to expect deliveries of additional radiation-induced fatal Cancers during the post-1990 follow-up years --- because 56% of the initial participants were still alive at the beginning of 1991 (Pierce 1996-b, p.6, Table 4). The database currently in use by RERF analysts consists of 86,572 initial participants, whose age-distribution is similar to the age-distribution of an earlier database (91,231 initial participants) shown in Part 5a of this chapter.

8b. Duration of the Carcinogenic Impact, for People of Same Age

A very important insight has emerged from continuous study, since 1950, of the various age-groups within the A-Bomb Survivors:

When a group of people of the same age is irradiated at the same time, the excess (radiation-induced) Cancers do not occur at the same time. Each irradiated age-group "delivers" or manifests its extra Cancers gradually, over many years (see Gofman 1990, Table 17-B, for example). This is not in dispute. In other words, the duration of the delivery time varies from one irradiated individual to another. How short is the shortest delivery time? We discuss the question of "a minimum latency period" in Chapter 5, Part 4.

Once deliveries begin in an irradiated group, how long do the deliveries continue? For most age-groups, probably "forever." As the follow-up study of the A-Bomb Survivors grows ever longer, the evidence grows ever stronger from those who were relatively young in 1945, that the carcinogenic impact of exposure to ionizing radiation probably endures (though not necessarily at a constant level) for the subsequent lifespan. Because about half of the participants in the A-Bomb Study are still alive, no one can say this with certainty, however. The RERF analysts assume a lifetime impact, and they make their lifetime risk-estimates accordingly (Pierce 1996-b, pp.12-14, p.21). So did the BEIR-5

Committee (BEIR 1990). We used lifetime assumptions when making independent risk-estimates in Gofman 1981 and Gofman 1990.

8c. Persistence of Radiation-Induced Mutations

The observation, that the carcinogenic effect of exposure to radiation endures for most (probably all) of the remaining lifespan, is consistent with another observation in the A-Bomb Study: In 1992 and 1993, Lucas and Kodama reported that, among the living A-bomb survivors, a positive dose-response between bomb-dose and number of chromosomal mutations was still apparent (Lucas 1992 Figure 6, + Kodama 1993). Radiation-induced genetic mutations are the CAUSE of the radiation-induced Cancers which are gradually delivered as clinically manifest malignancies. Thus, the clinical evidence and the cell-studies are consistent: In irradiated groups, the carcinogenic impact of exposure to ionizing radiation endures for most (probably all) of the group's remaining lifespan.

The persistence of radiation-induced mutations means, of course, that a person accumulates more and more of them with each additional exposure to ionizing radiation.

● Part 9. A Very Slow Arrival at Conceiving and Testing Hypothesis-1

We have been very slow in arriving at Hypothesis-1.

9a. A Hunch in 1971 ... and a Missed Insight

Back in 1971, it occurred to us that medical irradiation had to account for some significant part of the cancer problem (Gofman + Tamplin 1971, p.266):

"Medical uses of xrays presently are a major source of population exposure and are undoubtedly responsible for a significant part of our currently experienced cancer mortality rate. Morgan's suggestions for feasible reduction in medical xray exposure, without loss of medical diagnostic information, deserve immediate action (Morgan 1971)." The reference is to one of many articles on this topic by Dr. Karl Z. Morgan, a man of immense integrity who is widely recognized as the "father of the health physics profession." Morgan's remarkable memoir is now available (Morgan and Peterson 1999).

Also in 1971, we pointed out that xray induced Cancers are routinely treated as part of the "spontaneous" or "background" cancer-rate rather than as a radiation-induced rate (Gofman + Tamplin 1971, p.244). We noted then that this treatment can lead to underestimates of radiation's role in cancer causation. Much later we realized what a huge epidemiological pitfall such treatment might represent (Gofman 1995/96, Chapter 41, Part 2):

"... 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 percent of the [Cancer] problem."

9b. A Neglected Observation in Gofman 1981

In a 1976 paper, Frigerio and Stowe had claimed that they found a "consistent and continuous" INVERSE relationship between levels of natural background radiation and cancer mortality-rates in the 50 United States (Frigerio 1976, p.385). In Gofman 1981 (p.568), we grouped the states into 3 classes (high, medium, or low background radiation dose) and demonstrated the serious fault in their conclusion.

Then, keeping the same three groups of states, we looked at other data provided in the same paper by Frigerio and Stowe. We did a mini-analysis of physician-density versus cancer mortality rates, and we showed for the three groups that: "The values of physicians per 1,000 persons parallel the cancer death rates almost perfectly, and the background radiation data definitely do not" (Gofman 1981, p.569).

The higher the density of physicians, the higher the cancer death rate. We --- and everyone else, too --- failed to explore that "smoking gun" on page 569 of Gofman 1981.

9c. An Estimate in Gofman + O'Connor 1985

In our 1985 book, Gofman and O'Connor provided estimates of the personal cancer-risk associated with about 40 types of common diagnostic xray exams (Gofman 1985). The book was praised in the New England Journal of Medicine (Greenfield 1986) and attacked in the Journal of the American Medical Association (Adler 1986).

In Chapter 17 of that book, we tried to estimate how many FUTURE cases of Cancer could be prevented in the USA, if the average dose received from diagnostic xray exams were reduced to 33% . A reduction of this magnitude had been demonstrated, by Dr. Kenneth Taylor and colleagues in Ontario, Canada (Taylor 1979 + 1983), to be readily achieved in actual radiology facilities --- without any loss of diagnostic quality and without purchases of expensive equipment.

To prepare our estimate, of course we had to begin with the unreliable type of estimates (on frequencies of common diagnostic exams, and average doses therefrom) which we describe in Part 3a of this chapter. Such estimates were an unreliable foundation for our calculations. Moreover, they excluded all angiographies, CT scans, and (by definition) all interventional radiology. Nonetheless, we felt that even an underestimate would be preferable to no estimate at all.

Our estimate was that about 50,000 cases of future Cancer per year could be prevented in the USA by cutting average dose per exam, from diagnostic radiology, to 33% of the supposed average prevailing dose. Subsequent work (Gofman 1995/96 and this book) indicates that 50,000 cases was a vast underestimate. But it was the best estimate that we could provide in 1985, from using the customary but unreliable input. The result: Our own estimate in 1985 did not provoke us into considering that medical irradiation might be the PRINCIPAL cause of Cancer (USA) in the Twentieth Century.

9d. An Estimate in Gofman 1990

In Gofman 1990, we made two comments about the role of ionizing radiation (all sources) in the total cancer problem. We were still far short of conceiving Hypothesis-1.

First, we provided a list of some 13 medical uses of xrays and radium, plus some non-medical sources of exposure (use of radium-dials, fluoroscopic shoe-fitters, and tobacco whose smoke contains decay-products from uranium), and we said: "One needs to wonder seriously how much of the current cancer-rate is due to past exposure to ionizing radiation from such practices. It could be a meaningful part of the so-called 'spontaneous' rate" (Gofman 1990, p.24-20).

And in the next chapter (p.25-15), we combined (a) BEIR 1990's estimates of annual doses from radon, other natural radiation, medical xrays, and "all other" sources, with (b) our own estimates of Cancers per unit of dose, and thus we arrived at (c) the "ball-park estimate" that about 25% of cancer mortality is radiation-induced --- excluding any radiation-induced inherited predisposition.

9e. An Estimate at the AAAS Symposium of 1994

An event in February 1994 was crucial in the arrival at Hypothesis-1. At the invitation of Nancy Evans and Breast Cancer Action, I was invited to be a panelist for the symposium on Breast Cancer at the national meeting of the American Association for the Advancement of Science. Other panelists were Dr. Graham Colditz, Dr. Devra Lee Davis, Dr. Samuel Epstein, and Dr. Elihu Richter.

My assigned topic was "Ionizing Radiation and Breast Cancer." Radiation-induced Breast Cancer happens to be prominent in the literature on radiation carcinogenesis (see Gofman 1981, BEIR 1990, for instance). Indeed, it provides a large share of the evidence of radiation carcinogenesis at the lowest possible dose and dose-rate per exposure (Gofman 1990).

During preparation of the AAAS presentation, we decided to attempt a very rough estimate of what share of the current Breast-Cancer problem is attributable to radiation exposures. When we began trying to quantify it, we realized that it was much too big a task to complete in the available time. We presented just a preliminary estimate --- which was about 35 percent.

Even we (and certainly others) were startled by such a high estimate. If the estimate was in the right "ball-park," it would point at a way to make an appreciable dent in the FUTURE Breast-Cancer problem. So we decided to continue our inquiry. This meant exploration in the nearly deserted basement of the excellent medical-school library at the University of California, San Francisco.

Almost no one goes to the basement, because that is where the OLD issues of the medical journals reside. Our particular inquiry required extensive use of such journals. What happened decades ago matters, because of the long and variable latency-time for radiation-induced Cancer (Part 8, above). Illustration: The Breast Cancers, caused by radiation-induced mutations received in 1920, were gradually delivered over decades --- some cases not until 1965 (or later).

9f. An Estimate in April 1995

After a year of concentrated effort, we produced the monograph, "Preventing Breast Cancer: The Story of a Major, Proven, Preventable Cause of This Disease, First Edition" (Gofman 1995). The bottom line was that we concluded 35 percent to be a serious underestimate. Our best estimate in 1995 was that about 75 percent of Breast-Cancer cases (USA), recent and current, are due to earlier medical radiation (much of it received during the years 1920-1960).

Every step in our analysis was shown, and the unavoidable assumptions and uncertainties were made explicit.

By the end of 1995, the 75 percent estimate had received lots of peer-review. The criticisms involved the unavoidable assumptions. Most colleagues preferred assumptions which gave much lower estimates, but they were unable to show any basis for thinking that their assumptions were more likely to be right than our assumptions. A few of their competing assumptions were not reasonable, in view of existing evidence. Reasonable or not, all criticisms of which we were aware were included in the Second Edition (Gofman 1996).

9g. Arrival at Hypothesis-1 --- Almost Inescapable, Now

Since no one showed that our 75 percent estimate for Breast Cancer was either wrong or unlikely to be right, we were "stuck" with CONTINUING to believe our 75% estimate. The result: We knew it would be irrational, and even irresponsible, for us to evaluate ONLY Breast Cancer. Thus, Hypothesis-1 insisted upon its own birth and upon our respectful consideration.

Hypothesis-1: Medical radiation is a highly important cause (probably the principal cause) of cancer-mortality among U.S. males and females during the Twentieth Century.

Could we find any data capable of testing this hypothesis vigorously? At the outset, we were stumped. We could not possibly undertake all the work, required for our evaluation of xray-induced Breast Cancer (Gofman 1995/96), for every other kind of Cancer. Even if we could, we would still end up with vast gaps in the evidence on the frequency and organ-dosage from medical xrays --- as we did in the Breast-Cancer book. Such gaps would have to be filled by some assumptions, again.

Finally, we remembered the neglected "smoking gun" described in Part 9b, above. We decided to try testing Hypothesis-1 by combining two databases, which were each collected without any conceivable bias about Hypothesis-1: Physicians per 100,000 population, by Census Divisions (Chapter 3), and age-adjusted cancer mortality-rates per 100,000 population, also by Census Divisions (Chapter 4).

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