X-Radiation and Gamma Radiation: Comments on Their Nomination as Known Human Carcinogens for the Eleventh Report on Carcinogens (RoC).

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Submitted by Priority Mail to:
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For the convenience of the NTP, this submission includes a copy of the author's 1999 peer-reviewed monograph, *Radiation from Medical Procedures in the Pathogenesis of Cancer and Ischemic Heart Disease: Dose-Response Studies with Physicians per 100,000 Population.*

* The author's CV is summarized on the two final pages of this submission.

Part 1:
How Many U.S. Citizens Are Exposed to X-Rrays and Gamma Rays?

These comments apply primarily to x-ray exposure received during medical imaging procedures (during diagnosis, during surgery, during placement of catheters, needles). These comments do not address x-rays and gamma rays used at very high doses for cancer ***therapy*** because the Report on Carcinogens (RoC) lists ***causes*** of cancer, not potential treatments.

The number of x-ray imaging procedures performed annually in the USA was and remains poorly documented. For instance, the annual number for 1985-1990 in the USA was estimated to be at least 800 diagnostic x-ray exams per thousand population, excluding dental x-rays (UNSCEAR 1993, Table 6, p.279). That estimate "could be an underestimate by up to 60%" (UNSCEAR 1993, p.229/46).

X-ray imaging procedures are hardly limited to older, presumably less radio-sensitive persons. According to NCRP 1989 (at p.19, citing the FDA in 1985), 47% of all x-ray imaging exams were administered to patients below age 45 years.

Since 1990, the number of procedures giving the highest doses — namely fluoroscopy and CT scans — have increased dramatically. Despite earlier expectations that MRI would replace CT, the use of CT has increased ceaselessly at an estimated rate of about 10% per year "and will continue to increase for the foreseeable future" (Ravenel 2001, p.279). The estimated number in 1998 was about 33 million CT exams (Nickoloff 2001, p.285).

The use of fluoroscopy during diagnostic cardiac catheterizations (estimated over 1 million times per year), during cardiac angioplasty (estimated over 700,000 times per year), and during other procedures, also has increased substantially in recent years (Shope 1997, p.i). Fluoroscopy creates the potential for very high, localized x-ray doses (hundreds of centi-Grays or rads), because the x-ray beam stays "on" either continuously or in a pulsed fashion.

There can be no doubt that significant numbers of U.S. citizens are exposed every year to medical x-rays for imaging purposes. Moreover, the evidence is overwhelming now that there is no threshold dose (no risk-free dose); please see Part 4. Therefore, every exposure counts, and the consequences (including carcinogenic mutations) accumulate.

Part 2:
How Big Are X-Ray Doses in Medical Imaging? Tables 1 and 2

The mistaken assumption, that x-ray exposure from medical imaging is negligible, has been very widely embraced. Although the NTP Reports on Carcinogens explicitly exclude any risk-assessments, the NTP has the responsibility to evaluate whether or not exposure to a nominated carcinogen is literally negligible.

Part 2 will show that x-ray exposure from medical imaging has been, and continues to be, far from negligible. It is much higher than appreciated.

In 1990, the BEIR-5 Committee embraced without critique the 1987 estimate by the National Council on Radiation Protection, that the average annual per capita "effective" dose equivalent from "x-ray diagnosis" was only 0.039 centi-Sievert (cSv) or rem (BEIR 1990, p.18).

We have challenged that estimate as non-credible (Gofman 1999, pp.33-38), and have shown the basis for estimating that annual average per capita dose from diagnostic medical x-rays in 1950 may well have been as high as 0.65 centi-Gray or rad (Gofman 1999, pp.609-616).

Since 1950, there may be only a little net change. Because x-ray doses ***were*** not and still ***are*** not measured, this is a question where uncertainty will be permanent. But the immense growth in CT and fluoroscopy since 1975 may well have offset the post-1950 dose-lowering effects of tuberculosis-eradication, the phase-out of pre-delivery pelvimetry, and introduction of faster films and better beam collimation.

Patients More Exposed than Nuclear Workers and Japanese A-Bomb Survivors

Tables 1 and 2 are located between pages 3 and 4.

Table 1 shows why medical patients can readily accumulate doses from x-rays considerably higher than the average annual dose accumulated occupationally by civilian "nuclear workers," who now accumulate less than 0.5 centi-sievert per year, on the average.

Table 2 indicates why it is easy for patients to accumulate higher doses to some internal organs than did most survivors of the Hiroshima-Nagasaki bombs — a comparison which necessarily requires adjustment for the higher mutagenic potency of 90 kVp x-rays than the mutagenic potency of a-bomb gamma rays. Gofman 1999 (pp.46-48) provides a detailed analysis of this point, with many references from the peer-reviewed literature.

Table 1. COMPUTED TOMAGRAPHY (CT) X-RAY EXAMS:
Estimated Doses to Patients

- CT doses below are merely "ballpark" values. Entrance doses during CT scans are almost never measured. Actual doses --- even from the same equipment for the same patient --- can vary many-fold according to the settings selected for kVp, mAs, pitch, filtration, slice-width, and some other variables.
- Real doses in centi-Gray units (cGy) are distinctly different entities from "effective" doses in centi-Sievert units (cSv). Real doses quantify energy per gram of tissue delivered by an x-ray exam to the irradiated sections of the body, whereas "effective" doses are artificial values based on assumptions about risk ("detriment"). The calculated "effective" dose suggests what dose, if given to the ***entire*** body, might produce approximately the same amount of ***risk*** as would the real dose received by the irradiated ***sections***. Please see additional comments in the text, Part 2.
- The centi-Gray (cGy) and the rad are identical units. There are 10 milli-Gray (mGy) per centi-Gray (cGy) or rad. The centi-Sievert (cSv) and rem are interchangeable units.
- This table begins with the typical extra "effective" radiation dose from commercial flying in the USA, because medical patients are so often told that their x-ray dose is about the same as the extra radiation from one trip. For CT exams, the table shows that the claim would be very mistaken. The righthand column divides CT "effective" doses by the "effective" dose from a ten-hour airplane flight in the US (0.003 cSv). The lowest ratio is 50, for just one scan. The ratio for one CT "study" involving 2 or 3 scans would be 2 or 3 times higher than the ratios in the righthand column. Please see additional notes below the tabulation.

TOPIC	TYPE OF DOSE	ESTIMATED DOSE	SOURCE	Eff.Dose: CT/flying
Extra radiation during commercial airplane flights within USA.	"Effective" dose/hr. And per 10 hours.	0.0003 cSv per hour. And 0.003 cSv per 10 hours.	UNSCEAR 1993, p.38.	
CT scans, general.	Tissue dose per scan.	1-3 cSv.	Mettler 2000, p.352.	
CT head scan, adult.	Surface dose.	3-7 cGy (rads).	Nickoloff 2001, p.285.	
CT head scan, adult.	"Effective" dose.	0.15 cSv.	Mettler 2000, p.352.	50 to 1.
CT chest, typical.	Surface dose.	2-5 cGy (rads).	Nickoloff 2001, p.286.	
CT chest, typical.	"Effective" dose.	0.54 cSv.	Huda 2000, p.843.	180 to 1.
CT chest, unspecified.	Breast: Mean glandular dose.	Up to 5 cGy (rads).	Gray 1998-a, p.63.	
CT multi-slice of heart for calcium score.	Surface dose.	Up to 10-20 cGy.	Nickoloff 2001, p.286.	
CT chest angiograph.	Surface dose.	2-4 cGy (rads).	Nickoloff 2001, p.286.	
CT chest, cancer screening.	Surface dose.	0.2 - 0.4 cGy (rad).	Nickoloff 2001, p.286.	
Electron Beam CT chest angiography or cardiac calcium score. "EBCT."	X-ray beam travels from back to front.	Reduced dose to breasts and front chest wall.	Nickoloff 2001, p.286.	
CT abdominal, adult.	Surface dose.	2-5 cGy (rads).	Nickoloff 2001, p.285.	
Adult.	"Effective" dose.	0.39 cSv.	Ware 1999, p.64.	130 to 1.
Young adult.	"Effective" dose.	0.44 cSv.	Ware 1999, p.64.	147 to 1.
Child.	"Effective" dose.	0.61 cSv.	Ware 1999, p.64.	203 to 1.
CT-fluoroscopy, for imaging in biopsies, etc.	Range of typical dose-rates.	20-60 cGy (rads) per minute.	Nickoloff 2001, p.285.	

- The "effective" doses above, for medical procedures, have very probably ***not*** been properly adjusted upward yet for the greater mutagenic power per cGy (rad) of 90-120 kVp x-rays, compared with 250 kVp x-rays and a-bomb gamma rays (details in Gofman 1999, pp.46-48).
- The "effective" doses above do not yet incorporate the risk of x-ray-induced coronary artery disease (Gofman 1999, Chapters 39-46).
- A handy approximation is that, during helical CT scans, the real dose (cGy or rads) at the body's center is approximately half of the surface dose (Nickoloff 2001, p.285). Except for Electron Beam CT (EBCT), the CT procedures above irradiate the body by revolving the x-ray beams fully around the head or torso.
- A CT "study" may involve 2 or 3 repeats ("phases") on the same day. Over 90% of abdominal/pelvic CT studies use 2 or more CT scans (Mettler 2000, p.355). The dose from such studies is the sum of single per-scan doses above.

Table 2. FLUOROSCOPIC X-RAYS:
Dose-Rates per Minute, and One Estimate for Cardiac Balloon Angioplasty.

- Fluoroscopy creates the potential for very high, localized doses (hundreds of centi-Grays or rads), because the x-ray beam stays "on" either continuously or in a pulsed fashion. Dose to patients can be reduced by less "on-time," but reduced time is far from the only option for achieving dramatic dose-reductions. Many additional and demonstrated ways exist to obtain good images during fluoroscopy at much lower doses than the customary doses currently delivered (Gray 1998-b; Koenig 2001-b).

- The roentgen (R) is a dose-unit very close to the centi-Gray (cGy) and rad. Sometimes fluoroscopic dose-rates are stated in roentgens (R) per minute.

Fluoroscopy, general.	Dose-rate per minute, on equipment made before 1995. Upper limit can be restricted by choice to 20.	2 to 50 cGy (rads) per minute.	FDA 1994, pp.2-3.
	Equipment made after 1995.	2 to 20 cGy (rads) per minute.	Code of Fed. Regulations: 21 CFR 1020.32 (e) Flu Equip.
CT-fluoroscopy, e.g. for complex needle biopsies.	"Typical" dose-rates delivered per minute.	20 to 60 cGy (rads) per minute.	Nickoloff 2001, p.285.
Fluoroscopy during cardiac angioplasty.	Surface dose, estimated per stenosis.	60 cGy (rads) total, per stenosis.	NCRP 1989, p.31.

- Other procedures with long fluoroscopy times: Angioplasty of non-coronary vessels, stent and filter placement, thrombolytic or fibronolytic procedures, percutaneous transhepatic cholangiography, percutaneous nephrostomy, biliary drainage, urinary/biliary stone removal (FDA 1994).

- Procedures where localized skin-dose from fluoroscopy is likely to exceed 100 cGy (rads): RF cardiac catheter ablation, vascular embolization, transjugular intra-hepatic portosystemic stent placement, and percutaneous endovascular reconstruction (Shope 1996, p.1199). One exceptional patient accumulated an estimated local skin dose of 2,100 cGy from fluoroscopy during a series of biliary procedures (Shope 1996, p.1197).

- When the skin receives very high doses, the organs beneath receive high doses too. Skin injuries begin at accumulated doses of about 200 cGy (rads), and increase in severity with increasing dose (details in Gofman 1996, pp.184-186, and Koenig 2001-a., Table 3).

- Because cardiac procedures are so frequent, their rate of x-ray-induced skin injuries appears to be the highest (Koenig 2001-a, Table 1).

The Higher Mutagenic Power of Medical X-Rays than High-Energy Gamma

A reasonable estimate at this time is that the cancer-risk per rad or centi-gray is about three times higher from 90 kVp x-rays than from a-bomb gamma rays. Therefore, in risk-assessment, it would be a severe error to assume that results from the a-bomb study apply directly to medical patients.

Table 1: The Difference between Real Doses and "Effective" Doses

Doses are reported in units of grays or rads. A ***dose*** of ionizing radiation is a quantity of energy delivered per gram of tissue. A rad means 100 ergs of energy per gram of tissue. Since there are 100 rads per gray, 1 rad is exactly the same dose as one centi-gray (cGy). The roentgen is a dose-unit roughly equivalent to the rad or cGy.

By contrast, the term "***effective***" before a dose is a big flag which means, "This is not a dose at all; it is an artificial value which estimates relative detriment." The effective dose is an attempt to estimate what dose to the ***entire*** body would have caused the same amount of detriment (risk) as the actual exam which irradiated only ***specific parts*** of the body (McCullough 2000). Thus, "effective" doses are usually considerably lower than real doses --- as Table 1 shows. The dose-unit is the centi-Sievert (cSv), which is exactly the same as the rem. These units incorporate a crude adjustment for the different mutagenic potency of x and gamma (low LET) vs. alpha (high LET) radiation.

"Effective" doses are necessarily much less credible than real doses, because "effective" doses incorporate a long series of estimates and assumptions about "tissue weighting factors," which attempt (despite woefully inadequate evidence) to assess the attributable probability of fatal cancer in different organs, of the additional detriment from non-fatal cancer and hereditary disorders, and of the different latency periods for cancers of different kinds. By contrast, a real dose is an estimate or measurement of something objective: Energy delivered per gram of tissue.

McCullough emphasizes that "It is important to recall that these [effective doses] are ***estimates***, based on many assumptions, and are not directly applicable to any one individual ... These values, although not intended to describe the dose to an individual, can be used as a relative measure of stochastic injury (e.g., cancer induction or genetic effects)" (McCullough 2000, p.835).

Table 1: Why the Doses Are Merely "Ballpark" Estimates

With the rarest exceptions, actual surface doses are ***not measured*** during x-ray imaging procedures, even though small thermo-luminescent dosimeters (TLDs) have been shown ***not*** to interfere with images. Instead, some efforts have been made to measure doses on phantoms (dummies), but the limited exposure-circumstances during such tests provide unreliable dose information about exposures in real-world practice. After all, the very same equipment will deliver very different doses depending upon what settings and techniques the operator chooses (the first note in Table 1).

Part 3:

A Major New Addition to Evidence that X-Rays Are a Known Human Carcinogen

In November 1999, a major prospective dose-response study of unique design provided what is probably the most powerful confirmation anywhere, that virtually all types of human cancer are inducible by medical x-rays in both males and females. The study is entitled *Radiation from Medical Procedures in the Pathogenesis of Cancer and Ischemic Heart Disease: Dose-Response Studies with Physicians per 100,000 Population,* and I am its author (Gofman 1999).

That study has been independently peer-reviewed by a former chair of the BEIR Committee and former director of the National Cancer Institute (Arthur Upton, M.D.) and by a professor of physiology at Temple University School of Medicine (Prof. Howard S. Pitkow). Their comments are attached to this submission, after the Reference List.

Although prospective dose-response studies are the "gold standard" in epidemiology for establishing causation, they are inherently unable to ***prove*** that some "mystery agent" is not the real cause of a positive dose-response. However, many lines of evidence in Gofman 1999 do virtually rule out explanations ***other than*** medical radiation as the cause of its incontrovertible positive correlations (discussion in Chapters 68 and 69).

All-Cancers-Combined and Major Types, Males and Females Separately

Gofman 1999 reveals that by 1940, medical radiation in the United States had become a ***necessary*** co-actor in about 90% of the age-adjusted male cancer mortality rate, and about 58% of the age-adjusted female cancer mortality rate (Chapter 6 and 7). These percentages cannot be dismissed as irrelevant today, because average annual per capita exposure to medical x-rays may ***not be*** substantially lower now than it was in the years preceding 1940 (discussion in Part 2, above).

The prospective nature of the study is reflected by the fact that the 1940 age-adjusted national cancer mortality rates, for men and women separately, can be well predicted by analysis of the x-ray doses given in 1921 and 1931 (Gofman 1999, pp.213-214, p.222).

Three Meritorious Scientific Differences from Other Studies

The design of the 1999 study differs in three very positive ways from most other epidemiological analyses of low LET radiation.

First, such analyses are often based a) on highly unreliable dose-estimates (because individual doses are not measured — they are estimated later, often decades later) and (b) on highly unreliable estimates of risk per dose-unit (because such values

derive from unreliable dose-estimates and/or from unreliable assumptions about the relative carcinogenic potency of particular types of low LET radiation).

By contrast, the 1999 study avoids both of these pitfalls by using a sensible measure of ***relative*** accumulated x-ray exposure (Gofman 1999, Chapter 3).

Second, other radiation studies sometimes use databases where the opportunity has existed for subjective choices, particularly on dosimetry and on exclusions. This is particularly true of the A-Bomb Survivor Database, whose practices --- of changing input *after* the results are known --- are discussed in both Gofman 1990 (Chapters 4, 5, 6) and Gofman 1999 (pp.43-44, pp.54-55). Moreover, influential analysts of that database have sometimes chosen to discard selected pieces of it. For example, the BEIR-1990 analysis discarded the observations from the 1950-1955 period except for breast cancer (BEIR p.168), discarded the observations from the two highest dose-groups (BEIR p.165), discarded cancer deaths which occurred beyond age 75 (BEIR p.165), and made no use of its own finding that the dose-response was supra-linear (BEIR p.200).

By contrast, Gofman 1999 marries two databases which are utterly neutral with respect to radiation: The American Medical Association's database on physicians per 100,000 population, by the nation's nine Census Divisions, and the U.S. Vital Statistics on age-adjusted cancer mortality rates, by the nine Census Divisions. Moreover, the analysis does not discard data.

Third, other radiation studies suffer from the problem of small numbers. Even the Life Span Study of the A-Bomb Survivors has a (repeatedly revised) database of only about 100,000 participants. Subdivision of cancer by types in such a study often produces statistically marginal findings.

By contrast, the 1999 study of x-ray-induced cancer "enrolls" 130 million participants --- the entire 1940 population of the United States. For age-adjusted mortality rates for all cancers combined, by Census Divisions, the male dose-response with accumulated x-ray exposure has an R-squared value of 0.95, and for females, the value is 0.86. Subdivision of the data by the major types of cancer, separately for males and females, still yields ***highly significant*** dose-response relationships (summary table in Gofman 1999, p.217). The R-squared values are as follows: 0.92, 0.91, 0.76, 0.92, 0.94, 0.78, 0.72, 0.87, 0.96. The only exception to a highly significant, positive dose-response in all these studies was found in female genital cancers, with an R-squared value of 0.07.

<u>The Bottom Line: A Known Cause of Cancer, Lacking a Dose-Threshold</u>

We submit these data (Gofman 1999) as a ***major new addition*** to the human epidemiological evidence that x-rays are a known cause of human cancer.

Part 4:
The Absence of Any Risk-Free (Safe) Dose-Level of Low LET Radiation

Gofman 1999 also presents (in its Appendix B) a nine-page summary of the overwhelming evidence that cancer risk from x-rays and gamma rays extends all the way down to zero dose (with excerpts from Gofman 1990, UNSCEAR 1993, and NRPB 1995). After publication of Gofman 1999, the finding of excess breast cancer in a study of scoliosis patients (Doody 2000) provided additional epidemiological evidence against any threshold dose. In the Doody study, the patients received x-radiation in serial doses which were estimated (long afterwards) at only 0.6 cGy (rad) per exam — a dose which is the lowest conceivable dose (1 primary ionization track, on the average, per cell nucleus) with respect to DNA or chromosomal damage (Gofman 1999, p.522).

By any reasonable standard of biomedical proof, the evidence from human epidemiology and the physical evidence from track-analysis combine to demonstrate that cellular repair processes, for nuclear DNA and chromosome injuries, are unable to deliver a safe (risk-free) dose of low-LET radiation — including x-rays and gamma-rays.

Part 5:
Complex Mutations and Genomic Instability in Irradiated Cells

There is a vast literature on human cell-studies which demonstrates that x-rays and gamma rays are a potent cause of structural chromosomal mutations of every sort, including re-arrangements, acentric fragments, and ***deletions*** ranging in size from multiple genes probably down to single nucleotides. (The deletion of a single nucleotide is no small matter, since it can scramble the genetic code by causing a frame-shift.)

The dose-response shape for the easily detectable aberrations appears to be linear down to the 2 cGy dose-level (Lloyd 1992). One of the best sources, for evidence about the complex types of damage inflicted by low-LET radiation upon the human genome, are the studies by Ward (1991, 1994, 1995) and Sutherland (2000).

Sutherland's observations include ***double***-strand chromosome breaks (which are the basis for deletions, translocations and every other type of chromosomal re-arrangement) and other sorts of "clustered" DNA damage incorporating "two or more closely spaced damages" such as strand breaks, abasic sites and/or oxidized bases. Sutherland and colleagues are working experimentally with both gamma rays from cesium-137 and with 50 kVp x-rays (Sutherland 2000, p.107).

In the same paper, Sutherland and colleagues conclude that their work confirms that each cluster "results from a single radiation track" (Sutherland 2000, p.106). If so, this constitutes additional support for the conclusion that there is no risk-free dose-level of exposure to x-rays and gamma-rays.

The induction of single-strand and double-strand chromosome breaks by ionizing radiation is under study by Boudaiffa et al, who report on the role of the low-energy secondary electrons in strand breakage (Boudaiffa 2000).

Induction of Genomic Instability by X-Rays and Gamma Rays

Genomic instability refers to abnormally high rates (possibly accelerating rates) of genetic change occurring serially and spontaneously in cell-populations, as they descend from the same ancestral cell (Gofman 1999, p.533).

Many (not all) cancer biologists now believe that genomic instability "is one of the most important aspects of carcinogenesis" (Morgan 1996, p.247; additional references and discussion in Gofman 1999, Appendix D). In 1976, Peter C. Nowell published his classic paper proposing that "the biological events recognized in tumor progression represent (i) the effects of acquired genetic instability in the neoplastic cells, and (ii) the sequential selection of variant subpopulations produced as a result of that genetic instability" (Nowell 1976, p.25). In 1971, I saw in our lab the operation of selective advantage for certain gamma-ray-induced mutations in cultured human fibroblasts: "There is no question that the cells with profound structural re-arrangements of chromosomes became the dominant and finally, with adequate survival time, the only reproducing cells in the culture" (Minkler 1971, p.73).

Can exposure to x-rays and gamma-rays induce genomic instability?

Evidence appears to support an affirmative answer. The following references (which provide many additional references) can be recommended:

Holmberg 1993.
Kronenberg 1994.
Marder 1993.
Mendonca 1993.
Morgan 1996.

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Dr. Arthur C. Upton, former director of the National Cancer Institute, provided the statement below for the purpose of stimulating additional research and attention to ALARA measures. The message is reproduced with his permission, and may be reproduced ONLY in its entirety, verbatim. JWG.

Message

From: acupton@eohsi.rutgers.edu (Arthur Upton MD)
Date: Mon, Nov 29, 1999, 2:51pm (PST+3)
To: gofman123@webtv.net
Subject: Medical Radiation and Disease Rates

Dear Dr. Gofman:
Thank you for kindly sending me a copy of your recent book entitled "Radiation from Medical Procedures in the Pathogenesis of Cancer and Ischemic Heart Disease". Your observations are impressive and are consistent with the linear-nonthreshold dose-response hypothesis for the genetic and carcinogenic effects of ionizing radiation, and they support the wisdom of the ALARA principle in radiation protection. At the same time, however, the associations you have so skillfully demonstrated cannot be taken as proof of causal relationships, owing to the possible influence of confounding variables. Just as the inverse relationship between lung cancer rates and county residential radon levels, as reported by Bernard Cohen, does not suffice to prove that low-level exposure to radon protects against lung cancer, neither do your observations suffice to establish medical radiation as a causal factor in the associations you have identified. Nevertheless, I find your observations intriguing, and your interpretation of them to be thoughful and constructively hypothesis-generating. I hope that your book stimulates the productive follow-up research that your findings clearly call for. Many thanks, again, for sharing your findings with me, and best wishes for continuing productivity in the new millennium. Arthur C. Upton

ALARA: As Low As Reasonably Achievable.

Arthur C. Upton, M.D. is a former Director of the National Cancer Institute (1977-1979). Beforehand and afterwards, he has been a member of various Committees which produce reports on the health effects of ionizing radiation, including:

BEIR: The Committee on the Biological Effects of Ionizing Radiation (BEIR) of the National Research Council, National Academy of Sciences. 1972, 1980, Chair 1990.

NCRP: National Council on Radiation Protection; Chairman of Scientific Committee 1-6, to evaluate the linear non-threshold dose-response model. The Committee posted its 284-page draft report online in October 1998.

NIH: National Institutes of Health, Ad Hoc Working Group to Develop RadioEpidemiological Tables. 1985.

ICRP: International Commission on Radiological Protection. 1977, 1985-1989.

UNSCEAR: The United Nations Scientific Committee on the Effects of Atomic Radiation. 1977.

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Science and Technology-Health Sciences

Gofman, John W. **Radiation from medical procedures in the pathogenesis of cancer and ischemic heart disease: dose-response studies with physicians per 100,000 population** . ed. by Egan O'Connor. Committee for Nuclear Responsibility, 1999. 699p bibl index ISBN 0-932682-97-9, $35.00; ISBN 0-932682-98-7 pbk, $27.00 . Reviewed in 2000may CHOICE.

Renowned nuclear physics scholar Gofman (emeritus, Univ. of California, Berkeley), author of several books on heart disease and the effects of radiation on human health, combines these two areas to offer convincing statistical evidence of the deleterious effects of medical procedures that use ionizing radiation (i.e., X-rays) as a causative factor in both cancer and ischemic heart disease (IHD) mortality in the US. There are six sections: introduction; cancer mortality caused by medical radiation; noncancer and non-IHD mortality (i.e., strokes, diabetes, hypertension); IHD and medical radiation; cancer and IHD mortality after 1940 from medical radiation; analysis of a hypothesis that medical regimens using radiation contribute to cancer and IHD mortality in the US. The overall theme is the contention that even very low doses of ionizing radiation may be a contributing risk factor in the development of different forms of cancer and death from IHD. The reader will appreciate the various appendixes with their wealth of supplemental information as well as the alphabetically arranged, up-to-date reference list enabling the reader to pursue any topic. A work especially for professionals concerned about the effects of medically induced exposure to ionizing radiation, even at low doses and rates, on human health. Upper-division undergraduates through professionals; two-year technical program students. -- *H. S. Pitkow, Temple University*

18 April 2000
http://www.choicereviews.org/

The web identifies Howard S. Pitkow, Ph.D., as Professor Emeritus of Physiology, Temple University School of Medicine, Temple Health Science Center, 8th at Race Street, Philadelphia, PA 19107.

Radiation from Medical Procedures in the Pathogenesis of Cancer and Ischemic Heart Disease, by John W. Gofman, M.D., Ph.D. 1999. Library of Congress 99-045096. 699 pages.

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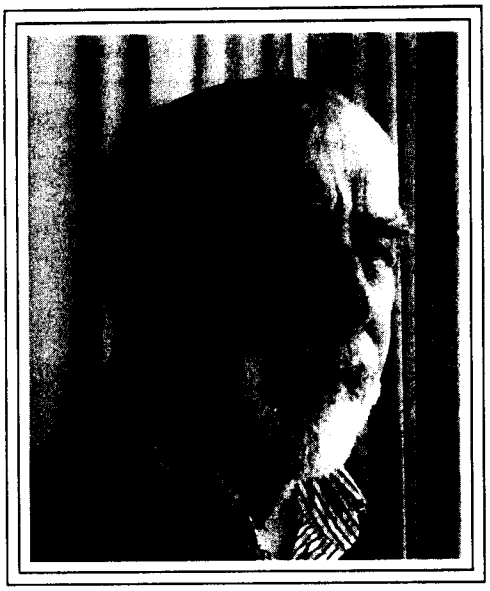

The Author's History
by Egan O'Connor

John William Gofman is Professor Emeritus of Molecular and Cell Biology, University of California at Berkeley, CA 94720-5706. He is also on the faculty at the University of California Medical School at San Francisco (UCSF). His life's work is divisible into three main areas, which converge for the first time in this monograph. Some of the earlier work is cited in the monograph's Reference List.

• (1) While a graduate student at U.C. Berkeley, Gofman earned his Ph.D. (1943) in nuclear/physical chemistry, with his dissertation on the discovery of Pa-232, U-232, Pa-233, and U-233, the proof that U-233 is fissionable by slow and fast neutrons, and discovery of the 4n + 1 radioactive series. His faculty advisor was Glenn T. Seaborg (who became Chairman of the Atomic Energy Commission, 1961-1971). Seaborg, Gofman, and Raymond W. Stoughton share Patent #3,123,535 on the slow and fast neutron fissionability of uranium-233, with its application to production of nuclear power or nuclear weapons. The work is recounted in Seaborg's book "Nuclear Milestones" (1972).

Post-doctorally, Gofman continued research related to the first atomic bombs --- particularly the chemistry of plutonium, at a time when the world's total supply was less than 0.25 milligram. He shares patents #2,671,251 and #2,912,302 on two processes for separating plutonium from the uranium and fission products of irradiated nuclear fuel. "We all were pushing the envelope in those years, and in the process, we learned the habit of observing details very closely."

• (2) After the plutonium work, Gofman completed medical school (1946) at UCSF, where the faculty and his classmates selected him to receive the annual Gold-Headed Cane Award for having the qualities of "a true physician."

In 1947, following his internship in Internal Medicine, Gofman joined the faculty at U.C. Berkeley (Division of Medical Physics), where he began his research on lipoproteins and Coronary Heart Disease at the Donner Laboratory. At the time, only two types of blood lipoproteins were known: Alpha and beta. By devising special flotation techniques with the ultracentrifuge, he and Frank T. Lindgren and co-workers at the Donner Lab began to reveal (1949-1950) the great diversity of very-low-density, intermediate-density, low-density, and high-density lipoproteins (VLDL, IDL, LDL, HDL) which truly exist in the bloodstream.

Their work on the chemistry of lipoproteins (e.g., the cholesterol-rich and triglyceride-rich varieties), and on dietary experiments, and on epidemiologic studies, soon produced evidence that high blood levels of the LDL, IDL, and VLDL lipoproteins are a risk-factor for Coronary Heart Disease.

In 1954, Gofman received the Modern Medicine Award for outstanding contributions to heart disease research. In 1965, he received the Lyman Duff Lectureship Award of the American Heart Association, for his research in atherosclerosis and Coronary Heart Disease. In 1972, he shared the Stouffer Prize for outstanding contributions to research in arteriosclerosis. In 1974, the American College of Cardiology selected him as one of twenty-five leading researchers in cardiology of the past quarter-century.

• (3) Meanwhile, in the early 1960s, the Atomic Energy Commission (AEC) asked Gofman to establish a Biomedical Research Division at the AEC's Livermore National Laboratory, for the purpose of evaluating the health effects of all types of nuclear activities. From 1963-1965, Gofman served as the division's first director and concurrently as an Associate Director of the full laboratory. Then he stepped down from the administrative activities in order to have more time for his own laboratory research on Cancer and chromosomes (the Boveri Hypothesis), on radiation-induced chromosomal mutations and genomic instability, and for his analytical work on the epidemiologic data from the Japanese atomic-bomb survivors and other irradiated human populations.

By 1969, Gofman and a Livermore colleague, Dr. Arthur R. Tamplin, had concluded that human exposure to ionizing radiation was much more serious than previously recognized. Because of this finding, Gofman and Tamplin spoke out publicly against two AEC programs which they had previously accepted. One was Project Plowshare, a program to explode hundreds or thousands of underground nuclear bombs in the Rocky Mountains in order to liberate (radioactive) natural gas, and to use nuclear explosives also to excavate harbors and canals. The second was the plan to license about 1,000 commercial nuclear power plants (USA) as quickly as possible. In 1970, Gofman and Tamplin proposed a 5-year moratorium on that activity.

The AEC was not pleased. Seaborg recounts some of the heated conversations among the Commissioners in his book "The Atomic Energy Commission under Nixon: Adjusting to Troubled Times" (1993). By 1973, Livermore de-funded Gofman's laboratory research on chromosomes and Cancer. He returned to teaching full-time at U.C. Berkeley, until choosing an early and active "retirement" in order to concentrate fully on pro-bono research into human health-effects from radiation.

His 1981, 1985, 1990, 1994, and 1995/96 books present a series of findings. His 1990 book includes his proof, "by any reasonable standard of biomedical proof," that there is no threshold level (no harmless dose) of ionizing radiation with respect to radiation mutagenesis and carcinogenesis --- a conclusion supported in 1995 by a government-funded radiation committee. His 1995/96 book provides evidence that medical radiation is a necessary co-actor in about 75% of the recent and current Breast Cancer incidence (USA) --- a conclusion doubted but not at all refuted by several peer-reviewers.

John W. Gofman is the son of David and Sarah Gofman --- who immigrated to the USA from czarist Russia in about 1905. JWG was born in Cleveland, Ohio, in September 1918.

Some Comments about Dr. John Gofman's Earlier Work and Books.

• In 1972, Dr. Gofman shared the 1972 Stouffer Prize, one of the top awards for research in combatting arteriosclerosis. The 1972 Prize Committee was chaired by Professor Ulf S. von Euler, M.D., former chairman of the Nobel Prize Committee for Physiology and Medicine. The Committee's citation:

"The 1972 Stouffer Prize is awarded to Dr. John W. Gofman for pioneering work on the isolation, characterization and measurement of plasma lipoproteins, and on their relationship to arteriosclerosis. His methods and concepts have profoundly stimulated and influenced further research on the cause, treatment, and prevention of arteriosclerosis."

Radiation and Human Health. 1981. ISBN 0-87156-275-8.

• From the Journal of the American Medical Assn., March 19, 1982, p.1637, a review by Victor E. Archer, M.D.: "This remarkable and important book enables any intelligent person with a high school education to understand the complexities involved in assessing the risks to man from low levels of ionizing radiation. Gofman not only demonstrates his mastery of this complex subject but carefully explains the basic concepts of epidemiology, genetics, birth defects, carcinogenesis, radiobiology, physics, chemistry and even mathematics, which are necessary to an understanding of the subject."

Xrays: Health Effects of Common Exams. 1985. ISBN 0-87156-838.1. E.O'Connor, co-author.

• From the New England Journal of Medicine, Feb. 6, 1986, p.393, a review by Maurice M. Greenfield, M.D (radiologist): "This book is practical and important. It is destined to represent a watershed in the controversial field of low-dose radiobiology and will be of inestimable value to radiologists, other physicians, dentists, and patients."

• From the American Journal of Roentgenology, April 1986, p.774, a review by David S. Martin: "From a radiologist's point of view, this book represents a well organized and concise attempt to quantify the cancer risk from diagnostic xray exposures by age, gender, organ, and examination. As such, it is a useful starting point for comparisons."

Radiation-Induced Cancer from Low-Dose Exposure. 1990. ISBN 0-932682-89-8.

• From the New England Journal of Medicine, Feb. 14, 1991, p.497, a review by G. Theodore Davis, M.D., and Andre J. Bruwer, M.D. (radiologist) of two books jointly: The 1990 book by Gofman (above) and the 1990 BEIR-5 Report from the National Research Council, National Academy Press: "Both these works agree that previous assessments of the dangers of radiation underestimated the risk, but they reach substantially different conclusions about the magnitude of the risk, especially when the radiation is at lower doses (below 10 rem) and the doses are delivered slowly ... We strongly recommend both these excellent and timely books for physicians, engineers, and public health officials concerned with radiation, the environment, and public health."

Preventing Breast Cancer. 1995. ISBN 0-932682-96-0 (Second Edition).

• From the Journal of the American Medical Assn. "Medical News & Perspectives," August 2, 1995, a two-page feature (pp.367-368) by Andrew A. Skolnick about Gofman's book: "A respected authority on the biological effects of ionizing radiation has just published a book claiming that the vast majority of breast cancers in the United States were caused by ... medical xrays ..." Skolnick quotes from interviews with the author and with critics of the book.

• On August 3, 1995, Channel 3 in Britain telecast a report ("The Xray Effect") featuring the book's findings. The 1995 broadcast included these statements:

"John Gofman is a superb analyst and has always been at the cutting edge of medical science, particularly when it comes to protecting people." • - Mortimer Mendelsohn, M.D., Ph.D., then Assoc. Director of the Radiation Effects Research Foundation (the A-Bomb Survivor Study).

"Dr. Gofman is owed a debt of gratitude by the scientific community because he was one of the first people to raise the issue of cancer risks from radiation exposure." • - Edward P. Radford, M.D., epidemiologist and Chairman of the 1980 Committee on the Biological Effects of Ionizing Radiation (BEIR-3) of the National Academy of Sciences, National Research Council.

Radiation from Medical Procedures in the Pathogenesis of Cancer and Ischemic Heart Disease,
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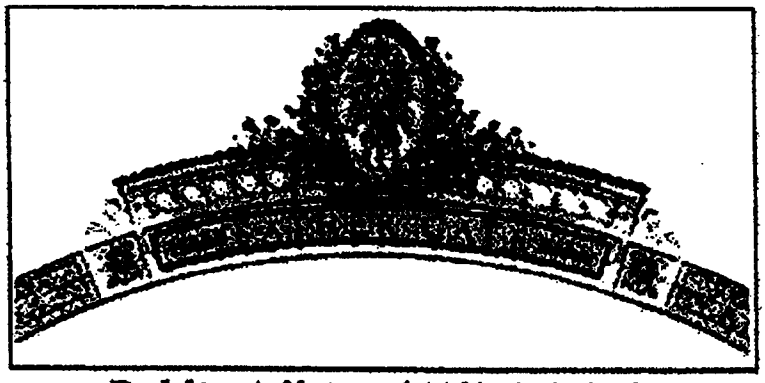

Public Affairs, (510) 642-3734

NEWS RELEASE, 11/16/99

Radiation expert warns of danger from overuse of medical X-rays, claiming they're responsible for many cancer and heart disease deaths

By Robert Sanders, Public Affairs

BERKELEY-- A noted University of California, Berkeley, expert on the health effects of radiation has concluded that a large proportion of deaths today from cancer and heart disease are due in part to past exposure to medical radiation.

John W. Gofman, professor emeritus of molecular and cell biology at UC Berkeley, conducted an intensive analysis comparing death rates in each of the country's nine census divisions with the average number of physicians per 100,000 people in these divisions.

The analysis turned up a major surprise. While death rates from almost all causes went down with increasing physician density, death rates rose with physician density in two categories: cancer and ischemic heart disease, also known as coronary heart disease.

Gofman, who for decades has warned of the dangers of low-level radiation, concluded that the cause is medical X-rays, including fluoroscopy and computed tomography or CT scans. The analysis and conclusions are published this week in a 700-page monograph by the book division of the Committee for Nuclear Responsibility, Inc., a non-profit, public interest association Gofman founded in 1971.

"This is a serious public health problem," Gofman said. "We're talking about the two biggest causes of death in this country - cancer and heart disease - which together amount to 45 percent of all deaths. Medical X-rays are a major cause of these deaths."

Gofman does not discount the role of other factors in these diseases, including diet and smoking, but maintains that more than half the deaths from cancer and heart disease would not have occurred but for medical X-rays.

He also acknowledges the value of X-rays in diagnosis and to monitor medical treatment. Nevertheless, he urges physicians to be careful of unnecessarily high doses of X-rays, and to advise patients of the pros and cons of X-rays, much as they alert patients to the possible side effects of drugs.

"My findings are not going to cause patients to reject the obvious benefits of medical X-rays," Gofman said. "People are smart. Very soon, patients may insist on seeing some evidence that they will receive the lowest possible X-ray doses."

He also urges radiologists to reduce radiation doses delivered in standard procedures, and in his study

The rest of this press release can be obtained by scrolling down to Nov. 16 on the University website: http://www.berkeley.edu/news/index.html --->