THE NEW JERSEY RADIUM RESEARCH PROJECT: FINAL REPORT

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The New Jersey Radium Research Project actively collected human material from November 1957 through June 1967. Original working papers and tissue specimens generated by the project pertained to industrial intoxication, and were turned over by the State Medical Examiner to the present writer, who has deposited them at the Center for Human Radiobiology at the Argonne National Laboratory, Argonne, Illinois. The present radium protection standard, defined in 1940, was based on a small number of radium workers who had relatively large burdens, and remains the only such standard based on human experience. The project hoped to test this standard by studies of larger numbers of clinically asymptomatic subjects with very much lower body burdens.

The project stopped active collection of material in June 1967, and in July 1967 the Newark riots broke out. By the spring of 1968, the present writer had summarized certain problems founded on partial review of histologic material from project subjects.¹ At that time, he was asked to become Director of Laboratories at Newark City Hospital, where Martland had done his original work. The medical school pathology department was a poorly balanced one, and from July 1968 until his resignation early in 1971, the writer with one part-time assistant pathologist was responsible for professional pathology services in a 500 bed city hospital locally known

as "the slaughterhouse on the hill." Neither time nor energy then permitted active study of material available during this interval, and this material was organized and transferred to the writer's home after he resigned from the full-time faculty early in 1971 -- and was replaced by three pathologists. This material has since been studied despite such interruptions as social upheaval, illness and the demands both of a busy hospital practice and of editing a medical journal.

The writer approached this material with only two assumptions: that this unique population would probably not again occur, and that nobody had any very clear idea as to what, if anything, lifetime (50 years or so) exposure to very small quantities of skeletally deposited alpha and beta emitting radionuclides did to people. The effects of large quantities (over 1 μCi pre-terminal burdens) of such elements are well known and probably require little further documentation, but the effect on man of lifetime exposure to burdens only one or two orders of magnitude above background levels remains unclear.

After several years of preliminary study, analysis of this material fell naturally into several distinct questions, each of which had to be investigated in its proper sequence. These seemed to be: 1. The historical background of the problem, including Harrison S. Martland's role,² the subjective reactions of one of the victims,³ and the New Jersey cases as a prototype of occupational carcinogenesis generally.⁴ 2. An epidemiologic description of the population,⁵ an offshoot of which was a description of the use of a standard nomenclature for the handling of data generated by the New Jersey studies.⁶ 3. A description and analysis of abnormalities

encountered during examination of bones from the New Jersey subjects, including the preliminary survey,¹ description and documentation in detail of radium osteitis based on this human material,⁷ review of age-related changes in human bone, most of the literature of which has appeared within the past decade,⁸ and an attempt to correlate the distribution of radium osteitis with pre-terminal radium-226 burdens.⁹

Review of death certificates available for 391 of the New Jersey subjects yielded only minor differences from mortality data reported by Polednak, Stehney and Rowland,¹⁰ differences too slight to add new information and therefore confirming their conclusions.

Clinicopathologic Studies

A detailed study of clinical and autopsy findings of 42 of the long-term New Jersey survivors was prepared,⁵ preliminary to analysis of bone findings, both as itself worthwhile and to exclude conditions other than internally deposited radium-226 and radium-228 which might have caused bone infarcts or aseptic necrosis of bone. These 42 subjects constituted 4.2 per cent of all of the workers whom the project could identify by name, and 8.5 per cent of those known to have survived twenty-five years or longer from their first occupational radium exposure. Pre-terminal radium-226 burdens were known for 31 of the 42, and ranged from background ($\leq 0.0042 \mu\text{Ci}$) to $9.1 \mu\text{Ci}$.

Twenty-four of these 42 had a malignant tumor or fatal blood dyscrasia. Women's but not men's life spans were shortened, and women subjects produced proportionately fewer living children than the wives of

men who were occupationally exposed. Deafness (conduction, sensorineural and mixed pattern) and histories of otitis media were more frequent than expected. Jaw necrosis and spontaneous fractures through the shafts of long bones were frequent at pre-terminal burdens above 0.6 μCi radium-226, and above 1.0 μCi , carcinoma of the paranasal sinuses behaved as a radium-induced cancer with a long latent period. Studies available twenty years ago to assess immune competence were neither precise nor sophisticated, but the subjects' erythrocyte sedimentation rates were increased and their serum alpha-1 globulin fractions were decreased consistently enough to suggest that changes in immune responses should be investigated among living subjects occupationally exposed in the nuclear industry. Modern techniques may indicate whether these are indices of at least potential radiation damage before the diagnosis of cancer or osteitis.

The latent period between occupational or environmental exposure to a pathogen and the diagnosis of a presumptively related cancer, blood dyscrasia or osteitis is so long that professionally frustrating studies extending over decades may lead to a despairing attitude of cui bono? The choice of a lethal cancer or blood dyscrasia or of a chronic disabling disease such as radium osteitis or osteomyelitis as the endpoint for determining the effects of noxious exposure is cynical, and offers only the advantage of neat columns of numbers and regression curves unmuddled by the balancing of probabilities and subjective interpretations inseparable from all human clinical studies. Radiation physicists and radiobiologists are obsessed with death from cancer as an endpoint and tacitly assume that if the subject does not actually die of cancer he suffered no radiation injury. The high incidence of deafness and serum protein changes among

the New Jersey subjects suggests that prospective long-term studies of these changes, considering the anatomic route of the eighth cranial nerve through the skull and the reticuloendothelial system's radiosensitivity, could profitably be undertaken among asymptomatic exposed populations to ascertain whether these may indicate early radiation injury before a fatal disease makes itself known. Such clinical tests are painless, inexpensive, and yield graphs or curves that admit of computer analysis, storage and regular comparison.

Observed versus Expected New Jersey Deaths

Table 1 lists observed and expected causes of death among the 391 New Jersey subjects whose death certificates were available for review. The "expected" number was calculated from the expected numbers reported by Polednak, Stehney and Rowland¹⁰ using a proportion of 0.9416 as explained in Table 1. The populations overlap, but this approximation is close enough considering the unreliability of death certifications and the errors introduced by extrapolating annual death rates per 100,000 of population to a base of 597 subjects over six decades of shifting diagnostic classifications. Any conclusions based on these numbers must be very carefully qualified. Deaths from external causes (ICD rubrics 800-998) exceeded the number expected, but agree with Polednak, Stehney and Rowland:¹⁰ 3.17 and 3.08 observed against 1.0 expected. Table 2 summarizes death certifications by categories and decades, and Table 3 presents detailed causes of deaths by ICD rubric and decade. These data were not corrected when autopsy or other evidence indicated that the death certificate diagnoses were in error.

More New Jersey subjects than expected died of cancer, and proportionately more than Polednak, Stehney and Rowland¹⁰ report, 2.92 versus 1.93 against 1.0 expected. If we assume that a ratio of 2.5 observed against 1.0 expected deaths suggests a real change, the New Jersey subjects had more deaths than expected from cancers in the following primary sites: buccal cavity and pharynx (ICD rubrics 140-149), large intestine (ICD 153), rectum (ICD 154), respiratory system (ICD 160-165), urinary bladder (ICD 181), bone (ICD 196), "other and unspecified sites" (ICD 198-199), and lymphatic-myeloma (ICD 200-203). Respiratory system cancers include paranasal sinus cancers (160) and a not unanticipated number of bronchogenic carcinomas. Four of five lymphatic-myeloma malignancies (ICD 200-203) were myelomas (ICD 203), and these four tumors explain the increased number of deaths in this category.

More subjects than expected died from diseases of the blood and blood-forming organs (ICD 290-299), but all seven deaths in this category had presumably radium-related aplastic anemia: five during the 1921-1930 decade, one during 1941-1950, and one during 1961-1970. These seven deaths explain the excess, and no other hematologic process need be implicated.

The excess of observed over expected deaths from diseases of the digestive system was slight (2.47/1.0). Five deaths from inflammatory conditions of the jaws (4) and mouth (1), three during 1921-1930, and one during each subsequent two decades, all apparently complications of radium-related mandibular or maxillary osteomyelitis. Seven died from cirrhosis of the liver (ICD 581), more than expected (6.93/1.0), but this real

increase is more likely due to northern New Jersey's drinking habits than to radiation exposure, provided that the deaths were in fact from cirrhosis and not from primary hepatoma or hepatic or peritoneal metastases from an unknown primary carcinoma misdiagnosed as cirrhosis. Without autopsies we can never be sure.

Not only are death certificates remarkably unreliable bases for epidemiologic surveillance, but clinical records of the New Jersey subjects have been reviewed in enough detail that their actual causes of death can sometimes be checked against their certified causes of death. Table 4 lists cancers known, on histologic grounds, to have been omitted from the 391 death certificates reviewed: 13 thus escaped entry, and our total of 119 malignant neoplasms should therefore be at least 132, but because we have no way to know how many more cancers were omitted from the other 272 death certificates, probably more than 132. Should we assume that at least ten per cent of cancers among radiation-exposed subjects are omitted from death certificates? If not ten per cent, then what per cent? And is this omission also true of subjects not exposed to radiation? This is not a trivial statistical peccadillo -- two of the omitted cancers were osteogenic sarcomas and one was a cancer of the temporal bone, tumors generally accepted as radiation-related. We therefore suggest that the real incidence of cancer and of blood dyscrasias among our 391 subjects is understated by at least ten per cent and probably more. Epidemiologic surveillance of occupational or environmental carcinogenesis based only on death certificates may thus understate real cancer death rates by at least ten per cent, and therefore understate potential risks by as much.

Table 5 lists the certifications of death that mentioned radium or radiation in some form, and includes 15 deaths from cancer or anemia and 11 from other causes. Most (14 of 15) cancer deaths certified as radium-related occurred in 1960 or earlier, and only one was thus certified after 1961. All 11 non-cancer, non-anemia but presumptively radium-related deaths were so certified before 1960, most of them during Harrison S. Martland's active career. Of the deaths not due to cancer or anemia but attributed to radiation, one each died of acute myocardial infarction, generalized arteriosclerosis, and urinary tract infection. It is difficult, in retrospect, to see the association although radium exposure is undoubted. The remaining eight deaths from this group may be accepted as directly due to ionizing irradiation: one from mastoiditis, four from inflammatory conditions of the jaws, one from chronic osteomyelitis, and two as due to radiation without further specification as to the manner of death.

Although the New Jersey Radium Research Project was active during the late fifties and most of the sixties, and although many of our subjects died during those years, radiation in fact appeared on death certificates only when these certificates were completed by medical examiners in New Jersey or elsewhere. Review of the hospital records of subjects admitted to hospitals and at that time participants in project studies very rarely found notes either of participation in these studies or of past occupational exposure to radium. Consequently, unless deaths of persons exposed to any toxic agent, whether radiation or anything else, are reported to the medical examiner and he issues the certificate, neither radiation nor any other external hazard can appear on the death certificate because most physicians, by statute, may certify only to "natural" deaths. The logical

agency to monitor and to investigate deaths suspected to be related to environmental or occupational causes is the local coroner's or medical examiner's office, but very few have the staff and resources to do so.

Radium Osteitis

This project began as a study of human radium and mesothorium osteitis among long-term survivors of the New Jersey radium industry, and this report has been delayed by analysis of bone changes that, after separation from the normal (and until the present decade not very clearly described) changes of skeletal senescence, could reasonably be attributed to radium. Appendix A is a draft version of a review of age changes in the human skeleton,⁸ Appendix B reviews and illustrates the pattern of radium osteitis,⁷ and Appendix C attempts to correlate estimated pre-terminal radium burdens to the distribution of radium osteitis in the New Jersey subjects.⁹ These three appendices constitute a part of this report, and are made a part of it by reference.

Martland described osteitis among the New Jersey subjects as early as 1929 and 1931.⁷ Morphologically, this resembles ischemic bone and marrow infarction or asepticⁱ necrosis of bone. When related to radium-226 (and presumably also to radium-228) deposits, these infarcts heal slowly, an observation in agreement with the generally poor healing capacity of irradiated tissues. Our material cannot answer whether radium osteitis represents a very slowly and incompletely healing "one shot" injury, one that requires decades of constant irradiation for its development and evolution, or both. Our subjects were old enough that extensive arterio-

sclerosis was present, and we cannot comment on any possible contribution of local circulatory insufficiency or capillary damage to the pattern of radium osteitis.

The bones we examined came from subjects whose pre-terminal radium-226 burdens fell between some level that could not be distinguished from background irradiation ($\leq 0.0042 \mu\text{Ci}$) and $1.78 \mu\text{Ci}$ radium-226. Ten of eleven subjects whose radium-226 could be measured above this background had radium osteitis, including six of the seven subjects whose burdens were above background but below the presently accepted "safe" industrial standard of $0.1 \mu\text{Ci}$, and six of the fourteen subjects whose pre-terminal burdens could not be distinguished from background levels also had radium osteitis. Whether pre-terminal body burdens are the best index of radiation exposure is not altogether clear and how much these subjects got from the shorter-lived but very potent radium-228 (mesothorium) is unknown. Many subjects were exposed to radium-228 (mesothorium), but unless body burdens during active radium industry employment reached $20 \mu\text{Ci}$ radium-228,⁵ the decay curve of radium-228 is such that none could have been measured by the time of the project's active patient studies thirty-five or forty years later. The first investigators of the New Jersey subjects blamed mesothorium, not radium, for their illness and deaths.

If, as seems on balance more likely than not, the New Jersey subjects experienced considerable additional but, because of its short half-life, now undeterminable amounts of irradiation from radium-228 (mesothorium), their total alpha and beta particle exposure must be regarded as unknown, and none of the New Jersey subjects can provide really reliable information as to "safe" levels or contribute to any dose-response calculations. Material

available from subjects known to have been exposed to pure radium-226 without admixture with other isotopes should be examined in detail for evidence of radium osteitis, and pending such review, the present occupational standard of 0.1 μ Ci of radium-226 equivalent must be prudently regarded as too high by one order of magnitude.

Discussion

Policy allocating federal funds (and therefore personnel, resources and influence) for medical research following World War II was defined by physicians whose training and professional maturity overlapped an unusually productive era in medical research that had controlled vitamin and endocrine deficiencies by replacement therapy and many common infections by immunization and chemotherapy. Much of this progress had been based on experimental animal models, and before the clinical application of vitamin B₁₂ and insulin, pernicious anemia and ketogenic diabetes mellitus were every bit as relentless as cancer. But the analogy proved inexact. Cancer is a group of diseases with many causes, some of them clearly occupational and environmental, and cancer research, thirty-odd years ago, elected to go the experimental, not the epidemiologic, route. The latter approach might have been much more fruitful: it could hardly have been more sterile.

The notion of an epidemiology of cancer was until very recently widely regarded in academic circles as a palpable eccentricity, comparable to disbelief in Darwinian evolution or to voting Republican, because cancer research involved things like rodents and tissue cultures. Human disease was not pure enough, not basic enough, to challenge academic minds and, anyhow, academic pathology deals with mice and rats, not human beings.

The writer, a hospital pathologist who makes the diagnosis of cancer, in a human being, several times a day and must often advise on therapy, sadly confesses that most basic research into the mechanisms of carcinogenesis -- whether the HeLa cell or the DNA strand -- strikes him as interesting in the sense that the decipherment of the Minoan B script or Lord Mansfield's reasoning in the Somerset decision are interesting, but clinically quite irrelevant. Cancer is increasing, and not all of this increase comes from fuller reporting, more accurate diagnosis or longer life spans, although some of it certainly does. Evidence for epidemiologic (occupational, environmental) factors in human carcinogenesis seems overwhelming, and those who read the autopsy protocols from fifty or a hundred years ago are struck by how few patients then died of cancer. Pathologists then could recognize cancer when they saw it, but they saw much less of it than we now do: in 1913, bronchogenic carcinoma was a pathologic curiosity.*

*From October 1908 through December 1911, Harrison S. Martland performed 546 autopsies, and his associate performed 2 autopsies, at Newark City Hospital, a total of 548 autopsies. They described exactly 30 deaths from cancer, 5.47 per cent of the total number of autopsies, distributed as follows: Colon 4; leukemia, rectum, esophagus, uterine cervix 3 each; tongue, pancreas, brain (glioma) 2 each; and one each of Hodgkin's disease, prostate, bronchus, stomach, larynx, "jaw," pleural epithelioma (in an 8 year old child), and vulva. Granting that more people died at home then than now, these numbers document a prodigious increase in cancer deaths over the years. Analysis of these old autopsy records might prove more than a pleasant antiquarian pastime.

Every medical student used to study the case of Dr. John Snow (1813-1858) and the Broad Street pump. Dr. Snow, the world's first full-time anesthesiologist and not an epidemiologist, noticed a large number of deaths from cholera among residents of one neighborhood who drew their drinking water from one pump. He sawed the handle off the pump, people had to draw water elsewhere, cholera subsided, and Dr. Snow went back to giving chloroform to obstetrical patients, among them Queen Victoria. He knew nothing of the Vibrio cholerae, its metabolism or manner of spread nor, at that time, did anyone. Our knowledge of most environmental carcinogenesis is now about where John Snow's knowledge of cholera was in 1854. But we may be able to act, as Snow acted, on epidemiologic grounds and with good effect, because the death rates of the most serious diseases (tuberculosis, syphilis, yellow fever, typhoid) of the early nineteenth century began to fall long before the rise of bacteriologic diagnosis purely from pragmatic steps based on observation of the patterns of these disease, without any detailed knowledge of etiology, microbiology or immunology.

Man's genetic diversity, species sensitivity to ionizing radiation, relatively large physical size, wide variety of spontaneously occurring malignant tumors, random breeding habits, and long life span during which he is surrounded by carcinogens and co-carcinogens, all suggest that useful information about human environmental carcinogenesis will emerge only from studies of man. Animal models, most of which are not even typical of animals, cannot define a risk of injury for man. Human radiation cancer is not an issue only for radiobiologists and physicists, and at present risks becoming the bloody shirt for hysterical, single-issue environmental

groups. It is a problem in medical epidemiology to be most efficiently approached through the prospective techniques of industrial epidemiologists, approaching exposed populations (such as entire nuclear plant workforces) in depth and without the wholly unacceptable, because inhumane, notion that the only index of radiation injury is a malformed infant or a patient dead of cancer or aplastic anemia.

Careful attention has to be paid to cancer as an epidemiologic, not a random, event. Some states (New Jersey, for example, or Connecticut) have made cancer a reportable disease by statute in the sense that anthrax and typhoid fever are reportable diseases. These cancer reporting programs are all grossly underfunded and as presently constituted seem unlikely to do more than collect raw data without appropriate follow-up. Great effort and expense are wasted, for example, chasing down the contacts of patients with syphilis, an easily curable disease from which few people die, resources better spent elsewhere than in harassing impecunious young homosexuals.

Pathologists make most diagnoses of cancer, and most pathologists use the College of American Pathologists' computer-compatible Systematized Nomenclature of Medicine (SNOMED) or its predecessor SNOP to index their tissue diagnoses.⁶ SNOMED includes an occupation code, and codes for at least major classes of chemical, ionizing, and physical agents. It would be simple to collect these already coded diagnoses, add standard demographic data (age, race, sex, etc.), occupation codes, probable exposure histories, and postal zip codes for residence and place of occupation, to generate a data base that would, for the first time, begin to describe regional, occupational, and exposure as well as age, race and sex differences in the pattern of recorded tissue diagnoses of cancer.

The United States, by treaty, records and analyses death certificate diagnoses using the International Classification of Disease. This is fine if one wishes to compare, for example, deaths from various forms of legal execution (garotting vs. electrocution) or from epizootics (Chaga's disease vs. Clonorchis sinensis infestation) between countries, but it is neither precise enough nor complete enough to be more than a very crude epidemiologic tool, and is at its worst exactly in those fields of oncology and teratology that are essential for studies of the impacts of environmental hazards, including ionizing irradiation. Analysis of the death certificates from our New Jersey subjects was a frustrating experience, partly because it was impossible to ascertain death rates from rare tumors. Not only does the International Classification of Disease group under a limited number of rubrics a variety of quite different malignant diseases and congenital malformations whose discrimination and identification are basic to accurate epidemiologic studies, but death certificates themselves are in at least a quarter of deaths quite simply wrong. Errors are so frequent on death certificates, without autopsy confirmation, that conclusions drawn from death statistics based on death certificate diagnoses are extremely unreliable, and are at least as misleading as helpful. All many death certificate diagnoses really mean is that the body had no obvious stab wounds or bullet holes.

Epidemiologic studies of causes of death can be reliably based only on autopsy diagnoses, with histologic confirmation. Identification of geographic or occupational clusters of specific cancers (or congenital malformations) in excess of background rates requires an enormous data base. The raw data for such a base already exist, in thousands of hospital

laboratory files, based on millions of slides, and could be mobilized to define real causes of death with very considerable accuracy. Prospective risks of cancer and congenital malformations from pollution by industrial processes or energy production will influence policy decisions, and sound planning demands very accurate human mortality and morbidity data that death certificates, without autopsy data, cannot provide. Large numbers (say at least a quarter of a million) of autopsies have not been collected on any significant scale, although efforts have been made in that direction for the decidedly atypical populations of federal hospitals. Popular fear of cancer "caused" by nuclear reactors will not be stilled by reports of animal studies or deeds of derring do with DNA molecules. Only human data will do, these data can come only from epidemiologic surveys, and the New Jersey subjects represent the only human population followed long enough to cover the period from young adult life to old age and death.

Martland identified the first New Jersey radium victims because he knew where they worked, and because he knew their family physicians. How many patients' clinical records today contain any reference to their occupations, let alone a chronological occupational history? To ask the question is to answer it. Teaching of undergraduate medical students and house officers has fallen into the hands of technicians so preoccupied by computerized print-outs of biochemical tests and physiological "parameters" that nobody listens to patients anymore. Not only must epidemiologic studies be founded on tissue diagnoses, but must incorporate the results of meticulously thorough clinical histories, the kind that demand rapport with patients and long, intelligent listening. Clinical research will be no better than the clinical records and observations on which it is based.

Who will monitor the pattern of cancer deaths to attempt to identify clusters that may implicate environmental or occupational factors? ERDA has succeeded the AEC, and neither has a dime's worth of credibility with the public, lay or medical. This writer's dealings, over almost fifteen years, with AEC and ERDA officials, and with those at the Argonne National Laboratory, convince him that they are honest and competent, and he is perplexed that the general public does not share this perception. This is unfair, but nuclear mishaps have been consistently presented by communications media in such a light as to compromise public confidence in existing federal nuclear safety surveillance mechanisms.

Many physicians cheerfully contribute substantial time, skill and experience to various medical society projects, whether sponsored by elite (e.g., the New York Academy of Medicine) or by specialist (e.g., the College of American Pathologists) organizations. The actual assembling and storage of cancer diagnoses, and supplemental occupational, demographic and geographic data, would be a simple enough computer programming exercise. Regular review and analysis of these data by an independent medical board might inspire more public confidence than ERDA or other federal agencies can muster, and medical societies have access to specialized knowledge and interests not always available to career physicians and scientists in government service. Serious thought should be given to the delegation of surveillance review of environmental (including radiation-related) cancer to an independent organization whose members' careers are financially and professionally independent both of the federal government and of the nuclear industry.

Studies of the New Jersey subjects indicate that more of them died of cancer than we expected, and that the bone changes of radium osteitis occurred in an unexpected number of the subjects. Uncertainty as to total irradiation exposure is introduced by the probability that many subjects had unknown exposures to radium-228 (mesothorium) that unless present in very large quantities would have decayed out by the time the subjects came under active project study. These subjects, whose general state of health did not radically differ from that of their non-exposed contemporaries, had undoubted irradiation from internally deposited alpha and beta emitters, but their total exposures are really unknown. Studies of individual patients may be too expensive, in physician-time and in money, to be applicable to whole exposed populations, and treating current nuclear industry workers as an epidemiologic population would probably yield more information.

Summary

Cancers among dead New Jersey subjects have been underreported by at least ten per cent, but even underreported, almost three times the expected number died of cancer. Their radiation experience apparently acted as a generalized carcinogen. Conventional clinical, laboratory and roentgenographic tests neither correlated with calculated radiation exposure nor predicted which subjects subsequently developed cancer.

More subjects than expected were deaf and enough of the subjects had increased erythrocyte sedimentation rates and decreased alpha-1 serum globulin levels that both hearing tests and tests of immune competence should be undertaken among asymptomatic exposed populations at regular

intervals to see whether these may indicate radiation effects prior to a fatal cancer or blood dyscrasia. Death is a very tidy endpoint, but not everyone agrees that it is the only indication of radiation injury.

If pre-terminal radium-226 burdens validly express total irradiation experience, and past exposure to shorter-lived radium-228 (mesothorium) makes it unlikely that this is so, the distribution of radium osteitis among our subjects suggests that anatomically demonstrable radiation injury occurs in the vast majority of subjects with any radium-226 burden that can be measured above background levels after twenty-five years, and in almost half of those exposed whose measured radium-226 burdens are indistinguishable from background levels. Until bones from patients exposed only to known quantities of radium-226 without additional exposure to other isotopes have been examined in comparable detail for radium osteitis two suggestions seem prudent: (1) dose-response calculations based on New Jersey subjects, because of added irradiation from radium-228 (mesothorium), provide no stable base for conclusions as to "safety," and (2) to the extent that the present occupational standard of 0.1 μ Ci radium-226 was based on New Jersey cases, it must be regarded as too high by about one order of magnitude.

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Table 1 : OBSERVED AND EXPECTED CAUSES OF DEATH, NEW JERSEY RADIUM WORKERS

I.C.D.		Polednak et al. (1978) 634 Women			N.J.R.R.P. 597 Cases		
		Obs.	Exp.	O/E	Obs.	Exp.*	O/E
	All Causes	240	188.52	1.27	391	177.21	2.21
001-139	Infective and Parasitic	7	11.30	.62	10	10.64	0.94
001-019	All tuberculosis	5	8.25	.61	8	7.76	1.03
140-205	Malignant Neoplasms	84	43.36	1.93	119	40.76	2.92
140-149	Buccal cavity, Pharynx	1	0.47	2.15	5	0.44	11.36
150-159	Digestive Organs, Peritoneum	15	12.53	1.20	28	11.73	2.38
151	Stomach	2	2.15	.93	4	2.02	1.98
153	Large Intestine	10	4.96	2.02	13	4.66	2.79
154	Rectum	0	1.48		4	1.39	2.88
155	Liver	0	1.63		0	1.53	
157	Pancreas	2	1.75	1.14	4	1.65	2.42
160-165	Respiratory system (Note 1)	4	2.35	1.70	19	2.21	8.60
161	Larynx	1	0.09	11.13	2	0.08	25.00
162-163	Lung	2	2.15	.93	14	2.02	6.93
170	Breast	9	9.45	.95	13	8.88	1.46
171-176	All genital organs	5	9.48	.53	5	8.91	0.56
180	Kidney	0	0.61		1	0.57	1.75
181	Bladder	1	0.57	1.76	4	0.54	7.41
185	Prostate	-	----		2		
193	Brain and C.N.S.	3	0.97	3.09	2	0.91	2.20
194	Thyroid (From 1950 only)	0	0.17		1	0.16	6.25
196	Bone	22	0.27	81.79	12	0.25	48.00
198-199	Other and unspecified sites	18	2.51	7.16	27	2.36	11.44
200-203	Lymphatic and Myeloma (Note 2)	0	0.81		5	0.76	6.58
204	Leukemia and Aleukemia	3	1.41	2.13	3	1.33	2.26
260	Diabetes mellitus	2	5.04	.40	2	4.74	0.42
290-299	Blood and blood forming organs	4	1.02	3.91	7	0.96	7.29
330-334	Vascular lesions of the C.N.S.	15	16.99	.88	32	15.97	2.00
400-468	Diseases of circulatory system	60	61.97	.97	108	58.25	1.85
420	Arteriosclerotic heart disease	39	37.22	1.05	25	34.99	0.71
470-527	Diseases of respiratory system	7	7.10	.99	19	6.67	2.85
530-587	Diseases of digestive system	9	9.04	1.00	21	8.50	2.47
581	Cirrhosis of liver	3	2.81	1.07	7	1.01	6.93
590-637	Diseases of genitourinary system	6	6.07	.99	7	5.71	1.23
800-998	External causes	31	10.06	3.08	30	9.46	3.17
918	Radiation accidents and sequelae	22			2		
	All other causes	13			5		
	Unknown cause of death	2			0		

* Expected N.J.R.R.P. deaths: $\frac{597 \text{ NJRRP Cases}}{634 \text{ Argonne Cases}}$ yields a factor of 0.9416, close enough for our purposes, considering the unreliability of death certificate diagnoses.

Note 1: 3 NJRRP deaths from cancer of the sinuses, ICD rubric 160.

Note 2: 4 NJRRP deaths from myeloma, ICD rubric 203.

Table 2 : SUMMARY OF CERTIFICATIONS AS TO CAUSE OF DEATH,

NEW JERSEY RADIUM WORKERS

ICD Class	1921 to 1920	1931 to 1930	1941 to 1940	1951 to 1960	1961 to 1970	1971 to	Total
I Infectious and Parasitis	2	4	1	3			10
II Malignant Neoplasms		5	12	23	31	35	119
III Endocrine and Metabolic				1		1	2
IV Blood and Blood-Forming Organs		5		1		1	7
V Nervous System			2			3	5
VII Circulatory System		6	14	27	27	73	165
VIII Respiratory System	2	4	2	3	1	3	19
IX Digestive System	1	3	3	2	5	5	21
X Genitourinary System		1		2	2	2	7
XI Complications of Pregnancy		1	1				2
XII Skin and Subcutaneous Tissues					1		1
XIII Musculoskeletal System		1					1
XIV Congenital Anomalies				1			1
XVI Symptoms and Ill-Defined Conditions						1	1
XVII Accidents	1	1	6	3	5	11	30
Total	6	31	41	66	72	134	391

Table 3a: CERTIFICATIONS AS TO CAUSE OF DEATH, NEW JERSEY RADIUM WORKERS

	Total	ICD	to 1920	1921 to 1930	1931 to 1940	1941 to 1950	1951 to 1960	1961 to 1970	1971 to
I. Infectious and Parasitic:									
Gastroenteritis and colitis	1	009.2			1				
Pulmonary Tuberculosis	7	011.9	1	4		2			
Tuberculosis: Intestine and Peritoneum	1	014	1						
Meningococcemia without Meningitis	1	036.1				1			
II. Malignant Neoplasms:									
Tongue	1	141.9						1	
Parotid Gland	1	142.0			1				
Floor of Mouth	2	144					1	1	
Mouth, Part Unspecified	1	145.9					1		
Esophagus	1	150				1			
Stomach	4	151						3	1
Colon	13	153			1	4	2	4	2
Rectum	4	154					2	1	1
Gall Bladder	1	156.0				1			
Ampulla of Vater	1	156.2					1		
Pancreas	4	157					3		1
Nasal Cavity and Paranasal Sinuses	3	160				1	2		
Larynx	2	161.9					1	1	
Bronchus and Lung	14	162.1			2	3	2	4	3
Bone	12	170		1	5	1	3	2	
Scalp, Neck	1	173.4				1			
Breast	13	174			1	2	4	4	2
Cervix Uteri	1	180				1			
Uterus, Unspecified Part	1	182.9							1
Ovary and Adnexa	3	183					1	2	
Prostate	2	185				1		1	
Urinary Bladder	4	188				1	1	2	

Table 36 : CERTIFICATIONS AS TO CAUSE OF DEATH, NEW JERSEY RADIUM WORKERS, CONTINUED

	Total	ICD	to 1920	1921 to 1930	1931 to 1940	1941 to 1950	1951 to 1960	1961 to 1970	1971 to
Kidney, Except Pelvis	1	189						1	
Eye	1	190			1				
Brain	1	191					1		
Thyroid Gland	1	193				1			
Suprarenal Gland	1	194						1	
Pelvis and Pelvic Viscera	3	195.1		2		1			
Ill-Defined Site	4	195.9		2	1	1			
Secondary to Liver, Primary Not Specified	1	197.8							1
"Carcinomatosis"	4	199.0				1		3	
Site Not Specified	2	199.1				1	1		
Other Primary Malignancy of Lymphoid Tissue	1	202.2					1		
Multiple Myeloma	4	203					1	3	
Chronic Myeloid Leukemia	1	205.1						1	
Acute Leukemia	1	207.0					1		
Acute Erythremia (DiGuglielmo's Disease)	1	207.2							1
Myelofibrosis	1	209					1		
Unclassified Neoplasm, Ovary	1	235				1			
Malignant Neoplasm, Spinal Cord	1	238.4					1		
III. <u>Endocrine and Metabolic:</u>									
Diabetes Mellitus with Acidosis, Coma	1	250.0							1
Diabetes Mellitus without Acidosis, Coma	1	250.9				1			
IV. <u>Blood and Blood Forming Organs:</u>									
Pernicious Anemia	2	281		2					
Aplastic Anemia	3	284		1		1		1	
Unspecified Anemia	2	285.9		2					

Table 3c: CERTIFICATIONS AS TO CAUSE OF DEATH, NEW JERSEY RADIUM WORKERS, CONTINUED

	Total	ICD	to 1920	1921 to 1930	1931 to 1940	1941 to 1950	1951 to 1960	1961 to 1970	1971 to
<u>V. Nervous System:</u>									
Chronic Brain Syndrome	1	309.9						1	
Paralysis Agitans	3	342			1			2	
Unspecified Mastoiditis	1	383.9			1				
<u>VII. Circulatory System:</u>									
Disease of Mitral Valve, Not Rheumatic	1	394.9				1			
Hypertensive Heart Disease	1	402						1	
Hypertensive Renal Disease	1	403							1
Hypertensive Heart and Renal Disease	5	404			1	1	1	2	
Acute Myocardial Infarct Without Hypertension	67	410.9		1	1	11	10	37	7
Acute and Subacute Ischemic Heart Disease Without Hypertension	2	411.9						2	
Coronary Arteriosclerosis With Hypertension	2	412.1					1	1	
Cardiovascular Disease Without Chronic Ischemic Heart Disease, With Hypertension	1	412.2						1	
Coronary Arteriosclerosis Without Hypertension	11	412.3				1	1	7	2
Cardiovascular Disease Without Chronic Ischemic Heart Disease, Without Hypertension	8	412.4			1		3	3	1
Angina Pectoris Without Hypertension	4	413.9		1	2				1
Acute Bacterial Endocarditis	2	421.0		1	1				
Other Acute Endocarditis	1	421.9			1				
Acute Myocarditis	1	422					1		
Chronic Disease of Endocardial Structure	2	424.9			2				
Other Myocardial Insufficiency	7	428		1	1	5			
Other and Unspecified Heart Disease	1	429.9			1				
Subarachnoid Hemorrhage Without Hypertension	2	430.9						2	
Cerebral Hemorrhage Without Hypertension	11	431.9		2		4	3	2	
Cerebral Thrombosis Without Hypertension	11	433.9					2	7	2

Table 3d: CERTIFICATIONS AS TO CAUSE OF DEATH, NEW JERSEY RADIUM WORKERS, CONTINUED

	Total	ICD	to 1920	1921 to 1930	1931 to 1940	1941 to 1950	1951 to 1960	1961 to 1970	1971 to
Acute But Ill-Defined Cerebrovascular Disease Without Hypertension	6	436.9			1		2	1	2
Generalized Ischemic Cerebrovascular Disease Without Hypertension	1	437.9			1				
Other and Ill-Defined Cerebrovascular Disease Without Hypertension	1	438.9						1	
Generalized and Unspecified Arteriosclerosis	11	440.9			1	3	3	4	
Aneurysm, Abdominal Aorta	1	441.2						1	
Phlebitis and Thrombophlebitis	1	451.0						1	
Other Venous Embolism and Thrombosis	1	453							1
Unspecified Circulatory Disease	2	458.9				1			1
VIII. <u>Respiratory System:</u>									
Pneumococcal Pneumonia	5	481	1	2		2			
Streptococcal Pneumonia	1	482.2						1	
Bronchopneumonia, Unspecified	4	485			1		1	1	1
Unspecified Pneumonia	4	486	1	1		1			1
Emphysema	3	492						1	2
Sinusitis (Chronic), Other and Unspecified	1	503.9			1				
Abscess of Lung	1	513		1					
IX. <u>Digestive System:</u>									
Inflammatory Condition of Jaw	4	526.4		2	1	1			
Stomatitis	1	528.0		1					
Ulcer of Stomach With Perforation	1	531.1			1				
Ulcer of Duodenum With Hemorrhage	1	532.0						1	
Ulcer of Duodenum, Other and Unspecified	1	532.9					1		
Acute Appendicitis With Peritonitis	1	540.0	1						

Table 3e: CERTIFICATIONS AS TO CAUSE OF DEATH, NEW JERSEY RADIUM WORKERS, CONTINUED

	Total	ICD	to 1920	1921 to 1930	1931 to 1940	1941 to 1950	1951 to 1960	1961 to 1970	1971 to
Volvulus	1	560.2					1		
Diverticulitis of Colon	2	562.1				1		1	
Regional Enteritis	1	563.0					1		
Other Chronic Enteritis	1	563.9			1				
Alcoholic Cirrhosis, Liver	1	571.0							1
Cirrhosis, Without Mention of Alcohol or Alcoholism	1	571.8					1		
Cirrhosis of Liver	5	571.9					1	3	1
<u>X. Genitourinary System:</u>									
Acute Nephritis	1	580				1			
Chronic Nephritis	3	582		1		1	1		
Chronic Pyelonephritis	1	590.0					1		
Urinary Tract Infection, Not Otherwise Specified	1	599.0						1	
Hyperplasia of Prostate	1	600						1	
<u>XI. Complication of Pregnancy:</u>									
Toxemia of Pregnancy	1	637.9			1				
Delivery Complicated by Placenta Previa	1	651.0		1					
<u>XII. Skin and Subcutaneous Tissues:</u>									
Cellulitis and Abscess of Other, Multiple and Unspecified Sites	1	682.9					1		
<u>XIII. Musculoskeletal System:</u>									
Chronic Osteomyelitis	1	720.1		1					

Table 3f: CERTIFICATIONS AS TO CAUSE OF DEATH, NEW JERSEY RADIUM WORKERS, CONCLUDED

	Total	ICD	to 1920	1921 to 1930	1931 to 1940	1941 to 1950	1951 to 1960	1961 to 1970	1971 to
<u>XIV. Congenital Anomalies:</u>									
Cystic Kidney Disease	1	753.1				1			
<u>XVI. Symptoms and Ill-Defined Conditions:</u>									
Senility Without Mention of Psychosis	1	794						1	
<u>XVII. Accidents:</u>									
Railway Accident, Involving Explosion, Fire	1	803E						1	
Motor Vehicle Accident, Pedestrian	3	814.7E						2	1
Fracture of Neck of Femur, Closed	1	820.4							1
Motor Vehicle Non-Traffic Accident: Collision With Stationary Object	1	821E			1				
Fall on Stairs or Steps	2	880E						1	1
Other and Unspecified Fall	4	887E			1		1	2	
Accident: Conflagration in Private Dwelling	1	890E						1	
Caught Accidentally Between Objects	1	918E	1						
Accident Caused by Ionizing Radiation	1	926.1E				1			
Complication and Misadventure: Surgical Operation	7	930.0E			2	1	2	2	
Complication and Misadventure: Anesthesia	1	930.1E			1				
Complication and Misadventure: Unspecified Therapeutic Procedure	1	931.8E					1		
Suicide: Self-Inflicted Poisoning	1	952.0E						1	
Suicide: Hanging, Suffocation	2	953E					1	1	
Toxic Effect of Caustic	1	983.9		1					
Effect of Radioactivity, Neither Diagnostic Nor Therapeutic	1	990.0			1				
Injury, Other and Unspecified, of Trunk	1	996.1				1			

Table 4: KNOWN CANCERS OMITTED FROM DEATH CERTIFICATES,
NEW JERSEY RADIUM WORKERS

	1921 to 1920	1931 to 1930	1941 to 1940	1951 to 1960	1961 to 1970	1971 to	Total	
Breast					1	2	3	
Lung and Bronchi					1		1	
Uterine Cervix				1			1	
Hepatoma					1		1	
"Temporal Bone"			1				1	
Osteosarcoma					2		2	
Urinary Bladder					3		3	
"Large Number of Cancers"					1		1	
Total				1	1	9	2	13

Table 5 : RADIATION OR RADIUM APPEARS ON DEATH CERTIFICATE,

NEW JERSEY RADIUM WORKERS

		1921 to 1920	1931 to 1930	1941 to 1940	1951 to 1950	1961 to 1960	1971 to 1970	Total	
<hr/>									
<u>With Cancer or Anemia:</u>		0	2	4	3	5	1	0	15
Paranasal Sinuses	160					2			2
Osteosarcoma	170			3	1	2			6
"Eye"	190			1					1
Pelvis, Pelvic Viscera	195.1		1						1
"Carcinomatosis"	199.0						1		1
Site Not Specified	199.1				1	1			2
Aplastic Anemia	284				1				1
Anemia, Unspecified	285.9		1						
<hr/>									
<u>Cause other than above:</u>		0	3	3	2	3	0	0	11
Unspecified Mastoiditis Without Mention of Otitis Media	383.9			1					1
Acute Myocardial Infarction	410.9					1			1
Generalized and Unspecified Arteriosclerosis	440.9					1			1
Inflammatory Condition of Jaw	526.4		2	1	1				4
Urinary Tract Infection	599.0					1			1
Chronic Osteomyelitis	720.1		1						1
Effect of Radioactivity, Neither Diagnostic Nor Therapeutic	990.0			1					1
Accident Caused by Ionizing Radiation	926.1				1				1