

HEALTH EFFECTS AMONG PLUTONIUM WORKERS

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Concern about health effects that may be associated with plutonium has existed since its discovery. For example, Dr. Glenn Seaborg allocated 10 mg of the first 500 mg of plutonium for health effects studies in animals. These early efforts demonstrated that plutonium is absorbed poorly by the gastrointestinal tract, significant deposition occurs on bone surfaces and in the liver, and small amounts are excreted in urine and feces.⁽¹⁾ Subsequent laboratory studies have demonstrated excess tumors of the lung, liver and bone among plutonium exposed animals.⁽²⁾ Investigations of human post mortem tissues have shown that principal concentrations of plutonium occur in the lung, liver, bone, and tracheobronchial lymph nodes.⁽³⁾

Health effects in humans have been demonstrated for a number of internal emitters. These include lung cancer among uranium miners exposed to radon-222,⁽⁴⁾ liver neoplasms among patients who received thorium-232 (thorotrast),⁽⁵⁾ leukemia among polycythemia vera patients who were treated with phosphorus-32,⁽⁶⁾ thyroid tumors among Marshall Islanders exposed to iodine-131 as a result of atmospheric nuclear tests,⁽⁷⁾ osteogenic sarcomas and sinus carcinomas in radium dial painters as a result of exposure to radium-226,⁽⁸⁾ and bone sarcomas, leukemia and liver tumors among ankylosing spondylitis patients treated with radium-224.⁽⁹⁾ Of these, the latter two have been the most useful for estimating health effects in humans due to plutonium exposures.

There are important differences between the biological behavior of radium and plutonium. For example, radium is absorbed from the gastrointestinal tract to a much greater extent than plutonium. Radium-226 deposits throughout the bone whereas plutonium deposits initially on the bone surface. Radium has produced bone sarcomas in exposed dial painters; however, the cumulative bone doses have been much greater than are estimated to be present in plutonium-exposed workers to date. Because of the differences between radium and plutonium, and concerns regarding extrapolating results from animal studies to humans, studies of potential effects in humans are necessary. The following studies summarize our investigations of workers who have been exposed to plutonium.

Human Studies of Plutonium Workers

In the early 50's a group of Manhattan Project workers with estimated systemic burdens ranging from 7 to 230 nCi were selected for clinical followup. Thirty-two years of follow-up with quinquennial clinical evaluations show no untoward health effects associated with plutonium deposition. These include clinical manifestations as well as mortality. Only two deaths occurred in these workers compared to four expected based on US male rates.⁽¹⁰⁾

Another investigation of Los Alamos workers included 241 who demonstrated systemic body burdens of 10 or more nCi. All of the 224 male and 17 females were contacted, or death certificates were obtained for those who were deceased. Life table analyses did not demonstrate excesses for any causes of death, and significant deficits were observed for total cancer, lung cancer and cardiovascular mortality when compared to US rates.⁽¹¹⁾ Although small in numbers, this group represents approximately one-third of all known plutonium exposed workers in the US with 25% or more of the maximum permissible body burden (40 nCi).

An investigation of cancer incidence among workers employed at Los Alamos National Laboratory from 1969-1978 has also been completed.⁽¹²⁾ Incident cancers were identified from records of the New Mexico Tumor Registry and compared with rates for the State of New Mexico. No significant excesses were found for any site specific cancers or for all cancers combined for males or females. For Anglo males (non-Hispanic white), significantly fewer than expected cancers were observed for all cancers combined, primarily because of marked deficits for smoking related neoplasms. For example, whereas 24.2 lung cancers were expected, only 6 were observed, and whereas 7.9 oral cancers were expected, only 2 were observed. Among females, no smoking related cancers were observed. However, slight excesses were discovered for breast and uterine cancers, although they were not statistically significant. In general, the distribution of cancers among Los Alamos workers appears similar to that found among high socioeconomic groups.

In response to a three-fold excess of melanoma reported for Lawrence Livermore workers, an investigation of melanoma incidence⁽¹³⁾ and a case control study of melanoma among Los Alamos workers employed from 1969-1978⁽¹⁴⁾ were conducted. No significant excesses of melanoma were found. Also, no differences were found between cases and controls for plutonium body burdens, cumulative external radiation exposure, or type of employment. However, it was found that cases were more likely than controls to be college graduates. This is consistent with other studies that suggest increased risk of melanoma among higher socioeconomic groups and also suggests that lifestyle characteristics may be important risk factors for melanoma.

Recent studies of standardized mortality and relative risk among workers at the Rocky Flats Plant have failed to demonstrate significant excesses for neoplasms of greatest concern for plutonium and other radiation workers.^(15,16) White male workers employed between 1952 and 1979 show significantly fewer than expected cancers for all neoplasms, and lung cancers when compared to the US population. We discovered an unhypothesized excess of benign and unspecified neoplasms (ICD 8th Rev. Codes, 210-239). All were intracranial in location, but the death certificate information was inadequate to identify specific origin or, in some cases, whether malignant or benign. No bone cancers were found and other radio-genic cancers did not differ from expectation. Analyses of duration of employment and latency did not affect these results. Standardized mortality ratios (SMRs) among workers cumulatively exposed to 1 or more rem of external radiation were significantly higher than expected for benign and unspecified intracranial tumors. However,

SMR's for all other causes of death were lower than, or did not differ from, expectation. Similarly, no SMR's were significantly higher than expected for workers demonstrating systemic plutonium body burdens of 2 or more nCi.

When workers who experienced 1 or more rem cumulative whole body exposures were compared to those with less than 1 rem, no significant excess risks were observed. The relative risk for unspecified intracranial tumors was not significantly elevated, probably because of the small numbers of exposed and unexposed cases available for analysis. In the case of plutonium exposure, relative risks could not be calculated because no exposed cases were observed.

The excess of brain tumors that was observed led to conduct of a case control study designed to investigate differences in exposure between brain tumor cases and three sets of controls selected from the same worker population. No significant differences were observed between cases and controls for cumulative external radiation exposures, plutonium exposures, or nonradiation occupational hazards.⁽¹⁷⁾

Conclusion

Although it is still too early to arrive at definitive conclusions regarding untoward health effects in humans, especially cancer, that may be associated with exposure to plutonium, the results of our early investigations have all been negative. A variety of study methods and populations have been employed, as shown in Table I, that range from in-depth clinical follow-up of a

TABLE I

SUMMARY OF HEALTH EFFECTS STUDIES AMONG PLUTONIUM WORKERS

<u>Study Population</u>	<u>Method</u>	<u>Results</u>
Manhattan Project Workers	Clinical follow-up	No suspicious health problems
Los Alamos Pu Workers (>10 nCi)	Mortality follow-up	No excess mortality
Los Alamos Workers	Incidence follow-up	No excess incidence
	Case-control study of melanoma	No association with exposure
Rocky Flats Workers	Mortality follow-up	Excess of benign and unspecified brain tumors associated with >1 Rem
	Case control study of brain tumors	No association with any type of exposure

small, highly exposed population to follow-up of mortality among an entire cohort of nuclear workers. In all instances, deleterious effects have not been discovered to be associated with the plutonium exposure. However, the excess of intracranial tumors discovered among one cohort of workers was associated with external radiation exposure >1 Rem. This latter finding was not replicated in a case-control study where no differences in exposure to external radiation (or to plutonium or other occupational exposures) were found when brain tumor cases were compared to controls.

These investigations of plutonium workers have suffered from the small populations of exposed workers available for study and from the limited periods of follow-up present for the majority of workers. These shortcomings can only be overcome through continued observation and study.

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