Occupational health studies at Los Alamos National Laboratory[1]

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Development, testing and production of nuclear weapons over the last 60 years has exposed workers and communities to hazardous substances (*1*). Some of these substances, including asbestos, silica and solvents, occur in many industrial settings, while others, most notably certain radioactive materials such as plutonium, are special products of the nuclear industry. Concerns about the impacts of toxic materials on workers and the public have been heightened by the nuclear industry's history of secrecy, its control over research on environmental and health consequences of weapons production, and the practice of human experimentation (*2, 3*). Public confidence in evaluations of exposures from this industry, as well as health consequences of those exposures, has been undermined by a lack of trust in the authorities who have been responsible for creating the exposures as well as evaluating their impact.

In this report we provide a critical review of occupational health studies at Los Alamos National Laboratory (LANL), one of the first facilities built by the U.S. government as part of the Manhattan Project to develop nuclear weapons. We begin by describing the weaknesses and strengths of the studies and their capacity to address health concerns of workers and the public. We next consider who has been included and excluded from occupational health studies. Building on this evaluation, we summarize results of LANL worker studies. Next we interpret the LANL studies in the context of studies of workers at other nuclear facilities and other types of research into the biological effects of ionizing radiation. We conclude with a discussion of what the studies mean for people with health concerns and we make suggestions for protection of occupational and public health.

Types of occupational health studies at LANL

Three general types of health studies of workers at LANL and other nuclear facilities can be distinguished. The first type focuses not on health and disease *per se* but on exposure to substances that could cause disease. A second type of study consists of medical follow-up of selected workers. The third type, epidemiologic studies, either compares workers' disease experience to the experience

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of non-workers, or evaluates whether measures of occupational exposure are related to disease rates among workers.

Exposure studies. A large number of toxic agents have been used in development and production of nuclear weapons. Work at LANL has involved use of arsenic, beryllium, asbestos, lead, organic and inorganic solvents, explosives, adhesives, and acids. Although these agents and others pose important health concerns, our review focuses on radiation hazards, which have been of primary interest in occupational health studies at LANL and other Department of Energy (DOE) facilities. The profession of health physics was created during the Manhattan Project as a response to concerns about special radiation hazards connected with development and production of atomic weapons. The primary focus of health physics in industrial settings is to minimize exposures and monitor radiation hazards in order to prevent exposures in excess of regulations.

In most industrial settings exposures of individual workers are not measured, therefore exposure levels must be inferred from information about the use of hazardous agents in particular jobs and departments, or, when available, information from monitors in work areas. However, radiation monitoring for individual workers has been conducted at many DOE facilities. Devices such as film badges and thermoluminescent dosimeters (TLDs) have been used at LANL to monitor exposures to external penetrating radiation including gamma rays, neutrons and x-rays. Although external penetrating radiation is generally easier to measure than radiation from internal radionuclide contamination, there are many problems with the use of historical monitoring records for research purposes including lack of monitoring for many workers and time periods, changes in sensitivity of dosimeters, errors in linking worker and dosimeter records, and failures in processing and reporting results.

Workers may also inhale, ingest or absorb (for example, through a wound or break in the skin) particles that emit alpha radiation, which is not detected by film badges or TLDs. Internal contamination from radionuclides such as plutonium may be assessed from tests of urine or by *in vivo* gamma spectroscopy, also referred to as whole body or lung counting. The ability of urine tests to detect internal contamination depends on the solubility of compounds, their route of entry into the body, and their rates of excretion. Therefore the accuracy of estimates of internal radiation doses depends on the quality of information about the chemical form, solubility, particle size, and route of entry of the radionuclide. The ability of urine tests to detect internal contamination also depends on the analytical method used and the completeness and frequency of monitoring.

In vivo counting works by measuring gamma emissions from the radioactive decay of particles within the body. If *in vivo* monitoring occurs infrequently, it is better suited to detection of radiological contaminants with long biological and physical half-lives than contaminants with short half lives. Plutonium, one of the major radionuclides of concern at LANL, has low gamma emissions and is difficult to detect by *in vivo* counting. Sometimes the presence of plutonium may be inferred from the gamma emissions of other radionuclides such as americium that occur along with plutonium. Internally deposited radionuclides can remain in the body until death, and autopsy studies of LANL workers, as well as workers at other DOE facilities, have compared plutonium body burdens estimated from autopsy tissues with estimates based on urinalysis studies. Discrepancies between these two methods can be large. Tritium, which emits beta radiation, has also been of concern at LANL and can be detected by urinalysis. Studies of internal radionuclide contamination also suffer from many of the same difficulties as studies of external radiation, including problems in sampling, laboratory processing, lack of coverage of many workers and time periods, and accuracy of record linkage.

Exposure studies are important tools for evaluating hazards in the workplace. Quantitative estimates of exposure, sometimes called dose reconstruction, can be used along with information from experimental studies of animals or epidemiologic studies of humans to estimate health risks from a given level of exposure. Of course, many assumptions are necessary to make such estimates, and they are based on averages, for example, they do not take into account an individual's susceptibility based on genetics, nutrition and other exposures. Additional problems with this approach are discussed later.

Medical follow-up study. A small group of plutonium-exposed LANL workers have had medical exams about every five years since they were identified for medical study in 1952 (*4*). Twenty-six young healthy men working in four types of plutonium operations were chosen for study because they were judged to have the highest internal depositions of plutonium in 1944 and 1945. These men have had medical histories, physical exams, tests of vision and hearing, cardiovascular and respiratory function, blood counts, sputum cytology, urine tests, and *in vivo* counts for plutonium and other radionuclides. The vital status of this group has been monitored and cause of death information has been obtained from medical records and death certificates.

Medical follow-up of a small number of workers can assemble large amounts of clinical data. However, the significance of such studies is unclear because of uncertainties about initial exposures, choice of workers for special study, lack of a comparison group, and low statistical power for studies of diseases of interest such as malignancies or genetic effects.

Epidemiologic studies. Two types of epidemiologic studies have been conducted at LANL - cohort and case control studies. Cohort studies identify workers from a roster of employees and follow them through time to evaluate mortality or cancer incidence using vital records or tumor registry data. Cohort studies of mortality can evaluate deaths from all types of specific causes, and cohort studies of cancer incidence can evaluate specific types of cancer.

Data collected in cohort studies can be analyzed in one of two ways. First, the observed number of deaths or cancer cases among workers can be compared to the number that would be expected if the workers had experienced the same death or disease rates as a standard population, typically the state or nation. These analyses simply address the question of whether death or disease rates of LANL workers differ from the state or the nation, and they do not consider specific occupational exposures. Employed persons must be healthy enough to work, and many, especially employees of large institutions, have regular income, medical insurance and other employment benefits. This means that industrial workers typically have low disease rates compared to populations that include people who are too ill to work and lack the benefits of regular employment. This phenomenon, sometimes called the "healthy worker effect," means that workers whose disease rates are increased by exposure to occupational hazards can have lower disease rates than the general population in spite of their exposures. Low disease or death rates among workers compared to the general population does not mean that the work environment is safe.

Cohort studies can also be used to conduct analyses of trends in disease rates with increasing occupational exposure, sometimes called dose response studies. Instead of comparing worker disease rates to a standard population, workers are divided into groups based on their occupational exposures, and disease rates for workers with higher exposures are compared to disease rates for workers with little or no exposure. The ability of dose response studies to detect effects of occupational exposures depends upon the quality of exposure measurements. When exposures are not accurately measured, workers with higher exposures may be incorrectly included in lower exposure groups, and *vice versa*, thus diluting differences between groups. In addition, accuracy of dose response studies depends on the ability to control other risk factors, such as smoking, diet, or other occupational risks, if histories of these exposures differ between workers with lower and higher levels of the occupational factor (for example, radiation) under study. The adverse effect of exposure could be obscured, for example, if workers in radiation areas were less likely to smoke than other workers (perhaps because of workplace restrictions), or if they were required to pass medical tests to work in those jobs. Although occupational cohort studies seldom have detailed data on potentially confounding exposures, they can provide important information about dose response relationships that are important to evaluating cause-effect relationships.

A second type of epidemiologic study of LANL workers is the case control study. Case control studies evaluate a specific disease in relation to exposures of interest. Occupational case control studies are conducted in order to obtain detailed exposure information for a sample of cases and controls when it would not be feasible to collect data for all workers in a cohort. First, cases of the disease are identified through death certificate or tumor registry data. Next, a group of disease-free controls is chosen. Then, records of cases and controls are compared to evaluate whether exposures to hazards at work were higher for cases than for controls. Case control studies are used to estimate risks of a particular disease associated with a variety of exposures. When quantitative information on exposures of individual workers is available, as in the case of external penetrating radiation at LANL, dose response relationships may be evaluated. Case control studies may suffer from the same problems of measurement and confounding that affect cohort studies.

Who has been included in occupational health studies?

Only employees of "prime contractors" have been included in occupational health studies at LANL. Since the beginning of operations, the University of California has been responsible for overall operation of the site for the DOE and its predecessor organizations, the Energy Research and Development Administration and the Atomic Energy Commission. Beginning in 1946, the Zia Company took over maintenance, construction and support services previously handled by the U.S. Army Corps of Engineers. In 1986, Pan American World Services took over the support contract from Zia, and in 1989 Pan American World Services was purchased by Johnson Controls, Inc. Maintenance, construction and support workers are referred to in this report as Zia employees.

Occupational health studies at LANL have included only University of California and Zia workers; health studies have not been conducted of employees of other contractors and subcontractors.

Most occupational health studies at LANL have been limited to white Anglo employees of the University of California. Radiation monitoring, personnel and medical records for the Zia workforce, which includes many Hispanics and Native Americans, have been much less complete than records for the University of California workforce. In one study personnel records were available for 97 percent of University of California workers but only 20 percent of Zia workers, and urinalysis records were available for 39 percent of University of California workers but only four percent of Zia workers (*5*). Hispanics, non-whites and women have been excluded from a number of occupational health studies of University of California employees at LANL.

Study findings

Our summary of occupational health studies at LANL emphasizes the direction of the results (for example, a deficit or excess of disease), biological mechanisms (for example, cancer in parts of the body where plutonium concentrates) and sample size. We do not discuss "statistical significance" because none of the studies use randomization to impart a specific meaning to these tests (*6*), and because such tests have been widely misused to interpret epidemiologic evidence (*7, 8*).

Medical follow-up of Manhattan project workers (*4*). Investigators conducting periodic medical exams of 26 white male workers exposed to plutonium during World War II at LANL have reported, for the most part, changes typical of an aging population. Some of the more highly exposed workers have elevated ratios of T-helper to T-suppressor lymphocytes, apparently due to decreased numbers of T-suppressor lymphocytes resulting from altered radiosensitivity. The clinical significance of these changes is not clear. Seven of the 26 men had died as of 1994, representing a death rate 57 percent lower than expected based on U.S. rates. Three of the seven deaths were due to cancer, including one from bone sarcoma. This case is of particular interest because bone sarcoma is rare, because plutonium deposits in the skeleton, and because bone sarcomas are a radiation-induced cancer that occurs among workers exposed to radium.

Cohort mortality study of plutonium exposed workers (*9*). A group of 224 white male LANL workers who were estimated to have internal plutonium depositions of 10 nanocuries or more as of January 1, 1974, was followed for mortality through April, 1980. Death rates from all causes and all cancers in this small cohort were lower than expected based on U.S. rates.

Cohort mortality study of Zia workers (*10*). Galke and colleagues studied workers employed by the LANL maintenance contractor. They identified a roster of 14,428 workers hired between 1946 and 1978 of whom 5,424 with adequate records were included. Approximately half of the workers were white Hispanics. Vital status was determined through 1984 for 97 percent of the workers, including 1,196 deaths. Death rates for cardiovascular disease, all cancers and lung cancers were low compared to U.S. rates, however excess deaths were observed for cancers of the stomach, liver, pancreas, bone, and leukemia. Elevated death rates were also observed for injuries and ill-defined conditions. Cancer death rates for plutonium exposed workers were about 30 percent higher than rates for unexposed workers but this finding was based on small numbers due to the lack of plutonium bioassay data for about half of the cohort.

Cohort mortality study of LANL workers (*11*). A cohort mortality study of 15,727 white male University of California workers hired between 1943 and 1977 has been conducted through 1990. Average follow-up was 29 years. The death rate from all causes was 37 percent below rates for U.S. white males, and cancer mortality was 36 percent below U.S. rates. Death rates for cancer of the bone, melanoma and leukemia were similar to U.S. rates. Cancer death rates for a group of 3,775 plutonium monitored workers were compared to rates for other workers. Death rates for all cancers were seven percent higher among plutonium workers than among other workers. Lung cancer rates were 78 percent higher among plutonium workers, based on eight observed deaths among plutonium workers. Positive dose response relationships with external ionizing radiation were observed for brain cancer and Hodgkin's disease, but not for lung cancer or cancers in general.

Cohort cancer incidence study of LANL and Zia workers (*12*). Incident cancers were ascertained from the New Mexico Tumor Registry for a group of LANL workers employed by University of California and the Zia Company between 1969 and 1978. Incident cancers among white Anglo employees were compared with the number expected based on rates for New Mexico. Among males, a 40 percent lower cancer incidence was observed in this group, primarily due to fewer than expected numbers of lung cancer. The one bone cancer observed represented a twofold excess over the expected. Five cases of lymphosarcoma and reticulosarcoma were observed where two were expected. Among females a 21 percent excess of cancer was observed. Investigators were not able to ascertain incident cancers among workers who left the state of New Mexico.

Case control study of melanoma (*13*). Incident cases of malignant melanoma were included in a special case control study. These included 15 male and five female cases. Four controls were selected for each case matched for sex, ethnicity (Anglo or Hispanic), date of birth and date of first employment at LANL. Estimates of plutonium body burden, external radiation exposure and employment as a chemist or physicist were not associated with malignant melanoma.

Case control study of multiple myeloma (*14*). This study compared 98 multiple myeloma deaths and 391 age-matched controls from LANL, Hanford, Oak Ridge National Laboratory, and the Savannah River Site. Information on prior work history, smoking, medical x-rays, and potential exposure to solvents, metals, welding fumes, asbestos, ionizing and non-ionizing radiation was derived from personnel, medical, industrial hygiene, and health physics records. African Americans, men, and workers first hired before 1948 had excess multiple myeloma compared to non-African Americans, women and workers hired after 1948. Occupational exposures to external penetrating radiation and tritium at older ages (above age 40), but not exposures at younger ages, showed a dose response relationship with multiple myeloma.

Discussion

All the types of occupational health studies have limitations in design and implementation. Hazardous occupational exposures are difficult to measure accurately even in situations where a worker has been monitored. Exposure measures for LANL workers are limited primarily to radiation hazards. In addition to the basic problems noted above, interpretation of badge data for external radiation may be complicated by situations particular to a job or individual worker, for example when tools or equipment shield the part of the body where the dosimeter is worn from a source that is exposing other parts of the body. In the case of internally deposited radionuclides, estimates of body burdens and internal doses are highly uncertain and do not take into account individual differences in metabolism, deposition and retention. Even if exposure measures are adequate, some studies lack adequate follow-up to detect diseases with long latencies.

Dose reconstruction may be used along with risk models, as in the "probability of causation" approach, to estimate a worker's risk of disease based on occupational exposure to radiation. In addition to accurate information about historical radiation exposures, the reliability of this calculation depends on the accuracy of risk values, or dose response coefficients, used to predict the increase in disease risk. Most risk models have been based on studies of a group of survivors of the atomic bombings of Hiroshima and Nagasaki that began in 1950. High mortality in the aftermath of the atomic attacks, selective survival of persons with low sensitivity to radiation, and uncertainties in estimating doses from the bombs, including a lack of data on doses from radioactive fallout, raise serious questions about the relevance of risk estimates from this population for U.S. radiation workers (*15, 16*). Other problems with the "probability of causation" concept come from its inability to recognize complex interactions of multiple factors in disease causation, and its lack of attention to situations in which exposure advances the time at which a person becomes sick (*17*).

Other nuclear worker studies have provided evidence of health risks from radiation exposures at levels similar to those that occurred at LANL (*16*). Excess risks in some populations are seen only when carefully considering potentially confounding factors, cancer latency and the modifying effects of age at exposure (*15*). As in the multiple myeloma case control study (*14*), some other studies of nuclear workers have suggested increased susceptibility of older workers to the carcinogenic effects of radiation exposure (*18*). The possible increased cancer risk for older workers has not been investigated in cohort studies of LANL workers. Effects of paternal occupational radiation exposures on the relative frequency of female vs. male births, still births and childhood cancers has been suggested in some other studies (*19-21*), but these issues have not been investigated at LANL. Further investigation of radiation health risks, as well as effects of other toxic agents, could be enhanced by involving workers and former workers in efforts to identify risky jobs and improve exposure estimates.

Risk estimation from dose reconstruction shares one problem with direct observation of risks in epidemiologic studies of nuclear workers. Both estimates represent an average of risks for many persons. In reality, an individual's risk of disease depends not only upon exposure level, but upon a myriad of factors that are particular to individuals, including genetics and historical exposures that influence susceptibility. Not only does the risk estimate depend upon accurate information at each stage of dose reconstruction and risk estimation, it represents an average whose relevance to a particular worker is uncertain. Even in the case of strong risk factors such as cigarette smoking, epidemiologic studies do a poor job of predicting who will get cancer (*22*). For these reasons, even the best health studies have limited utility for individual workers and community members concerned about individual health risks from exposures at LANL. However, these studies can contribute to identifying factors that cause disease, risks at exposure levels faced by workers or the public, and populations that are more sensitive to exposure.

Despite serious measurement problems and a lack of exposure data for many workers and time periods, excesses of certain cancers and dose response relationships for others have been observed among workers at LANL and other DOE facilities. Because workers as a group are more highly exposed than members of the general population, their experience may be considered in evaluating whether health effects might occur off site. Non-workers may be exposed because of contaminants carried home by workers, airborne emissions, water pollution, or exposures through the food chain. These exposures should in general be much lower than worker exposures, however many more people are potentially exposed. Furthermore, the general population includes children, pregnant women, older persons, and people with existing disease who may be more susceptible to hazardous agents. Direct evaluation of health effects of chronic, low-level environmental exposures through epidemiologic research is difficult because of complex exposure pathways that include air, water and food, a lack of individual exposure measurements, and migration in and out of potentially exposed areas.

Uncertainties about the health effects of exposures at LANL reflect basic limitations in knowledge about exposures and diseases. For example, unlike infectious diseases, which are classified based on their causal agents, cancers can only be classified according to the tissues they affect and the characteristics of the malignant cells. Given these uncertainties, it is important that occupational and environmental exposures to hazardous agents be minimized, and that workers and the general public be involved in decision-making about exposure standards and health related research.

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