Paper

CHARACTERIZATION OF INTERNAL EXPOSURE TO ENRICHED URANIUM AT A FORMER GASEOUS DIFFUSION PLANT

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Abstract—**The National Institute for Occupational Safety and Health (NIOSH) is conducting a nested case-control study of mortality from multiple myeloma involving 581 subjects who worked at the Oak Ridge K-25 Gaseous Diffusion Plant. Internally-deposited uranium is the primary agent being considered in the exposure assessment. Routine operation and maintenance of the plant presented the potential for inhaling uranium of various enrichments. As part of the exposure assessment, records describing the various plant processes and procedures, documentation on the medical monitoring program, uranium urinalysis data, and procedures and analytical methods for monitoring uranium exposure were retrieved and reviewed. Uranium urinalysis data consisted of 161,055 uranium urinalysis results obtained by fluorometry and 171,914 results obtained by alpha particle counting. Approximately 20% of the workers were monitored for internal exposure using urine sampling. Mean and median uranium concentrations in urine for the monitored study subjects were slightly lower than for the entire population of monitored K-25 workers. The specific activity of uranium excreted in urine was determined by comparing results obtained using fluorometric and alpha activity measurements and indicate that the majority of internal exposure involved uranium that was depleted or enriched to no more than 4% ^{235}U.**
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Key words: bioassay; exposure, internal; exposure, occupational; uranium

INTRODUCTION

A NESTED case-control study is being conducted by the National Institute for Occupational Safety and Health (NIOSH) to evaluate the relationship between occupational internal exposure to uranium and mortality from multiple myeloma at the Oak Ridge Gaseous Diffusion Plant (ORGDP) in Oak Ridge, Tennessee. Between 1945 and 1985, approximately 48,000 workers at ORGDP, also known as K-25, were involved in a national war time (World War II and Cold War) project to construct and operate the world's first large scale uranium enrichment plant for the U.S. atomic weapons program. These workers were potentially exposed to a range of enriched, natural, and depleted uranium products as well as other chemical and physical agents, some of which are unique to the special barrier materials used in the gaseous diffusion process.

Previous epidemiological studies of this working population have focused largely on the health effects from external exposures to low-linear energy transfer (low-LET) radiations (Frome et al. 1997). However, K-25 workers were exposed primarily to soluble uranium compounds via inhalation and ingestion. Generally, internal exposure data are relatively sparse and dose reconstruction methods often rely on supplemental process knowledge and work history information to sufficiently characterize exposures for epidemiological study. This article focuses on the collection and assessment of historical information and urinalysis data and their subsequent use to characterize worker internal exposures to uranium compounds at the K-25 facility. Much of the presented background information can be generalized to other similar facilities within the U.S. nuclear weapons development complex and may be useful for subsequent dose reconstructions and related purposes. Finally, this characterization forms the basis for dose estimates to be used in subsequent epidemiological analyses, which are provided elsewhere (Anderson et al. 2007).

BACKGROUND

History of the K-25 facility

During World War II, the United States, under the auspices of the Manhattan Engineer District (MED), supported research at Columbia University to develop methods for increasing the abundance of ^{235}U above that of 0.72 wt % present in natural uranium. The MED designated the facility at Columbia University as the S. A. M. Laboratories, from the code words "Substitute Alloy Materials" (Benedict and Williams 1949). The responsibility for research on gaseous diffusion remained with Columbia University until 1945, when the War

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Department reassigned this project to the Carbide and Carbon Chemical Corporation.

The M. W. Kellogg Company was designated by the Office of Scientific Research and Development to study the feasibility of constructing a large-scale gaseous diffusion plant in Oak Ridge. The Kellex Corporation, established by the M. W. Kellogg Company, was responsible for design, planning, and engineering of the K-25 uranium enrichment facility (Benedict and Williams 1949). However, delay in developing the critical diffusion barrier material made it necessary to construct an interim facility, designated as the S-50 plant, which used an older, less efficient liquid thermal diffusion process to meet an urgent, wartime need for enriched uranium. The S-50 plant started operation at Oak Ridge in the summer of 1944 and continued through August 1945, when the gaseous diffusion plant became operational. The S. A. M. Laboratories at Columbia University were closed on 1 July 1946 and all activities associated with gaseous diffusion research were transferred to Oak Ridge.

Uranium enrichment

The ^{235}U isotope is significantly more fissionable than ^{234}U and ^{238}U, thus making it an essential component for nuclear fuels and weapons material. Because the atom abundance of the ^{235}U isotope in naturally-occurring uranium ore is too low for most nuclear applications, it is necessary to concentrate (i.e., enrich) ^{235}U in uranium compounds used in nuclear fuel and weapons. The gaseous diffusion process employed at the K-25 facility was the principal enrichment process adopted during the Manhattan Project. This process involves movement of a gaseous uranium compound through a diffusion barrier contained in a single unit known as a converter, many hundreds of which are connected in series to create a cascade. The gaseous uranium compound is introduced into the cascade at a pressure that is high relative to the rest of the system but below atmospheric pressure. Since the molecular diffusivity of the ^{235}U isotope is greater than ^{238}U, two streams of gaseous uranium are formed in the cascade, one increased and one depleted in the ^{235}U isotope. (Bailey 1975; Benedict and Pigford 1957). The ^{234}U isotope is also enriched with ^{235}U since both the mass and molecular diffusivity of these isotopes are nearly identical.

The change in the specific activity (*SA*) of each uranium isotope with increasing enrichment is shown in Table 1 and illustrates that ^{234}U is the predominant isotope for radiation dosimetry whenever the material is even slightly enriched. As the degree of enrichment progresses from natural uranium to highly-enriched uranium, ^{234}U becomes the predominant source of alpha activity. Exposure to uranium at the end of the cascade, where ^{234}U is most concentrated, is likely to result in much greater risk than a release earlier in the process. Thus, the evaluation of dose arising from occupational exposure to uranium at a gaseous diffusion plant can be very dependent upon location where work or maintenance is being performed on or around the cascade.

Table 1. Specific activity (Bq g^{-1}) of uranium isotopes[a] in UF_6 with increasing uranium enrichment.

Isotope	Natural	3 %	10 %	93 %
^{234}U	1.2×10^4	6.3×10^4	1.5×10^5	2.5×10^6
^{235}U	5.8×10^2	2.4×10^3	8.1×10^3	7.5×10^4
^{236}U	—	1.4×10^1	9.0×10^2	4.9×10^3
^{238}U	1.2×10^4	1.2×10^4	1.1×10^4	6.8×10^2
Total activity	2.4×10^4	7.8×10^4	1.7×10^5	2.6×10^6

[a] Calculated using ORIGEN2 computer code, ORNL, Oak Ridge, TN, 1991.

Conventional fuels for most commercial nuclear reactors require uranium enrichment of only about 4%, whereas the enrichment for nuclear fuels used in naval and research reactors or for nuclear weapons may exceed 90% (Rucker and Johnson 1988). Enrichment levels of uranium products at K-25 typically ranged from 3% to 93%. K-25 produced primarily high-enriched uranium ($>$90%) prior to 1964 after which portions of the cascade system were shut down and the plant continued to produce low-enriched uranium ($<$4%) (U.S. DOE 1997).

Biokinetics of uranium

The primary form of uranium at the enrichment facility is uranium hexafluoride (UF_6), which reacts violently with moisture in ambient air producing uranyl fluoride (UO_2F_2), hydrofluoric acid (HF), and considerable heat (Gindler 1973; Morrow et al. 1982). Uranyl fluoride is a very soluble compound and is likely to enter the bloodstream if inhaled or ingested. In the uranium recovery and feed manufacturing areas of the gaseous diffusion plant, workers also had potential for exposure to a mixture of soluble and insoluble uranium compounds such as various oxides of uranium (Schultz and Becher 1963).

Uranyl fluoride is rapidly transported from the lungs to blood with about 60% being excreted in urine in the first 24 h (Eidson 1994; Morrow et al. 1982; Wrenn et al. 1994). A small fraction of the uranium ($\sim$8%) in blood eventually deposits on bone surfaces where it is retained with a half-life of about 880 d (Wrenn et al. 1994). Although uranium is initially deposited on all bone surfaces, it tends to concentrate in areas of growth (Rowland and Farnham 1969). Other significant sites of deposition include the kidneys and liver (Morrow et al. 1982; Wrenn et al. 1994).

Inhaled soluble uranium compounds are transferred from lungs to blood more quickly than the dissolution rates of most industrial uranium compounds (Eidson 1994; Heffernan et al. 2001). Rapid translocation from the lungs to the blood leads to more uptake of uranium in other tissues such as the bone surfaces and potentially more radiation exposure to those tissues compared to insoluble materials (Morrow et al. 1982).

Inhalation of insoluble uranium compounds can lead to increased radiation exposure of the respiratory tract since uptake to blood is much slower than for a soluble material. Insoluble particles can be translocated to thoracic or pulmonary lymph nodes where the local tissue dose can be very high but the health consequence is very low. Accordingly, an insoluble uranium compound will deliver less dose to the skeleton, kidney, liver, and other systemic organs and tissues than a soluble compound. Depending on particle size, a fraction of the insoluble uranium particles deposited in the lungs will be cleared via the mucociliary escalator, enter the gastrointestinal (GI) tract, and be eliminated in the feces. Alternatively, a fraction ($f_1 = 0.02$) of the uranium entering the GI tract can dissolve and enter the blood stream where it can be transported to other organs or tissue.

Uranium urinalysis methods at K-25

The conventional method for monitoring internal exposure to uranium is to periodically analyze single void samples of urine. The frequency of sample collection is determined by evaluating many factors including the sensitivity of the analytical method, the solubility of the uranium compound, and the *a priori* administrative or regulatory requirement for limiting internal dose to the workers.

Routine monitoring for internal exposure to uranium at the K-25 plant involved analyzing a small portion of single void urine samples using a conventional uranium fluorometric method (Centanni et al. 1956). The majority of the remaining sample volume was used for other analyses including measurement of alpha activity to monitor exposure to enriched uranium. Historical urinalysis records indicate that additional aliquots of the single void urine sample could be analyzed for fluorides, mercury, nickel, and other chemical and physical agents.

Typically, 1 mL of urine was analyzed fluorometrically to determine the concentration of uranium mass being excreted by the worker. The fluorometric method involved adding 1 mL of urine to a solid pellet of sodium and lithium fluoride in a small platinum dish that was then melted (fused) to form a uranium fluoride. The formulation for the sodium-lithium fluoride pellet changed with time. The fluorescence of uranium in the fused sample was measured optically either by comparison with standards (up to February 1955) or using a fluorophotometer (after 1955). Uranium fluorometry would eventually be replaced with the method of laser-induced phosporimetry after 1985. Since the K-25 plant ceased operation in 1985, this change does not impact the epidemiological study. The lower limit of detection for this method was reported to be 1 μg U L^{-1} or 10 $\pm$ 3 μg U L^{-1} at 95% confidence (Schultz and Becher 1963).

Fluorometric analysis does not provide information on the enrichment or *SA* of uranium being excreted which would lead to underestimating internal radiation dose if the worker was exposed to uranium that was enriched in the ^{235}U isotope. Thus, each single void sample of urine was also analyzed radiometrically to determine the alpha activity concentration. The radiometric analysis involved chemically ashing 100 mL of urine with hydrochloric acid. Aluminum nitrate and ammonium hydroxide were added to form a precipitate that was dissolved and evaporated onto a metal disk for alpha counting in a low background gas flow proportional counter. Hurd and Fox (1947) reported that 10 μg of natural uranium and 0.01 μg of ^{233}U per 100 mL of sample could be detected. No information could be found regarding precision of these measurements at the K-25 facility. However, another uranium facility in Oak Ridge calculated a percent limit of error of 12% to 99% for gross alpha counting of electro-deposited uranium from undigested urine samples (Patterson 1958). Omitting the digestion, or ashing, step significantly decreases the chemical yield, thereby decreasing the precision.

Personnel monitoring for internal uranium exposure at K-25

Recently declassified documents and historical records from the 1940's describing the objectives of the Division of Health (DOH) at Oak Ridge demonstrate that there was a significant emphasis placed upon monitoring the health of workers who could be exposed to potentially hazardous chemical and radioactive materials. Specifically, the DOH at Oak Ridge was responsible for protecting the health of personnel in the laboratories and that of the public in surrounding areas from hazards resulting from the operation of the laboratories.[†] The DOH served as the main health care provider for workers during plant startup by conducting routine medical examinations and collecting and analyzing excreta for radioactive materials. Clinical procedures were developed by the DOH to measure uranium in urine and studies were conducted to relate uranium urinary excretion to exposure of personnel to uranium and other metals (Stone 1946).

[†] Murphy EJ. Memorandum to Col. Stafford L. Warren. Proposed Health Program for the Metallurgical Laboratory. Oak Ridge, TN: Army Service Forces, U.S. Engineer Office, Manhattan District; 21 July 1945.

Prior to 1949, there were no limits established for exposure to uranium, although there were considerable data on uranium toxicology in experimental animals indicating that uranium could cause kidney damage due to its behavior as a heavy metal. Therefore, in 1944, the Medical Division of the Manhattan District adopted the maximum permissible concentration in air (MPC_a) for lead, another heavy metal, of 150 $\mu g\ m^{-3}$ as the standard for uranium (Spoor and Hursh 1973). Then, in 1949, a group at the University of Rochester Atomic Energy Project recommended an MPC_a of 50 $\mu g\ m^{-3}$ for soluble uranium based on chemical toxicity to the kidney determined from animal experiments and 100 $\mu g\ m^{-3}$ based on radiation injury to the lung (Hursh 1975). Neuman (1950) calculated a urinary excretion level of 320 μg U per day for an average working day (8 h) exposure to the MPC_a of 50 $\mu g\ m^{-3}$ of soluble uranium and suggested a urinary limit of 250 μg U per day for samples collected on evenings after exposure and 50 μg U per day for samples collected after a weekend with no exposure. He also estimated a urinary excretion level of 60 μg U per day for exposure to an insoluble uranium compound at the maximum permissible lung burden of 25 mg U. In 1953, the National Council on Radiation Protection and Measurements (NCRP) recommended an MPC_a of 73 $\mu g\ m^{-3}$ for both soluble and insoluble uranium compounds (Hursh 1975).

The K-25 facility eventually established administrative control limits for urinary excretion of uranium in accord with the recommendations of nationally recognized groups. K-25 set an excretion rate limit of 26 μg per day for natural uranium or equal activity (~650 mBq per day) for enriched uranium. A urine sample with a uranium concentration of 0.005 $\mu g\ mL^{-1}$ was considered to be a "positive" sample (Henry et al. 1957). This urinary level was based on the radiological toxicity of an insoluble uranium compound in the lung and a maximum permissible lung burden of 330 Bq.[‡]

For the period between 1948 and 1985, the historical records do not indicate that baseline or pre-employment uranium samples were collected from newly hired workers. Thus, estimating the uranium excreted in urine arising solely from natural sources in diet and drinking water could not be determined using K-25 urinalysis records. Likewise, there was insufficient information in the K-25 historical records to determine the concentration of uranium in drinking water or the natural background excretion of uranium in the general population. The geometric mean concentration of uranium excreted in urine due to natural sources is 0.009 $\mu g\ U\ L^{-1}$ (0.007–0.010 95% confidence interval), as ascertained for the U.S. population as part of the National Health and Nutrition Examination Survey (NHANES) for 2001–2002 (DHHS 2005). This concentration is significantly below the reported limits of detection for uranium fluorometric and alpha activity measurements (~1–10 $\mu g\ U\ L^{-1}$) prior to 1985.

[‡] Bailey JC. Suggested P.A.L. [Plant Acceptable Limit] for Urinary Uranium. Exhibit III of Memorandum from A.P. Huber to L.B. Emlet. Radiation Protection at Production Plants. Union Carbide Nuclear Company inter-company correspondence. Oak Ridge, TN: Union Carbide Nuclear Company; 14 May 1959.

METHODS

Epidemiological study subject selection

The current research supports the dose reconstruction efforts for a future nested case-control study. The cases and matched controls ($n = 581$) for the study were drawn from a population of 39,403 workers, which includes all workers who were hired prior to 1 January 1985, and employed at the K-25 facility for at least 30 d. Over half of these workers were hired in 1945 and 1946, a period of time when both construction and uranium enrichment were in progress. The 581 study subjects include 98 cases of multiple myeloma mortality and five controls matched to each case by age (i.e., birth date ±5 y), race, and sex. The five controls were randomly selected from each risk set (i.e., those K-25 workers meeting the match criteria of the case) with the exception that each control must reach the attained age of the case. Incidence density sampling methods were used for control selection, thus a control could be selected to more than one risk set (Beaumont et al. 1989). A discussion of the relationship between multiple myeloma and exposure to radiation and uranium is found elsewhere (Anderson et al. 2007).

Evaluation of urine sample data

A comprehensive search was done of K-25 plant records, including early health division reports, correspondence, and interdepartmental memos. The scientific literature, and declassified Atomic Energy Commission (AEC) reports, War Department correspondence and reports, and Manhattan District reports were also examined to ascertain dose monitoring philosophy and practices in the 1940s' and 1950's. Plant history and monitoring program practices were reconstructed by extracting information from these various sources.

Paper records and computerized files containing individual urinalysis data for workers were retrieved from the K-25 facility and from Oak Ridge Associated Universities. The descriptive statistics and frequency distributions for the urinalysis data were obtained using PROC UNIVARIATE procedure in SAS version 9 (SAS Institute 2006).

Urine data were also evaluated and records were examined to attempt to determine whether levels of uranium measured in urine were due to occupational exposures or due to uptake of naturally-occurring uranium from food and water sources. Again, the scientific literature was searched for reported levels of naturally-occurring uranium in urine.

Determination of uranium enrichment in urine samples

Retrospectively, none of the historical records provided adequate information to relate job title or work location to a potential for exposure to a specific isotopic composition of uranium. However, since most of the urinalysis monitoring data included results of uranium mass (mg L^{-1}) and alpha activity (dpm per 100 mL), it is possible to estimate whether potential exposures involved enriched uranium. In this study, the *SA* of uranium excreted in each sample of urine was calculated by dividing the measured uranium alpha activity by the measured uranium mass. The *SA* of uranium (Bq g^{-1}) per enrichment percentage was calculated using the following equation (U.S. DOE 2001):

$$SA(\text{Bq g}^{-1}) = [(3.4 \times 10^{-9})\,X^2 + (3.8 \times 10^{-7})\,X + (4 \times 10^{-7})] \times (3.7 \times 10^{10}), \quad (1)$$

where X is equal to the enrichment percentage. A curve was plotted of *SA* vs. enrichment percentage using eqn (1) and the observed *SA* in the urine samples was compared to this curve to estimate enrichment levels in the samples.

Specific activity does not increase linearly with enrichment because in the gaseous diffusion process ^{234}U increases more rapidly than ^{235}U. Also, the plant could produce various blends of uranium isotopes that result in a product having an *SA* that could differ from that predicted by calculation.

Much of the information gathered for the study of K-25 workers is applicable to other uranium enrichment facilities managed under the auspices of the U.S. government, thus facilitating a means to compare activities and health risks. To explore this further, the *SA* of uranium excreted in urine collected from workers at the Portsmouth Gaseous Diffusion Plant (PORTS) in Piketon, Ohio, was compared with results for workers at the K-25 plant to assess differences in excreted uranium enrichments. Uranium urinalysis data for PORTS were obtained as part of a previous epidemiological study of uranium exposure to workers conducted in 1983 (Rinsky et al. 2001). Approximately 8,900 workers were employed at PORTS since it began enriching uranium in September 1954. The total workforce at PORTS was significantly smaller than at K-25. The PORTS cascade contains 4,020 stages and processes uranium from low to a much higher enrichment (i.e., 97.65%) than produced at K-25. Thus, it is expected that the average *SA* of uranium excreted in urine from workers at PORTS would be higher than at K-25. The method described above for determining the *SA* of uranium excreted in urine was applied to the urinalysis data obtained from PORTS.

RESULTS

Results of urine sample data analysis

A total of 161,055 uranium fluorometric and 171,914 alpha activity measurement results were identified in the historical records dating back to 1948. Many of these records were incomplete because some of the record was missing or data were censored (i.e., result recorded as "less than" some value). Thus, excluding incomplete or censored records, 139,095 fluorometric results for 7,541 workers and 112,292 alpha activity results for 7,642 workers were available for analysis. Only 16% of the total K-25 work force between 1948 and 1988 was monitored by urinalysis for internal uranium exposure. Urinalysis data were available for only 118 workers (20%) out of 581 study subjects. Figs. 1 and 2 show the number of uranium fluorometric urinalysis results reported for each year for the K-25 worker population and study subjects, respectively. Fig. 3 shows the annual number of uranium fluorometric urinalysis results reported for the 98 multiple myeloma fatalities (cases), while Fig. 4 shows the annual number of uranium fluorometric results reported for the randomly-selected controls.

Table 2 shows the statistics for the distributions of the number of fluorometric and alpha results for workers with uranium urinalysis monitoring results. Table 3 shows the mass and activity concentrations of uranium measured in the urine samples.

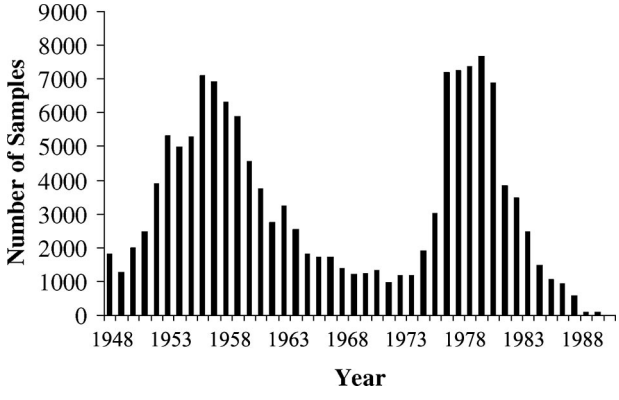

Fig. 1. Number of uranium fluorometric urinalysis results per year (1948–1990) for the 47,941 K-25 worker population.

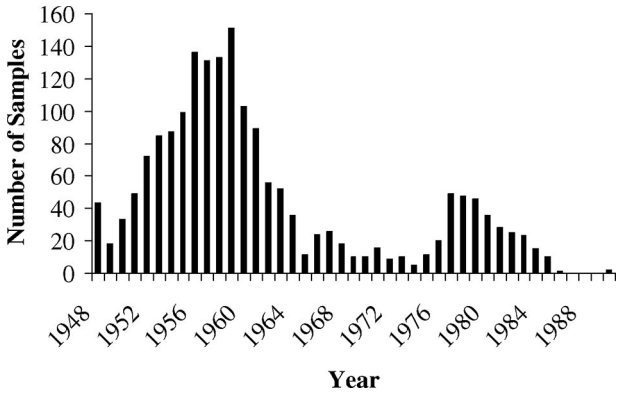

Fig. 2. Number of uranium fluorometric urinalysis results per year (1948–1990) for the 581 study subjects.

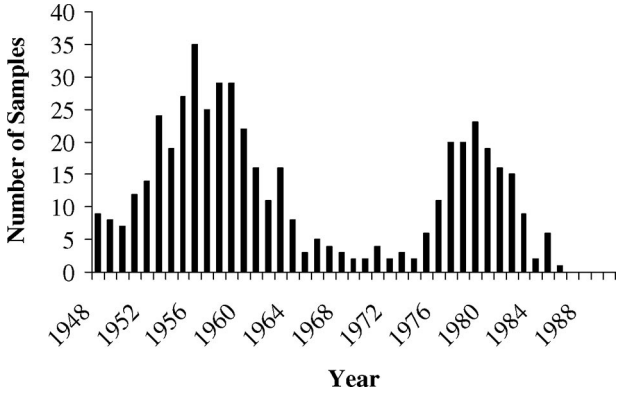

Fig. 3. Number of uranium fluorometric urinalysis results per year (1948–1990) for the 98 multiple myeloma fatalities.

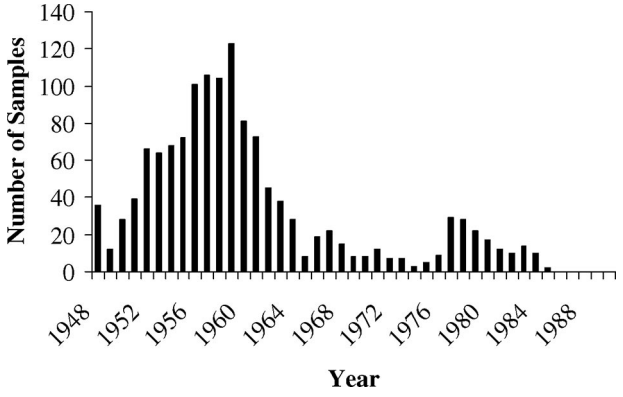

Fig. 4. Number of uranium fluorometric urinalysis results per year (1948–1990) for the control group.

All K-25 workers who were monitored for internal exposure to uranium using urinalysis submitted an average of 18 samples that were analyzed fluorometrically and 15 samples analyzed for alpha activity. An average of 15 urine samples (ranging from 1 up to about 150) were submitted by study subjects who were monitored for internal exposure

Table 2. Distribution of the number of uranium bioassay results among K-25 workers.

Statistic	K-25 workers		Study subjects	
	Fluorometric	Alpha	Fluorometric	Alpha
Mean	18	15	15	15
Median	9	7	7	6
Mode	1	1	1	1
Minimum	1	1	1	0
Maximum	337	298	154	145
No. of monitored workers	7,541	7,642	118	115
Total workers	47,941	47,941	581	581

to uranium. The distribution of the number of urine samples submitted for uranium analysis is highly skewed toward unity. The median and mode for the sample number distribution is 9 and 1, respectively, for K-25 workers and 7 and 1, respectively, for the study subjects.

Enrichment of uranium in urine samples

Exposure assessment for enriched uranium was performed using 644 urine samples containing at least a detectable quantity of uranium out of a total of 1,755 samples that were analyzed both for uranium mass and activity. The *SA* of uranium for increasing levels of enrichment is shown in Fig. 5.

Table 4 lists descriptive statistics for the *SA* determined in samples obtained from K-25 workers and the study subjects, based upon the assumption that the results are lognormally distributed. For the 581 cases and controls, approximately 48% of the urine samples contained depleted uranium, 55% contained depleted to 1% enriched, and 83% contained depleted to 4% enriched.

Internal exposure to uranium at PORTS and K-25 is most likely to occur by inhalation of material released to air during routine operation or as a result of an accident. Urinalysis for uranium at PORTS was performed using fluorometric and alpha counting methods similar to those used at K-25. The descriptive statistics for the concentration of uranium mass and activity excreted in urine samples from workers at K-25 and PORTS are listed in Table 5. Table 6 compares the *SA* of uranium excreted in urine determined from eqn (1) for workers at K-25 and PORTS and demonstrates, as expected, that workers at PORTS were exposed to a higher enrichment of uranium than workers at K-25.

DISCUSSION

Unexpectedly, differences were observed in the collection of urine samples over time for study subjects (Fig. 2) compared to those for the K-25 cohort (Fig. 1). These differences may indicate variations in exposure patterns among cases or their matched controls when compared with those of the full cohort. In

Table 3. Concentration of uranium excreted in urine by K-25 workers.

Statistic	K-25 workers		Study subjects	
	Fluorometric (μg L^{-1})	Alpha (dpm per 100 mL)	Fluorometric (μg L^{-1})	Alpha (dpm per 100 mL)
Mean	8.2	1.68	5.6	1.24
Standard deviation	200	15	31	7.2
Median	2	0.4	1.0	0.40
Mode	0	0	0	0
Minimum	0	0	0	0
Maximum	56,000	991	800	197
Count	139,095	112,292	1,826	1,764

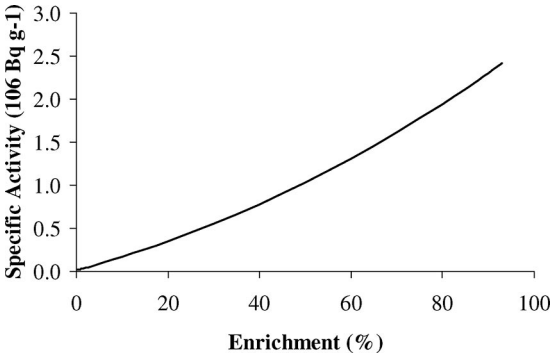

Fig. 5. Specific activity of uranium as a function of enrichment percentage.

the latter case, the random selection of controls should minimize these differences within a population. However, it appears that during the period of operation of the K-25 facility, the years with the greatest number of workers employed were 1945 (~25,000 workers) and 1946 (~15,000 workers), with annual employment levels dropping to an average of about 4,500 workers (approximate range 1,100–9,200) thereafter. The early year workers supported construction and initial operations of the facility and continued employment for a short time relative to those workers hired after 1946; thus, these workers exhibit uniquely different employment histories and exposure patterns than those hired in later years. Controls were more likely to be drawn from the subcohort of workers hired prior to 1947 given their large number (n = 24,454 or 62%) relative to those hired after 1947 (n = 14,949 or 38%). In contrast, very few controls were selected from a small group of workers (100–600 workers in three departments) who submitted a large number of urine samples as a result of enhanced urinalysis monitoring for special project work during the late 1970's and 1980's. Thus, the differences in the pattern of urine sampling of study subjects over time compared with the cohort suggest that controls may be selected from a population of workers that is different than those of the cases. This is an important finding for continuing research and demands careful consideration when conducting and interpreting the results of subsequent epidemiological analyses.

Although the workforce was smaller and length of operation was shorter at PORTS than at K-25, the number of urine samples collected at PORTS was much greater than at K-25. Comparison of urinalysis data obtained from K-25 to that obtained from PORTS (Table 6) shows that the average uranium enrichment observed in urine was 7.8% compared to 2.9% for K-25. Over 29 years of operation at PORTS, 96% of the uranium fluorometric results and 50% of the alpha activity results were reported as zero values, whereas at K-25, 40% of the uranium fluorometric results and 23% of the alpha activity results were reported as zero values. The number of non-zero results for uranium alpha activity at PORTS was nearly the same magnitude as K-25. However, the ratio of the number of non-zero results of alpha activity to the number of non-zero results of uranium mass was a factor of 8 greater at PORTS than at K-25. This indicates a higher *SA* for uranium in the urine samples from PORTS, which suggests that those workers were exposed to a higher level of uranium enrichment. This finding, and the descriptive statistics for uranium mass and activity provided in Table 5 for K-25 and PORTS workers, helps to validate the method described in this manuscript for determining the *SA* of uranium excreted in urine.

Job categories perceived by the facility as having a higher potential risk of exposure to uranium could be identified retrospectively by observing an increase in the number of urine sample results recorded for workers in this category. Workers involved in suspected or known exposure incidents would also have an unusually high number of sample results. In general, however, the urine sampling frequency was quite low compared to contemporary practices that, depending upon solubility and particle size of the uranium product, collect samples weekly or monthly.

From the limited number of urine samples submitted by K-25 workers and, specifically, those subjects selected for the epidemiological study, it has been determined that exposure to uranium involved mainly depleted, natural, or very low enrichments.

Table 4. Distribution of the specific activity of uranium in urine at K-25.

	K-25 workers		Study subjects	
Statistic	Specific activity (Bq g^{-1})	Enrichment	Specific activity (Bq g^{-1})	Enrichment
Mean	5.69×10^4	2.9%	5.01×10^4	2.5%
Median	2.50×10^4	Natural	2.50×10^4	Natural
Mode	1.67×10^4	Depleted	1.67×10^4	Depleted
Minimum	1.67×10^1	Depleted	8.33×10^1	Depleted
Maximum	2.64×10^7	>99.9%	1.64×10^6	71%
Count	50,569		644	

Table 5. Comparison of urinalysis data for workers at K-25 and PORTS.

	K-25		PORTS	
	Fluorometric	Gross alpha	Fluorometric	Gross alpha
Number of samples (all observations)	139,095	112,292	212,085	142,126
	(μg L^{-1})	(dpm per 100 mL)	(μg L^{-1})	(dpm per 100 mL)
Mean	8.2	1.7	16	2.2
Median	2	0.4	0	0.1
Mode	0	0	0	0
Minimum	0	0	0	0
Maximum	56,000	991	15,000	7,322
	Fluorometric	Gross alpha	Fluorometric	Gross alpha
Number of samples (all non-zero results)	83,934	86,324	9152	71,403
	(μg L^{-1})	(dpm per 100 mL)	(μg L^{-1})	(dpm per 100 mL)
Mean	14	2.2	37	4.5
Median	4	0.6	10	1.0
Mode	1	0.2	10	1.0
Minimum	1	0.001	10	0.10
Maximum	56,000	991	15,000	7,322

Table 6. Comparison of specific activities of urine samples from workers at K-25 and PORTS.

	K-25		PORTS	
Statistic	Specific activity (Bq g^{-1})	Enrichment	Specific activity (Bq g^{-1})	Enrichment
Mean	5.69×10^4	2.9%	1.31×10^5	7.8%
Median	2.50×10^4	Natural	3.89×10^4	1.7%
Mode	1.67×10^4	Depleted	1.67×10^4	Depleted
Minimum	1.67×10^1	Depleted	8.33×10^1	Depleted
Maximum	2.64×10^7	>99.9%	5.10×10^6	>99.9%
No. of observations[a]	50,569		5,018	

[a] Each observation consists of a mass and activity result for a single urine sample.

This is a particularly interesting finding considering that K-25 enriched uranium to more than 90% prior to 1964 (U.S. DOE 1997).

CONCLUSION

Approximately 16% of K-25 workers were monitored for internal exposure to uranium using fluorometric and alpha activity measurements of uranium in urine. About 20% of the cases and controls in the current study were directly monitored for internal exposure to uranium using routine urinalysis. Study subjects that were monitored submitted an average of only 15 samples during their employment for which both fluorometric and alpha activity results were reported, which is similar to the number of samples submitted by monitored workers in the K-25 population. Comparison of the concentration of uranium measured in urine for all K-25 workers with those of the study subjects suggests that the study subjects received slightly less exposure on average than the K-25 population as a whole. Mean *SA* levels for the study subjects were also slightly lower than for the

K-25 workers, although the majority of urine samples for both K-25 workers and the study subjects indicated workers were exposed mainly to depleted to low-enriched uranium.

Controls were more likely to be selected from the larger group of construction and start-up workers who were employed for a comparatively brief period at the plant in 1945 and 1946. The characteristics of these workers may differ significantly from those of the remaining cohort, thus introducing complexities in the interpretation of subsequent epidemiological results. This potential heterogeneity of the study population will be examined in the epidemiological analyses to determine the magnitude of, and adjustment for, any biases that may result.

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