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URANIUM MINING AND LUNG CANCER IN NAVAJO MEN

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Abstract We performed a population-based case–control study to examine the association between uranium mining and lung cancer in Navajo men, a predominantly nonsmoking population. The 32 cases included all those occurring among Navajo men between 1969 and 1982, as ascertained by the New Mexico Tumor Registry. For each case in a Navajo man, two controls with nonrespiratory cancer were selected. Of the 32 Navajo patients, 72 per cent had been employed as uranium miners, whereas no controls had documented experience in this industry. The lower 95 per cent confidence limit for the relative risk of lung cancer associated with uranium mining was 14.4. Information on cigarette smoking was available for 21 of the 23 affected uranium miners; eight were nonsmokers and median consumption by the remainder was one to three cigarettes daily. These results demonstrate that in a rural nonsmoking population most of the lung cancer may be attributable to one hazardous occupation. (N Engl J Med 1984; 310:1481-4.)

URANIUM miners work in an atmosphere that is contaminated by radon daughters, the short-lived decay products of radon gas. Investigations of uranium miners and other underground miners have established a causal association between inhalation of radon daughters and the occurrence of lung cancer.[1-3] However, only limited data have been available from nonsmoking miners.

In the United States, the uranium industry developed during the late 1940s in the Colorado Plateau region of Colorado, Utah, Arizona, and New Mexico, including portions of the Navajo Indian Reservation near Shiprock, New Mexico (Fig. 1).[4,5] Uranium production from this portion of the Navajo reservation reached a peak during the 1950s and declined through the mid-1960s. Navajo men who were employed as uranium miners worked primarily in this area, but some mined off the reservation as well. Little information has been published concerning working conditions in the mines on the Navajo reservation. Limited surveys by the Public Health Service and other agencies have documented exposures to radon gas and silica dust.[1,6,7] Anecdotal accounts describe dusty mines with little effective ventilation.[8-10]

Excess mortality from lung cancer has been demonstrated in Navajo men who mined uranium in this region. A follow-up study of 780 American Indian miners, primarily Navajos, showed 11 deaths from respiratory cancer through 1974, with only 2.6 expected.[11] Among 17 Navajo men with lung cancer who were admitted to the Shiprock Hospital between 1965 and 1979, 16 had mined uranium.[12]

Since 1969, the New Mexico Tumor Registry, a member of the National Cancer Institute's Surveillance, Epidemiology, and End Results Program, has ascertained all incident cancer cases in the Navajo population of New Mexico, Arizona, and Utah.[13] We have used this resource to describe further the importance of uranium mining as a cause of lung cancer in Navajo men, a largely nonsmoking group. To accomplish this goal, we have performed a population-based case–control study of all 32 cases of lung cancer diagnosed among Navajo men between 1969 and 1981.

METHODS

For this investigation, all cases of primary lung cancer (n = 33) (*International Classification of Diseases for Oncology*, code 162) in Navajo males included in the New Mexico Tumor Registry file on August 31, 1982, were selected. One subject with a histologically confirmed carcinoid tumor was excluded. Of the 32 remaining cases, 28 were histologically confirmed, two were diagnosed by x-ray film, and two were identified by review of death certificates. Twelve of these cases were included in the series of Gottlieb and Husen,[12] six in a report by Archer et al.,[11] and six in both.

For each case, two deceased Navajo male controls with cancer other than lung cancer were selected from the Registry files. Deceased controls were used because only two of the Navajo subjects with lung cancer remained alive at the time of this investigation and death certificates were one source for occupational histories. The controls were matched to the cases for age (± five years) and diagnosis date (± five years). The primary tumor sites for the 64 controls were digestive (n = 35), male genital (n = 5), kidney (n = 4), brain

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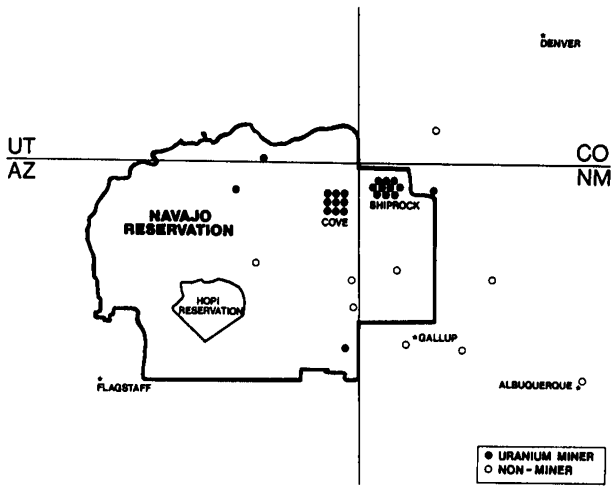

Figure 1. Residence at the Time of Diagnosis of Navajo Men with Lung Cancer.

(n = 3), lymphoma (n = 2), multiple myeloma (n = 3), leukemia (n = 4), and other, ill-defined and unknown sites (n = 8).

Sources of Data on Exposure

Multiple sources were used for all subjects to obtain information concerning occupation and smoking. For occupation, these included records maintained by the National Institute for Occupational Safety and Health (NIOSH), the Registry abstract of medical records, the occupation and industry stated on the death certificate, and listings of New Mexico uranium miners. Data from these sources were combined to determine whether each subject had ever been employed as a uranium miner. Each source is described separately below.

The major source of occupational data was the NIOSH rosters of uranium miners in the Colorado Plateau region, originally developed from annual censuses by the Public Health Service during the 1950s and 1960s and then maintained by NIOSH.[1,11] We were able to match 20 subjects, all cases, with this source on the basis of name and identical birth date or Social Security number (or both).

New Mexico Tumor Registry abstracts, completed for all cases and controls, sometimes mention occupation, although this item is not always available in charts and is not routinely collected. Relevant data from the abstracts were available for 21 cases and 26 controls. Death certificates could not be located for one case and five controls, and two cases remain alive. The 88 available death certificates provided information concerning occupation or industry for 21 cases and 32 controls.

Finally, we matched two cases with lists of New Mexico uranium miners that had been prepared for an ongoing mortality study.[14] The lists included most persons who had had a mining-related physical examination in the Grants, New Mexico, area between 1957 and 1976.

The cigarette-smoking history is not routinely collected by the New Mexico Tumor Registry but was obtained repeatedly in the Public Health Service longitudinal study. Smoking histories were unavailable for controls and were available for only 21 cases — from the Public Health Service data for 19 and from the New Mexico Tumor Registry for 2. For seven subjects who reported inconsistently over time, we selected the maximum amount smoked. Five of the seven stated on at least one questionnaire that they had never smoked cigarettes, and none reported a maximum greater than a few cigarettes daily.

The dates of exposure and the cumulative doses of radon daughter exposure were available from NIOSH records.[1] Exposure to radon daughters is measured in working-level months (WLM). The working level is any combination of radon daughters in 1 liter of air that ultimately releases 1.3×10^5 MeV of alpha energy during decay. Working-level months of exposure are calculated as the product of duration of exposure (measured as 170-hour working months) and the working-level values in the mines.

Statistical Analysis

The data were analyzed with standard techniques for a matched case–control study.[15] The statistical significance of the association between lung cancer and uranium mining was tested with an exact test developed by Gart.[16] A lower 95 per cent one-sided confidence level for the relative risk (rr) was calculated from the binomial distribution by setting $(rr/rr + 2)^n = 0.05$, where n equals the number of exposure-discrepant triplets.[16]

For a further description of the effects of uranium mining in Navajo men, incidence rates were calculated with and without the cases in uranium miners. Mid-period (1975) denominators derived from Indian Health Service population estimates[17] were used. Rates were adjusted by the direct method to the age of the 1970 U.S. population for comparison.

Results

Of the 32 Navajo men with lung cancer in the period 1969-1981, 23 had been employed as uranium miners. This occupational history was documented for 20 by the NIOSH rosters and for the remaining 3 by New Mexico Tumor Registry abstracts. For 16 of the 20 included on the NIOSH lists, death certificates or New Mexico Tumor Registry abstracts were confirmatory.

A history of uranium mining could not be documented for any of the controls. One had worked in a lead, zinc, and silver mine. The association between uranium mining and lung cancer was statistically significant ($P = 1.1\times10^{-11}$). The estimate of relative risk was infinite because no controls were exposed. However, with use of the binominal distribution, the lower 95 per cent confidence limit for the relative risk was 14.4.

The age distribution of the affected Navajo uranium miners differed markedly from that of the affected Navajos who were not uranium miners and from that of men with lung cancer in the white U.S. population. The median age of the affected miners was 44 years, whereas that of the affected non-miners was 63 years — similar to that of affected men in the white U.S. population. The residences of the cases with a history of uranium mining were clustered in the northeast portion of the reservation around the Shiprock, New Mexico, and Cove, Arizona, area where the mines had been located (Fig. 1). In 1975, the Indian Health Service unit that included these communities comprised 24 per cent of the total Navajo population. In contrast, the residences of the nine affected non-miners were scattered across Arizona and New Mexico, as were the residences of the controls. During the 12-year study period, the number of lung cancer cases among uranium miners did not decline; 11 were diagnosed during 1969-1972, and 9 during 1978-1981. The median age for the earlier group of cases was 42 years, as compared with 54 years for the more recent ones.

For the 23 cases with uranium-mining experience, the median duration of employment in underground mines was 13 years. Six were employed there for less than 10 years. The median duration from the start of employment in uranium mining until diagnosis (in-

duction–latency period) was 23.5 years (range, 12 to 38), excluding one case for whom this period could not be determined.

Lifetime working-level months, calculated from job histories, were known for 14 cases and ranged from 30 to 2698, with a median of 1207. However, the two lowest values, 30 and 103 WLM, appear from our review of the records to be based on incomplete work histories. The third lowest value was 830.

Information concerning cigarette smoking was available for 21 of the 23 affected uranium miners (Table 1). Although the majority had smoked cigarettes, the amounts reported were low. Only five had smoked as much as four to eight cigarettes daily. No data on cigarette smoking were available for controls because the major source of these data was the Public Health Service records.

Table 1. Cigarette-Smoking Habits of 21 Male Navajo Uranium Miners with Lung Cancer.*

Cigarette Usage	No. of Men
Nonsmoker	8
Smoker	
<1 cigarette/day	2
1–3 cigarettes/day	6
4–8 cigarettes/day	5

*Data were not available for 2 of the 23 cases in uranium miners.

Discussion

American Indians have substantially lower rates of lung cancer than white and other nonwhite populations of the United States.[18-20] This pattern has been confirmed in the Navajo and other southwestern tribes by autopsy, mortality, and incidence data.[21-24] A low prevalence of cigarette smoking by American Indians, as suggested by the limited available data,[22,25] is the most obvious explanation for these differences. Of the American Indian miners in the Colorado Plateau investigation, 62 per cent had never smoked, and the median consumption by smokers was only four cigarettes per day.[11] Of a sample of adult Navajos admitted to the Phoenix Public Health Service Indian Hospital from 1961 through 1965, only 4.3 per cent smoked more than one pack of cigarettes daily.[26] In a 1977 survey of Navajos, only 13 per cent smoked and only 6 per cent of the smokers consumed at least one pack daily.[27]

The present investigation thus offers an assessment of the role of a single occupational risk factor, uranium mining, in a population at low risk for lung cancer. Case ascertainment through a population-based tumor registry for the Navajo tribe facilitated examination of the effects of this exposure in the entire tribe in this study, unlike previous studies.[11,12]

The association between uranium mining and lung cancer among the Navajos was strong, with a lower 95 per cent confidence limit of 14.4 for the relative risk. In fact, 72 per cent of the cases (23 of 32) are attributable to this industry. For all male Navajos, the average annual age-adjusted incidence rate of lung cancer for the period 1969-1981 was 16.6 per 100,000. Exclusion of the affected uranium miners lowered the rate to 5.2 per 100,000. This finding demonstrates that in a population at low risk for a specific cancer, exposure to a single risk factor may have readily detectable consequences and cause the majority of cases.

Bias cannot satisfactorily explain the results, although selection and information bias are possible. With regard to selection bias, the diagnosis of lung cancer may be more vigorously pursued in younger men with a history of uranium mining. However, in the younger age groups in which the proportion of cases attributable to uranium mining is highest, contact with medical care and intensity of evaluation were probably comparable for miners and non-miners. With regard to information bias, death certificates and the New Mexico Tumor Registry abstracts provided more complete occupational information for the cases. The Public Health Service censuses, however, were the major source used for identifying uranium miners. These censuses were prospectively collected and uniformly applied to cases and controls. Because of the size of the Public Health Service study group (n = 780), we expected to find that several controls had worked as uranium miners. The failure to identify any exposed controls may reflect better occupational information for cases or may have resulted from chance. Nevertheless, even if several controls had been uranium miners, the relative risk associated with this exposure would have remained high.

Differing smoking habits of cases and controls also cannot explain the effect of uranium mining. Because smoking histories were unavailable for controls, we could not directly assess the relative risk associated with cigarette smoking. In other populations, the relative risk for smokers of less than one pack per day ranges from approximately 2 to 10.[28] With a formula derived from a prospective study of British doctors,[29] we have calculated that the relative risk of lung cancer associated with smoking three cigarettes daily, the average consumption of affected Navajos who smoked, was only 2.3.

This investigation provides confirmation that uranium mining, without cigarette smoking, increases the risk of lung cancer in human beings. In animal models, inhalation of radon daughters alone causes respiratory neoplasms.[30,31] Supporting epidemiologic evidence has been available from few populations, including Colorado Plateau miners[1,11,12] and Swedish metal miners.[32,33] Smoking was probably not a prevalent risk factor among the early Schneeberg and Joachimsthal miners either, but documentation of their smoking habits is unavailable.[1,3]

Further follow-up will be needed for a complete characterization of the consequences of uranium mining in Navajos. The affected Navajos in this study were primarily younger men who began mining in the early 1950s. Exposure levels have declined since that

time,[14] and a federal standard of 4 WLM annually was implemented in 1971. More recent miners should have lower risks. However, the number of lung-cancer cases in Navajo uranium miners did not decline from 1969 through 1981, and more cases must be anticipated as these early miners age.

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References

1. Lundin FE Jr, Wagoner JK, Archer VE. Radon daughter exposure and respiratory cancer: quantitative and temporal aspects. Washington, D.C.: United States Department of Health, Education, and Welfare, June 1971. NIOSH NIEHS joint monograph no. 1.
2. Committee on the Biological Effects of Ionizing Radiations. The effects on populations of exposure to low levels of ionizing radiation. Washington, D.C.: National Academy of Sciences, 1980.
3. Myers DK, Stewart CG, Johnson JR. Review of epidemiological studies on hazards of radon daughters. In: Gomez M, ed. International conference: radiation hazards in mining: control, measurement, and medical aspects. New York: American Institute of Mining, Metallurgical, and Petroleum Engineers, Inc., 1981:513-24.
4. Chenoweth WL. Historical review of uranium-vanadium production in the northern and western Carrizo mountains, Apache County, Arizona. Grand Junction: United States Department of Energy, January 1980.
5. *Idem*. Historical review of uranium-vanadium production in the eastern Carrizo mountains, San Juan County, New Mexico and Apache County, Arizona. Grand Junction: United States Department of Energy, November 1980.
6. Holaday DA, David WD, Doyle HN. An interim report of a health study of the uranium mines and mills. Federal Security Agency, Public Health Service, and Colorado State Department of Public Health. May 1952.
7. Holaday DA. History of the exposure of miners to radon. Health Phys 1969; 16:547-52.
8. Occupational health hazards of older workers in New Mexico. Washington, D.C.: Government Printing Office, 1980. (Hearing before the Special Committee on Aging, United States Senate).
9. Kay J. Long-dead uranium mines strike Navajos from grave. Arizona Daily Star 1981 Aug 16.
10. Stanton KL. Uranium: in the atom's shadow. Arizona Republic 1982 Dec 5-10.
11. Archer VE, Gillam JD, Wagoner JK. Respiratory disease mortality among uranium miners. Ann NY Acad Sci 1976; 271:280-93.
12. Gottlieb LS, Husen LA. Lung cancer among Navajo uranium miners. Chest 1982; 81:449-52.
13. Young JL Jr, Percy CL, Asire AJ, eds. Surveillance, epidemiology, and end results: incidence and mortality data, 1973-77. Natl Cancer Inst Monogr 1981; 57:1-1082.
14. Samet JM, Morgan MV, Buechley RW, Key CR, Valdivia AA. Study of Grants, New Mexico, uranium miners: current status. In: Gomez M, ed. International conference: radiation hazards in mining: control, measurement, and medical aspects. New York: American Institute of Mining, Metallurgical, and Petroleum Engineers, Inc., 1981:363-8.
15. Schlesselman JJ. Case-control studies: design, conduct, analysis. New York: Oxford University Press, 1982.
16. Gart JJ. Point and interval estimation of the common odds ratio in the combination of 2×2 tables with fixed marginals. Biometrika 1970; 57:471-5.
17. United States Indian Health Service. Selected vital statistics for Indian Health Service areas and service units, 1972 to 1977. Washington, D.C.: Government Printing Office, 1979. (DHEW publication no. (HSA)79-1005).
18. Smith RL. Recorded and expected mortality among the Indians of the United States with special reference to cancer. JNCI 1957; 18:385-96.
19. Creagan ET, Fraumeni JF Jr. Cancer mortality among American Indians, 1950-67. JNCI 1972; 49:959-67.
20. Dunham LJ, Bailar JC III, Laqueur GL. Histologically diagnosed cancers in 693 Indians of the United States, 1950-65. JNCI 1973; 50:1119-27.
21. Reichenbach DD. Autopsy incidence of diseases among southwestern American Indians. Arch Pathol 1967; 84:81-6.
22. Sievers ML, Cohen SL. Lung cancer among Indians of the southwestern United States. Ann Intern Med 1961; 54:912-5.
23. Samet JM, Key CR, Kutvirt DM, Wiggins CL. Respiratory disease mortality in New Mexico's American Indians and Hispanics. Am J Public Health 1980; 70:492-7.
24. Smith RL, Salsbury CG, Gillian AG. Recorded and expected mortality among the Navajo, with special reference to cancer. JNCI 1956; 17:77-89.
25. Muggia AL. Diseases among the Navajo Indians. Rocky Mt Med J 1971; 68:39-49.
26. Sievers ML. Cigarette and alcohol usage by southwestern American Indians. Am J Public Health 1968; 58:71-82.
27. DeStefano F, Coulehan JL, Wiant MK. Blood pressure survey on the Navajo Indian Reservation. Am J Epidemiol 1979; 109:335-45.
28. Office on Smoking and Health. The health consequences of smoking: cancer. Washington, D.C.: Office on Smoking and Health, 1982. (DHHS publication no. (PHS) 82-50179).
29. Doll R, Peto R. Cigarette smoking and bronchial carcinoma: dose and time relationships among regular smokers and lifelong non-smokers. J Epidemiol Community Health 1978; 32:303-13.
30. Chameaud J, Perraud R, Masse R, Lafuma J. Contribution of animal experimentation to the interpretation of human epidemiological data. In: Gomez M, ed. International conference: radiation hazards in mining: control, measurement, and medical aspects. New York: American Institute of Mining, Metallurgical, and Petroleum Engineers, Inc. 1981:222-7.
31. Chameaud J, Perraud R, Lafuma J, Masse R, Pradel J. Lesions and lung cancers induced in rats by inhaled radon 222 at various equilibriums with radon daughters. In: Karbe E, Park JF, eds. Experimental lung cancer: carcinogenesis and bioassays. New York: Springer-Verlag, 1974:411-21.
32. Axelson O, Sundell L. Mining, lung cancer and smoking. Scand J Work Environ Health 1978; 4:46-52.
33. Edling C, Axelson O. Quantitative aspects of radon daughter exposure and lung cancer in underground miners. Br J Ind Med 1983; 40:182-7.