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Lung Cancer in a Nonsmoking Underground Uranium Miner

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Working in mines is associated with acute and chronic occupational disorders. Most of the uranium mining in the United States took place in the Four Corners region of the Southwest (Arizona, Colorado, New Mexico, and Utah) and on Native American lands. Although the uranium industry collapsed in the late 1980s, the industry employed several thousand individuals who continue to be at increased risk for developing lung cancers. We present the case of a 72-year-old Navajo male who worked for 17 years as an underground uranium miner and who developed lung cancer 22 years after leaving the industry. His total occupational exposure to radon progeny was estimated at 506 working level months. The miner was a life-long nonsmoker and had no other significant occupational or environmental exposures. On the chest X-ray taken at admission into the hospital, a right lower lung zone infiltrate was detected. The patient was treated for community-acquired pneumonia and developed respiratory failure requiring mechanical ventilation. Respiratory failure worsened and the patient died 19 days after presenting. On autopsy, a 2.5 cm squamous cell carcinoma of the right lung arising from the lower lobe bronchus, a right broncho-esophageal fistula, and a right lower lung abscess were found. Malignant respiratory disease in uranium miners may be from several occupational exposures; for example, radon decay products, silica, and possibly diesel exhaust are respiratory carcinogens that were commonly encountered. In response to a growing number of affected uranium miners, the Radiation Exposure Compensation Act (RECA) was passed by the U.S. Congress in 1990 to make partial restitution to individuals harmed by radiation exposure resulting from underground uranium mining and above-ground nuclear tests in Nevada. **Key words:** mining, lung cancer, occupational lung disease, radon. *Environ Health Perspect* 109:305–309 (2001). [Online 5 March 2001]

<http://ehpnet1.niehs.nih.gov/docs/2001/109p305-309mulloy/abstract.html>

A 72-year-old Navajo male with a 2–3 month history of increased cough, shortness of breath, decreased appetite, and an 18-pound weight loss was admitted to a rural Indian Health Service hospital. His diagnosis at the time of admission was right lower-lobe pneumonia (Figure 1). After 10 days of broad-spectrum antibiotics and with progressing infiltrates, a computed tomography scan of the chest revealed a right lung abscess, a tracheo-esophageal fistula, and a right pleural effusion. Worsening respiratory distress (Figure 2) required intubation and ventilatory support, and the patient was transferred to the University Hospital, Albuquerque, New Mexico.

Because the patient spoke only Navajo, his history was obtained through translation from his son. The patient's past medical history included hypertension, degenerative joint disease, hypercholesterolemia, history of a positive PPD (purified protein derivative; tuberculin) skin test, no surgical history, and

no drug allergies. His only current medication was lisinopril. He had been treated with isoniazid in 1972 for an unknown length of time, and retreated in 1974 and in 1986 due to the uncertain duration of isoniazid therapy. The patient was a lifelong nonsmoker, he did not use other tobacco products, and he had no history of alcohol abuse. His family history was noncontributory.

The patient lived alone in housing without running water or electricity in an isolated area of the Navajo Reservation in Arizona. His son reported that the patient had started to experience significant emesis after eating approximately 6 months before his hospitalization. He had lost 30–40 pounds from the time these symptoms began. The patient at first remained active and often herded sheep in the hills near his home. His family thought his weight loss was due to his lack of nutritious food when he was herding. The patient had been a uranium miner for 17 years from 1950 to 1968. He worked in seven different

underground mines primarily on the Navajo Reservation. He worked as a driller and general laborer, shoveling ore into wheelbarrows or ore cars and hauling the ore out of the mine by wheelbarrow. During his employment he worked underground without any personal protection equipment. On one occasion, he described nearly fainting after inhaling smoke from a blast in a mine. His total exposure to radon progeny as a uranium miner was 506 working level months (WLM). The highest single-year exposure was 82 WLM.

At the University Hospital, bronchoscopy and endoscopy revealed a broncho-esophageal fistula. Biopsies of the esophagus showed a poorly differentiated squamous cell carcinoma, which was determined to be unresectable (Figure 3). The patient had progressive respiratory compromise, decreased blood pressure, and bradycardia, which progressed to asystole. The patient expired 19 days after presenting to the referring hospital.

Autopsy findings included a patent broncho-esophageal fistula measuring 1.0×1.5 cm on the esophageal side and 1.0×1.8 cm on the right lower lobe bronchus, a 2.5 cm squamous cell carcinoma of the right lung arising from the lower lobe bronchus (Figure 4), and invasion of the esophageal submucosa by the squamous cell carcinoma. There were no asbestos bodies noted in the lung tissue, but there were occasional polarizable foreign bodies, consistent with silica particles.

Discussion

The history of uranium mining on the Navajo Reservation has its roots in 18th-century Europe. In 1789 uranium oxide was

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D.S.J. was supported by a grant from the National Heart, Blood, and Lung Institute, National Institutes of Health (HL02949).

Received 27 July 2000; accepted 30 October 2000.

extracted from pitchblende, a uranium-containing ore discovered in Bohemia. Named after the planet Uranus, uranium was first used in pottery glazes and iridescent glass. By the late 1890s, Antoine-Henri Becquerel and Marie and Pierre Curie had discovered the radioactive elements contained within uranium ore, and radium isolated by Marie Curie from uranium-containing ores was thought to hold promise for curing cancer (1).

In 1898, while on an archaeological expedition to the southwestern region of the United States, John Wetherill recognized the significance of the yellow crumbly mineral formations on the Colorado Plateau. News of the new valuable mineral carnotite, containing both uranium and vanadium (used to harden steel), had reached the United States (2). During World War I there was a dramatic increase in the use of radium for luminous paint for nighttime warfare machinery, and Congress was continually pressured to open tribal lands for mineral development leases. In 1919, authorization for the Secretary of the Interior to open Indian lands to prospecting and mining was added to a Bureau of Indian Affairs bill (2).

Revisions in the mining leasing agreements on tribal lands and changes in the laws that governed the development of vanadium and uranium on the Navajo Reservation during the late 1930s allowed a rapid increase of mining operations by the 1940s. When Hitler invaded Czechoslovakia, the richest known source of uranium fell into German hands. Scientists who had fled Germany warned the U.S. government of the possibility of Germany producing an atom bomb. The U.S. government, led by Franklin D. Roosevelt, started a program for military research on uranium; in January 1942, the Manhattan Project was born.

The U.S. government demand for uranium spurred a boom in uranium milling and mining in the Colorado Plateau and Four Corners region, a large area of land in New Mexico, Arizona, Utah, and Colorado that encompasses the Navajo and Hopi Nations (Figure 5) (3). From the 1940s through the 1960s there were 2,500 uranium mines and four uranium mills both on and off the Navajo Reservation (Figure 5) (4–6). There were up to 3,000 Navajo miners and millers. Since the 1980s when the market for U.S.-mined uranium collapsed, there has been little mining activity in underground or surface operations. *In situ* leach mining is taking place in some states, but it is not known whether there will be extensive underground or surface mining of uranium in the near future. Uranium is still being mined in countries such as Czechoslovakia, the former German Democratic Republic (GDR), China, Namibia, the former Soviet Union,

and Canada. Long-term medical problems among these miners are significant. Kreuzer et al. (7) reported that among 64,000 uranium miners in East Germany (GDR) who worked between 1946 and 1989, there have been 1,436 lung cancer deaths, with a total of 3,000 lung cancer deaths expected by the year 2002 (7).

Mining operations in the early years involved drilling holes in the soft sandstone rocks, blasting, and hand loading the ore into bins; the ore was then loaded into trucks and hauled to the mills for processing. The miners often went back into the mines immediately after the blasting operation where they were exposed to dust and smoke. Few underground mines at that time had adequate ventilation, and miners described thick smoke that made them acutely ill and long hours of working in heavy dust conditions.

An underground mine is a unique, complicated, and potentially hazardous environment for the worker. Work is often performed under adverse conditions of excessive heat or cold, water and mud, uneven walking surfaces, poor lighting, and confined, often limited work areas. Underground miners are at risk for several occupational injuries and illnesses. Musculoskeletal-, hearing-, and respiratory-related injuries and illnesses are the most common. Traumatic injuries can result from crush-type injuries from machinery, from falls, from electrical injuries, or from material falling from the roof or vertical walls of the mine. Rates of injuries in miners are some of the highest in any occupation (8). Fortunately, injuries and deaths from explosions have dramatically decreased in the past half-century. The average annual fatality rate from all causes has declined from 329/100,000 miners during 1911–1915 to 25/100,000 miners during 1996–1997 (9). Miners are at risk for degenerative arthritis from the long-term sequelae of acute traumatic injuries and repetitive motion injuries (10). Noise from machinery, drilling, and blasting can result in noise-induced hearing impairment or loss. A recent analysis of audiograms for a large

cohort of noise-exposed miners by the National Institute for Occupational Safety and Health revealed that 90% of the U.S. miners studied have hearing impairment by 50 years of age as compared to 10% of the general population (11).

Exposure to dust, gases, exhaust, and fumes can result in nonmalignant or malignant respiratory disease in underground miners. Chronic exposure to inorganic dusts can result in a fibrotic process in the lung parenchyma. This form of pneumoconiosis is typically diagnosed by chest X-ray. Uranium ores are often found in silica-containing deposits. Silicosis has been observed in 9% of uranium miners (12). Underground uranium miners may be at risk for diffuse fibrotic lung disease that is different from silicosis, but the cause of this type of damage is not clear. Animal studies show that radon-decay product exposure can result in pulmonary fibrosis and emphysema (13). In a recently reported case series of pulmonary fibrosis in uranium miners, Archer et al. (14) argue that this fibrosis is most likely due to exposure to radiation from the radon decay products. Another likely cause of pulmonary fibrosis in underground uranium miners is a fibrotic effect of the inorganic silica dust. Silica dust and coal dust can result in a more diffuse fibrotic process on the chest X-ray, rather than the more commonly observed or classically described discrete nodular lesions of silicosis and coal workers' pneumoconiosis (15,16). Inorganic dusts such as silica can also damage the airways. Underground uranium miners



Figure 1. Chest radiograph on admission. An infiltrate is visible in the right lower lung field.



Figure 2. Chest radiograph on day 11 of the hospital stay. There has been progression since the admitting radiograph, with more extensive airspace disease in the right lower lung fields and new changes in other regions of the right and left lung. There is an abnormal amount of air in the stomach and bowel despite placement of an enterogastric tube as a consequence of a broncho-esophageal fistula. A right chest tube is in place.

are at increased risk for developing obstructive lung disease (17). Mortality in underground miners is greater than average for nonmalignant respiratory diseases in general, and specifically for pneumoconiosis, tuberculosis, and lung cancer (18,19); the increased risk of silico-tuberculosis among miners has been well established (20). Studies among various groups of miners have indicated a relative risk of tuberculosis of 1.5–10. Even in the absence of radiographic evidence of silicosis, there is an increase in incidence of tuberculosis among workers exposed to silica (21).

Malignant respiratory disease in underground miners may result from several different exposures. Arsenic and silica dust in the mined ores, diesel exhaust from mining machinery, and radon and its decay products are all suspected or known carcinogens that can occur in the mining environment. The respiratory carcinogenic effect of silica has been debated (22–24). However, in 1996 the International Agency for Research on Cancer (IARC), after reviewing epidemiologic and experimental studies on the link between silica exposure and lung cancer, classified inhaled crystalline silica as a class 1 human carcinogen (25). IARC (25) reports the relative risk (RR) of 1.02–5.38 in studies of miners. In a recent review, however, Checkoway and Franzblau (26) point out the uncertainty in the existing epidemiologic literature as to whether silicosis is a necessary co-condition for silica-related lung cancer. Previous reviews have indicated that lung cancer risks are highest for workers with silicosis who have received the highest doses [RR = 2.3, confidence interval (CI), 2.2–2.4, across 19 studies] (27). Diesel exhaust is considered a probable human carcinogen by IARC (28). The epidemiologic evidence has rested on studies of lung cancer among bus drivers, truck drivers, shipyard workers, and railroad workers. In a recent study, Steenland et al. (29) report a significant positive trend in lung cancer risk among truck drivers with increasing cumulative exposure (a lifetime excess risk of lung cancer of 1–2% above the background risk of 5%). Although no excess mortality rate in lung cancer has been observed between miners working in mines with diesel and those without, the Mine Safety and Health Administration is considering regulating levels of diesel exhaust. This is based on the fact that miners may be exposed to diesel exhaust particle concentrations similar to levels that have induced lung cancer in mice and rats (30).

The greatest occupational risk factor for lung cancer in underground uranium miners is exposure to radon decay progeny. Radon is a clear, odorless gas that has a half-life of 3.82 days. Its decay to lead-210 is associated with the production of alpha particles that

are capable of damaging DNA in respiratory cells. Radon exposure is reported in WLMs. One working level (WL) is any combination of radon progeny in 1 L air that ultimately releases 1.3×10^5 MeV of alpha energy during decay (31). Exposure to 1 WL for 170 hours equals 1 WLM, which is the average number of hours a miner would work underground in 1 month (32). The concentration of radon found in a typical home is 50–100 times less than the lowest level found in uranium mines (33). In an average home the annual WLM is 0.2 and a lifetime exposure is 10–20 WLM. In an analysis of 11 studies on underground uranium miners, the average WLM was 158 (34). In a study of Colorado Plateau underground uranium miners who had worked before 1974, WLM exposures ranged from 465 to 16,467 in miners who developed lung cancer and did not smoke (18). The current limit for miners is 4 WLM/year (35). The lifetime risk of lung cancer in nonsmokers is $\leq 1\%$ (36). The risk of lung cancer in miners who have never smoked tobacco increases with age. The risk of lung cancer for a 72-year-old male (the age of the patient presented here) who had no occupational exposure would be approximately 0.3/1,000 person-years (37). The lung cancer risk resulting from an occupational exposure to radon progeny of 506 WLM is approximately 3/1,000 person-years, 100 times higher than the individual without occupational exposure (37).

On average, underground uranium miners have mortality rates from lung cancer that are 3.6 times those of nonminers (32). For underground uranium miners, it has been estimated that 70% of lung cancer deaths in nonsmoking miners and 40% of lung cancer deaths in smoking miners are due to exposure to radon progeny (33). For the same cumulative dose of radon, miners who were exposed at lower doses over a longer period have a higher risk of developing lung cancer than those exposed over a shorter period (32). This effect is called the inverse dose–rate effect. The age at which the miner

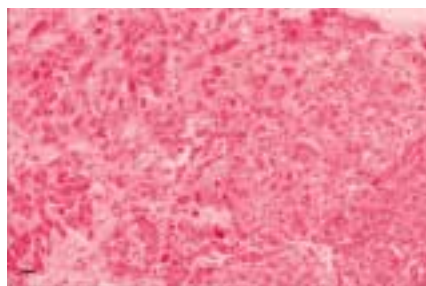


Figure 3. Esophageal biopsies taken during endoscopy. The mucosa is replaced by diffuse sheets of atypical epithelial cells with abundant eosinophilic cytoplasm. Numerous mitoses are present. Bar = 10 μ m.

was first exposed to radon does not appear to have an effect on the risk for developing lung cancer. In a study examining mortality in Navajo uranium miners, the mean age at death for the 34 miners who died from lung cancer was 53 years (range 33–81), the mean time since the first exposure was 27 years (range 13–45 years), and the mean WLM was 1,517 (range 30–3,896) (19) (Figure 6). Approximately 59% of the Navajo miners who died had never smoked tobacco (19). Miners who smoke and who also are exposed to radon have a relative risk of lung cancer that is between the sum (additive) and the product (multiplicative) of the two individual risks (32,38). The risk of lung cancer decreases after the exposure ceases. On average, the risk decreased by 50% 15 years after the exposure ceased (38). There are no marked differences in the cell type of primary lung cancer resulting from radon exposure in underground miners compared to cancers resulting from cigarette smoking. Underground uranium miners are not at increased risk for nonrespiratory malignancies from radon exposure (39).

Other behavioral and environmental factors can modify the risk of developing cancer from occupationally related carcinogens. A multicenter case–control study of diet and lung cancer among nonsmokers showed a protective effect with high consumption of tomatoes, lettuce, carrots, margarine, and cheese; only weak protective effects are linked to high consumption of carotenoids, β -carotene, and retinol (40). With high consumption of fruits, protective effects were seen for squamous cell carcinoma [odds ratio (OR) = 0.7; 95% CI, 0.4–1.2] and small cell carcinoma (OR = 0.9; 95% CI, 0.6–1.3). Excess risk for squamous and small cell carcinomas was associated with high meat, butter, and egg consumption. In a study examining

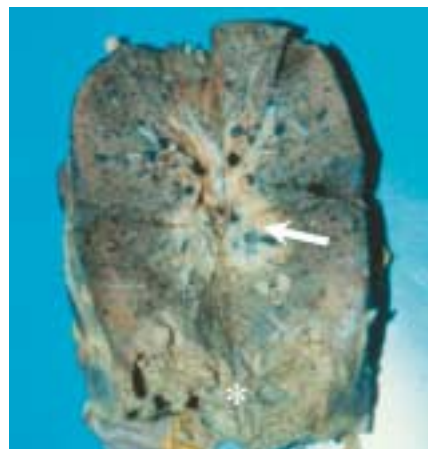


Figure 4. Whole right lung specimen at autopsy showing tumor (pale color) in the central, hilar region (arrow) and an abscess in the right lower lobe (asterisk).

cattle that grazed in regions of underground uranium mines and mills in New Mexico, Lapham et al. (41) reported elevated levels of radon progeny in muscle, liver, kidney, and bone tissue as compared to animals from another location. The calculated radiation dose was low in humans, however, unless large quantities of liver or kidney were ingested, and the public health risks were estimated as minimal (41).

In 1990, the Radiation Exposure Compensation Act (RECA) (42) was passed by the U.S. Congress to make partial restitution to individuals harmed by radiation exposure resulting from above-ground nuclear tests in Nevada and from uranium mining. The act was amended in 1999 and 2000. Miners who worked in underground or surface mines in Arizona, Colorado, Idaho, New Mexico, North Dakota, Oregon, South Dakota, Texas, Utah, Washington, or Wyoming between 1 January 1942 and 31 December 1971 are eligible. Also eligible are uranium mill workers or ore transporters. The years of eligibility cover the period that the U.S. Government was the sole purchaser of uranium (1942–1971). For uranium miners, compensated diseases are *in situ* and primary lung cancer and nonmalignant respiratory diseases. The nonmalignant respiratory diseases include pulmonary fibrosis, pneumoconiosis, silicosis, and cor pulmonale. Miners are required to show that they have been exposed

to radiation doses of ≥ 40 WLM. Uranium mill workers and ore transporters are also eligible if they have developed renal cancer or other chronic renal diseases including nephritis and renal tubular disease.

To be eligible for compensation under RECA, written medical documentation is required as proof of all conditions. For non-malignant diseases, biopsy or chest imaging documentation is required. Chest X-rays must be interpreted by two B-readers according to the 1980 International Labor Organization (ILO) standard for pneumoconiosis (43). Parenchymal abnormalities of a severity or profusion of 1/0 or greater is the criteria used for establishing disease. Computed tomography findings consistent with pneumoconiosis are also acceptable to establish the presence of disease. In addition to biopsy or chest imaging documentation of nonmalignant disease, spirometry or arterial blood gas studies are required. Qualifying spirometry values are a forced expiratory volume in the first second or forced vital capacity of $\leq 80\%$ of predicted using the Knudsen 1983 lung function predicted equations (44). Arterial blood gas (ABG) values must meet or be lower than those published in “Claims under the Radiation Exposure Compensation Act” (45). Arterial blood gas values meeting the criteria are based on the partial pressure of carbon dioxide (P_{CO_2}) and the altitude. To qualify, the partial pressure of oxygen (P_{O_2})

should be ≤ 75 mmHg for an ABG obtained at an altitude of 0–2,999 feet and a P_{CO_2} of 30 mmHg; for the same ABG obtained at an altitude of $\geq 3,000$ feet, the P_{O_2} should be ≤ 70 mmHg.

The amount of the compensation award for uranium miners who qualify or their survivors is \$100,000. Since the passage of RECA in 1990–1998, there have been 1,405 claims approved for uranium miners and 1,429 claims have been denied (46). It has been difficult for some former uranium miners to document their exposures. Radon monitoring may not have been performed consistently or at all in some mines, particularly in small operations. Variability in the B-reading interpretation of the chest X-ray for pneumoconiosis has been problematic. Because a large number of former uranium miners in the southwestern United States were Hispanic or Native American, the frequent lack of ethnic or race-specific lung function prediction equations can bias against some miners (17). Access to diagnostic resources, distance to primary care, and disease recognition and its cause in remote, rural areas of the Navajo Nation has also contributed to difficulties in obtaining compensation among the Navajo miners and their families.

Conclusion

We have presented the case of a nonsmoking former underground uranium miner who died from complications resulting from a primary lung cancer 22 years after leaving the industry. His risk of developing lung cancer due to radon progeny was 100-fold greater than if he had never mined uranium.

Workers such as our patient may be compensated under RECA, which was recently amended to compensate not only former underground uranium miners but also surface miners, millers, and uranium ore transporters for malignant and nonmalignant respiratory diseases. Uranium millers and ore transporters with certain malignant

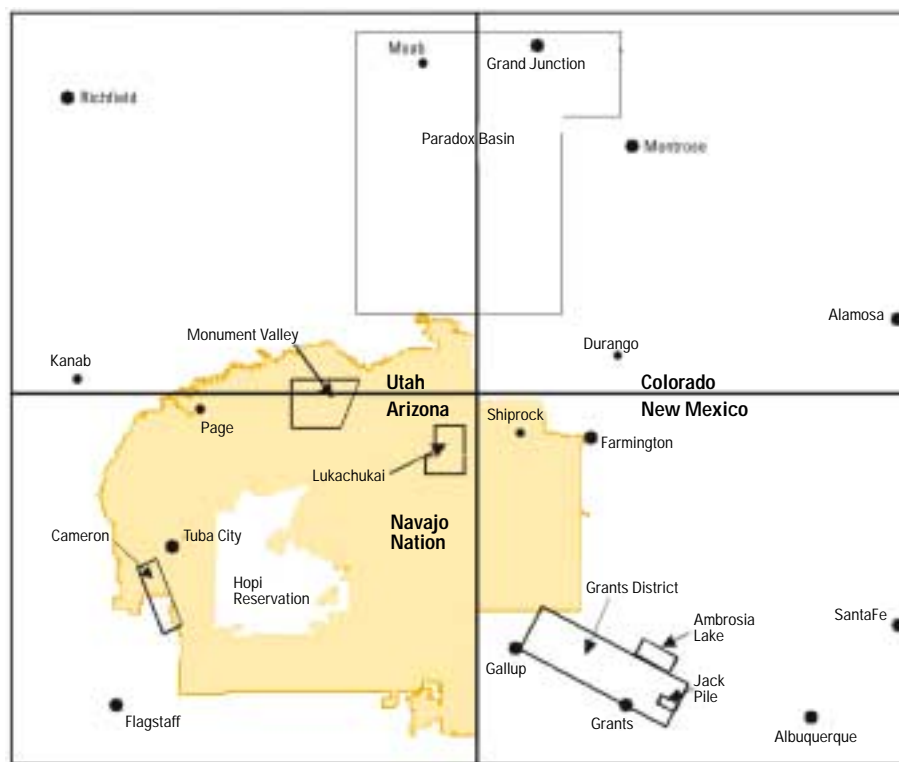


Figure 5. Map of the Four Corners region of the United States showing the location of the Navajo Nation. Regions of uranium mining are indicated with boxes. Information from Baars (5) and the Energy Information Administration (6).

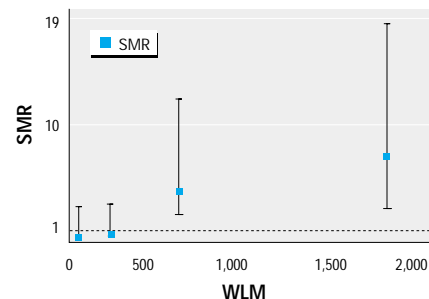


Figure 6. Standardized mortality ratios (SMRs) for lung cancer for Navajo uranium miners from the Colorado Plateau. Error bars indicate median WLM and lower and upper 95% confidence intervals. Data from Roscoe et al. (19).

and nonmalignant diseases of the kidney are also eligible.

There has been little mining of uranium in the United States since the late 1980s, but if uranium mining increases in the future, the health and safety of all workers in uranium mines (underground and surface miners millers, and uranium ore transporters) should be protected.

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