FAST TRACK

The Presence of Asbestos in the Natural Environment is Likely Related to Mesothelioma in Young Individuals and Women from Southern Nevada

Francine Baumann, PhD, Brenda J. Buck, PhD,† Rodney V. Metcalf, PhD,† Brett T. McLaurin, PhD, ‡ Douglas J. Merkler, MSc,§ and Michele Carbone, MD, PhD**

Background: Inhalation of asbestos and other mineral fibers is known causes of malignant mesothelioma (MM) and lung cancers. In a setting of occupational exposure to asbestos, MM occurs four to eight times more frequently in men than in women, at the median age of 74 years, whereas an environmental exposure to asbestos causes the same number of MMs in men and women, at younger ages.

Methods: We studied the geology of Nevada to identify mineral fibers in the environment. We compared MM mortality in different Nevada counties, per sex and age group, for the 1999 to 2010 period.

Results: We identified the presence of carcinogenic minerals in Nevada, including actinolite asbestos, erionite, winchite, magnesioriebeckite, and richterite. We discovered that, compared with the United States and other Nevada counties, Clark and Nye counties, in southern Nevada, had a significantly higher proportion of MM that occurred in young individuals (<55 years) and in women.

Conclusions: The elevated percentage of women and individuals younger than 55 years old, combined with a sex ratio of 1:1 in this age group and the presence of naturally occurring asbestos, suggests that environmental exposure to mineral fibers in southern Nevada may be contributing to some of these mesotheliomas. Further research to assess environmental exposures should allow the development of strategies to minimize exposure, as the development of rural areas continues in Nevada, and to prevent MM and other asbestos-related diseases.

Key Words: Mesothelioma, Environmental exposure, Asbestos, Lung cancer, Mineral fibers.

(*J Thorac Oncol.* 2015;10: 731–737)

*Cancer Center, University of Hawaii, Honolulu, Hawaii; †Department of Geoscience, University of Nevada Las Vegas, Las Vegas, Nevada; ‡Department of Environmental, Geographical and Geological Sciences, Bloomsburg University of Pennsylvania, Pennsylvania; and §USDA, Natural Resources Conservation Service, Las Vegas, Nevada

This work was supported by National Institute of Health (grant numbers R01CA106567, P01CA114047, and P30CA071789) and the University of Hawai'i Foundation, which received donations to support mesothelioma research from Honeywell International Inc., to M. Carbone.

M. Carbone has pending patent applications on BAP1 and provides consultation for mesothelioma expertise and diagnosis. The remaining authors declare no competing financial interests.

Address for correspondence: Francine Baumann, PhD, University of Hawaii Cancer Center, 701 Ilalo Street, Honolulu, HI 96813. E-mail: fbaumann@cc.hawaii.edu

DOI: 10.1097/JTO.0000000000000506

ISSN: 1556-0864/15/1005-0731

Malignant mesothelioma (MM) is a rare and highly fatal form of cancer of the pleura or more rarely, peritoneum or pericardium[1] that is caused by the inhalation of asbestos and other mineral fibers. Median survival is 6 to 12 months from diagnosis.[2,3] In 1997, the International Expert Meeting on Asbestos, Asbestosis, and Cancer estimated that around 10,000 MM and 20,000 lung cancer cases are attributable each year to asbestos in Western Europe, North America, Japan, and Australia.[4] In the United States, there are around 3200 new MM cases every year with an annual incidence of 5.8 cases per million in states with no commercial asbestos use and up to 16.5 cases per million in the states where asbestos was used industrially in large amounts.[5] These numbers reflect a significant increase in MM during the past 40 years in men, whereas rates in women have not significantly increased, as they are rarely occupationally exposed to asbestos.[1,5,6]

The MM male-to-female (M/F) sex ratio ranges from 4:1 to 8:1, the highest in countries with asbestos industry.[7] Instead, a sex ratio of 1:1 is found when MM are caused by environmental exposure and genetics.[8] In the United States, the median age at diagnosis is 74 years, as most MMs develop because of occupational exposure to asbestos and the mean latency from exposure is 30 to 50 years.[9,10] During the years 1999 to 2005, MMs in individuals younger than 55 years represented only 6.7%.[9] Because of the long latency from the time of exposure to the development of MM, MMs in individuals younger than 55 years are rarely associated with occupational exposure.[8] Instead, these MMs are related to exposure since childhood, such as environmental exposure or secondary exposure to occupationally exposed family members.[10] Thus, MM in young individuals and increased MM rates in women, and particularly a M/F ratio less than 3:1, are indicators of environmental exposures to mineral fibers.[10–12]

Asbestos also causes other cancers, in particular more lung cancers than MMs[13]; however, the risk of lung cancer attributable to asbestos is difficult to estimate[14] because of the confounder of cigarette smoking.

Asbestos is a commercial and regulatory term applied to six fibrous silicate minerals historically mined for industrial use.[8] Most research efforts have focused on occupational exposure to asbestos and have demonstrated their carcinogenicity in animals and humans. However, environmental exposure to other nonregulated mineral fibers can also cause MM and other diseases.[8,15] Documented examples include exposure to erionite

in the Cappadocia region of Turkey;[16–19] exposure to the amphibole minerals winchite, richterite, and magnesioriebeckite at Libby, Montana, United States[20–25]; and exposure to antigorite in New Caledonia.[8,15] All these exposure have been linked to the development of MM in humans. These mineral fibers share some physical and biological properties that are thought to contribute to their carcinogenicity, such as a fibrous shape (length/diameter [aspect] ratio >3:1), a high surface area, and a width of less than 0.25 μm,[26] because ultrathin fibers are more likely to reach the pleura[27] and to resist biological degradation.[28,29]

Naturally occurring asbestos (NOA) is a term used to describe fibrous minerals that may or may not meet the regulatory definitions of asbestos but are natural components of rocks and soils.[30] Areas with NOA in soils and sediments are a potential source of exposure for nearby populations especially if these fibers become airborne through natural erosion or human activities producing dust: mines, quarries, roads, and outside activities.[8] Increasing road traffic in rural areas and other dust producing activities are also causing exposure to NOA to a growing number of people.[8,18] In arid and semiarid climates, natural wind erosion can be a significant process for dust emissions, which can increase fiber exposures.[31] Such exposures can occur since birth, resulting in MM in young individuals, in both genders.[32,33] NOA presents a significant health risk primarily where the close proximity of NOA occurrences to large populations provides a pathway for human exposure.

Because of both anecdotal reports of MM in young individuals in southern Nevada and the recent finding of NOA in soil, dust, and air near the Las Vegas metropolitan area,[34,35] we tested the hypothesis that MM would be increased in that region in a pattern consistent with environmental exposure.

MATERIALS AND METHODS

We studied several health indicators suggestive of a possible environmental exposure to carcinogenic mineral fibers, including increased proportion of female MMs and a higher percentage of MM in individuals under the age of 55 years.

We analyzed MM mortality data obtained from the Centers for Disease Control and Prevention (CDC) in United States for the period 1999 to 2010, by gender, by age group, and by county, which included a total of 31,526 MM cases. We also used data from the CDC to study MM incidence and death rates by state and by gender.[36] Because MM is a rare disease, confidence intervals (CIs) per county and per age groups were calculated assuming that the MM cases followed a Poisson distribution. Because of the small numbers, we grouped the two southern counties of Clark and Nye, defined here as southern Nevada, and compared the proportion of women and of young cases (<55 years old) in these two southern counties to those in all other Nevada counties grouped together. Percentages were compared between southern Nevada, all other Nevada counties, and all other U.S. counties, by using the Pearson χ^2 test with Yates correction or Fisher's exact test when the expected numbers were less than five, and were considered statistically significant when the p value was less than 0.05. Incidence and death rates are given with their 95% CI.

We compiled and integrated known presence of fibrous minerals in Nevada from published sources.[19,34,35,37–39] We used population data by county from the 2010 census (accessible at: http://www2.census.gov/geo/maps/dc10_thematic/2010_Profile/2010_Profile_Map_Nevada.pdf) to better interpret the potential for populations to come in contact with naturally occurring carcinogenic fibrous minerals. The 2010 census measured just over 2.7 million people in the state, with 74% living in Clark and Nye counties, southern Nevada (http://censusviewer.com/state/NV). The vast majority of the population in southern Nevada and the largest concentration of people in the entire state live in the Las Vegas metropolitan area. This includes the cities of Las Vegas, Henderson, North Las Vegas, and Boulder City with a population of over 1.9 million. Washoe County in northwestern Nevada has the next highest population, with over 400,000 people. Vast areas of central and northern Nevada have fewer than one person per square mile.

RESULTS

Mesothelioma Rates in Nevada

For the 2006 to 2010 period, Nevada has a global MM age-standardized incidence rate of 10 cases per million inhabitants per year (95% CI: 8–12).[36] This rate is similar to the mean U.S. rate (10 per million; 95% CI: 10–10) and places Nevada in a middle position among the states for MM incidence (minimum, 5 [Hawaii]; maximum, 15 [Alaska and Maine] MM cases per million in 2006–2010).[36] Nevada is not listed among the 15 states having produced asbestos or showing a high occupational exposure[40]; thus a standardized MM incidence of 10 per million in this state is unexpectedly high, compared with the background MM incidence of 5 per million in other U.S. states without known occupational exposure.[5,36]

The analysis of all MM deaths recorded in Nevada for the 1999 to 2010 period shows a constant mortality rate over these 12 years. To respect confidentiality, we cannot show detailed data per subgroup. In all Nevada counties, excluding the southern Nevada counties of Clark and Nye, the MM M/F ratio was 6.33:1, as expected when MM occurs prevalently in a setting of occupational exposure (Table 2). In contrast, in southern Nevada (Clark and Nye counties), the MM M/F ratio was significantly lower (2.69:1; $p = 0.0468$; Table 2). The southern Nevada MM sex ratio was also significantly lower compared with the United States (4.97:1; $p = 0.0422$; Table 2). The low sex ratio of MM in the southern Nevada counties cannot be explained by the characteristics of this population; the percentage of women was exactly the same (49.1% in 2000) in Clark and Nye counties and all other Nevada counties.

The percentage of MMs in individuals younger than 55 years—a possible indicator of environmental exposure—was significantly higher in the southern Nevada counties (11.28%) than in all other U.S. counties (6.21%; $p = 0.0249$; Table 2). These young cases were residents of Clark and Nye counties, southern Nevada, where we identified 21 MMs with a M/F ratio of 1:1 (11 males and 10 females), and the youngest cases being recorded in the age group of 15–19 years. No difference in the population distribution per age groups could explain the increased rate of young MM cases in Clark and Nye counties; compared with the other Nevada counties, in 2000, the 0–54 years age group in Clark

