



Familial Clustering of Mesothelioma: A Report on Three Affected Persons in One Family

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Pleural mesothelioma developed in at least three members of a family of first-degree relatives. Only one member had probable direct asbestos exposure. An analysis of these cases and their circumstances leads us to suspect that a latent genetic susceptibility may be present in this cancer-prone family. [Am J Prev Med 1986;2:186-8]

Some malignant and premalignant neoplasms, such as familial polyposis, retinoblastoma, malignant melanoma, and breast cancer, are known to be associated with genetic aberrations.¹⁻³ In addition, several investigators⁴⁻⁹ have described familial clusterings of specific cancers, including lung cancer, that implicate a genetic defect.

Mesothelioma, a rare neoplasm associated with asbestos exposure¹⁰ has been reported in two pairs of siblings: a sister and brother who had minimum household asbestos exposure during childhood and identical twin brothers who had been exposed to asbestos on their jobs for eight years.¹¹ Also, Lynch et al.¹² reported a family in which two brothers with prolonged occupational asbestos exposure manifested malignant mesotheliomas of similar histology. The occurrence of this rare neoplasm in three siblings led us to question whether a hereditary predisposing factor may be operational in this type of cancer. Here we describe a family of first-degree relatives in which pleural mesothelioma occurred in at least three members. Only one of these subjects possibly had direct asbestos exposure.

REPORT OF CASES

The proband, a 74-year-old woman, had papillary epithelioid mesothelioma of the pleura diagnosed by open biopsy at age 68 (Figure 1). There was no evidence of asbestos fibers on microscopic examination. Born and raised in Iberville Parish, a rural

Louisiana county, she had spent the previous 30 years in urban Orleans Parish. From ages 26 to 38 she worked as a clothing salesperson and candle-maker, after which she was a homemaker. She was a nonsmoker.

The proband's first husband worked as a laborer for a lumber and shingle company for ten years. The family lived within one mile of the company, which used asbestos insulating material as wrapping for its steam pipes. That husband died in an accident at the age of 33. Her second husband, who worked at the same lumber and shingle company for most of his life, died at age 65 of carcinoma of the lung. Both husbands had smoked about one pack of cigarettes a day since early adulthood.

The proband's daughter, aged 40, was diagnosed as having pleural malignant mesothelioma, of which she died one year later. On microscopic examination, there was no evidence of asbestos fibers. Born in Iberville Parish, she moved at age 11 to urban Orleans Parish, where she spent the rest of her life. At age 16, she began working as a PBX operator, continuing in that job for two years. She later worked as a telephone operator for three years before becoming a housewife for her remaining years. Her husband was an electrician in various industries during their married life. She was a nonsmoker, but her spouse smoked cigarettes.

The proband's son was diagnosed as having pleural malignant mesothelioma at age 35, in the same year his sister's mesothelioma was diagnosed. There was no microscopic evidence of asbestos fibers on histopathologic examination. His diagnosis was confirmed at autopsy. He too had been born in Iberville Parish, but he moved to Orleans Parish at age 5. Starting at age 18, he was a torpedo-man aboard a nuclear submarine for five years

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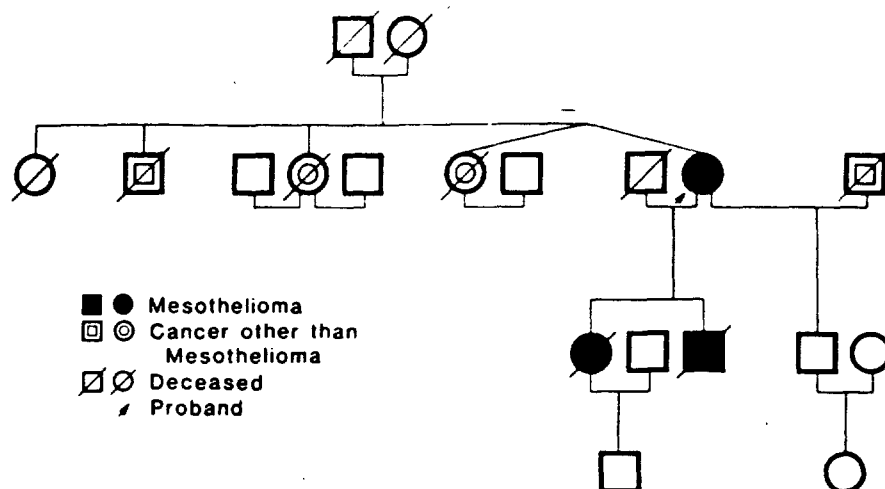


Figure 1. Pedigree of family with three persons with mesothelioma.

and then worked as a shipyard helper (one month), cement pipe maker (two months), stock manager in a drugstore (eight months), lineman (seven years), and board controller for a power company (seven years). During this time he also worked part-time as a carpenter, perhaps handling asbestos materials. He smoked about one pack of cigarettes a day.

Other types of cancer also occurred in this family. The proband's brother died at age 52 of renal carcinoma, her fraternal twin sister died at age 58 of a metastatic carcinoma of uncertain origin, and her elder sister died at age 66 with infiltrating bronchiolar carcinoma. In addition, a nephew was found to have colon polyps.

DISCUSSION

Mesothelioma is a public health concern because of its association with occupational, environmental, and domestic exposure to asbestos. We obtained careful histories of asbestos exposure that could have occurred either directly through work experiences or indirectly through environmental or household exposure. Although the proband did not have any direct occupational exposure to asbestos, she and her family may have been subject to indirect household exposure from her husband's clothes or had environmental exposure from the neighborhood lumber and shingle company.¹³ Although the proband's daughter did not have any occupational asbestos exposure, she and her husband lived within a mile of a factory that used asbestos in the manufacture of its products. This putative environmental exposure began when she married at age 20 and lasted until her death. Although the proband did not have an occupational exposure to asbestos, laundering her husband's clothes could have exposed her and her children in-

directly. In only one of the four cases, the proband's son, can a direct occupational exposure be documented.

The latency period between asbestos exposure and disease development for mesothelioma has been reported to be about 34 ± 8 years.¹⁴⁻¹⁷ Consequently, if asbestos exposure were a factor in the tumor development in our patients, the ages of the proband's daughter and son when mesothelioma developed (40 and 35 years, respectively) would indicate that their exposure most probably occurred while they lived in Iberville Parish with the proband during early childhood. The fact that the cases were all diagnosed within a seven-year span (1975-1982) suggests that the subjects could each have had a similar exposure, inasmuch as the environment was similar for all. Therefore, the likely sources for the putative environmental exposure could have been the immediate home environment (such as asbestos dust, primarily through the laundering of work clothing), the school environment, or neighborhood exposure to various asbestos industries.¹³

From 1938 to 1948, the roofs of the school and the home where the family was raised were made of asbestos shingles. The family also lived 0.5 to 1.5 miles from a lumber and shingle company that used asbestos insulating material to wrap its steam pipes. The company stated that only millwrights were responsible for working with the steam pipes, yet the possibility existed that other workers might have come into contact with the pipes while moving or cleaning them. The proband's first husband and brother worked as laborers for the lumber and shingle company at that time. In neither man did mesothelioma develop. Although the proband visited the mill, none of the other subjects did. She also laundered her husband's work clothes while he worked for that company. The laundering could

have resulted in a household exposure, as has been reported in the past.¹⁸

The lumber and shingle company, so near to the family dwellings, could have been a source of asbestos exposure and contamination for this family and others nearby. The proband and her brother and three sisters lived for the most part within two miles of each other while residing in Iberville Parish. The proband's affected son and daughter and her nieces and nephews, all about the same ages, had frequently played together, attended the same schools, and occasionally spent entire summers together. Nevertheless, no additional cases of mesothelioma or asbestosis have been reported from this family and there were no other cases of mesothelioma recorded in the local hospitals' pathology departments during the seven-year span of mesothelioma development in this family.

From the information obtained, asbestos exposure cannot be related with certainty to the cancers in the proband and her two offspring. An analysis of the cases and their circumstances leads us to suspect that a latent genetic susceptibility may be present in this cancer-prone family, thus raising the question of other operational risk factors, e.g., genetic predisposition.

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