

Travis et al.¹²⁹ also conclude that treatment (as opposed to genetic susceptibility to tumors) probably explains much of the observed excess tumors in testicular cancer patients, an interpretation supported by the lower risks in the first 10 years of follow-up.

Accordingly, it is our view that ionizing radiation may play a causal-contributory role in the genesis of some mesotheliomas, probably as a cofactor along with innate susceptibility to cancer development (as demonstrated by one or more antecedent cancers), with or without past asbestos exposure, but the number of such radiation-related cases is small in comparison to the burden of asbestos-related MMs, for which radiation is not a co-factor.

Malignant Mesotheliomas in Children (and the Concept of Spontaneous Mesotheliomas)

In 1985 Talerman et al.¹⁵² reported a case of a diffuse malignant deciduoid peritoneal mesothelioma in a 13-year-old girl and reviewed the literature identifying 41 previously reported cases of mesothelioma in children. Thirty-three of the 41 previously reported cases began in the pleura, and 40 of the 41 children died 2 weeks to 21 months after diagnosis, a clinical course similar to that in adults. In many reported cases of mesothelioma in children, a history of exposure to asbestos was not documented, and in Talerman et al.'s case and in two other cases reviewed, there was no history of exposure to asbestos.

Fraire et al.¹⁵³ independently reviewed slides available of 17 children previously diagnosed as having mesothelioma. Upon review, only three cases were confirmed as mesothelioma. Therefore, they concluded mesothelioma in children might be rarer than suspected. Fraire et al.¹⁵⁴ conducted an extended evaluation of 80 reported cases of mesothelioma in childhood. Of the 80 cases, tissue slides were available for review in 22 cases, of which 10 were considered MM, nine nonmesothelial malignant tumors, and three malignant neoplasms of uncertain type. The authors found no relationship between childhood MM and asbestos, radiation, or isoniazid therapy. Lin-Chu et al.¹⁵⁵ reported a confirmed case of MM in a 19-month-old girl. In their review of the literature, they found three other cases of MM in infants. In their case, there was no information concerning exposure to asbestos.

The occurrence of mesothelioma during infancy, childhood, and adolescence supports the notion of true spontaneous mesotheliomas. Diagnosis of mesothelioma during infancy and childhood poses greater difficulties than for adults, especially the distinction from pleuropulmonary blastomas of childhood¹⁵⁶ and perhaps desmoplastic small round cell tumors of the pleura,³⁷ but there is little doubt that childhood mesotheliomas do

occur. From a review of three studies, McDonald and McDonald¹⁵⁷ suggest that the incidence of childhood mesothelioma may be within the range of 0.5 to 1.0 case/10⁷/yr.

Background Exposure to Asbestos and Background or Spontaneous Mesotheliomas: Do They Exist? It is our perception that background asbestos exposure from the environment at large represents general environmental exposure unrelated to the use of asbestos-containing materials in the workplace or at home, or from significant point sources of asbestos such as factories. We consider background exposure to include exposures related to the passive weathering of in-place asbestos-containing materials, including asbestos-cement roofing materials with very low or unmeasurably low airborne fiber concentrations, and environmental exposure derived from the brakes of passing automobiles; we exclude from "background" any exposure arising from active disturbance of any asbestos-containing materials such as asbestos-cement building products or insulation materials.

It is also important to recognize that absence of a history of asbestos exposure does not equate to absence of exposure. Many cases of seemingly background MM can be attributed to long-past forgotten or unrecognized asbestos exposures. For example, many of the cases that are encountered in our everyday or referral practice are accompanied by a clinical statement that no asbestos exposure has been identified, but subsequent and more detailed history-taking usually does yield a history of brief exposure to asbestos, and in some of those cases the mesothelioma patient was unaware that the material used (e.g., fibrous cement building materials) did in fact contain asbestos. The problem of detailed and systematic history-taking is also exemplified by some of the data in the Australian Mesothelioma Surveillance Program, in which a substantial number of the cases initially classified as having no known exposure history in fact had asbestos exposure documented upon more detailed review.⁴³

The often-cited background MM rate of 1 to 2 per million person-years, was derived partly from backward extrapolation of the incidence rates in men, to the point where the rates for men and women diverged from each other, based on a presupposition that the female incidence rate for mesothelioma has been stable, and that most MMs in women represent background cases.¹⁵⁸ In reality, there is persuasive evidence that both of these assumptions are false: (1) in the United Kingdom the death rate for MM in females increased from 4.67/10⁶/yr in 1989–1991 to 5.77 in 1995–1997,¹⁵⁹ and to 9.75 in 2002–2004; (2) the female incidence rate in Australia rose about threefold over a period of ~20 years; (3) Strickler et al.¹⁶⁰