

**COMMITTEE ON CARCINOGENICITY OF CHEMICALS IN FOOD,  
CONSUMER PRODUCTS AND THE ENVIRONMENT****Relative Vulnerability of Children to Asbestos compared to Adults –  
Epidemiology and Case Reports on asbestos exposure in childhood and  
the risk of mesothelioma in later life.**

1) Mesothelioma is a rare type of cancer that can develop in the tissues covering the lungs or the abdomen and accounts for less than 1% of all cancers diagnosed in the UK. In the UK in 2007, around 2,400 people were diagnosed with mesothelioma (Cancer Research UK, 2011). The overall incidence rate in the UK is 2.9/100,000. Mesothelioma is five times more common in men than in women, with an incidence rate of 5.2/100,000 in men and an incidence rate of 0.9/100,000 in women. Around 9 out of 10 mesothelioma cases occur in people aged 60 and over. Mesothelioma incidence rates have increased almost four-fold since the early 1980s. The incidence of mesothelioma is still increasing and is expected to peak circa 2020 and to decline rapidly thereafter. About two thirds or three quarters of mesotheliomas occur in the chest (67 to 75%). They start in the two sheets of tissue known as pleural membranes (or pleura) that cover the lungs. Mesothelioma of the tissues lining the abdominal cavity is known as peritoneal mesothelioma. Between a quarter and a third of mesotheliomas occur in the abdomen (25 to 33%). Around 2,150 people died from mesothelioma in the UK in 2008. More than 80% of mesothelioma deaths occur in men. Mesothelioma death rates have increased by more than a quarter in women in the last five years to 0.8/100,000 people, but have remained fairly stable in men at a rate of 4.6/100,000 population. The overall mortality rate in the UK is 2.5/100,000 people (Cancer Research UK, 2011).

2) There is little information concerning mesothelioma of childhood, limited mainly to individual case reports (Fraire et al., 1988). Mesothelioma is rarely diagnosed in children as the disease has a long latency period and typically associated with occupational exposure to asbestos. However, few publications (case reports and epidemiological studies) have addressed the issue of exposure to asbestos in childhood and the risk of mesothelioma in later life. In these studies detailed below, exposure to asbestos occurred either through paraoccupational exposure, domestic exposure or environmental exposure.

3) Grundy and Miller (1972) identified 13 cases of mesothelioma in children from 42,597 death certificates for all children less than 15 years of age who died of cancer in the US from 1960-1964 and for those under 20 years of age from 1965-1968. Using a population based approach; Cooper et al. (1989) identified cases of childhood mesothelioma in Texas and the US. They identified 6 cases in total of childhood mesothelioma, 2 from 1969 to 1971

from the National Cancer Institute and 4 cases from 1973 to 1984 from Surveillance, Epidemiology and End-Results Program (SEER). Using the SEER population at risk from 1973 to 1984, Copper et al. estimated that the average annual incidence rate in children, aged 0-19 years was 0.5 cases per 10 million population (95% CI 0.0 – 1.0 per 10 million). In the UK, Muir et al. (1992) and Niggli et al. (1994) found only 4 cases of peritoneal mesothelioma among 918 malignancies registered by the West Midlands Regional Research Group in the UK in the time period 1987 to 1994. The calculated annual incidence of mesothelioma was approx 0.6 cases per million children younger than 15 years. In an IARC publication in 1980, Wasserman and Wasserman (1980) reviewed the literature from the late 1970s and presented the available data on childhood mesothelioma. The biggest difference that they could identify between the characteristics of mesothelioma between adults and children was the latency period. They found that the latency of the tumour was up to 14 years in children but ranged from 25-55 years in adults. They did not include any comment on the causes of the childhood mesotheliomas.

### **Epidemiological Studies**

4) Metintas et al. (1999) reported prospective epidemiological data of diffuse malignant pleural mesothelioma (DMPM) diagnosed in their clinic in Eskisehir in central Turkey from 1989-1997. The use of “white soil” (containing tremolite asbestos) was common in this area as whitewash or plaster material for the walls, for insulating and water proofing floors and roofs of houses. Of the 113 DMPM patients, 59 were men and 54 were women. They found that 97 patients (86%) had non occupational asbestos exposure. 28 of the patients had lived in the villages their entire lives and thus formed the ‘continuous exposure’ group. The other 69 patients had been born in the village but migrated to a city or gave up “white soil” usage for various reasons and they formed the partial exposure group. The mean length of exposure was 55 years for the continuous exposure group and 25 years for the partial exposure group. The mean age of disease appearance was 56 years (range 26-81 years) and there was no significant difference between age at appearance of disease between the two groups. As patients had been exposed to asbestos from birth, the latency period was equivalent to the age of the patients. Mentintas et al. (2002) conducted a field based epidemiological study to determine the mesothelioma rate in an Eshisehir cohort with environmental exposure to asbestos from birth through the use of white soil in the area. They reported that the annual mesothelioma incidence rate was 114.8/100,000 for men and 159.8/100,000 for women. These data indicate that the risk of mesothelioma is 88.3 and 799 times greater in men and women, respectively compared to the world background incidence rates of 1.3/100,000 for men and 0.3/100,000 for women.

5) Luce et al. (2000) performed a case-control study on a population in New Caledonia where a high incidence of malignant pleural mesotheliomas (MPM) have been observed. Only data relevant to MPM are presented here. They found that in the high mesothelioma incidence area, a very friable rock from local outcropping has been used by residents as a whitewash for indoor and outdoor walls of houses. Sampling of the whitewash found it to consist of

virtually pure tremolite asbestos. The authors found the risk of pleural mesothelioma was strongly associated with exposure to whitewash with 14/15 patients reporting exposure. They found that 13/14 cases were exposed since birth with no case of exposure starting after 16 years of age. The risk of mesothelioma increased with the duration of exposure. Exposure for < 20 years gave an Odds ratio (OR) = 22.2 (95 % CI 2.33-211)) and exposure for ≥ 20 years gave an OR of 65.1 (95% CI 7.69 – 551).

6) Libby is a small community located in North Western Montana close to the Zonolite Mountain containing high concentrations of vermiculite ore. The vermiculite ore contains amphibole asbestos composed of 6% tremolite, 84 % winchite and 11 % richterite. The ore was mined from 1920s until the closure of the mine in 1990. A case report by Whitehouse et al. (2008) describes 11 cases of mesothelioma from non occupationally exposed individuals. From the study exposure and pathology data, a number of cases were exposed to asbestos in childhood, either through the presence of the asbestos in the gardens, in their homes or through paraoccupational exposure. In one case, a 65 year old male diagnosed with mesothelioma had lived in Libby from birth to 18 years of age. His father had worked at the mine throughout the 18 years and he was paraoccupationally exposed to vermiculite through him. He was also exposed to the vermiculite from its use in their garden and in their attic of his childhood home. Whitehouse et al. (2008) describes another case of mesothelioma in a 45 year old female who lived 100 miles from Libby. Her father worked at the mine when she was 14 years old. During the time that her father worked at the mine, the patient would launder his clothes at the weekend. In another case, a 48 year old female died of mesothelioma in 1998 diagnosed 2 years earlier. It was reported that she lived from birth in Libby and her home was near contaminated ball fields and railroad tracks. She also played on piles of vermiculite ore as a child.

7) Crocidolite (blue) asbestos was mined and milled at Wittenoom Gorge, Western Australian from 1943 to 1966. Reid et al. (2007) reported on the malignant mesothelioma that occurred in residents of the town who did not work at the mill or mine and tried to determine if children were more susceptible to asbestos exposure than adults. Most residents moved to the town during the 1950s and 1960s, with 10% of residents born in Wittenoom and 42 % of residents were < 15 years when they first resided there. The authors reported that there was evidence that children < 15 years of age had lower rates of mortality with mesothelioma than those ≥ 15 years at first exposure, with a 40 % lower death rate of 47 per 100,000 versus 112 mesothelioma deaths per 100,000 person years by age at first exposure. They found that the two groups had similar mean residence time in Wittenoom, cumulative exposure and lengths of follow up.

8) Hansen et al. (1998) estimated the exposure-response relationship between environmental exposure to crocidolite and mesothelioma in a cohort of former residents of Wittenoom. The cohort consisted of individuals who resided in Wittenoom between 1943 and 1993 for at least one month and were not directly employed by the asbestos industry. Of the 27 subjects, 11 cases were children of men who had worked with crocidolite at Wittenoom

and thus experienced "domestic exposure". They found that the standardised incidence of mesothelioma was 260 per million person years and was similar for both males and females. They reported that time from first exposure, duration of exposure and cumulative exposure all increase the rate of mesothelioma significantly. They also found that those first exposed as children under the age of 10 years had a lower rate of mesothelioma than subjects first exposed after that age (RR = 0.7, 95% CI 0.3-1.5). Of the 27 cases of mesothelioma in the Wittenoom cohort, Hansen et al. reported that nine (33 %) were younger than 40 years at the time of diagnosis resulting from first exposure to crocidolite during childhood. This result of lower rates for children aged < 10 years than those 10 and older at first exposure is a much smaller difference than those found by Reid et al. (2007).

9) Schneider et al. (1996) investigated the development of asbestos induced malignant mesothelioma after non-occupational exposure to asbestos through contact with occupationally exposed household members in their clinic in Germany. Between 1986 and 1994, five women and one young man (aged 42-65 years) with no occupational exposure to asbestos, died of asbestos-induced mesothelioma. For the five women, asbestos exposure was exclusively through residential inhalation of asbestos from contaminated work clothes or shoes that were brought home from the workplace by the husband. As a child, the young man regularly delivered lunch to his father's place of work. The length of household exposure varied from 7 to 23 years, while the latency period from onset of exposure to development of the disease varied from 17 to 39 years.

10) Miller (2005) identified 32 cases of mesotheliomas from the files of nine plaintiff law firms in the US who had no occupational, environmental or other exposure to asbestos other than as a household member of a worker with a clear occupational exposure. Of the 32 cases identified, 12 cases were younger than 7 years of age at first exposure. In total 15 cases were younger than 18 years at first exposure. In terms of relationship to the occupationally exposed individual, the authors found that 11 of the cases were parent – daughter relationships and 3 cases were parent – son relationships.

### **Case Reports**

11) Inase et al. (1991) reports on a case of a 38 year female presenting with pleural mesothelioma, with a history of neighbourhood and domestic asbestos exposure during her childhood. She lived in an area until the age of 4 years, close to cement factories, nitrogen comp factories and a coal mine. She regularly went to the cement factory as her mother worked there. She also played in the hills covered in white dust. She left the area at 4 years of age and had no other known exposure during the subsequent 34 years.

12) Magee et al. (1986) investigated a case of malignant mesothelioma in a 41 year old male. This individual was exposed as a child to chrysotile product from the Canari mine and to other asbestos products in Corsica such as

crushed serpentine using in road paving. They report that the individual's pulmonary chrysotile fibre burden was well within the range of the general population and the size distribution of the chrysotile fibres also resemble that found in the general population. The individual had an elevated tremolite and actinolite asbestos in his lungs compared to the general population. The tremolite asbestos fibres were long in size, with a geometric mean of 3.7  $\mu$ m. The size data indicated that the geometric mean fibre length were much longer than the tremolite found in chrysotile miners with or without mesothelioma (Churg et al., 1984).

13) Yano et al. (2009) provided details of a case report of a 35 year old male worker in an asbestos textile plant in China. The worker developed mesothelioma after 4 years of employment in the plant. The typical long latency of mesothelioma was highlighted by the authors. The paper provided details of his domestic exposure to asbestos as a child through his parents and domestic duties in the home. He resided from birth in workers residences adjacent to an asbestos containing factory. It was common practice for family members to visit the factory and it was also common for the children to spin asbestos thread in the home. The author concluded that it was the early childhood exposure that contributed to the early development of mesothelioma in this Chinese worker.

14) A case report by Martensson et al. (1984) describes the presence of malignant mesotheliomas in two siblings exposed to asbestos in their homes during childhood. Their father worked at a foundry where asbestos was used for insulation purposes. The cases were exposed to asbestos from their father's working clothing that was hung in the kitchen.

15) Ascoli et al. (2003) identified a cluster of mesothelioma in five siblings. The affected siblings were born and grew up in a small habitation in Naples in Italy where the ground floor and basement of the same building contained a workshop that recycled jute bags. The authors did not have formal confirmation that the recycled jute bags contained asbestos but they indicated that it was very likely that a large proportion of the jute bags that came for recycling came from asbestos cement factories located in Naples. For the five siblings, the period of time spent together was from 1954 -1963. The low mean patient age at diagnosis of 45 years indicates a childhood exposure and corresponds to the 10 year period where the patients lived above the jute bag recycling operation. The time period of exposure also overlaps with time spent by two of the siblings working occasionally in the workshop.

16) In a case report by Cassadori et al. (1992), a 37 year old woman was diagnosed with diffuse malignant mesothelioma of mixed pattern. The patient did not have any occupational exposure to asbestos but lived from birth to 10 years of age in a house next to an asbestos processing factory. Asbestos exposure was confirmed by identification of asbestos bodies in the bronchoalveolar lavage at a concentration of 0.3 asbestos bodies/ml.

17) Arul and Holt, (1977) described a case report of a 42 year old female diagnosed with a malignant pleural mesothelioma. It was noted that at the

time of diagnosis that the patient had no history of asbestos exposure and that the tumour appeared to be a spontaneous mesothelioma. Fifteen months into treatment, the patient recollected that she lived near an asbestos factory as a child (from the age of 5-7 years) and played in the neighbourhood of the factory. White dust from the factory settled on houses and after heavy winds, floors and furniture has to be cleaned in the house. The patient left the area after two years and had no other known exposure to asbestos. A post mortem of the patient revealed asbestos bodies in sections of the left lung. Asbestos fibres were also seen and identified as amosite and chrysotile.

18) Li et al. (1989) describes a familial cluster of mesothelioma in a household. One daughter died of mesothelioma at the age of 32 years. Throughout her life, she was paraoccupational exposed to asbestos through her father soiled work clothes. It was also noted by the authors that during her infancy she was also exposed to asbestos. Cotton cloth sacks in which moulded asbestos insulation had been transported had been utilized to make nappies for the young children of the household. The mother had laundered the nappies and her husband's work clothes, and she died of mesothelioma at age 49. The father, an insulator, died with asbestosis and cirrhosis of the liver at age 53.

## **Conclusions**

19) To date, few epidemiological studies have investigated exposure to asbestos in childhood and the risk of mesothelioma in later life. The majority of the information available is in the form of case reports. It has been suggested that those exposed to asbestos in early life are at greater risk to the development of asbestos related diseases than those exposed later in life. Reasons for this suggestion include the long term retention of asbestos fibres in the lungs and the long latency period for onset of asbestos related diseases like mesothelioma. However, in the updated Toxicological profile of Asbestos of the US Agency of Toxic Substances and Disease Registry (ATSDR), Hanley (2001) has not found direct evidence of this and he found no definitive evidence to suggest that children have a greater susceptibility to asbestos toxicity than adults. Hanley (2001) suggested the need for lifetime studies to assess the long term effects of childhood exposure to asbestos. Comparison to occupationally exposed adults would help assess the susceptibility of children compared to adults. Efforts are continuing and currently an ATSDR and EPA funded study is investigating the effect of low level exposure to asbestos in children who attended high school in Libby, Montana from 1950 through 1990 and their risk of developing asbestos-related diseases such as mesothelioma or autoimmune disorders later in life.

## **Questions for the Committee**

- 1) What are the views of the Committee on the available epidemiological and case report data on non-occupational exposure to asbestos in childhood and the development of mesotheliomas?

- 2) Thus far, does the data provided enable the Committee to make any statements on the relative susceptibility of children to asbestos?
- 3) Can the Committee suggest other areas that would help in this discussion?

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