Committee on CARCINOGENICITY

CC/13/S1

COMMITTEE ON CARCINOGENICITY OF CHEMICALS IN FOOD, CONSUMER PRODUCTS AND THE ENVIRONMENT

STATEMENT ON THE RELATIVE VULNERABILITY OF CHILDREN TO ASBESTOS COMPARED TO ADULTS.

Executive Summary

I. We were asked for advice on the relative vulnerability of children to asbestos to inform the discussions of the independent "Asbestos in Schools Steering Group" of the Department for Education (DfE). There are two key components to assessing children's vulnerability to asbestos. These are 1) the effect of age at exposure and life expectancy and 2) a child's intrinsic susceptibility to injury. Accurate definitions of the terms "susceptibility", "sensitivity" and "vulnerability" were integral to the discussion. We considered the following information: relevant epidemiological studies, animal studies, levels of exposure which children may experience, and anatomical and physiological differences between children and adults.

II. There are 24,372 schools in England and it is estimated that more than 75% of these schools have some buildings which contain asbestos-containing products (ACPs). If buildings contain ACPs, there is increased potential for occupants, including children, to be exposed to asbestos. When asbestos is present and is disturbed or damaged, exposure can increase.

III. All forms of asbestos are carcinogenic to humans, causing mesothelioma and cancer of the lung, larynx, and ovary. From an epidemiological perspective, there is good evidence that childhood exposure to asbestos can cause mesothelioma in later life.

IV. There are respiratory and immunological differences between adults and children but their impact on the susceptibility of children to asbestos-induced cancer is unclear.

V. From the available, albeit limited, data it is not possible to say whether children are intrinsically more susceptible to asbestos-related injury. However, it is well recognised by this committee that, due to the increased life expectancy of children compared to adults, there is an increased lifetime risk of mesothelioma as a result of the long latency period of the disease. Because of differences in life expectancy, for a given dose of asbestos the lifetime risk of developing mesothelioma is predicted to be about 3.5 times greater for a child first exposed at age 5 compared to an adult first exposed at age 25 and about 5 times greater when compared to an adult first exposed at age 30. In reaching our evaluation and taking into consideration that

there are a number of uncertainties and data gaps, we conclude that exposure of children to asbestos is likely to render them more vulnerable to developing mesothelioma than exposure of adults to an equivalent asbestos dose.

Background and Terms of Reference

1. In 2011, the Department for Education (DfE) sought advice from the Committee on Carcinogenicity (COC) on the relative vulnerability of children to asbestos. This request arose from discussions in an independent advisory group called the "Asbestos in Schools Steering Group", which reports to the DfE. This Steering Group aims to promote effective management of asbestos in schools and to contribute to the development of guidance on such management. DfE subsequently asked the Department for Health (DH) for an evaluation of the risk of asbestos to children and DH facilitated this request by referral to the COC.

Strategy

2. The information assessed by the Committee included –

i) An evaluation of the available epidemiology literature on childhood exposure to asbestos and risk of mesothelioma in later life.

ii) A review of the available animal studies investigating the comparative changes and consequences of juvenile exposure to asbestos compared to those from exposure in later life.

iii) A discussion on the differences between children and adults in relation to respiratory physiology, inflammation and dosimetry.

iv) Information on the levels of asbestos to which children may be exposed, in particular in school buildings and in residential properties.

v) Consideration of the WATCH statement and of their deliberations on low level exposure to asbestos for background information into the subject matter (http://www.hse.gov.uk/aboutus/meetings/iacs/acts/watch/240211/asbestos-final-position-statement.pdf). WATCH is a Health and Safety Executive (HSE) committee, which advises the Advisory Committee on Toxic Substances (ACTS) and HSE on scientific and technical issues relating to the assessment and control of health risks from chemicals.

A number of health and other experts were consulted by the Committee. Appendix A provides a list of these professionals, and of other individuals who provided oral and written information to the COC on this item.

3. From the outset, we agreed that two factors required careful consideration, when assessing children's vulnerability to asbestos. These were 1) the effect of age at exposure and life expectancy and 2) a child's intrinsic susceptibility to injury. A clear understanding of the term "vulnerability" was integral to the discussion. The following definitions of "susceptibility", "sensitivity" and "vulnerability" are based on Hines et al. (2010); they reflect the Committee's understanding of the terms and are used accordingly throughout. Susceptibility is defined as a capacity characterized by

biological (intrinsic) factors that can modify the effect of a specific exposure, leading to an altered health risk at a given relevant exposure level. Sensitivity describes the capacity for higher risk due to the combined effect of susceptibility (biological factors) and differences in exposure. Vulnerability incorporates the concepts of susceptibility and sensitivity, as well as additional factors that include social and cultural parameters (e.g., socio-economic status and location of residence) that can contribute to an altered health risk. We agreed that consideration should be given to all children up to school leaving age.

Asbestos

4. Asbestos is the name given to a group of six different fibrous minerals that occur naturally in the environment: chrysotile (white asbestos), amosite (brown asbestos), crocidolite (blue asbestos), and the fibrous varieties of tremolite, actinolite, and anthophyllite. Chrysotile belongs to the serpentine family of minerals, while all of the others belong to the amphibole family. Asbestos minerals consist of thin, separable fibres that have a parallel arrangement. Amphibole asbestos fibres are generally brittle and often have a rod- or needle-like shape, whereas chrysotile asbestos fibres are flexible and curved. The term "regulated asbestos fibres" encompasses chrysotile, amosite, crocidolite, tremolite, actinolite or anthophyllite fibres with a length to width ratio (aspect ratio) of at least 3:1 and a length of 5 micrometres (µm) or more, which are visible in the phase-contrast optical microscope (PCM) at a magnification of at least 500 (Control of Asbestos at Work Regulations UK (CAWR, 2012). Annex A details the different types of asbestos.

Sources of asbestos in the UK

5. Over 5.3 million tonnes of asbestos have been imported into the UK since the 1940s, peaking between the 1960s and mid-1970s and then falling sharply. Historically, chrysotile was the main type of asbestos imported into the UK (around 95% of all asbestos imported) but between the late 1950s to the mid-1970s in excess of 20,000 tonnes of amosite were imported annually, approximately 15% of the asbestos imported in this period. Crocidolite imports were around 6000 tonnes per year from 1950 to the early 1960s, constituting around 5% of the total asbestos imported (Asbestos Information Centre UK website, http://www.aic.org.uk/Asbestos_imports.htm). Asbestos was extensively used in a wide range of manufactured products (more than 3,000) in the UK from the 1950s through to the mid-1980s, mostly in building materials, friction products, and heat-resistant fabrics, because of its sound absorption, average tensile strength, its resistance to fire, heat, electrical and chemical damage, and affordability. The importation, supply and use of amosite and crocidolite were banned in 1985 and of chrysotile in 1999. However, due to its earlier extensive use, asbestos is still present in buildings such as schools, houses, flats and offices built prior to 2000 and in products manufactured before the bans. UK residents, including children, are potentially exposed to asbestos from such buildings. Consideration must also be given to low level exposure from ambient[1] levels indoors and outdoors.

[1] Ambient is defined as "the normal conditions surrounding a person, i.e. sampling location" http://ieh.cranfield.ac.uk/ighrc/cr10.pdf

6. Asbestos is present in the three main environmental media, namely air, water and soil. For humans, the main route of exposure of asbestos fibres is inhalation and, to a lesser extent, ingestion (HPA, 2007). Following inhalation, asbestos fibres are deposited on the epithelial surface of the respiratory tract. The fate of the asbestos fibres depends on the site of deposition and on their aerodynamic characteristics (HPA, 2007). Shorter, thicker fibres are usually deposited in the upper respiratory tract, whereas longer, thinner fibres may be carried deeper into the distal airways and alveolar regions (ASTDR, 2001). Amphibole fibres are retained for longer periods in the lung than chrysotile fibres (Albin et al. 1994; Churg 1994; Churg et al. 1993; Davis 1989).

7. During our discussions, an HSE official with expertise in asbestos analysis informed us that the usual procedure for the determination of airborne concentrations of respirable fibres in buildings involves filtering air through a membrane filter. After some manipulations of the filter, the fibres are counted using either an optical phase contrast microscope (PCM) or an electron microscope (EM). Both the scanning electron microscope (SEM) and the transmission electron microscope (TEM), if fitted with an analytical X-ray detector, can be used to verify that the fibre counted is asbestos. The TEM is also used in the non-occupational environment for asbestos analysis of small thin asbestos fibres and structures (see Annex A). Annex B provides further details on the methodologies used for asbestos measurement. The Control of Asbestos Regulations 2012 came into force on 6 April 2012. The control limit for asbestos is 0.1 asbestos fibres per cubic centimetre (or millilitre, ml) of air (0.1 f/cm^3; 0.1 f/ml). The control limit is not a 'safe' level and exposure from work activities involving asbestos must be reduced to as far below the control limit as possible (HSE website, 2013a).

Asbestos levels

8. A review by the Institute of Environmental Health (IEH) in 1997 indicated that background outdoor (ambient) levels of respirable asbestos fibres may range from 0.000001 to 0.0001 f/ml (IEH, 1997). In 1991, a report by the UK Department of the Environment (DoE) estimated a level of 0.0004 f/ml of regulated asbestos fibres in buildings which contain asbestos-containing products (ACPs) (DoE, 1991). Using data from a number of publications, the IEH considered most indoor air concentrations of asbestos were below 0.0002 f/ml. IEH also commented that a mean level of 0.0005 f/ml asbestos fibres was found inside buildings containing asbestos materials in good condition but the significance of this is difficult to interpret because no information on distribution of levels or median level was supplied (IEH, 1997).

9. Information provided by the DfE indicated that there were16,818 primary schools, 3,268 secondary schools and 2,420 independent schools in England (DfE, 2012a). It is estimated that more than 75% of schools in England have some buildings which contain asbestos (DfE, 2012b; http://www.education.gov.uk/schools/adminandfinance/schoolscapital/buildingsanddesign/managementofpremises/b00215518/asbestosmanagementschools/whatasbestosis). According to the report by IEH, "*in general, in school buildings constructed before 1946, exposure will be limited mainly to chrysotile lagging and asbestos cement roofing. Exposure in buildings constructed after 1946 will have been to a*

much broader range of materials including amphiboles in more "vulnerable" locations with a higher risk of damage and potential fibre release. Of the estimated 2,360 secondary schools built between 1945 and 1975, approximately 47% would have been "system built" rather than traditionally[2] built. In general, extensive use was made of sprayed coatings (amphiboles), Asbestolux ceiling panels and asbestos board (amosite) and asbestos cement partitioning in system-built buildings in the 1960s" (IEH, 1997).

10. We were provided with background information on indoor levels of asbestos in school buildings. The background paper is available on the COC website (http://www.iacoc.org.uk/papers/documents/CC-2011-13version2_000.pdf). There are data in the literature that result from a variety of analyses of asbestos levels in schools. Some analyses are continual measurements of normal (background) levels and presented in comparison with levels in areas where asbestos has been disturbed or damaged, some measurements were made during normal occupancy including following remediation or during/following routine maintenance, and other results were from re-enactment studies. The data presented suggest that schools not built with asbestos still contain low ambient background levels of asbestos of the same order of magnitude as indoor asbestos levels in other buildings. Although it is beyond the remit of this Committee to evaluate rigorously these diverse data on asbestos levels, it is clear that, if the school building contains asbestos products, there is increased potential for occupants, including children, to be exposed to asbestos. When asbestos is present and is disturbed or damaged, the data indicate that exposure can increase.

11. In addition to levels of asbestos in schools, we sought information on the asbestos levels found in residential dwellings, as children spend a large proportion of their time in their home environment. In 2010, there were approximately 22.4 million dwellings in England (EHS, 2012). The majority (80%) of dwellings are houses or bungalows while flats make up 20% of the stock. Traditionally built homes represent 95% of all homes built in the UK and 'non-traditional" construction methods (often referred to as 'system built') had been used for the remaining 5% of the stock. The ECHS (1993) indicated that the majority of system-built flats (73%) were built between 1945 and 1980 with ACPs such as lagging, board partitions and ceiling tiles. There may be other sources of asbestos in dwellings, such as ironing boards, gaskets in stoves and backing for vinyl flooring. The IEH report states that, as there is no evidence of fibre release from these products in buildings, exposure to asbestos in traditionally built houses can be considered to be part of ambient exposure to asbestos (IEH, 1997).

12. Few publications have specifically cited levels of asbestos in residential homes and flats, but there have been some reports from the UK and the US. We were provided with background information, which is available on the COC website (http://www.iacoc.org.uk/papers/documents/CC201201AsbestoslevelsinResidentialhomesandFlats.pdf). Overall, we conclude that, in general, the levels of asbestos found in traditionally built residential houses and flats are of the same order of magnitude as ambient indoor levels. There is potential for children to be exposed to increased levels of asbestos in their home environment in homes where ACPs were

[2] 'Traditionally' built is used to describe brick/block or rendered block/block cavity construction.

used in their construction. We note that airborne concentrations vary depending on the amount of activity in the area where ACPs were present, as evidenced by there being higher concentrations during the day when there is greater movement. We note the greater volume and dynamic flow of individuals in other buildings such as schools and the likelihood of higher disturbance of asbestos than in homes. We also note that uncontrolled releases of asbestos fibres due to DIY home maintenance and renovation are difficult to account for and could lead to increased exposure of children.

Asbestos-related diseases

13. Inhalation exposure to any type of asbestos is associated with diseases such as lung cancer, mesothelioma (cancer of the mesothelium, the protective lining that covers many of the internal organs of the body), asbestosis (a non-malignant scarring of the lung tissue) and non-malignant pleural disorders such as pleural plaques and diffuse pleural thickening (HSE, 2013b http://www.hse.gov.uk/statistics/causdis/asbestos.htm). The effects of asbestos exposure on an individual can be affected by factors such as 1) dose, 2) duration of exposure and time since exposure, 3) size, shape and chemical composition of the asbestos fibres and 4) individual risk factors such as smoking or pre-existing lung disease. Asbestos-associated respiratory diseases have long latency periods (the time period between first exposure to asbestos and disease onset). Most cases of non-malignant pleural disorders, lung cancer and asbestosis occur 15 or more years after initial exposure to asbestos (ASTDR, 2001) while the latent period between inhalation of asbestos and mesothelioma is seldom less than 15 years and may exceed 60 years (Bianchi et al., 1997).

14. A recent International Agency for Research on Cancer (IARC) evaluation of asbestos (2012) considered that there was sufficient evidence that all forms of asbestos (chrysotile, amosite, crocidolite, tremolite, actinolite and anthophyllite) are carcinogenic to humans (Group 1) and that it causes mesothelioma and cancer of the lung, larynx and ovary. IARC also considered that there is evidence (in some cases limited) in humans for positive associations between exposure to asbestos and cancer of the pharynx, stomach and colorectum.

15. In the context of advising on the relative vulnerability of children to asbestos, we concentrated on the risk of mesothelioma rather than other cancer endpoints as mesothelioma is nearly always associated with asbestos exposure and hence is less likely to be confounded by other factors. The lung cancer risk caused by childhood asbestos exposure is lower than the mesothelioma risk (HEI, 1991), and the risk for other cancers is much lower still. There is a synergistic interaction between smoking and asbestos exposure for lung cancer risk, but not for mesothelioma. Mesothelioma can develop in the tissues covering the lungs or the abdomen. Most cases of mesothelioma (~ 75%) occur in the chest, with a lesser proportion (~25%) occurring in the abdomen (Cancer Research UK, 2012).

16. Mesothelioma is the 20th most common cancer in the UK (2009), accounting for less than 1% of all cancers. In men, it is the 17th most common cancer in the UK, accounting for over 1% of all new cases of cancer. In the UK in 2010, 2,543 people were diagnosed with mesothelioma (Cancer Research UK, 2012). The overall

incidence rate in the UK is 2.8 cases in 100,000 people (2.8/100,000). Mesothelioma is five times more common in men than in women, with incidence rates of 5.3/100,000 in men and 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 2016 and to decline rapidly thereafter. The lifetime risk of developing mesothelioma in the UK is estimated to be 1 in 150 for men and 1 in 773 for women (calculated using 2006-2008 data) (Cancer Research Statistical Team, 2011). The potential causes of mesothelioma relevant to Great Britain have been summarised in a report by the HSE and are provided in Table 1 (HSE, 2007).

17. There is a consistent increase in risk of mesothelioma with increasing exposure to asbestos. This has been reported in cohort studies as well as in analyses of asbestos fibres in the lungs (Hansen et al, 1998; Churg et al., 1993, McDonald et al., 1989 and Roggli et al., 1986). The dose-response is thought to be approximately linear for pleural mesothelioma (Hodgson and Darnton 2000). The sub-linear relationship seen in some cohort studies may be a statistical effect of inaccuracies in exposure assessment. Studies have suggested that the amphibole forms of asbestos may be more potent than chrysotile, particularly for mesothelioma risk, because of the apparent longer retention of amphibole fibres in lung tissue (ASTDR, 2001; Mossman et al. 1990). Hodgson and Darnton (2000) analysed exposure-response relationships for mesothelioma mortality in studies of 17 asbestos-exposed occupational cohorts and concluded that relative potencies ("exposure specific risk of mesothelioma") are in a ratio of 1:100:500 for chrysotile, amosite, and crocidolite, respectively. We agree with Hodgson and Darnton (2000) that there is no evidence of any threshold for mesothelioma risk. This view was reflected in the statement on low level exposure to asbestos from the UK HSE WATCH committee, published in 2011, which stated that "*there are risks of asbestos-induced cancer arising from work-related cumulative exposures below 0.1 fibres/ml.years. The risk will be lower, the lower the exposure, but "safe" thresholds are not identifiable. Where potential exposures to amphiboles, particularly crocidolite, are below 0.1 fibres/ml.years (for example, 0.01 fibres/ml.years), the available scientific evidence suggests no basis for complacency, but rather a basis for active risk management*".

Epidemiological and case reports on the effect of asbestos exposure in childhood and the development of mesothelioma in later life

18. We reviewed the available case reports of mesothelioma in children with caution, due to the possibility of misdiagnosis. Few epidemiological studies have investigated exposure to asbestos in childhood and the risk of mesothelioma in later life. Most of the information available is in the form of case reports. We were provided with a review of available studies, attached as Annex C, and this review included studies where exposure to asbestos occurred either through para-occupational exposure, domestic exposure or environmental exposure. A recent study by Reid et al. (2013) examined the cancer incidence and all-cause mortality of people exposed to crocidolite as children in the town of Wittenoom, Western Australia. In the study, individual asbestos exposures were estimated by assigning all residents an intensity of exposure of 1.0 f/ml of air between 1943 – 1957 (time period when new mill was in commission) and an intensity of exposure of 0.5 f/ml between 1958 -1966 (time

period when the milling operation had ceased). Interpolation between the dust surveys that used personal monitors allocated exposures from 0.5 f/ml in 1966 to 0.01 f/ml in 1992. We note that these exposure values are several orders of magnitude higher than the levels typically reported in school buildings and residential homes with asbestos in good condition in the UK. We agreed that the exposure assessment was fairly crude and probably underestimated exposure for some residents. The study reported an overall increase in all-cause mortality and cancer incidence rates in adults that grew up as children in Wittenoom compared with the Western Australian adult population. The increase was predominantly but not solely due to malignant mesothelioma. There was a statistically significant increased incidence of mesothelioma. There were also consistently increased rates of some other cancers namely ovarian and brain cancers in females and leukaemia, prostate, brain, and colorectal cancers in males. We note two earlier studies (Hansen et al. (1998) and Reid et al. (2007)), involving the same cohort of former residents of Wittenoom, Western Australia. In both studies, individual asbestos exposures were estimated using the method described above. Hansen et al. (1998) found no significant association between incidence of mesothelioma up to the end of 1993 and age of first exposure to crocidolite in these subjects, who had no history of occupational exposure to asbestos. Reid et al. (2007) presented evidence that children < 15 years of age at first exposure had lower rates of mortality with mesothelioma compared to those ≥ 15 years at first exposure, but this could reflect age-related differences in environmental exposure. Although the study indicates that the lifetime risk of mesothelioma is lower in children with a young age at first exposure, compared with older children, we do not consider it appropriate to draw conclusions from this one study. Overall, we consider there is evidence that childhood exposure to asbestos can cause mesothelioma but the epidemiological data are too limited to assess differential susceptibility between children and adults.

Effect of children's age and life expectancy on mesothelioma risk

19. We discussed the trends in the national mesothelioma mortality rates and other epidemiological data. It was notable that the death rate from mesothelioma at 85 years of age is ten times higher than at 55 years. Among British men, the rate for those born in 1945 is much higher than that for those born in 1955, but the mortality rates in women are not declining much even in the population born in 1960, a cohort born at the peak of asbestos use. It is possible that this is because the majority of mesotheliomas in females are the result of environmental or para-occupational exposure to asbestos (Table 1) which may have occurred before the age of 20 and possibly before the age of 10. It is acknowledged that the lifetime mesothelioma risk following asbestos exposure at any age would be increased as life expectancy increased, and this should be allowed for. However, the effect could not be predicted reliably, particularly for childhood exposure, due to uncertainties about future changes in overall mortality rates and the rate of increase in the mesothelioma incidence rate beyond 60 years after first exposure.

20. In terms of lifetime risk of developing mesothelioma, it is well recognised that the younger a person is when they are exposed, the greater the risk of developing mesothelioma, which reflects the latency of the disease as younger people are more likely to live long enough for the disease to manifest itself. The effect of age of exposure on the risk could be large, as risk increases to the third or fourth power of

time after first exposure (Peto et al., 1982). Because of differences in life expectancy, for a given dose of asbestos the lifetime risk of developing mesothelioma following exposure to asbestos is predicted to be about 3.5 times greater for a child first exposed at age 5 compared to an adult first exposed at age 25 and about 5 times greater when compared to an adult first exposed at age 30 (Darnton, 2013, personal communication to the Committee and available on the COC website, http://www.iacoc.org.uk/papers/documents/CC20132EffectofAgeonMesotheliomaRisk-AnnexA.pdf). This value is broadly consistent with that derived using the life-table approach in an unpublished report presented to the Committee by Howie (2012). It is also in line with the value calculated by the HEI (1991) where, based on life expectancy, the lifetime risk of developing mesothelioma following 10 years' exposure is expected to be about 5 times greater for a child first exposed at age 5 than for an adult first exposed at age 30.

Animal Studies

21. As part of our strategy, we considered whether animal studies which compare the changes and consequences following juvenile exposure to asbestos with those following exposure in adult life may be informative. Only one such study, which specifically addressed the effect of age at exposure to asbestos on the occurrence of mesothelioma in rats, was found. Berry and Wagner (1976) injected Wistar rats of both sexes with crocidolite asbestos intrapleurally at either 2 months or 10 months of age and found by observation and by statistical analysis a higher rate of mesothelioma in the latter group, compared to the former group after exclusion of mortality due to other causes.

22. Overall, the animal study provided data on age related susceptibility to asbestos in rodents. We noted that the rodent data do not support the hypothesis that exposure at a younger age increases susceptibility to mesothelioma due to asbestos exposure. Consideration was given by members to the methodologies used in the study, their impact on the results and the relevance of the study to humans in particular children. Issues raised included route of exposure used (intrapleural injection), and differences in physiology and maturation processes between young rats and children. Although the Committee does not dismiss animal data as an experimental pathology approach to understanding human disease processes, we agreed that this study did not offer any significant insight into the relative vulnerability of children compared to adults to asbestos. The Committee considered that further animal studies would probably not be helpful in view of the difficulties involved in conducting valid studies and the scarce availability of facilities in which to conduct such studies in juvenile animals.

Comparative differences in respiratory physiology, inflammatory response and dosimetry between children and adults

23. An understanding of the physiological differences between adults and children in the respiratory and immune systems, and the issue of inhalation dosimetry would play a key part in addressing the relative vulnerability of children to asbestos compared to adults. We thus sought the advice of Professor Andy Bush (Professor

of Paediatric Respirology at Imperial College & Consultant Paediatric Chest Physician, Royal Brompton & Harefield NHS Foundation Trust), an expert in juvenile respiratory physiology, on the behaviour of asbestos in a child's respiratory tract and whether this might make them more or less susceptible.

24. The structure and physiology of the lung differ significantly between adults and children although it is not clear how this impacts on the uptake and disposition of any inhaled fibres. While it is not possible to be definitive, we were advised that the lungs could be considered to reach the adult stage around the mid-teenage (post pubescent) years. It was noted that foetal lung development occurs as zonal growth with all the airway branches being determined by the 16th week of pregnancy. The number and size of alveoli increase with age. Therefore, in a child there would be a lower surface area for gaseous exchange. We suspect that deposition of asbestos fibres could be different from that in adults given the differences in airway dimension and structure. However, we are not aware of any studies specifically assessing this in relation to fibres. Similarly, we are not aware of any study which demonstrates differences between the transit of asbestos fibres through the pleura to the site of carcinogenic action in a juvenile compared to an adult. During our discussions we were informed that the juvenile lung was particularly susceptible to injury and any lung damage received in the first 4 years of life, in terms of air flow obstruction, would remain for life. This could manifest later in life as increased susceptibility to some smoking-related disorders and conditions such as chronic obstructive pulmonary disease (COPD), although it is not known whether this would have an effect on life-time lung cancer risk.

25. While the lung is the primary target organ for asbestos toxicity, a number of clinical and experimental studies have shown that the immune system may also be altered by exposure to asbestos at occupationally relevant concentrations (Rosenthal et al., 1998). Reported immunological effects include the influence of asbestos exposure on non-specific immunity (natural killer cells, epithelial cells and lung macrophages), on specific immunity and asbestos-induced pathophysiologic responses associated with generation of various reactive oxygen species (ROS). We are unclear how the development of the immune system in childhood would impact on these reported immunological responses to asbestos. It was noted that immunologic responses associated with antibody production are very different from birth until 2 years of age from those in the adult.

26. In terms of the susceptibility of children, we reviewed the International Commission on Radiological Protection (ICPR) modelling framework for particle dosimetry and the US EPA inhalation dosimetry methods for application to children for risk assessment. In 2005, the US EPA described how risk assessment in childhood can be assessed as a sequence of life stages. As an infant develops into a child and a child into an adult, there may be periods of time in their development where they are more susceptible and have enhanced sensitivity to environmental agents. We recognise that changes in behaviour and physiology as a child ages can increase a child’s exposure to chemicals and dose of chemicals. Toxicokinetic differences between children and adults can cause children to have increased

uptake and reduced clearance of certain chemicals from their bodies. Inhalation dosimetry can differ across age groups as children's breathing rate is greater than adults' per kilogram body weight and per respiratory tract surface area (in particular in the pulmonary region).

27. In our discussion on lung dosimetry we considered that surface area or lung surface area might be the most appropriate metric for converting the dose/body weight from an adult to a child. We noted that the deposition of inhaled fibres could be different in children compared to adults due to their narrower airways and also due to the lower volume of air inhaled by children each day, resulting in fewer fibres being inhaled in a given situation. We discussed the potential for dilution of the fibres deposited as a child grows which would, therefore, reduce the body burden. We emphasise that it cannot be assumed that deposition would be the same at age 2 compared to age 18, however we are not clear whether there would be greater or less deposition.

28. An invited expert, Professor Jonathan Grigg (Professor of Paediatric Respiratory and Environmental Medicine at Barts and the London School of Medicine, Queen Mary University of London, and a consultant paediatrician at the Royal London Hospital (Whitechapel, London)) provided an insight on whether it is possible to extrapolate information on the effects of particulates in the juvenile lung to fibres. Modelling data generated specifically for the Committee's assessment were discussed. The calculations took into account the fact that children have higher metabolic rates and faster breathing rates than adults which, it was noted, initially suggests greater exposure in children compared to adults. This is the basis of the general assumption that children are exposed to double the dose of a substance compared to adults on the basis of lung surface area. Children also have shallower breathing, which interacts with the faster rate in a complex way to alter where fibres and particles are deposited in the lung, with less deposition in the lower airways. In the modelling, the geometry of the airways was scaled down by approximately a third for children; clearance mechanisms are more effective as there is less distance for inhaled particulates/fibres to travel to be removed. Therefore, the underlying assumption that children will inhale more fibres does not hold. The Committee considered that, for the same dose, this modelling provided evidence that children would not be more sensitive to fibres than adults.

Uncertainties and data gaps

29. We acknowledge a number of uncertainties and data gaps in our assessment of the relative vulnerability of children to asbestos. One such uncertainty relates to exposure assessment. The levels of asbestos at various sites reported in many references are uncertain given the problems in measurement, suitability of the analytical method used, and comparability of results. In many cases, the exposure measurements are largely historical and it would be valuable to have more contemporary measurements, especially from schools in the UK.

30. From an epidemiological perspective, few studies have specifically investigated the effect of childhood exposure to asbestos and the risk of developing mesothelioma in later life. We note that the levels of asbestos exposure tended to be

very high in these studies and not comparable to the UK situation. We also note uncertainties in interpreting data from many of the epidemiology studies. Issues include the accuracy of exposure measurements or estimates of uncertainty in such measurements; unknown accuracy of cancer diagnosis; limited cohort size and loss to follow up; and inadequate statistical analysis in some studies.

31. We also acknowledge uncertainties in the risk estimation. Issues include the extrapolation of data from adult age-related cancers to children and the assumption that the risk model from first exposure as a function of age, which was derived from occupational studies in adults, is the same for a child as for an adult. From our discussion on the intrinsic susceptibility of children compared to adults, we identify one key data gap, namely the behaviour of fibres in children's respiratory tracts compared to those of adults.

Conclusions

32. Following our deliberations, we make the following conclusions:

a) Asbestos is classified by IARC as a group 1 carcinogen, i.e. it is carcinogenic to humans. Asbestos causes mesothelioma, and cancer of the lung, larynx, and ovary. In their recent evaluation, IARC also considered that there is evidence (in some cases limited) in humans for positive associations between exposure to asbestos and cancer of the pharynx, stomach and colorectum.

b) In general terms, the levels of respirable asbestos fibres in air range from lowest to highest in the following order:

- background outdoor ambient levels (lowest levels)
- background indoor ambient levels in buildings not built with asbestos
- levels in buildings built with asbestos where the asbestos is in good condition
- levels in buildings built with asbestos where the asbestos has been disturbed or damaged and/or is in bad condition (highest levels)

c) The data in general suggest that the levels of asbestos found in schools with no asbestos in their construction are of the same order of magnitude as indoor asbestos levels in other buildings. When asbestos is present and is disturbed or damaged, the data indicate that exposure to asbestos fibres can increase. However, the information on levels found in schools is largely historical and there is a lack of contemporary data on asbestos in schools. In view of the importance of this issue, there would be a benefit in generating new exposure data.

d) There is also potential for children to be exposed to asbestos in their home environment in homes where asbestos-containing products (ACPs) were used in their construction. In general, the reported levels of asbestos found in traditionally built houses and flats are of the same order of magnitude as ambient indoor levels. However, activities such as maintenance can disturb asbestos and increase exposure both at home and at school.

e) From an epidemiological perspective, there is good evidence that childhood exposure to asbestos can cause mesothelioma in later life. However, the

epidemiological data are too limited to assess differential susceptibility between children and adults. We recognise the effect of increased life expectancy of children compared to adults and the increased likelihood of mesothelioma as a result of the long latency period for this cancer. Because of differences in life expectancy, for a given dose of asbestos, the lifetime risk of developing mesothelioma is predicted to be about 3.5 times greater for a child first exposed to asbestos at age 5 compared to an adult first exposed at age 25 and about 5 times greater when compared to an adult first exposed at age 30.

f) There are respiratory and immunological differences between adults and children but their impact on the susceptibility of children to asbestos-induced cancer is unclear. We were informed that the juvenile lung is particularly susceptible to injury and that any lung damage received in the first 4 years of life, in terms of air flow obstruction, would remain for life. However, it is not possible to determine what effect fibre inhalation before the age of 5 would have on lung function, and whether any effect would persist. Some physiological differences (e.g. respiratory rates, total volume, and airway dimension) have the potential to modify the susceptibility of children compared to adults to asbestos. However, modelling of fibre deposition in children has indicated that children are unlikely to inhale more fibres than adults.

g) While the available relevant animal study provides data on age-related susceptibility to asbestos in rodents, it does not offer any significant insight into the relative vulnerability of children compared to adults to asbestos.

h) From the available data, it is not possible to say that children are intrinsically more susceptible to asbestos-related injury. However, it is well recognised by this Committee that, due to the increased life expectancy of children compared to adults, there is an increased lifetime risk of mesothelioma as a result of the long latency period of the disease. In reaching our conclusion and taking into consideration that there are a number of uncertainties and data gaps, we conclude that exposure of children to asbestos is likely to render them more vulnerable to developing mesothelioma than exposure of adults to an equivalent asbestos dose.

COC May 2013

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Table 1: Potential causes of mesothelioma relevant to Great Britain*

Group	Attributable cause
1.	**Occupational asbestos exposures** Exposure during work activities – either due to an individual's own work, or due to the work of others in the same workplace.
2.	**Paraoccupational and environmental exposures** Exposure outside work activities but resulting from the work activities of others, for example, laundering overalls used by asbestos workers Living close to industrial sites using or producing asbestos / asbestos products Living or working in buildings containing asbestos in poor condition DIY activities involving work with asbestos
3.	**Background cases (cases that would have occurred in the absence of any industrial exploitation of asbestos)** Spontaneous cases occurring in the absence of any exposure Environmental exposures via naturally occurring asbestos or other mineral deposits (such exposures are unlikely to occur in Great Britain)

***Table obtained from HSE (2007)**

Appendix A. Experts, Advisors and other individuals who provided information on this item to the COC

Those whom attended the COC meetings and/or provided written information

Professor Andy Bush[3] MB BS(Hons) MA MD FRCP FRCPCH
Mr Brendan Beckett (DfE)
Dr Garry Burdett (HSL)
Mr Andy Darnton (HSE)
Professor Jonathan Grigg BSc MB BS MD MRCP FRCPCH
Mr Michael Lees (Asbestos in Schools Group)
Ms Julie Winn (Chair of the Joint Union Asbestos Committee)
Mr Robin Howie (Robin Howie and Associates)

[3] By teleconference link

ANNEX A to Asbestos Statement CC/13/S1

ISO definitions of different fibres/asbestos types (ISO 13794:1999)

asbestos structure	term applied to an individual asbestos fibre, or any connected or overlapping grouping of asbestos fibres or bundles, with or without other particles
fibril	single fibre of asbestos which cannot be further separated longitudinally into smaller components without losing its fibrous properties or appearances
fibre	elongated particle which has parallel or stepped sides. For the purposes of this International Standard, a fibre is defined to have an aspect ratio equal to or greater than 5:1 and a minimum length of 0.5 µm.
fibre bundle	Structure composed of parallel, smaller-diameter fibres attached along their lengths. A fibre bundle may exhibit diverging fibres at one or both ends.
fibrous structure	fibre, or connected grouping of fibres, with or without other particles
PCM-equivalent fibre	fibre of aspect ratio greater than or equal to 3:1, longer than 5 µm, and which has a diameter between 0.2 µm and 3.0 µm. For the purposes of this International Standard, PCM is the abbreviated term for phase-contrast optical microscopy.
PCM-equivalent structure	fibrous structure of aspect ratio greater than or equal to 3:1, longer than 5 µm, and which has a diameter between 0,2 µm and 3,0 µm
primary structure	fibrous structure that is a separate entity in the TEM image
structure	single fibre, fibre bundle, cluster or matrix
twinning	occurrence of crystals of the same species joined together at a particular mutual orientation, and such that the relative orientations are related by a definite law
unopened fibre	large diameter asbestos fibre bundle which has not been separated into its constituent fibrils or fibres

ANNEX B – Measurements of asbestos

	Description	Measurements
PCM analysis		Countable fibres are defined as particles with length >5µm, width <3µm and aspect ratio (length: width ratio) >3:1. Fibres having widths <0.2µm may not be visible using this method. The PCM count represents only a proportion of the total number of fibres present. PCM does not determine whether fibres are asbestos or not. Therefore the count is only an index of the numerical concentration of fibres and not an absolute measure of the number of fibres present
PCM equivalent fibres (PCME):		these are a sub set of the > 5 µm long fibres that would be expected to be counted by the WHO PCM method and counts those fibres with a minimum width of 0.2 µm and a maximum width of 3 µm.
TEM analysis:	TEM is the "gold standard" and a range of measurements can be used. In practice a combination of energy dispersive x-ray analysis and selective area electron diffraction is used to identify the asbestos type for any size of fibre. Energy dispersive x-ray analysis can be made quantitatively in terms of % weight of each element and electron diffraction can measure the d-spacing and angles of the atomic structure to meet the highest standards for defining minerals.	All > 5 µm long fibres: particles with an aspect ratio of >3:1 which has parallel or stepped sides.

	Description	Measurements
All fibres:		All >0. 5 µm long particles with an aspect ratio of >3:1 which has parallel or stepped sides. In practice the 3:1 and 5:1 aspect ratios make only a minor difference to asbestos fibres but 3:1 is used for optical microscopy and epidemiology exposures
SEM analysis	SEM in its normal form is much more limited than TEM for identification and has only energy dispersive x-ray analysis to "classify" the fibre type. It cannot fully identify the fibre as the TEM can. The sample is mounted on a filter and stub "thick sample" so there are many more problems and limitations to the energy dispersive x-ray analysis than the TEM which uses a "thin sample." Often only fibres of width of >0.25 µm can be classified based on the ratio of peak heights. High resolution field emission SEM's are now more common but have not been used for asbestos measurements reported in the data reviewed by the CoC. High resolution field emission SEM have the same limitations as tungsten SEMs except smaller fibre widths could be classified.	These are similar to PCM equivalent fibres but have lower visibility and may use a slightly high minimum width 0.25 µm. Some early methods counted fibre >2.5 µm long as well.

Annex C to Asbestos Statement CC/13/S1

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. 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 para-occupational exposure, domestic exposure or environmental exposure.

2. 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

3. 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.

4. 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).

5. 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.

6. Crocidolite (blue) asbestos was mined and milled at Wittenoom Gorge, Western Australian from 1943 to 1966. A recent study by Reid et al. (2013) examined the cancer incidence and all-cause mortality of people exposed to crocidolite as children in the town of Wittenoom, Western Australia. In the study, individual asbestos exposures were estimated by assigning all residents an intensity of exposure of 1.0 f/mL of air between 1943 – 1957 (time period when new mill was in commission) and an intensity of exposure of 0.5 f/mL between 1958 -1966 (time period when the milling operation had ceased). Interpolation between the dust surveys that used personal monitors allocated exposures from 0.5 f/ml in 1966 to 0.01 f/ml in 1992. The study reported an overall increase in all-cause mortality and cancer incidence rates in adults that grew up as children in Wittenoom compared with the Western Australian adult population, predominantly but not solely due to malignant mesothelioma. There was a statistically significant increased incidence of mesothelioma. There were also consistently increased rates of some other cancers namely ovarian and brain cancers in females and leukaemia, prostate, brain, and colorectal cancers in males but whether these increases were significant or not depended on the method analysis used.

7. Two other studies (Hansen et al. (1998) and Reid et al. (2007), involving the same cohort of former residents of Wittenoom in Western Australia investigated the effect of childhood exposure to crocidolite. In both studies, individual asbestos exposures were estimated using the method as described in Reid et al. (2013). 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 Witternoom, 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 the 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 occupational 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-old female presenting with pleural mesothelioma, with a history of neighbourhood and domestic asbestos exposure during her childhood. She lived until the age of 4 in an area that was close to cement factories, nitrogen production 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 products 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 resembled that found in the general population. The individual had an elevated level of 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 µm. The size data indicated that the geometric mean fibre length was 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 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 indicated 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 overlaped 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) described a familial cluster of mesothelioma in a household. One daughter died of mesothelioma at the age of 32 years. Throughout her life, she was paraoccupationally exposed to asbestos through her father's 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.

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