Primary, Secondary and Tertiary
Prevention of Asbestos-related disease

Pitchaya Phakthongsuk, MD., Ph.D.
Occupational Health Unit, Community Medicine Department,
Faculty of Medicine, Prince of Songkla University,
Hatyai, Songkhla, Thailand

20 April 2011
"Knowing is not enough, we must apply. 
Willing is not enough, we must do"

-Goethe-
I would like to express my sincere gratitude to all those who gave me the possibility to complete this e-book.

I am deeply indebted to Dr. Somkiat Siriruttananapruk, Director of the Bureau of Occupational and Environmental Diseases, Department of Disease Control, Ministry of Public Health, who provided both the opportunity to write this book and unknowingly inspired me through his brave deed, not words all along the Asbestos ban Thailand. He also supported me to distribute this e-book as public domain materials.

Further thanks I feel compelled to mention is SAICAM (Strategic Approach to International Chemicals Management), who supported me for this writing.

I have furthermore to thank Saifar Suwanasam and Book Unit, Faculty of Medicine, Prince of Songkla University for index system.

Especially, I would like to give my special thanks to my husband Ray and my closed friends Mug and Tum, whose love and support enabled me to complete this e-book.
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<td>Arterial Blood Gas Analysis</td>
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<td>ACCP</td>
<td>American College of Chest Physician</td>
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<td>ACGIH</td>
<td>American Conference of Industrial Hygienists</td>
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<td>ACM</td>
<td>Asbestos Containing Material</td>
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<td>ADL</td>
<td>Active Daily Life</td>
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<td>AMA</td>
<td>American Medical Association</td>
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<td>AHERA</td>
<td>Asbestos Hazard Emergency Response Act</td>
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<td>ASTM</td>
<td>American Society for Testing and Materials</td>
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<td>ATS</td>
<td>American Thoracic Society</td>
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<td>ATSDR</td>
<td>Agency for Toxic Substances and Disease Registry (US)</td>
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<td>BAL</td>
<td>Brochoalveolar lavage</td>
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<td>BTS</td>
<td>British Thoracic Society</td>
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<td>BWI</td>
<td>Building and Wood Workers International</td>
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<td>CIS</td>
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<td>CPET</td>
<td>Cardiopulmonary Exercise Test</td>
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<td>Computer Tomogram</td>
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<td>CXR</td>
<td>Chest X-Ray</td>
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<td>DHSS</td>
<td>Department of Health and Human Services</td>
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<td>DL&lt;sub&gt;co&lt;/sub&gt;</td>
<td>Carbon monoxide Diffusing Factor</td>
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<td>DTS</td>
<td>Dutch Thoracic Society</td>
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<td>EBUS-FNA</td>
<td>Endobronchial Ultrasound Fine Needle Aspiration</td>
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<td>EDXA</td>
<td>Energy-dispersive X-ray analysis</td>
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<td>EFBWW</td>
<td>European Federation of Building and Wood Workers</td>
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<td>EMA</td>
<td>Epithelial Membrane Antigen</td>
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<td>EORTC</td>
<td>European Organization for Research and Treatment of Cancer</td>
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<td>EPA</td>
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<td>EPP</td>
<td>Extrapleural Pneumonection</td>
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<td>ERS</td>
<td>European Respiratory Society</td>
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<td>ESTS</td>
<td>European Society of Thoracic Surgeons</td>
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<td>ESMO</td>
<td>European Society for Medical Oncology</td>
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<td>FAM</td>
<td>Fibrous Aerosol Monitor</td>
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<td>FDG PET</td>
<td>18F-Fluorodeoxyglucose Positron Emission Tomography</td>
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<td>FEV1</td>
<td>Forced Expiratory Volume in 1 second</td>
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<td>FEF25-75</td>
<td>Forced Expiratory Flow at 25-75% which is a mean of the flow during an interval of FVC, usually between 25–75%</td>
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<td>FVC</td>
<td>Forced Vital Capacity</td>
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<td>HRCT</td>
<td>High Resolution Computer Tomogram</td>
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<td>HSE</td>
<td>Health and Safety Executive (UK)</td>
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<td>IARC</td>
<td>International Agency for Research on Cancer</td>
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<td>IAV</td>
<td>Institute of Asbestos Victims (Netherland)</td>
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<td>ICOH</td>
<td>International Commission on Occupational Health</td>
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<td>Acronym</td>
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<td>ICOERD</td>
<td>International Classification of HRCT for Occupational and Environmental Respiratory Disease</td>
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<td>INCHEM</td>
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<td>ILO</td>
<td>International Labour Organization</td>
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<td>IMRT</td>
<td>Intensity Modulated Radiotherapy</td>
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<td>IPF</td>
<td>Idiopathic Pulmonary Fibrosis</td>
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<td>ISO</td>
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<td>MET</td>
<td>Metabolic Equivalents</td>
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<td>MMF</td>
<td>Man Made Fiber</td>
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<td>MMOF</td>
<td>Man Made Organic Fiber</td>
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<td>MPM</td>
<td>Malignant Pleural Mesothelioma</td>
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<td>MRI</td>
<td>Magnetic Resonance Imaging</td>
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<td>MVV</td>
<td>Maximal Voluntary Ventilation</td>
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<td>NAIMA</td>
<td>North American Insulation Manufacturer Association</td>
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<td>NCI</td>
<td>National Cancer Institute (US)</td>
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<td>NIOSH</td>
<td>National Institute for Occupational Safety and Health (US)</td>
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<td>NOHSC</td>
<td>National Occupational Health and Safety Commission</td>
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<td>NPEAD</td>
<td>National Program for Elimination of Asbestos-related Diseases (ILO)</td>
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<td>NTP</td>
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<td>OEL</td>
<td>Occupational Exposure Limit</td>
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<td>OSHA</td>
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<td>PACM</td>
<td>Presumed Asbestos Containing Material</td>
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<td>PAHP</td>
<td>Plaintiff-Attorney-Hired B-readers</td>
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<td>PCM</td>
<td>Phase Contrast Microscopy</td>
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<td>PFT</td>
<td>Pulmonary Function Test</td>
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<td>PLM</td>
<td>Polarized Light Microscopy</td>
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<td>PVA</td>
<td>Polyvinyl alcohol</td>
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<td>RFP</td>
<td>Respiratory sized, Fiber-shaped Particulates</td>
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<td>SAEDP</td>
<td>Selected Area Electron Diffraction Pattern</td>
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<td>SAICM</td>
<td>Strategic Approach to International Chemicals Management</td>
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<td>SEM</td>
<td>Scanning Electron Microscopy</td>
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<td>SSA</td>
<td>Social Security Administration (US)</td>
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<td>STEL</td>
<td>Short Term Exposure Limit</td>
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<td>SUV</td>
<td>Standardized Uptake Value</td>
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<td>TEM</td>
<td>Transmission Electron Microscopy</td>
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<td>TCO</td>
<td>Transfer Factor</td>
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<td>TLC</td>
<td>Total Lung Capacity</td>
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<tr>
<td>Abbreviation</td>
<td>Description</td>
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<tr>
<td>TLV-TWA</td>
<td>Threshold Limit Value – Time Weighted Average</td>
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<tr>
<td>TNM</td>
<td>T stands for tumor size and invasiveness. T can range from T1 to T4; N stands for nodal involvement (lymph nodes) and is staged from N1 to N3; M stands for the presence (1) or absence (0) of metastases (spread to a distant site)</td>
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<tr>
<td>TWA</td>
<td>Time Weighted Average</td>
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<tr>
<td>UNEP</td>
<td>United Nations Environment Programme</td>
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<td>VATS</td>
<td>Video Assisted Thoracic Surgery</td>
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<td>VO₂max</td>
<td>Maximal Oxygen Consumption</td>
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<td>WHO</td>
<td>World Health Organization</td>
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<td>WTO</td>
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PREFACE

In Thailand, deadly asbestos, that causes lung cancer, asbestosis, and mesothelioma, has been imported for more than 40 years. Thailand was the world top 5 countries that imported and used asbestos. Asbestos is used in several industries, for example, 90% of imported raw materials are used in cement manufacture, e.g., roof tile and cement pipe. The others are used in production of brake and clutch (8%) and in production of vinyl floor tile, gasket, or heat insulating materials (2%). Several initiatives have been made to combat with cancerous asbestos.

In 2006, the Bangkok Declaration, which contains the aspirations and commitments of the Asian region, declared on elimination of asbestos and asbestos-related diseases. Since then, the asbestos ban movement in Thailand has persistently and officially started.

In 2007, National asbestos workshop in Thailand by National Board of Occupational Health and Environmental set ultimate goal on “Asbestos Ban in 2012”.


In 2010, the National Economic and Social Advisory Council (NESAC) passed the ban asbestos proposal to the Prime Minister and the Thailand National Health Assembly (NHA) also passed asbestos ban resolution.

In 2011, the resolution from NHC is going to the government cabinet for policy implementation. The cabinet resolution for asbestos ban is still in waiting.

This e-book has comprehensively reviewed the international and national litigation, guideline and recommendations of primary, secondary and tertiary prevention and control for asbestos. The purpose of this review is to provide candid and critical measures that will assist any institution in making decision on primary, secondary and tertiary prevention and control for asbestos as sound as possible. I wish this e-book will be useful to all those involved in asbestos ban programs both in my country and abroad, who from time to time need a reference to which they can refer to in the management of asbestos prevention and control programs.

Pitchaya Phakthongsuk, MD., Ph.D.
20 April 2011
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Health effect of chrysotile asbestos in aspect of some international and national health agencies

Chrysotile, like all other forms of asbestos, has produced malignant tumors in people who were occupationally exposed, family members of people who occupationally exposed, and residents who lived close to asbestos factories and mines. The main aim of this review part is to focus on the position of numerous national and international health agencies around the world towards health effect of chrysotile asbestos. The following information collected and provided the resources relevant to asbestos health effect from many respectable international and national agencies. These evidences address that both amphibole and chrysotile as carcinogenic substance and chrysotile carcinogenicity is no longer under debate but a widely accepted fact.

i) World Health Organization -WHO

WHO stated clearly that all forms of asbestos (amphibole or chrysotile) are carcinogenic to humans, and may cause mesothelioma and cancer of the lung, larynx and ovary. Asbestos exposure is also responsible for other diseases, such as asbestosis (fibrosis of the lungs), pleural plaques, thickening and effusions.

Currently, about 125 million people in the world are exposed to asbestos at the workplace. According to the most recent WHO estimates, more than 107 000 people die each year from asbestos-related lung cancer, mesothelioma and asbestosis resulting from exposure at work. One in every three deaths from occupational cancer is estimated to be caused by asbestos. In addition, it is estimated that several thousand deaths annually can be attributed to exposure to asbestos in the home.

ii) International Agency of Research on Cancer –IARC

According to IARC, asbestos in all forms has been classified as carcinogen class 1 or having carcinogenicity evidence in human. Moreover, IARC also address on sufficient evidence for carcinogenicity to animals as follow:

Evidence for carcinogenicity to humans (sufficient)

Numerous reports from several countries have described cases or series of pleural and peritoneal mesothelioma in relation to occupational exposure to various types and mixtures of asbestos (including talc containing asbestos), although
occupational exposures have not been identified in all cases. Mesothelioma of the tunica vaginalis, testis and of the pericardium have been reported in persons occupationally exposed to asbestos.

Environmental exposure either in the houses of asbestos workers or in the neighborhood of asbestos mines or factories has been noted in some of the cases. It has been estimated that a third of the mesothelioma occurring in the USA may be due to nonoccupational exposure. In a study from Israel, the incidence of mesothelioma was found to be higher among those born in the USA or in Europe relative to those born in Israel.

In some of these case reports and in other studies, asbestos fibres were identified in the lung. Amphibole fibres usually predominated, but in a few cases mainly or only chrysotile fibres were found.

The long latency required for mesothelioma to develop after asbestos exposure has been documented in a number of publications. An increasing proportion of cases has been seen with increasing duration of exposure.

A number of epidemiological studies of respiratory cancer and mesothelioma have been reported in relation to exposure to unspecified or complex mixtures of asbestos in shipyard work. The risk ratio for lung cancer has usually been moderately increased, both in these studies and in studies on various other occupational groups with similarly job-related but unspecified or complex asbestos exposures. Risk ratios of about 2-5 have been reported in some studies, but the ratio was considerably higher in one rather small study and did not exceed unity in another. In one study, individuals suffering from asbestosis had a considerably greater risk for lung cancer, with a risk ratio of 9.0. In some of the studies, a number of mesotheliomas were also observed. Abdominal mesotheliomas have sometimes been mistaken for pancreatic cancer. Mesothelioma cases have been observed to have relatively lower fibre content in the lungs than lung cancer cases.

Laryngeal cancer has been considered in two case-control studies, resulting in risk ratios of 2.4 and 2.3 that relate to exposure to unspecified or complex asbestos exposure, respectively. A cohort study of insulation workers showed a relative risk of 1.9, based on nine cases. A case series indicated a high frequency of exposure to asbestos, especially in low-grade smokers. A risk ratio of 3.2 for laryngeal cancer was reported among chrysotile miners in an area with generally high incidence, but no increased risk was seen in a cohort of workers with exposure to crocidolite. Two correlation studies have also indicated a relationship between laryngeal cancer and exposure to asbestos.

Mesotheliomas related to shipyard work and other exposures, including household contact with asbestos workers, have also been subject to epidemiological
studies, resulting in risk ratios of about 3-15 in comparison with background rates not clearly referable to asbestos exposure.

Some studies have specifically considered environmental exposures with reference to mesotheliomas. Three correlation studies and one case-control study considering exposure to piped drinking-water did not show consistently increased risks for any type of cancer, whereas another study considering chrysotile contamination mainly from natural sources gave some indication of an increase in the incidence of peritoneal and stomach cancers in persons of each sex, although no other cancer site was consistent in this respect.

Exposure to crocidolite has been studied with regard to risk of lung cancer, and risk ratios of about 2-3 have been reported. Three lung cancers and two mesotheliomas occurred in 20 individuals after one year of high exposure to crocidolite; at least 17 of the cases had asbestos-induced lung changes on X-ray films.

One study of histological types of lung cancers showed that among persons exposed to crocidolite, 45.7% of cases were squamous cell carcinomas, as compared to 35.2% among unexposed persons. In the context of unspecified and complex exposures, small cell carcinoma was found to be relatively more prevalent than other forms.

Exposure to chrysotile was found in some studies to result in virtually no increase in risk ratios, or a slightly elevated relative risk of lung cancer. Somewhat higher risk ratios, up to 2.5, 3.5 and 2, respectively, were obtained in one study of chrysotile miners and in two independent studies from one asbestos (chrysotile) textile plant, the latter being the more comprehensive. With regard to mesotheliomas, one study suggested a particularly high risk of combined exposure to chrysotile and amphiboles (risk ratio), thus almost multiplying the risk ratios (6 and 12, respectively) of exposures to chrysotile and to amphiboles alone. Another study showed no mesothelioma among a large worker population with exposure to chrysotile only.

A slight excess of lung cancer and some mesotheliomas appeared in some groups with mixed exposures involving amosite, chrysotile and crocidolite. Exposure predominantly to amosite, but also to chrysotile, was reported to be the probable cause of at least four of five mesotheliomas (one peritoneal) observed in a UK insulation-board factory. One cohort with exposure to cummingtonite-grunerite, which is closely related to amosite, had no clear excess of lung cancer, although one case of mesothelioma was observed.

Exposure to tremolite and actinolite has been the subject of a few studies in investigations of vermiculite mining and milling and environmental exposure. The
studies of miners indicated a risk ratio for lung cancer of up to approximately six fold. Deaths from mesothelioma were found in the occupational studies, whereas the study of environmental exposure showed no increased risk, although pleural plaques were reported. Publication of one case report of a mesothelioma after environmental exposure suggests that tremolite was of etiological importance. Cancers other than of the lung or mesothelioma have been considered in many studies. Some indicated an approximately two-fold risk with regard to gastrointestinal cancer in connection with shipyard work, and some increased risk was also seen in association with exposure to both chrysotile and crocidolite, to crocidolite or to chrysotile. Cancer of the colon and rectum was associated with asbestos exposure during chrysotile production, with an approximately two-fold risk; a similar excess was found for unspecified asbestos exposure. Some excess of ovarian cancer has been reported in two studies but not in another; exposure to crocidolite was probably more predominant in the studies that showed excesses. Bile duct cancer appeared in excess in one study based on record linking, and large cell lymphomas of the gastrointestinal tract and oral cavity appeared to be strongly related to asbestos exposure in one small study covering 28 cases and 28 controls, giving a risk ratio of 8; however, ten cases and one control also had a history of malaria. An excess of lymphopoietic and haematopoietic malignancies has been reported in plumbers, pipe-fitters, sheet-metal workers and others with asbestos exposure.

The relationship between asbestos exposure and smoking indicates a synergistic effect with regard to lung cancer. Further evaluations indicate that this synergistic effect is close to a multiplicative model. As noted previously, the risk of mesothelioma appears to be independent of smoking, and a significantly decreasing trend in risk was observed with the amount smoked in one study.

The studies of the carcinogenic effect of asbestos exposure, including evidence reviewed earlier, show that occupational exposure to chrysotile, amosite and anthophylite asbestos and to mixtures containing crocidolite results in an increased risk of lung cancer, as does exposure to minerals containing tremolite and actinolite and to tremolitic material mixed with anthophylite and small amounts of chrysotile. Mesotheliomas have been observed after occupational exposure to crocidolite, amosite, tremolitic material and chrysotile asbestos. Gastrointestinal cancers occurred at an increased incidence in groups occupationally exposed to crocidolite, amosite, chrysotile or mixed fibres containing crocidolite, although not all studies are consistent in this respect. An excess of laryngeal cancer has also been observed in some groups of exposed workers. No clear excess of cancer has been associated with the presence of asbestos fibres in drinking-water. Mesotheliomas
have occurred in individuals living in the neighborhood of asbestos factories and mines and in people living with asbestos workers.”

**Evidence for carcinogenicity to animals (sufficient)**

Asbestos has been tested for carcinogenicity by inhalation in rats, by intrapleural administration in rats and hamsters, by intraperitoneal injection in mice, rats and hamsters and by oral administration in rats and hamsters.

Chrysotile, crocidolite, amosite, anthophyllite and tremolite produced mesotheliomas and lung carcinomas in rats after inhalation and mesotheliomas following intrapleural administration.

Chrysotile, crocidolite, amosite and anthophyllite induced mesotheliomas in hamsters following intrapleural administration. Intraperitoneal administration of chrysotile, crocidolite and amosite induced peritoneal tumours, including mesotheliomas, in mice and rats. Given by the same route, crocidolite produced abdominal tumours in hamsters, and tremolite and actinolite produced abdominal tumours in rats. A statistically significant increase in the incidence of malignant tumours was observed in rats given filter material containing chrysotile orally. In more recent studies, tumour incidence was not increased by oral administration of amosite or tremolite in rats, of amosite in hamsters or of chrysotile in hamsters. In two studies in rats, oral administration of chrysotile produced a low incidence of benign adenomatous polyps of the large intestine in males (9/250 versus 3/254 pooled controls) and of mesenteric haemangiomas (4/22 versus 0/47 controls). Synergistic effects were observed following intratracheal administration of chrysotile and benzo(a)pyrene to rats and hamsters and of intratracheal administration of chrysotile and subcutaneous or oral administration of N-nitrosodiethylamine to hamsters.

**Other relevant data**

Insulation workers exposed to asbestos displayed a marginal increase in the incidence of sister chromatid exchanges in lymphocytes in one study.

Chrysotile did not induce micronuclei in bone-marrow cells of mice or chromosomal aberrations in bone-marrow cells of rhesus monkeys treated in vivo. In cultured human cells, conflicting results were reported for the induction of chromosomal aberrations and negative results for the induction of sister chromatid exchanges by chrysotile and crocidolite; amosite and crocidolite did not induce DNA strand breaks, and crocidolite was not mutagenic. Amosite, anthophyllite, chrysotile and crocidolite induced transformation of Syrian hamster embryo cells, chrysotile and crocidolite transformed BALB/c3T3 mouse cells, and chrysotile
transformed rat mesothelial cells. Neither amosite nor crocidolite transformed CH3 10T1/2 cells. In cultured rodent cells, amosite, anthophyllite, chrysotile and crocidolite induced chromosomal aberrations, and amosite, chrysotile and crocidolite induced sister chromatid exchanges; chrysotile and crocidolite induced aneuploidy and micronuclei. Chrysotile induced unscheduled DNA synthesis in rat hepatocytes. Amosite, chrysotile and crocidolite were inactive or weakly active in inducing mutation in rodent cells in vitro; none was mutagenic to bacteria.

iii) United Nation Environmental Program – UNEP ³

In 1998, the report on “chrysotile asbestos: Environmental health criteria series no.203”, under the sponsorship of UNEP, ILO and WHO produced under the framework of the inter-organization program for the sound management of chemicals. The report consisted of 9 parts: 1) identify, physical properties, sampling 2) sources of occupational and environmental exposure 3) occupational and environmental exposure levels 4) uptake, clearance and translocation 5) effects on animals and cells 6) effects on humans 7) environmental fate and effects on biota 8) evaluation of health risks of exposure to chrysotile asbestos and 9) conclusion and recommendation.

The full text of this report is available at http://www.inchem.org/documents/ehc/ehc/ehc203.htm. This documented included the summary part of asbestos health effects as follows:

**Effects on humans**

Commercial grades of chrysotile have been associated with an increased risk of pneumoconiosis, lung cancer and mesothelioma in numerous epidemiological studies of exposed workers.

The non-malignant diseases associated with exposure to chrysotile comprise a somewhat complex mixture of clinical and pathological syndromes not readily definable for epidemiological study. The prime concern has been asbestosis, generally implying a disease associated with diffuse interstitial pulmonary fibrosis accompanied by varying degrees of pleural involvement.

Studies of workers exposed to chrysotile in different sectors have broadly demonstrated exposure-response or exposure-effect relationships for chrysotile-induced asbestosis, in so far as increasing levels of exposure have produced increases in the incidence and severity of disease. However, there are difficulties in defining this relationship, due to factors such as uncertainties in diagnosis and the possibility of disease progression on cessation of exposure.

Furthermore, some variation in risk estimates is evident among the available studies. The reasons for the variations are not entirely clear, but may relate...
to uncertainties in exposure estimates, airborne fibre size distributions in the various industry sectors and statistical models. Asbestotic changes are common following prolonged exposures of 5 to 20 f/ml.

The overall relative risks for lung cancer are generally not elevated in the studies of workers in asbestos-cement production and in some of the cohorts of asbestos-cement production workers. The exposure-response relationship between chrysotile and lung cancer risk appears to be 10-30 times higher in studies of textile workers than in studies of workers in mining and milling industries. The relative risks of lung cancer in the textile manufacturing sector in relation to estimated cumulative exposure are, therefore, some 10-30 times greater than those observed in chrysotile mining. The reasons for this variation in risk are not clear, so several hypotheses, including variations in fibre size distribution, have been proposed.

Estimation of the risk of mesothelioma is complicated in epidemiological studies by factors such as the rarity of the disease, the lack of mortality rates in the populations used as reference, and problems in diagnosis and reporting. In many cases, therefore, risks have not been calculated, and cruder indicators have been used, such as absolute numbers of cases and deaths, and ratios of mesothelioma over lung cancers or total deaths.

Based on data reviewed in this UNEP monograph, the largest number of mesotheliomas has occurred in the chrysotile mining and milling sector. All the observed 38 cases were pleural with the exception of one of low diagnostic probability, which was pleuro-peritoneal. None occurred in workers exposed for less than 2 years. There was a clear dose-response relationship, with crude rates of mesotheliomas (cases/1000 person-years) ranging from 0.15 for those with cumulative exposure less than 3530 million particles per m³ (mpcm)-years (< 100 million particles per cubic foot (mpcf)-years) to 0.97 for those with exposures of more than 10590 mpcm-years (> 300 mpcf-years).

Proportions of deaths attributable to mesotheliomas in cohort studies in the various mining and production sectors range from 0 to 0.8%. Caution should be exercised in interpreting these proportions as studies do not provide comparable data stratifying deaths by exposure intensity, duration of exposure or time since first exposure.

There is evidence that fibrous tremolite causes mesothelioma in humans. Since commercial chrysotile may contain fibrous tremolite, it has been hypothesized that the latter may contribute to the induction of mesotheliomas in some populations exposed primarily to chrysotile.

The extent to which the observed excesses of mesothelioma might be attributed to the fibrous tremolite content has not been resolved.
The epidemiological evidence that chrysotile exposure is associated with an increased risk for cancer sites other than the lung or pleura is inconclusive. There is limited information on this issue for chrysotile per se, although there is some inconsistent evidence for an association between asbestos exposure (all forms) and laryngeal, kidney and gastrointestinal tract cancers. A significant excess of stomach cancer has been observed in a study of Quebec chrysotile miners and millers, but possible confounding by diet, infections or other risk factors has not been addressed.

It should be recognized that although the epidemiological studies of chrysotile-exposed workers have been primarily limited to the mining and milling, and manufacturing sector, there is evidence, based on the historical pattern of disease associated with exposure to mixed fibre types in western countries, that risks are likely to be greater among workers in construction and possibly other user industries.

**Environmental fate and effects on biota**

Serpentine outcroppings occur world-wide. Mineral components, including chrysotile, are eroded through crustal processes and are transported to become a component of the water cycle, sediment population and soil profile. Chrysotile presence and concentrations have been measured in water, air and other units of the crust.

Chrysotile and its associated serpentine minerals chemically degrade at the surface. This produces profound changes in soil pH and introduces a variety of trace metals into the environment. This has in turn produced measurable effects on plant growth, soil biota (including microbes and insects), fish and invertebrates. Some data indicate that grazing animals (sheep and cattle) undergo changes in blood chemistry following ingestion of grasses grown on serpentine outcrops.

**iv) World bank**

The World Bank has issued construction guidance to decrease the use of asbestos in construction projects around the world. The report on construction guidance was commissioned in 2006 but was not reviewed for another two years. However, this guidance was stalled for final administrative approval in 2009 and the World Bank now offered low interest loans and technical assistance to developing countries and expected loan recipients to avoid the use of asbestos-containing materials and use alternative materials wherever feasible.

The guidance report warns against the use of asbestos as “Health hazards from breathing asbestos dust include asbestosis, a lung scarring disease, and various forms of cancer. Mesothelioma, a signal tumor for asbestos exposure, occurs among
workers’ family members from dust on the workers’ clothes and among neighbors of asbestos air pollution point sources. Some experimental animal studies show that high inhalation exposures to all forms of asbestos for only hours can cause cancer.”

Furthermore, the report “Good practice Note on asbestos: Occupational and community health issues” which reviewed the health effect of asbestos stated clearly as follows:

**What is Asbestos, and Why are We Concerned with its Use?**

Asbestos is a group of naturally occurring fibrous silicate minerals. It was once used widely in the production of many industrial and household products because of its useful properties, including fire retardation, electrical and thermal insulation, chemical and thermal stability, and high tensile strength. Today, however, asbestos is recognized as a cause of various diseases and cancers and is considered a health hazard if inhaled. The ILO estimates that over the last several decades 100,000 deaths globally have been due to asbestos exposure, and the WHO states that 90,000 people die a year globally because of occupational asbestos exposure.

Over 90% of asbestos fiber produced today is chrysotile, which is used in asbestos-cement (A-C) construction materials: A-C flat and corrugated sheet, A-C pipe, and A-C water storage tanks. Other products still being manufactured with asbestos content include vehicle brake and clutch pads, roofing, and gaskets. Though today asbestos is hardly used in construction materials other than asbestos-cement products, it is still found in older buildings in the form of friable surfacing materials, thermal system insulation, non-friable flooring materials, and other applications. The maintenance and removal of these materials warrant special attention.

Because the health risks associated with exposure to asbestos area now widely recognized, global health and worker organizations, research institutes, and some governments have enacted bans on the commercial use of asbestos, and they urge the enforcement of national standards to protect the health of workers, their families, and communities exposed to asbestos through an International Convention.

**Health Concerns Linked to Asbestos-Containing Products**

Health hazards from breathing asbestos dust include asbestosis, a lung scarring disease, and various forms of cancer (including lung cancer and mesothelioma of the pleura and peritoneum). These diseases usually arise decades after the onset of asbestos exposure.
Mesothelioma, a signal tumor for asbestos exposure, occurs among workers’ family members from dust on the workers’ clothes and among neighbors of asbestos air pollution point sources.

Some experimental animal studies show that high inhalation exposures to all forms of asbestos for only hours can cause cancer. Very high levels of airborne asbestos have been recorded where power tools are used to cut A-C products and grind brake shoes.

For chrysotile asbestos, the most common variety, there is no threshold (non-zero) of exposure that has been shown to be free from carcinogenic risks. Construction materials are of particular concern, because of the large number of workers in construction trades, the difficulty of instituting control measures, and the continuing threat posed by in-place materials that eventually require alterations, repair, and disposal. Renovations and repairs in buildings containing A-C materials can also endanger building occupants. In addition to the problems from products made with commercial asbestos, asbestos also occurs as a contaminant in some deposits of stone, talc, vermiculite, iron ore, and other minerals. This can create health hazards for workers and residents at the site of excavation and in some cases in the manufacture and use of consumer products the materials are used to make.

While asbestos is a known carcinogen when inhaled, it is not known to be carcinogenic when ingested, as through drinking water, although pipe standards have been issued for asbestos-cement pipes conducting “aggressive” water.

From the industrial hygiene viewpoint, asbestos creates a chain of exposure from the time it is mined until it returns to the earth at landfill or unauthorized disposal site. At each link in the chain, occupational and community exposures coexist.

Workers in the mines are exposed to the fibers while extracting the ore; their families breathe fibers brought home on work clothes; workers in the mills and factories process the fiber and manufacture products with it; and their families are also secondarily exposed. Communities around the mines, mills, and factories are contaminated with their wastes; children play on tailings piles and in contaminated schoolyards; transportation of fiber and products contaminates roads and rights-of-way. Tradesmen who install, repair and remove ACM are exposed in the course of their work, as are bystanders in the absence of proper controls. Disposal of asbestos
wastes from any step in this sequence not only exposes the workers handling the wastes but also local residents when fibers become airborne because of insufficient covering and erosion control.

Finally, in the absence of measures to remove ACM from the waste stream and dispose of them properly, the cycle is often repeated when discarded material is scavenged and reused.

v) **World Trade Organization –WTO**

In 2000, WTO released a preliminary judgment upholding a French ban on the import of chrysotile asbestos. The ban, which was challenged by Canada as violating global free trade rules, was designed to protect French workers and consumers from this highly toxic material. WTO ruled that a French ban on the import of all products containing asbestos is legal on health grounds, despite protests from Canada. A WTO panel of experts rejected Canada's claim that the ban, which was imposed in January 1997 and also included the manufacturing, processing and sale of asbestos within France, was illegal because it damaged Canadian economic interests and was a barrier to free trade.

The Panel and the Appellate Body in this case both rejected Canada’s challenge to France import ban on asbestos and asbestos-containing products. These events reinforced the view that the WTO Agreements support members’ ability to protect human health and safety at the level of protection they deem appropriate. The key message of dispute by European Communities “Measures Affecting Asbestos and Asbestos-containing Products” on its hazardous effect was elaborated in the box below and full documents also could be found at http://www.wto.org/english/tratop_e/envir_e/edis09_e.htm.

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**Chrysotile asbestos is generally considered to be a highly toxic material, exposure to which poses significant threats to human health (such as asbestosis, lung cancer and mesothelioma).** However, due to certain qualities (such as resistance to very high temperature), chrysotile asbestos has been widely used in various industrial sectors. To control the health risks associated with asbestos, the French Government, which had previously been an importer of large quantities of chrysotile asbestos, imposed a ban on the substance as well as on products that contained it.

The European Communities justified its prohibition on the grounds of human
health protection, arguing that asbestos was hazardous not only to the health of construction workers subject to prolonged exposure, but also to population subject to occasional exposure. Being the second largest producer of asbestos world-wide, Canada contested the prohibition in the WTO. While it did not challenge the hazards associated with asbestos, it argued that a distinction should be made between chrysotile fibres and chrysotile encapsulated in a cement matrix. The latter, it argued, prevented release of fibres and did not endanger human health. It also argued that the substances which France was using as substitutes for asbestos had not been sufficiently studied and could themselves be harmful to human health.

Canada claimed that the Decree violated GATT Articles III:4 and XI, and Articles 2.1, 2.2, 2.4 and 2.8 of the TBT Agreement, and also nullified or impaired benefits under GATT Article XXIII:1(b). The EC argued that the Decree was not covered by the TBT Agreement. With regard to GATT 1994, it requested the panel to confirm that the Decree was either compatible with Article III:4 or necessary to protect human health within the meaning of Article XX(b).

Despite finding a violation of Article III, the Panel ruled in favor of the European Communities. Under Article III (which requires countries to grant equivalent treatment to like products) the Panel found that the EC ban constituted a violation since asbestos and asbestos substitutes had to be considered “like products” within the meaning of that Article. The panel argued that health risks associated with asbestos were not a relevant factor in the consideration of product likeness. However, the Panel found that the French ban could be justified under Article XX(b). In other words, the measure could be regarded as one which was “necessary to protect animal, human, plant life or health.” It also met the conditions of the chapeau of Article XX. It therefore ruled in favor of the European Communities.

On appeal, the WTO Appellate Body upheld the panel’s ruling in favor of the EC, while modifying its reasoning on a number of issues. For instance, it reversed the Panel’s finding that it was not appropriate to take into consideration the health risks associated with chrysotile asbestos fibres in examining the “likeness” of products under GATT Article III:4. The Appellate Body also argued that the case should have been looked at under the TBT Agreement rather than under GATT rules, but did not itself pursue the analysis under TBT since the Appellate Body only has a mandate to examine issues of “law” in dispute settlement (and cannot itself embark on new analyses).
vi) International Labour Organization -ILO

The intention of the ILO Asbestos Convention (C162) in 1986 when it was adopted was to eliminate the risk caused by asbestos by gradually banning and replacing asbestos. The Convention readily bans certain types of asbestos and processes in its use. It provides clear restrictions on any use, demolition and disposal of asbestos containing products.

In particular, article 10 gives two alternatives:

- replacement of asbestos or of certain types of asbestos or products containing asbestos by other materials or products or the use of alternative technology, scientifically evaluated by the competent authority as harmless or less harmful, whenever this is possible;
- total or partial prohibition of the use of asbestos or of certain types of asbestos or products containing asbestos in certain work processes. The text refers to "asbestos" meaning all types of it (both amphiboles and chrysotile). This was recently confirmed unanimously by the tripartite ILO/WHO Joint Committee recommending "the elimination of asbestos related diseases".

The 95th annual Conference of the International Labour Organization (ILO) in 2006 also adopted a Resolution concerning exposure to asbestos which causes some 100,000 deaths worldwide per year.

The Resolution declares that the elimination of the future use of asbestos and the identification and proper management of asbestos currently in place are the most effective means to protect workers from asbestos exposure and to prevent future asbestos-related diseases and deaths. It also resolves that the ILO's Asbestos Convention 1986 (No. 162) should not be used to provide a justification for, or endorsement of, the continued use of asbestos.

vii) Building and Wood Workers International (BWI), the World Federation of Building Workers (WFBW) and the Trades Union International of Workers in the Building, Wood and Building Materials Industries (UITBB)

BWI, WFBW, and UITBB are committed to actively promote the global ban of all forms of asbestos from the construction industry and from all other industrial sectors, and to promote the effective regulation of work with in-situ asbestos in demolition, conversion, renovation and maintenance works by law.

Considering that:

- All forms of asbestos, including chrysotile, are classified as known human carcinogens by the International Agency for Research on
Cancer -IARC and by the International Programme for Chemical Safety.

- 90 percent of chrysotile asbestos is used in asbestos cement materials.
- 100,000 workers die every year from diseases caused by exposure to asbestos.
- It has taken three decades of protracted efforts and the emergence of suitable alternatives for a comprehensive ban on the manufacture and use of asbestos and asbestos-containing products to be adopted in a number of countries. Furthermore that these countries now permit the handling of in situ asbestos only during asbestos removal, demolition, renovation and maintenance work carried out under strictly controlled working conditions.

**viii) International Social Security Association –ISSA**

ISSA issued a brochure ‘Asbestos: Towards a worldwide ban and advertized that “The purpose of this brochure of ISSA’s Special Commission on Prevention is to remind the reader that whilst asbestos may still be seen as a "miracle mineral", it is above all a time bomb and the moment has now come to ban it once and for all.”. The part on asbestos health effect of asbestos from its brochure was quoted as follows:

**Mechanisms of action**

Asbestos fibres break down into fibrils and are inhaled in the form of very fine dust that penetrates deep into the lungs. The longer and thinner these fibres are, the harder it is for the body to eliminate them. The body’s defense mechanisms cannot cope, and the physiochemical properties of the fibres trapped within the respiratory system mean that they cannot be broken down and destroyed.

They then very gradually cause inflammation and then fibrosis of the lung tissue (asbestosis) or the membrane - the pleura - which covers the lungs and may cause a variety of pleural conditions. On contact with the lining of the bronchi they can interfere with cell division and, after a lengthy latency period, cause cancerous changes leading to a lung tumour. The risk is exacerbated if there is simultaneous exposure to other carcinogenic agents.

Certain fibres may migrate outside the pleural cavity, where they evoke localized fibrosis (pleural plaques) or cancer of the pleura (mesothelioma). The most dangerous fibres are those which are long (more than 5 μm) and thin (less than 3 μm), with a length-to-diameter ratio greater than 3:1. However, whilst the likelihood
of developing an illness depends very largely on the size and nature of the asbestos fibres, and thus varies according to the type of asbestos concerned.

**Non-malignant respiratory diseases caused by asbestos**

*Pulmonary fibrosis (asbestosis)*

The disease is triggered by heavy exposure to asbestos fibres, over a variable length of time. The latency period between exposure and the onset of disease is usually 10 to 20 years or more, and the higher the exposure, the shorter the latency period will be. The symptom of asbestosis is breathlessness, which may progress to respiratory and cardiac insufficiency. There is no specific treatment, apart from alleviation of the symptoms. Patients with asbestosis are at higher risk than others of developing lung cancer, and that risk is significantly higher if they smoke.

**Benign pleural conditions**

Asbestos fibres migrate very readily from the lung to the pleura, where they cause a range of lesions: pleural plaques, pleurisy, diffuse pleural fibrosis. Pleural plaques are areas of fibrosis, with pleural thickening and sometimes calcification. Unlike asbestosis, these benign pleural plaques do not in general cause problems. They are usually identified on a chest X-ray. Regarded as a marker of asbestos exposure, they are not a predictor of mesothelioma.

**Asbestos-related cancers**

*Lung cancer*

High and protracted exposure to asbestos fibres increases the risk of developing bronchopulmonary cancer, even where there is no asbestosis. There is clearly a dose-effect relationship here, but the threshold for cancer induction cannot be identified.

Exposure to other carcinogens, especially tobacco smoke, exacerbates the risk. At the same level of exposure, the risk to smokers is ten times that of non-smokers. Latency periods between exposure to asbestos and the onset of pathological symptoms are on average 15–20 years, and may be as long as 30 years. The disease and its progression have no specificity compared with other cancers of the lung. The same applies to the options for treating it, which vary depending on the nature of the tumour, its stage and site. Whilst the prognosis is still often very poor, lung cancer can be cured, especially if it is diagnosed early.

**Pleural mesothelioma**
Mesothelioma is a primitive cancer of the pleura (and very rarely of the peritoneum and pericardium). This particularly malignant tumour is highly specific for exposure to asbestos. Onset typically follows a latency period of 20–40 years.

Unlike lung cancer it may be triggered by even very low-level and brief exposures. There is no link to smoking. Chest pain, cough and breathlessness are the principal symptoms. The prognosis for this cancer is very poor and no treatment has yet proved effective, though therapeutic trials are ongoing.

Other cancers

Scientific writing has looked at other cancer sites for a possible link with asbestos exposure:

- throat cancer, recognized as an occupational disease in some European countries;
- digestive cancers;
- urogenital cancers.

ix) Health and Safety Executive –HSE, British

There are four main diseases associated with inhalation of asbestos fibres. These are asbestosis (a scarring of the lung tissue caused by asbestos), two kinds of cancer (mesothelioma and asbestos related lung cancer), and diffuse pleural thickening (a non-malignant disease affecting the lung lining). The latest available statistics for each of these diseases are reported and discussed in the following web pages:

- Asbestosis
- Mesothelioma
- Asbestos-related lung cancer
- Diffuse pleural thickening

x) Occupational Safety and Health Administration –OSHA, US

OSHA’s position on asbestos health effect was elaborated as follows:

What is asbestos?

Asbestos is the name given to a group of naturally occurring minerals that are resistant to heat and corrosion. Asbestos has been used in products, such as insulation for pipes (steam lines for example), floor tiles, building materials, and in vehicle brakes and clutches. Asbestos includes the mineral fibers chrysotile, amosite, crocidolite, tremolite, anthophyllite, actinolite and any of these materials that have been chemically treated or altered. Heavy exposures tend to occur in the construction
industry and in ship repair, particularly during the removal of asbestos materials due to renovation, repairs, or demolition. Workers are also likely to be exposed during the manufacture of asbestos products (such as textiles, friction products, insulation, and other building materials) and during automotive brake and clutch repair work.

What are the hazards of asbestos?

Asbestos is well recognized as a health hazard and its use is now highly regulated by both OSHA and EPA. Asbestos fibers associated with these health risks are too small to be seen with the naked eye, and smokers are at higher risk of developing some asbestos-related diseases. Breathing asbestos fibers can cause a buildup of scar-like tissue in the lungs called asbestosis and result in loss of lung function that often progresses to disability and death. Asbestos also causes cancer of the lung and other diseases such as mesothelioma of the pleura which is a fatal malignant tumor of the membrane lining the cavity of the lung or stomach.

What can be done to reduce the hazards of asbestos?

Worker exposure to asbestos hazards is addressed in specific OSHA standards for the construction industry, general industry and shipyard employment sectors. These standards reduce the risk to workers by requiring that employers provide personal exposure monitoring to assess the risk and hazard awareness training for operations where there is any potential exposure to asbestos. Airborne levels of asbestos are never to exceed legal worker exposure limits. Where the exposure does, employers are required to further protect workers by establishing regulated areas, controlling certain work practices and instituting engineering controls to reduce the airborne levels. The employer is required to ensure exposure is reduced by using administrative controls and provide for the wearing of personal protective equipment. Medical monitoring of workers is also required when legal limits and exposure times are exceeded.

xi) National Institute of Occupational and Safety Health –NIOSH, USA

The NIOSH’s guideline for asbestos (regarded it as potential human carcinogen), has summarized pertinent information and recommendation to conduct effective occupational safety and health programs for asbestos. The part mentioned on asbestos health hazard included:

Substance identification

According to NIOSH, asbestos has various forms as:

Asbestos forms:
(1) Asbestos (mixed forms);
(2) Chrysotile;
(3) Amosite;
(4) Crocidolite;
(5) Tremolite;
(6) Anthophyllite;
(7) Actinolite.

If unspecified, NIOSH suggested that the information and recommendation still apply to all forms.

**Composition:**
(1) Not Available;
(2) \(3\text{MgO-2SiO}_2\text{-2H}_2\text{O}\);
(3) \((\text{FeMg})\text{SiO}_3\);
(4) \(\text{NaFe(SiO}_3\)\text{-2-FeSiO}_3\text{-H}_2\text{O}\);
(5) \(\text{Ca}_2\text{Mg}_5\text{Si}_8\text{O}_{22}(\text{OH})_2\);
(6) \((\text{MgFe})_7\text{Si}_8\text{O}_{22}(\text{OH})_2\);
(7) \(\text{CaO-3(MgFe)O-4SiO}_2\)

**Synonyms:**
(1) Asbestos fiber, serpentine, amphibole;
(2) Canadian chrysotile, white asbestos, serpentine;
(3) Brown asbestos, fibrous grunerite;
(4) Blue asbestos;
(5) Fibrous tremolite;
(6) Azbolen asbestos;
(7) Not available

**Health hazard information**

**Routes of exposure**

Asbestos may cause adverse health effects following exposure via inhalation or ingestion.

**Summary of toxicology**

1. Effects on animals: Single intrapleural injections of asbestos in rats, rabbits, and hamsters produced mesothelioma (cancer of the chest or abdominal linings). In rats, chronic inhalation or oral administration of asbestos produced cancers of the lungs, stomach, kidneys, liver, or mammary glands. All forms of asbestos were found to be carcinogenic in treated animals.
2. Effects on humans: Exposure to asbestos has been found to significantly increase the risks of contracting asbestosis, lung cancer, and mesothelioma.

*Signs and symptoms of exposure*

1. Short-term (acute): Exposure to asbestos can cause shortness of breath, chest or abdominal pain, and irritation of the skin and mucous membranes.

2. Long-term (chronic): Exposure to asbestos can cause reduced pulmonary function, breathing difficulty, dry cough, broadening and thickening of the ends of the fingers, and bluish discoloration of the skin and mucous membranes.

NIOSH also recommended the occupational health and safety measures for workers with potential exposures to chemical hazards. Workers should be monitored in a systematic program of medical surveillance intended to prevent or control occupational injury and disease. The program should include education of employers and workers about work-related hazards, placement of workers in jobs that does not jeopardize their safety and health, earliest possible detection of adverse health effects, and referral of workers for diagnostic confirmation and treatment. The occurrence of disease (a "sentinel health event," SHE) or other work-related adverse health effects should prompt immediate evaluation of primary preventive measures (e.g., industrial hygiene monitoring, engineering controls, and personal protective equipment).

A medical surveillance program is intended to supplement, not replace, such measures.

A medical surveillance program should include systematic collection and epidemiologic analysis of relevant environmental and biologic monitoring, medical screening, and morbidity and mortality data. This analysis may provide information about the relatedness of adverse health effects and occupational exposure that cannot be discerned from results in individual workers.

Sensitivity, specificity, and predictive values of biologic monitoring and medical screening tests should be evaluated on an industry-wide basis prior to application in any given worker group. Intrinsic to a surveillance program is the dissemination of summary data to those who need to know, including employers, occupational health professionals, potentially exposed workers, and regulatory and public health agencies.

*xii) National Cancer Institute –NCI, USA* ¹²

NCI, which is the federal government’s principle agency for cancer research and training in America, provided information on asbestos hazard as follows:
What is asbestos?
Asbestos is the name given to a group of minerals that occur naturally in the environment as bundles of fibers that can be separated into thin, durable threads. These fibers are resistant to heat, fire, and chemicals and do not conduct electricity. For these reasons, asbestos has been used widely in many industries.
Chemically, asbestos minerals are silicate compounds, meaning they contain atoms of silicon and oxygen in their molecular structure.
Asbestos minerals are divided into two major groups: Serpentine asbestos and amphibole asbestos. Serpentine asbestos includes the mineral chrysotile, which has long, curly fibers that can be woven.
Chrysotile asbestos is the form that has been used most widely in commercial applications.
Amphibole asbestos includes the minerals actinolite, tremolite, anthophyllite, crocidolite, and amosite. Amphibole asbestos has straight, needle-like fibers that are more brittle than those of serpentine asbestos and are more limited in their ability to be fabricated.

What are the health hazards of exposure to asbestos?
People may be exposed to asbestos in their workplace, their communities, or their homes. If products containing asbestos are disturbed, tiny asbestos fibers are released into the air. When asbestos fibers are breathed in, they may get trapped in the lungs and remain there for a long time. Over time, these fibers can accumulate and cause scarring and inflammation, which can affect breathing and lead to serious health problems.
Asbestos has been classified as a known human carcinogen (a substance that causes cancer) by the U.S. Department of Health and Human Services, the EPA, and the International Agency for Research on Cancer.
Studies have shown that exposure to asbestos may increase the risk of lung cancer and mesothelioma (a relatively rare cancer of the thin membranes that line the chest and abdomen).
Although rare, mesothelioma is the most common form of cancer associated with asbestos exposure. In addition to lung cancer and mesothelioma, some studies have suggested an association between asbestos exposure and gastrointestinal and colorectal cancers, as well as an elevated risk for cancers of the throat, kidney, esophagus, and gallbladder. However, the evidence is inconclusive.
Asbestos exposure may also increase the risk of asbestosis (an inflammatory condition affecting the lungs that can cause shortness of breath, coughing, and
permanent lung damage) and other nonmalignant lung and pleural disorders, including pleural plaques (changes in the membranes surrounding the lung), pleural thickening, and benign pleural effusions (abnormal collections of fluid between the thin layers of tissue lining the lungs and the wall of the chest cavity). Although pleural plaques are not precursors to lung cancer, evidence suggests that people with pleural disease caused by exposure to asbestos may be at increased risk for lung cancer.

Who is at risk for an asbestos-related disease?

Everyone is exposed to asbestos at some time during their life. Low levels of asbestos are present in the air, water, and soil. However, most people do not become ill from their exposure. People who become ill from asbestos are usually those who are exposed to it on a regular basis, most often in a job where they work directly with the material or through substantial environmental contact.

Since the early 1940s, millions of American workers have been exposed to asbestos. Health hazards from asbestos fibers have been recognized in workers exposed in the shipbuilding trades, asbestos mining and milling, manufacturing of asbestos textiles and other asbestos products, insulation work in the construction and building trades, and a variety of other trades. Demolition workers, drywall removers, asbestos removal workers, firefighters, and automobile workers also may be exposed to asbestos fibers. Studies evaluating the cancer risk experienced by automobile mechanics exposed to asbestos through brake repair are limited, but the overall evidence suggests there is no safe level of asbestos exposure. As a result of Government regulations and improved work practices, today’s workers (those without previous exposure) are likely to face smaller risks than did those exposed in the past.

Individuals involved in the rescue, recovery, and cleanup at the site of the September 11, 2001, attacks on the World Trade Center (WTC) in New York City are another group at risk of developing an asbestos-related disease. Because asbestos was used in the construction of the North Tower of the WTC, when the building was attacked, hundreds of tons of asbestos were released into the atmosphere. Those at greatest risk include firefighters, police officers, paramedics, construction workers, and volunteers who worked in the rubble at Ground Zero. Others at risk include residents in close proximity to the WTC towers and those who attended schools nearby. These individuals will need to be followed to determine the long-term health consequences of their exposure.

One study found that nearly 70 percent of WTC rescue and recovery workers suffered new or worsened respiratory symptoms while performing work at the WTC.
The study describes the results of the WTC Worker and Volunteer Medical Screening Program, which was established to identify and characterize possible WTC-related health effects in responders. The study found that about 28 percent of those tested had abnormal lung function tests, and 61 percent of those without previous health problems developed respiratory symptoms. However, it is important to note that these symptoms may be related to exposure to debris components other than asbestos.

Although it is clear that the health risks from asbestos exposure increase with heavier exposure and longer exposure time, investigators have found asbestos-related diseases in individuals with only brief exposures. Generally, those who develop asbestos-related diseases show no signs of illness for a long time after their first exposure. It can take from 10 to 40 years or more for symptoms of an asbestos-related condition to appear.

There is some evidence that family members of workers heavily exposed to asbestos face an increased risk of developing mesothelioma. This risk is thought to result from exposure to asbestos fibers brought into the home on the shoes, clothing, skin, and hair of workers. To decrease these exposures, Federal law regulates workplace practices to limit the possibility of asbestos being brought home in this way. Some employees may be required to shower and change their clothes before they leave work, store their street clothes in a separate area of the workplace, or wash their work clothes at home separately from other clothes.

Cases of mesothelioma have also been seen in individuals without occupational asbestos exposure who live close to asbestos mines.

**What factors affect the risk of developing an asbestos-related disease?**

Several factors can help to determine how asbestos exposure affects an individual, including:

- Dose (how much asbestos an individual was exposed to).
- Duration (how long an individual was exposed).
- Size, shape, and chemical makeup of the asbestos fibers.
- Source of the exposure.
- Individual risk factors, such as smoking and pre-existing lung disease.

Although all forms of asbestos are considered hazardous, different types of asbestos fibers may be associated with different health risks. For example, the results of several studies suggest that amphibole forms of asbestos may be more harmful than chrysotile, particularly for mesothelioma risk, because they tend to stay in the lungs for a longer period of time.
How does smoking affect risk?

Many studies have shown that the combination of smoking and asbestos exposure is particularly hazardous. *Smokers who are also exposed to asbestos have a risk of developing lung cancer that is greater than the individual risks from asbestos and smoking added together (multiplicative risk).* There is evidence that quitting smoking will reduce the risk of lung cancer among asbestos-exposed workers.

*Smoking combined with asbestos exposure does not appear to increase the risk of mesothelioma.* However, people who were exposed to asbestos on the job at any time during their life or who suspect they may have been exposed should not smoke.

**General Information**

Significant exposure to any type of asbestos will increase the risk of lung cancer, mesothelioma and nonmalignant lung and pleural disorders, including asbestosis, pleural plaques, pleural thickening, and pleural effusions.

This conclusion is based on observations of these diseases in groups of workers with cumulative exposures ranging from about 5 to 1,200 fiber-year/ml. Such exposures would result from 40 years of occupational exposure to air concentrations of 0.125 to 30 fiber/ml. The conclusion is supported by results from animal and mechanistic studies.
Diseases from asbestos exposure take a long time to develop. Most cases of lung cancer or asbestosis in asbestos workers occur 15 or more years after initial exposure to asbestos. Tobacco smokers who have been exposed to asbestos have a "far greater-than-additive" risk for lung cancer than do nonsmokers who have been exposed, meaning the risk is greater than the individual risks from asbestos and smoking added together.

The time between diagnosis of mesothelioma and the time of initial occupational exposure to asbestos commonly has been 30 years or more. Cases of mesotheliomas have been reported after household exposure of family members of asbestos workers and in individuals without occupational exposure who live close to asbestos mines.

**Asbestos Facts**

When asbestos fibers are inhaled, most fibers are expelled, but some can become lodged in the lungs and remain there throughout life. Fibers can accumulate and cause scarring and inflammation. Enough scarring and inflammation can affect breathing, leading to disease.

The term “naturally occurring asbestos” refers to the mineral as a natural component of soils or rocks as opposed to asbestos in commercial products, mining or processing operations. Naturally occurring asbestos can be released from rocks or soils by routine human activities, such as construction, or natural weathering processes. If naturally occurring asbestos is not disturbed and fibers are not released into the air, then it is not a health risk.

People are more likely to experience asbestos-related disorders when they are exposed to high concentrations of asbestos, are exposed for longer periods of time, and/or are exposed more often.
Inhaling longer, more durable asbestos fibers (such as tremolite and other amphiboles) contributes to the severity of asbestos-related disorders. Exposure to asbestos can increase the likelihood of lung cancer, mesothelioma, and non-malignant lung conditions such as asbestosis (restricted use of the lungs due to retained asbestos fibers) and changes in the pleura (lining of the chest cavity, outside the lung).

Changes in pleura such as thickening, plaques, calcification, and fluid around the lungs (pleural effusion) may be early signs of asbestos exposure. These changes can affect breathing more than previously thought. Pleural effusion can be an early warning sign for mesothelioma (cancer of the lining of the lungs).

Most cases of asbestosis or lung cancer in workers occurred 15 years or more after the person was first exposed to asbestos. Most cases of mesothelioma are diagnosed 30 years or more after the first exposure to asbestos.

Asbestos-related disease has been diagnosed in asbestos workers, family members, and residents who live close to asbestos mines or processing plants. Health effects from asbestos exposure may continue to progress even after exposure is stopped.

Smoking or cigarette smoke, together with exposure to asbestos, greatly increases the likelihood of lung cancer.

Health Risks of Asbestos Exposure

Chronic exposure to asbestos may increase the risk of lung cancer, mesothelioma, and nonmalignant lung and pleural disorders. Evidence in humans comes from epidemiologic studies as well as numerous studies of workers exposed to asbestos in a variety of occupational settings.

Tremolite asbestos exposure has been associated with an increased incidence of disease in vermiculite miners and millers from Libby, Montana. This evidence is supported by reports of increased incidences of nonmalignant respiratory diseases, lung cancer, and mesothelioma in villages in various regions of the world that have traditionally used tremolite-asbestos whitewashes in homes or have high surface deposits of tremolite asbestos and by results from animal studies.

Risk Factors

Various factors determine how exposure to asbestos affects an individual:

- Exposure concentration - what was the concentration of asbestos fibers?
- Exposure duration - how long did the exposure time period last?
- Exposure frequency - how often during that time period was the person exposed?
- Size, shape and chemical makeup of asbestos fibers:

Long and thin fibers are expected to reach the lower airways and alveolar regions of the lung, to be retained in the lung longer, and to be more toxic than short and wide fibers or particles. Wide particles are expected to be deposited in the upper respiratory tract and not to reach the lung and pleura, the sites of asbestos-induced toxicity. Short, thin fibers, however, may also play a role in asbestos pathogenesis. Fibers of amphibole asbestos such as tremolite asbestos, actinolite asbestos, and crocidolite asbestos are retained longer in the lower respiratory tract than chrysotile fibers of similar dimension.

Individual risk factors, such as a person’s history of tobacco use (smoking) and other pre-existing lung disease, etc.

Of note is that cigarette smoking and asbestos together significantly increase the chance of getting lung cancer. Therefore, if the workers have been exposed to asbestos, they should stop smoking. This may be the most important action that they can take to improve their health and decrease their risk of cancer.

Conditions Associated with Asbestos

Asbestosis

Asbestosis is a serious, progressive, long-term disease of the lungs. Asbestosis is not a cancer. Inhaling asbestos fibers irritate and inflame lung tissues, causing the lung tissues to scar, and asbestosis. The scarring makes it hard to breathe and difficult for oxygen and carbon dioxide pass through the lungs. Asbestosis generally progresses slowly. The latency period for the onset of asbestosis is typically 10-20 years after the initial exposure. The disease can vary from asymptomatic (no symptoms) to disabling and potentially fatal.

Figure 1.2 Microscopic view of lung tissue with asbestosis

Pitchaya Phakthongsuk, Occupational Health Unit, Community Medicine Department, Faculty of Medicine, Prince of Songkla University, Songkhla province, Thailand
Signs and Symptoms of asbestosis can include:

- Shortness of breath is the primary symptom
- A persistent and productive cough (a cough that expels mucus)
- Chest tightness
- Chest pain
- Loss of appetite
- A dry, crackling sound in the lungs while inhaling.

**Pleural Abnormalities**

Persons with significant exposure to asbestos are at risk for developing various types of pleural (lining of the chest cavity, outside the lungs) abnormalities. These abnormalities include pleural plaques, pleural thickening, pleural calcification, and pleural mesothelioma.

**Mesothelioma**

Mesothelioma is a rare cancer, which may affect the lining of the chest cavity, outside the lung (pleura) or the abdominal contents (peritoneum). *Most mesotheliomas are caused by exposure to asbestos.*

**Lung Cancer**

Lung cancer is a malignant tumor that invades and obstructs the lung's air passages. Cigarette smoking greatly increases the likelihood of a person developing lung cancer as the result of asbestos exposure. The most common symptoms of lung cancer are cough, wheezing, unexplained weight loss, coughing up blood, and labored breathing. Other symptoms of lung cancer include shortness of breath, persistent chest pain, hoarseness, and anemia. People who develop these symptoms do not necessarily have lung cancer, but they should consult a physician for advice.
xiv) Environmental Protection Agency – EPA, USA  
EPA declared that one of the highest priorities is to make significant and long overdue progress in assuring the safety of chemicals in US products. EPA provided the public with general information concerning asbestos as follows:

**What is asbestos?**

Asbestos is the name given to a number of naturally occurring fibrous minerals with high tensile strength, the ability to be woven, and resistance to heat and most chemicals. Because of these properties, asbestos fibers have been used in a wide range of manufactured goods, including roofing shingles, ceiling and floor tiles, paper and cement products, textiles, coatings, and friction products such as automobile clutch, brake and transmission parts. The Toxic Substances Control Act defines asbestos as the asbestiform varieties of: chrysotile (serpentine); crocidolite (riebeckite); amosite (cummingtonite/grunerite); anthophyllite; tremolite; and actinolite.

**Asbestos health effects**

Exposure to asbestos increases your risk of developing lung disease. That risk is made worse by smoking. In general, the greater the exposure to asbestos, the greater the chance of developing harmful health effects. Disease symptoms may take several years to develop following exposure. If you are concerned about possible exposure, consult a physician who specializes in lung diseases (pulmonologist).

Exposure to airborne friable asbestos may result in a potential health risk because persons breathing the air may breathe in asbestos fibers. Continued exposure can increase the amount of fibers that remain in the lung. Fibers embedded in lung tissue over time may cause serious lung diseases including asbestosis, lung
cancer, or mesothelioma. Smoking increases the risk of developing illness from asbestos exposure.

Three of the major health effects associated with asbestos exposure include:

- **Asbestosis** - Asbestosis is a serious, progressive, long-term non-cancer disease of the lungs. It is caused by inhaling asbestos fibers that irritate lung tissues and cause the tissues to scar. The scarring makes it hard for oxygen to get into the blood. Symptoms of asbestosis include shortness of breath and a dry, crackling sound in the lungs while inhaling. There is no effective treatment for asbestosis.

- **Lung Cancer** - Lung cancer causes the largest number of deaths related to asbestos exposure. People who work in the mining, milling, manufacturing of asbestos, and those who use asbestos and its products are more likely to develop lung cancer than the general population. The most common symptoms of lung cancer are coughing and a change in breathing. Other symptoms include shortness of breath, persistent chest pains, hoarseness, and anemia.

- **Mesothelioma** - Mesothelioma is a rare form of cancer that is found in the thin lining (membrane) of the lung, chest, abdomen, and heart and almost all cases are linked to exposure to asbestos. This disease may not show up until many years after asbestos exposure. This is why great efforts are being made to prevent school children from being exposed.
Bibliography


Primary prevention: prevent disease development

2.1 Total asbestos ban

The use of amphibole asbestos has been worldwide banned in 1990s and decreased the amount of asbestos world consumption for a while. Amphibole trade included 5 asbestos species: amosite, crocidolite, tremolite, anthophyllite and actinolite. Two of these are the most commercially valuable forms: amosite, or “brown asbestos,” and crocidolite, or “blue asbestos.” The other amphibole minerals are of little commercial importance. Since then, the other type of asbestos derived from serpentine asbestos, chrysotile, which is also known as “white asbestos accounts for nearly all asbestos used in the world today.

All forms of asbestos cause asbestosis, a progressive, debilitating fibrotic disease of the lungs. All forms of asbestos also cause malignant mesothelioma, lung, laryngeal, and ovarian cancers; and might may cause gastrointestinal and other cancers. Asbestos was declared a proven human carcinogen by the US Environmental Protection Agency (EPA), the International Agency for Research on Cancer (IARC) of the World Health Organization, and the National Toxicology Program (NTP) more than 20 years ago. The scientific community is in overwhelming agreement that there is no safe level of exposure to asbestos. Moreover, there is no evidence of a threshold level below which there is no risk of mesothelioma.

Chrysotile now represents 95 percent of all the asbestos ever used worldwide and is the only variety in international trade in the 21st century. Early suggestions that chrysotile might be less dangerous than other forms of asbestos have not been substantiated. There is general agreement among scientists and physicians, and widespread support from numerous national and international health agencies around the world, e.g., ACGIH, ATSDR, ILO, ISSA, NTP, NCI, OSHA, UNEP, WHO, WTO, that chrysotile causes various cancers, including mesothelioma and lung cancer. In 2006, WHO called for the elimination of diseases associated with asbestos. WHO supports individual countries in developing national plans to ban asbestos and eliminate asbestos-related disease, stating that “the most efficient way to eliminate asbestos-related disease is to stop using all types of asbestos”.

The 95th annual Conference of the International Labour Organization (ILO) in 2006 expressed concern about an evolving epidemic of asbestos-related diseases
which causes approximately 100,000 deaths worldwide per year. The Resolution from this conference called for the elimination of the future use of asbestos and the identification and proper management of asbestos currently in place are the most effective means to protect workers from asbestos exposure and to prevent future asbestos-related diseases and deaths. Likewise, the World Trade Organization (WTO) has also reached the same conclusion and stated that the “controlled use” of asbestos is a fallacy.

The Collegium Ramazzini, an international academic society which is independent of commercial interests and is dedicated to the prevention of occupational and environmental disease and the promotion of health. The name of the Collegium derives from Bernardino Ramazzini, the father of occupational medicine, a professor of medicine of the Universities of Modena and Padua in the early 1700s. Currently, 180 renowned clinicians and scientists from around the world, each of whom has been elected to membership, comprise the Collegium. The Collegium Ramazzini stated clearly that the so-called “controlled use” of asbestos is also a fallacy. In 2010, it has called again, as previously did in 1999, on all countries of the world to join in the international endeavor to ban all forms of asbestos and seriously consider an international ban on asbestos an urgent need. Up to now, Asbestos is now banned in 55 countries as shown in the table 2.1.
Table 2.1 National Asbestos Bans

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<th>National Asbestos Bans:^{1}</th>
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<td>Croatia^{2}</td>
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<td>Cyprus*</td>
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Note. Singapore and Taiwan have been removed from the ban list (Oct 2010). Although no further use of asbestos is anticipated in these two countries we have no hard evidence that comprehensive formal bans exist in either Singapore or Taiwan.

^1 Exemptions for minor uses are permitted in some countries listed; however, all countries listed must have banned the use of all types of asbestos. Additionally, we seek to ensure that all general use of asbestos, i.e. in construction, insulation, textiles, etc., has been expressly prohibited. The exemptions usually encountered are for specialist seals and gaskets; in a few countries there is an interim period where asbestos brake pads are permitted.

^2 Croatia banned asbestos as of January 1, 2006. Six weeks later, the Ministry of Economy, under political and commercial pressure, forced the Ministry of Health to reverse its position with the result that the manufacture of asbestos-containing products for export was permitted again.

^3 As the result of a series of restrictions on the use of asbestos introduced from the 1980s onwards, a de facto ban on asbestos exists in Israel.

^4 An immediate ban on amosite and crocidolite was imposed on August 16, 2005; a grace period of one year was allowed for the phasing out of the use of tremolite, chrysotile, anthophyllite and actinolite in friction products, brake linings and clutch pads. After August 16, 2006, all forms of asbestos were to be banned for all uses.

^5 Although an order banning the import of all types of asbestos including chrysotile was adopted in July 2010, the enforcement of this legislation is not without problems.

* January 1, 2005 was the deadline for prohibiting the new use of chrysotile, other forms of asbestos having been banned previously, in all 25 Member States of the European Union; compliance with this directive has not been verified in countries with an asterisk (*). As of May 2009 there are 27 Member States, with Romania and Bulgaria joining the EU in 2007.

Source: http://ibasecretariat.org/lka_alpha_asb_ban_280704.php
2.2 Prevention of new cases of asbestos-related diseases by hygienic controls

2.2.1 International convention

The International Labor Organization (ILO) established an C162 Asbestos Convention\textsuperscript{12} and R172 Asbestos Recommendation\textsuperscript{13} in 1986 to promote national laws and regulations for the “prevention and control of, and protection of workers against, health hazards due to occupational exposure to asbestos”. The convention outlines aspects of best practice: scope and definitions, general principles, protective and preventive Measures, surveillance of the working environment, and workers’ health and information and education. As of March 4, 2008, 31 countries had ratified the convention; 17 of them have banned asbestos\textsuperscript{14}.

2.2.2 Some international/ national standards and regulations for asbestos control at work

Standards and regulations for work involving ACM and asbestos abatement/ removal/ restoration have been published by non-governmental organizations and government agencies. This book provides a list of some resources including international organizations (e.g., WHO, ISO, ASTM) and national governments (e.g., UK, US, Canada, South Africa).

Of note is that some international and national organization which declared asbestos ban or elimination of asbestos-related diseases has provided only asbestos removal method; while some might cover both safe works with asbestos method and asbestos removal methods.

Some international standards

i) World Health Organization (WHO)

WHO provided no guideline on safety work with asbestos. The issue relevant to asbestos focused on the policy of elimination of asbestos-related disease as follows:

The 58\textsuperscript{th} World Health Assembly (WHA) resolution 58.22 (2005) on cancer prevention and control\textsuperscript{15-16} urged member states to pay special attention to cancers for which avoidable exposure is a factor, particularly exposure to chemicals and tobacco smoke in the workplace and the environment, certain infectious agents, and ionizing and solar radiation. This resolution is not directly addressed to chrysotile
asbestos but the WHO recommendation 2006 addressed directly on the cancer control caused by chrysotile asbestos as a result of WHA resolution 58.22.

**WHO recommendation 2006 on elimination of asbestos-related diseases**

...elaborated that all types of asbestos (amphiboles or chrysotile) have been classified by the International Agency for Research on Cancer (IARC) as being carcinogenic to humans and raised concern for some countries which have remained or even increased their production or use of chrysotile because that world production of chrysotile asbestos has been relatively stable at between 2,050,000 and 2,400,000 metric tons per annum in the period 2000-2005.

WHO regarded asbestos as one of the most important occupational carcinogens causing about half of the deaths from occupational cancer. There is no evidence for a threshold for the carcinogenic effect of asbestos and that increased cancer risks have been observed in populations exposed to very low levels, and the most efficient way to eliminate asbestos-related diseases is to stop using all types of asbestos. The 4 strategic directions towards elimination of asbestos-related diseases are recognizing that the most efficient way to eliminate asbestos-related diseases is:

- to recognize that the most efficient way to eliminate asbestos-related diseases is to stop the use of all types of asbestos
- to provide information about solutions for replacing asbestos with safer substitutes and developing economic and technological mechanisms to stimulate its replacement
- to take measures to prevent exposure to asbestos in place and during asbestos removal (abatement)
- to improve early diagnosis, treatment, social and medical rehabilitation of asbestos-related diseases and to establish registries of people with past and/or current exposures to asbestos

**The 60th World Health Assembly –WHA resolution 60.26 (2007) on workers’ health: global plan of action** underlined that member states should strengthen the capacities of the ministries of health to provide leadership for activities related to workers’ health, to formulate and implement policies and action plans, and to stimulate intersectoral collaboration. Its activities will include global campaigns for elimination of asbestos-related diseases –bearing in mind a differentiated approach to regulating its various forms.
WHO outline for the development of national programmes for elimination of asbestos-related diseases (2007)\textsuperscript{18} demonstrated the model for national programme for elimination of asbestos-related diseases in details as follows:

1. Introduction and purpose

This section should outline the magnitude of the problem, provide public health and other arguments for focusing on elimination of asbestos-related diseases as a priority and note the linkage to the relevant international binding and non-binding instruments.

*Health aspects:*

A short summary of the health effects of asbestos, which can be based on WHO and ILO documents Exposure to asbestos causes asbestosis, pleural plaques, thickening and effusions, lung cancer, mesothelioma, laryngeal and possibly other cancers with varying latency periods. This part should specifically underline that although the incidence of asbestos-related diseases is related to fibre type, fibre dose and industrial processing of asbestos, all types of asbestos are known human carcinogens and no threshold has been identified for the carcinogenic risk of chrysotile asbestos that accounts for 95% of all uses of asbestos today.

*Magnitude of the problem:*

This section should highlight the most important figures from the national asbestos profile, including a summary of the national inventory of main past and current uses of chrysotile and other forms of asbestos and asbestos-containing materials. Such an inventory can be prepared using customs information and domestic data on industrial products. This section should also deal with the number of exposed workers and the levels of exposure. High-risk groups, industries and occupations need to be clearly identified. Estimates of the future burden of disease attributable to current and past asbestos exposure may be more useful to determine potential health impacts than actual incidence and prevalence of reported asbestos-related diseases. Asbestos-related malignant diseases have very long latency period (up to 40 years) and currently they may not be manifest in countries that have recently increased their use of asbestos.

*Economic aspects:*

This section should include strategic economic arguments for elimination of asbestos-related diseases, e.g., direct costs, such as avoiding treatments costs and compensation claims (reference to the experience of other countries may be given
here, costs for demolition of buildings containing asbestos, costs for ensuring adequate health protection when working with asbestos already in place, and indirect costs, such as loss of potential income from asbestos-containing tourist facilities, depreciation of house stock built with asbestos etc).

Social aspects:

This section should address current and expected social impacts of the use of asbestos and asbestos-containing materials that need to be taken into account to ensure a just transition during the conversion to non-asbestos substitutes and technologies. Data should be presented on the number of jobs related to the import and domestic production of asbestos (in asbestos producing countries) and asbestos-containing materials, specific social networks and communities which are dependent on the consumption of asbestos. The social justice and equity aspects should be also tackled here, since living with asbestos may put some communities in a position of social disadvantage.

2. Political and legal background

Any national and international political decisions and statements that call for the elimination of asbestos-related diseases should be included here, e.g., resolutions and policy documents of WHO, ILO and UNEP. Reference should also be made to existing pieces of national legislation which directly or indirectly legitimize action for elimination of asbestos-related diseases, as well as obligations arising from international legal instruments.

Additionally information should be provided about the status of ratification by the country and/or the level of transposition of the provisions of the international legal instruments into the national legislation (ILO Convention No.139 and Recommendation No. 147 on Occupational Cancer; ILO Convention No. 162 and Recommendation 172 on Asbestos; Basel Convention on the Control of Transboundary Movements of Hazardous Wastes and Their Disposal; Rotterdam Convention on the Prior Informed Consent Procedure for Certain Hazardous Chemicals and Pesticides in International Trade). This section should also include reference to any enforceable national occupational exposure limits for the various forms of asbestos and how they compare to the best practice of other countries.

3. Strategy for elimination of asbestos related diseases

Preventive strategies:

Bearing in mind that there is no evidence of a threshold for the carcinogenic effect of both chrysotile and amphibole forms of asbestos and that increased cancer
risks have been observed in populations exposed to very low levels, the most efficient way to eliminate asbestos-related diseases is to stop using all types of asbestos.

Continued use of chrysotile asbestos cement in the construction industry is a particular concern, because the workforce is large, it is difficult to control exposure and in-place materials have the potential to deteriorate and pose a risk to those carrying out alterations, maintenance and demolition. In its various applications, asbestos can be replaced by some fibre materials and by other products which pose much less or no risk to health. Materials containing asbestos should be encapsulated and, in general, it is not recommended to carry out work that is likely to disturb asbestos fibres. Measures should be taken to avoid replacement of non-asbestos products with those containing asbestos, for example car brake pads.

When working with asbestos already in place, it is necessary to apply strict engineering measures to control exposure, such as encapsulation, wet processes, local exhaust ventilation with filtration and regular cleaning. Determining the form of asbestos (e.g. chrysotile or amphiboles) and monitoring of the level of exposure accordingly is also necessary to assess the effectiveness of engineering measures. The use of personal protective equipment special respirators, safety goggles, protective gloves and clothing - and the provision of special facilities for their decontamination are also needed for persons involved in work with asbestos.

Medical surveillance should be organized for early detection of any symptoms and health conditions resulting from asbestos exposure and the assessment of the adequacy of exposure control measures according to the ILO and WHO recommendations.

It is also necessary to establish national registries of workers exposed to the various forms of asbestos with data storage for at least 40 years. The registries should contain information on the exposure records (intensity, frequency and duration of exposure), medical examinations data, as well as information on the employer and the undertaking. Measures for controlling exposure to asbestos and medical surveillance require significant resources, and may be very difficult to carry out, particularly in countries with constrained resources, limited expertise and infrastructure for occupational health practice and insufficient level of general protection of health and the environment.

The enforcement of such measures may be practically impossible in small- and medium- sized enterprises and in the informal economy. Also, even the strictest occupational exposure limits are associated with health risks for asbestos-related diseases as no threshold has been identified for carcinogenic risks of asbestos. Therefore, the national strategy for elimination of asbestos-related diseases should
strive towards stopping the use of all forms of asbestos and replacing it with safer substitutes. The preventive strategy should envisage measures to encourage voluntary efforts by industry and be based on cooperation and consultation with the interested parties at national and enterprise levels. It should set up a framework for elimination of asbestos-related diseases, promote partnerships, commitments and cooperation.

Strategic actions:
National level

Action at the national level should create a political, regulatory and social environment and appropriate institutional framework conducive to elimination of asbestos-related diseases. Such action would include:

(a) political commitment to the elimination of asbestos-related diseases, e.g., prepare a national report on elimination of asbestos-related diseases to be presented to the government or the parliament, including information about past and current use, estimates of the health, economic and social consequences of continuing use of chrysotile asbestos and proposals for a package of measures to be taken to phase out its use and to prevent/contain the epidemic of asbestos-related diseases;

(b) ratification of international legal instruments (ILO conventions No 162 and 139, Basel and Rotterdam conventions) and development of specific laws and regulations to prevent exposure to the different forms of asbestos, to phase out their use and to ensure the prevention of asbestos-related diseases;

(c) introduction of fiscal mechanisms to reduce the use of chrysotile asbestos, e.g., import and excise duties, loans for conversion to non-asbestos technologies, establishment of a national fund for elimination of asbestos-related diseases with contribution from duty holders, insurance and compensation boards, governmental subsidy, etc.;

(d) updating and enforcement of occupational exposure limits for various forms of asbestos, e.g. align national occupational exposure limits to those listed in the IPCS Chemical Safety Card for Chrysotile, establishment of resources for determining the mineralogical form of asbestos and for measuring and monitoring its concentration in the air, introduction of practical tools for assessment and management of the risk from potential exposure and creation of a national reference laboratory;

(e) provision of an effective system of inspection and enforcement of technical standards and safety measures through strengthening the authority of the enforcement agencies in the areas of labour, building maintenance and construction, environment, public health, accreditation and standardization; provision of
guidelines for enterprises and economic undertakings for management of asbestos-related health risks, etc.;

(f) organization of early detection, notification, registration, reporting and compensation of asbestos-related diseases through improving diagnostic capacities for early detection of asbestosis and non-malignant asbestos-related disorders, clinical and pathological diagnosis of mesothelioma; establishing the causal relationship between lung and laryngeal cancer with exposure to asbestos; inclusion of all asbestos-related diseases in the national list of occupational diseases and development of diagnostic and exposure criteria for their recognition; establishing a fund for compensation of victims of asbestos-related diseases;

(g) provision of governmental advisory services to industry, trade and other economic undertakings, workers and their organizations and building owners on the use of safer substitutes for asbestos, application of preventive measures, and raising awareness about the risks related to the use of asbestos;

(h) enhancement of international collaboration to stimulate the transfer of know-how on alternatives to asbestos and best practices for prevention of asbestos-related diseases.

**Regional (provincial) level**

Local authorities should be involved in the efforts for elimination of asbestos-related diseases. Local authorities are usually responsible for issuing building licenses, monitoring the housing stock, landfills etc. In addition, municipalities may employ workers for building maintenance, reparation and demolition works that may involve exposure to asbestos. Local authorities may be able to take the following actions:

(a) introduce requirements for the use of safer substitutes for asbestos products and/or prohibit and enforce the prohibition of the production and use of chrysotile asbestos and asbestos-containing products;

(b) ensure that work involving potential exposure to the various forms of asbestos, e.g., demolition of structures containing asbestos, reparation and removal of asbestos from structures in which it is liable to become airborne, are carried out only by certified employers or contractors;

(c) take measures to dispose properly of asbestos-containing waste - wetted, transported covered, buried at special landfills and impregnated with agents that form a crust resistant to erosion;

(d) increase awareness among the general public of the hazards of demolition, removal and reparations of friable asbestos insulation in buildings and disseminate
information about the risks related to the presence of undisturbed asbestos in buildings;

(e) organize medical surveillance of municipal workers who might be exposed to asbestos in their work.

**Enterprise level**

Actions at this level should aim at reducing and eliminating the risks of exposure to asbestos. Enterprises can take the action in the following directions:

(a) replace chrysotile asbestos with safer substitutes and prevent potential exposure to any other type of asbestos already in place

(b) promote the elimination of the use of chrysotile asbestos among their contractors and suppliers.

(c) monitor the work environment for contamination with various forms of asbestos

(d) ensure compliance with exposure limits and technical standards for working with asbestos

(e) establish engineering measures for control of the exposure to asbestos at source

(f) provide special training for workers involved in activities with potential exposure to asbestos

(g) provide appropriate personal protective equipment;

(h) ensure registration and medical surveillance of workers exposed to asbestos.

Detailed guidance on actions to be taken at the enterprise level can be found in the ILO Code of Practice on Safety in the Use of Asbestos (1984) and in the Practical guide on best practice to prevent or minimize asbestos risks in work that involves (or may involve) asbestos: for the employer, the workers and the labour inspector developed by Senior Labour Inspectors Committee of the European Union (2006).

4. Institutional framework and principal partners

The National Program for Elimination of Asbestos-related Diseases (NPEAD) should be developed, implemented and evaluated in collaboration between principal stakeholders including governmental agencies, various national institutions, organizations and bodies responsible for and operating in the field of occupational safety, public health and environmental protection. This section of the document should also include a description of the general responsibilities of each of the principal stakeholders. Stakeholders may include:
- ministries responsible for health, labour, environment, industry, mines (in the case of asbestos-producing countries), transport, construction, science and technology, as well as national agencies and organizations such as national institutes and inspectorates responsible for occupational health, public health and the environment;
- organizations of employers, workers and civil society;
- professional associations, e.g. National Association on Occupational Health, National Safety Council, National Hygiene Association, National Lung Association, National Asbestos Awareness Association, Radiological Society, other professional associations and public interest groups;
- workers’ compensation and social security bodies;
- research, development and training institutions.

5. Knowledge management

National asbestos profile

A comprehensive National Asbestos Profile should be a compilation of all relevant information reflecting the current situation. It should serve as a baseline for measuring progress made towards the objectives of the NPEAD. For this reason, the profile should be updated periodically. In this section the NPEAD can indicate the frequency of the update and assign responsibility for this task.

Information about substitutes, alternative technologies and technical solutions

This section should deal with how information about asbestos substitutes and non-asbestos solutions will be collected, updated, evaluated and made available to the concerned and interested parties in the country.

Registry of workers exposed to asbestos

A central registry of all workers exposed to asbestos, including past exposures should be established and maintained. The registry should contain information about the enterprise, occupation, form of asbestos, level and duration of exposure.

Mobilization of resources

This section should provide strategic directions for releasing the existing resources for elimination of asbestos-related diseases and identifying further resources if necessary. Particular efforts are needed for strengthening the capacities and mobilizing the resources of ministries and enforcement agencies involved in the programme, as well as in local authorities and at the enterprise level.
Such work should also include training and licensing of contractors for asbestos abatement. There may be a need for increasing the level of expertise in practical measures for detecting potential exposure to the different forms of asbestos, measuring their concentrations in the air and preventive measures. Furthermore, it may be necessary to provide training of health professionals on screening, clinical and pathological diagnosis, recognizing and reporting asbestos-related diseases.

6. Programme implementation

An intersectoral mechanism for coordination and steering the development and implementation of the NPEAD (committee or task force) should be established as described above. The tasks of such mechanisms could be:

- to provide guidance for the development, implementation and evaluation of NPEAD;
- to ensure collaboration of the different stakeholders in implementing the national programme;
- to promote the programme objectives into the agenda of the government agencies concerned, private sector, workers, employers and the general public;
- to monitor and evaluate the progress made towards achieving the programme objectives and targets;
- to adopt plans of action for the different phases of the NPEAD implementation;
- to report to the government on the completion of the different phases of the programme and to recommend amendments and modifications of the NPEAD.

It is advisable to incorporate the activities related to the implementation of NPEAD into the work plans of participating governmental agencies, institutions and partners. It might be extremely useful to designate a focal point or a steering committee for providing leadership to the national program and to establish specific working groups for its major components. The members of this committee should be required to declare if they have any conflict of interests that might influence their attitudes in the work of the committee.

A specific budget should be allocated to the NPEAD. This budget may be in the form of a lump sum from the government, or through pooling together resources of the participating organizations. It might be useful to establish a special fund for implementation of the programme, e.g. using the import and excise duties on asbestos and asbestos-containing materials, contributions from workers’
compensation and insurance funds, governmental contribution, international assistance and voluntary donations.

The programme could be implemented step-by-step as follows:

Preparatory phase - the goal of this phase is to build up political commitment for starting the programme (accumulate data on current and past uses of the various forms of asbestos, particularly uses that have been already banned, those that are subject to restrictions and those that are not, as well as on morbidity and mortality from asbestos-related diseases; develop sufficient level of awareness of health risks posed by asbestos hazards; framing arguments, conducting feasibility studies and consultations; establishing intersectoral mechanisms; obtaining governmental approval; etc.) and to ensure that workers are fully protected from exposure to asbestos (introduce authorization of works involving asbestos, amend building codes with requirements for prevention of asbestos exposure; develop and introduce asbestos information and education campaigns, etc.);

First phase - the goal of this phase is to reduce substantially the use of chrysotile asbestos and the number of exposed workers in the country, focusing first on the uses of most health concern identified in the preparatory phase (introduce restrictions on the import, manufacture and use of asbestos, replace asbestos with safer alternatives wherever possible, increase awareness about asbestos and asbestos-related diseases);

Second phase - the goal is to phase out the use of chrysotile asbestos, make financial resources available for stopping the use of asbestos, strengthen legal, financial and enforcement mechanisms; create further incentives for the use of safer materials, ensure access to information and expert advice; improve registration and compensation of asbestos-related diseases;

7. Monitoring and evaluation

Evaluation criteria and indicators for monitoring progress in implementing NPEAD should be developed by the national intersectoral mechanism (steering committee/task force on elimination of asbestos-related diseases). This section should either describe these criteria or mandate their development and monitoring.

Indicators may include those related to:

(a) Outcome (impact): Such indicators should allow for answering the following:

Questions: Are the key outcomes established by the preventive strategy being met? Are over-exposures being reduced? Are dust control technologies being introduced? Are health and hazard surveillance systems established? The specific outcomes should be related to the overall strategy.
Examples: reduction of asbestos consumption per year; reduction of number of workers exposed to asbestos, estimated burden of asbestos-related diseases, level of public awareness about health risks arising from different uses of asbestos.

(b) Process: These indicators help answer the following questions: Are actions or processes that support prevention taking place? Has there been appropriate training, information dissemination, professional certification (e.g., laboratories, occupational health professionals, x-ray classification using the ILO 2000 System). Are the quality and quantity of workplace inspections improving? Again, these indicators should be linked to the prevention strategy.

Examples: number of physicians trained in diagnosis of asbestos-related diseases; percentage of asbestos workers covered with medical surveillance; number of labour inspectors and professionals from occupational health services trained in risk assessment and management of asbestos exposures; number of workers and employers trained in prevention of asbestos-related diseases; existence of national registry of workers exposed to asbestos; existence of system for authorization of works involving asbestos; amount of fund raised for the NPEAD; number of enterprises signing up to voluntary initiatives to reduce and eliminate the use of asbestos.

(c ) Administration: Is the program coordination and administration effective and efficient?

Examples: number of meetings of the steering committee per year; average level of attendance of meetings; rate of technical implementation of the individual activities; rate of financial implementation; percentage of activities completed by the deadline; evaluation of programme performance by committee members, partners and stakeholders.

The coordinating or steering committee should discuss progress on the NPEAD execution at least annually and formulate recommendations aiming at its further improvement.

WHO Factsheet no. 343 (2010) on elimination on asbestos-related disease addressed WHO role in relation to WHA resolution 58.22 and 60.26 that the World Health Assembly requested WHO to carry out a global campaign for the elimination of asbestos-related diseases "...bearing in mind a differentiated approach to regulating its various forms - in line with the relevant international legal instruments and the latest evidence for effective interventions...".

To eliminate asbestos-related diseases, WHO will particularly target at countries still using chrysotile asbestos, in addition to assistance in relation to exposures arising from historical use of all forms of asbestos. WHO, in collaboration
with the International Labour Organization and with other intergovernmental organizations and civil society, worked with countries towards elimination of asbestos-related diseases in four strategic directions: to stop the use of all types of asbestos; to provide information about solutions for replacing asbestos with safer substitutes; to take measures to prevent exposure to asbestos in place and during asbestos removal; and to improve early diagnosis, treatment, social and medical rehabilitation of asbestos-related diseases as previously stated in WHO recommendation 2006.

Emergency preparedness and response: Asbestos - hazards and safe practice for clear-up after tsunami

WHO recommended, before starting any work on site, the contractors or consultants should be given this guideline, and possibly information about the toxic substances the employees will be exposed to while on worksite, and the precautions they may take to decrease the risk of exposure. For example, external contractors involved in the construction or demolition of buildings used for industrial or other commercial purposes, may need to move asbestos ceiling tiles or wire installations. They should be given maps to identify asbestos-containing materials and instructed to use the proper personal protective equipment.

A contract may include a requirement to sign a statement indicating that programme guidelines were reviewed and understood. Orientation and training responsibilities should be clearly defined.

After the disaster, damage to asbestos-containing material can result in the release of small asbestos fibres that become airborne and are readily inhaled. These fibres can remain in the lungs for long periods thereby causing serious lung disease. WHO has also issued the guideline for risk assessment at clear-up ACM, general protection, work protection and disposal of ACM.

**ii) The International Programme on Chemical Safety (IPCS)**

The International Programme on Chemical Safety (IPCS), established in 1980, is a joint programme of three cooperating organizations - WHO, ILO and UNEP, implementing activities related to chemical safety. WHO is the executing agency of the IPCS, whose main roles are to establish the scientific basis for safe use of chemicals, and to strengthen national capabilities and capacities for chemical safety.

International Chemical Safety Cards (ICSCs)
IPCS INCHEM is a public online tool on basic chemical safety and its management produced through cooperation between the international programme on Chemical Safety (IPCS) and the Canadian Centre for Occupational Health and Safety (CCOHS); IPCS INCHEM directly responds to one of the Intergovernmental Forum on Chemical Safety (IFCS) priority actions to consolidate current, internationally peer-reviewed chemical safety-related publications and database records from international bodies, for public access.

The identification of the chemicals on the Cards is based on the UN numbers, the Chemical Abstracts Service (CAS) number and the Registry of Toxic Effects of Chemical Substances (RTECS/NIOSH) numbers. It is thought that the use of those three systems assures the most unambiguous method of identifying the chemical substances concerned, referring as it does to numbering systems that consider transportation matters, chemistry and occupational health.

Great similarities exist between the various headings of the ICSCs and the manufacturers' Safety Data Sheet (SDS) or Material Safety Data Sheet (MSDS) of the International Council of Chemical Associations, as can be seen in the following table 2.2.

Table 2.2 Comparison safety data sheets between ICCA and IPCS

<table>
<thead>
<tr>
<th>INTERNATIONAL CHEMICAL COUNCIL OF CHEMICAL PROGRAMME (ICCA) ASSOCIATIONS (IPCS) of</th>
<th>INTERNATIONAL PROGRAMME</th>
<th>CHEMICAL SAFETY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headings of Material Safety Data Sheets</td>
<td>Headings of International Chemical Safety Cards</td>
<td></td>
</tr>
<tr>
<td>2. Composition/Information on ingredients</td>
<td>2. Composition/formula</td>
<td></td>
</tr>
<tr>
<td>3. Hazards identification</td>
<td>3. Hazard identification from fire and explosion, and from exposure by inhalation, skin, eyes and ingestion, and Prevention measures (with personal protective equipment)</td>
<td></td>
</tr>
<tr>
<td>4. First-aid measures</td>
<td>First-aid measures</td>
<td></td>
</tr>
<tr>
<td>5. Fire-fighting measures</td>
<td>Fire-fighting measures</td>
<td></td>
</tr>
<tr>
<td>6. Accidental release measures</td>
<td>4. Spillage, disposal</td>
<td></td>
</tr>
</tbody>
</table>
7. Handling and storage

8. Exposure controls/Personal measures

See 3. above

7. Important data:

See 15. below

Occupational exposure limits

9. Physical & chemical properties

See 8. below

10. Stability & reactivity

Physical & chemical dangers

11. Toxicological information

Routes of exposure

Effects of short- and long-term exposure

See 9. above

8. Physical properties

9. Environmental data

10. Notes

12. Ecological information

13. Disposal considerations

See 4. above

14. Transport information

See 6. above

15. Regulatory information

See 7. above

11. Additional information

16. Other information

However, SDSs and the ICSCs are not the same. The SDS, in many instances, may be technically very complex and too extensive for shop floor use, and secondly it is a management document. The ICSCs, on the other hand, set out peer-reviewed information about substances in a more concise and simple manner. While not a legal document, the ICSC is an authoritative document emanating from WHO/ILO/UNEP.

This is not to say that the ICSC should be a substitute for an MSDS nothing can replace management's responsibility to communicate with workers on the exact chemicals, the nature of those chemicals used on the shop floor and the risk posed in any given work place.

Indeed, the ICSC and the SDS can even be thought of as complementary. If the two methods for hazard communication can be combined, then the amount of knowledge available to the safety representative or shop floor workers will be more than doubled. The ICSC could serve as a model for disseminating chemical safety information to workers.

iii) **International Organization for Standardization –ISO**

ISO (International Organization for Standardization) is the world's largest developer and publisher of International Standards. ISO is a non-governmental international organization which is network of the national standards institutes of 163 countries, one member per country, with a Central Secretariat in Geneva, Switzerland, that coordinates the system. The standards involving Asbestos mainly focused on the sampling strategy and laboratory analysis of asbestos.

**ISO 30007:2010 Ships and marine technology -Measures to prevent asbestos emission and exposure during ship recycling**

ISO 30007:2010 provides effective methods for minimizing the dangers of asbestos during ship recycling, reducing both the release of asbestos into the environment and worker exposure to asbestos. It helps ship recyclers to fulfill the requirements of The Hong Kong International Convention for the Safe and Environmentally Sound Recycling of Ships, 2009.

**ISO 8336:2009 Fibre-cement flat sheets -Product specification and test methods**

ISO 8336:2009 specifies methods for the inspection and testing of fibre-cement flat sheets and gives the acceptance conditions for their use in one or more of the following applications:

- external wall and ceiling finishes;
- internal wall and ceiling finishes;
- internal and external backing sheets.

Products covered by ISO 8336:2009 can be used for other purposes, provided they comply with the appropriate national or international application code or standard.

ISO 8336:2009 does not apply to sheets for fire protection purposes
ISO 8336:2009 does not include calculations for installation design requirements, wind uplift or water proofing of the installed sheets.
ISO 8336:2009 does not apply to the following products:
- boards of Portland or equivalent cement reinforced with fibrous wood particles;
- fibre-reinforced boards of calcium silicate or cement for thermal insulation or fire protection;
- sheets containing asbestos fibre reinforcement;
- sheets containing steel fibre reinforcement;
- fibre-cement roofing slates
ISO 9125:2009 Fibre-cement slates and fittings -- Product specification and test methods

ISO 9125:2009 specifies technical requirements and methods for the inspection and testing of fibre-cement slates and shingles and their fibre-cement fittings, designed to protect the weather-exposed surfaces on roofs and claddings of buildings. Products covered by ISO 9125:2009 can be used for other purposes provided they comply with the appropriate national or international application code or standard.

ISO 9125:2009 applies to fibre-cement slates with a height dimension not exceeding 850 mm for overlapping assembly.

The type tests described in ISO 9125:2009 are not intended to evaluate the performance of the coating in isolation (colour fastness, adhesion, etc.). Specific performance requirements for coatings are referenced in other ISO or national standards.

ISO 9125:2009 does not apply to fibre-cement slates reinforced with asbestos fibres.

ISO 9125:2009 does not include calculations for installation requirements, wind uplift or rain proofing of the installed products. National standards for installation requirements can be adopted.

ISO 16000-7: 2007 Indoor air - Part 7: Sampling strategy for determination of airborne asbestos fibre concentrations.

ISO 16000-7:2007 specifies procedures to be used in planning of air measurements to determine the concentrations of asbestos in indoor atmospheres. Careful planning of the measurement strategy is important, because the results can become the basis of recommendations for major building renovations, or for the return of a building to normal occupancy status after removal of asbestos-containing materials.

ISO 16000-7:2007 uses the following definition for indoor environments as specified in ISO 16000-1: dwellings having living rooms, bedrooms, do-it-yourself (DIY) rooms, recreation rooms, cellars, kitchens and bathrooms; workrooms or workplaces in buildings which are not subject to health and safety inspections in regard to air pollutants (for example, offices and sales premises); public and commercial buildings (for example, hospitals, schools, kindergartens, sports halls, libraries, restaurants and bars, theatres and other function rooms); cabins of vehicles and public transport.
ISO 1833-19:2006 Textiles -Quantitative chemical analysis -Part 19: Mixture of cellulose fibres and asbestos (method by heating)

ISO 1833-19:2006 specifies a method, by heating, to determine the percentage of cellulosic fibre in textiles made of binary mixtures of cotton or regenerated cellulose and chrysotile and crocidolite asbestos. This method may be applicable to other types of asbestos, subject to agreement between the interested parties.

ISO 14966:2002 Ambient air -Determination of numerical concentration of inorganic fibrous particles -Scanning electron microscopy method

ISO 14966:2002 specifies a method using scanning electron microscopy for determination of the concentration of inorganic fibrous particles in the air. The method specifies the use of gold-coated, capillary-pore, track-etched membrane filters, through which a known volume of air has been drawn. Using energy-dispersive X-ray analysis, the method can discriminate between fibres with compositions consistent with those of the asbestos varieties (e.g. serpentine and amphibole), gypsum and other inorganic fibres. Annex C of ISO 14966:2002 provides a summary of fibre types which can be measured.

ISO 14966:2002 is applicable to the measurement of the concentrations of inorganic fibrous particles in ambient air. The method is also applicable for determining the numerical concentrations of inorganic fibrous particles in the interior atmospheres of buildings, for example, to determine the concentration of airborne inorganic fibrous particles remaining after the removal of asbestos-containing products.

The range of concentrations for fibres with lengths greater than 5 micrometres, in the range of widths which can be detected under standard measurement conditions, is approximately 3 fibres to 200 fibres per square millimetre of filter area. The air concentrations, in fibres per cubic metre, represented by these values are a function of the volume of air sampled.

The ability of the method to detect and classify fibres with widths lower than 0.2 micrometres is limited. If airborne fibres in the atmosphere being sampled are predominantly less than 0.2 micrometres in width, a transmission electron microscopy method such as ISO 10312 can be used to determine the smaller fibres.


This standard specifies a reference method using transmission electron microscopy (TEM) for determination of the concentration of asbestos structures in ambient atmospheres. The specimen preparation
procedure incorporates ashing and dispersion of the collected particulate, so that all asbestos is measured, including the asbestos originally incorporated in particle aggregates or particles of composite materials. The lengths, widths and aspect ratios of the asbestos fibres and bundles are measured, and these, together with the density of the type of asbestos, also allow the total mass concentration of airborne asbestos to be calculated. The method allows determination of the type(s) of asbestos fibre present.

The method cannot discriminate between individual fibres of the asbestos and non-asbestos analogues of the same amphibole mineral.

The method is defined for polycarbonate capillary-pore filters or cellulose ester (either mixed esters of cellulose or cellulose nitrate) filters through which a known volume of air has been drawn. The method is thus suitable for determination of asbestos in both exterior and building atmospheres.

The upper limit for the range of concentration that can be measured on the analytical filter is 7000 structures/mm². The lower limit of the range that can be measured on the analytical filter corresponds to detection of 299 structures in the area of specimen examined. The air concentrations represented by these values are a function of the volume of air sampled and the degree of dilution or concentration selected during the specimen preparation procedures. The method is particularly applicable for measurements in areas with high suspended-particulate concentrations (exceeding 10 μg/m³), or where detection and identification of asbestos fibres are likely to be prevented or hindered by other types of particulate in direct-transfer TEM preparations. In theory, there is no lower limit to the dimensions of asbestos fibres which can be detected. In practice, microscopists vary in their ability to detect very small asbestos fibres. Therefore, a minimum length of 0.5 μm has been defined as the shortest fibre to be incorporated in the reported results.

The limit of detection theoretically can be lowered indefinitely by filtration of progressively larger volumes of air, concentrating the sample during specimen preparation, and by extending the examination of the specimens in the electron microscope. In practice, the lowest achievable limit of detection for a particular area of TEM specimen examined is controlled by the total suspended particulate concentration remaining after the ashing and aqueous dispersal steps, and this depends on the chemical nature of the suspended particulate.
For total suspended particulate concentrations of approximately 10 μg/m³, corresponding to clean, rural atmospheres, and assuming filtration of 4 000 litres of air, an analytical sensitivity of 0.5 structure/litre can be obtained, equivalent to a limit of detection of 1.8 structures/litre, if an area of 0.195 mm² of the TEM specimens is examined. Lower limits of detection can be achieved by increasing the area of the TEM specimen that is examined or by concentration of the sample during specimen preparation. In order to achieve lower limits of detection for fibres and bundles longer than 5 μm, and for PCM-equivalent fibres, lower magnifications are specified which permit more rapid examination of larger areas of the TEM specimens when the examination is limited to these dimensions of fibre.

ISO 8672 (1993): Air quality - Determination of the number concentration of airborne inorganic fibres by phase contrast optical microscopy - Membrane filter method [Method similar to AIA RTM1]

The principle of the method specified is collecting a sample by drawing a measured quantity of air through a membrane filter by means of a battery-powered sampling pump, transforming the filter from an opaque membrane into a homogeneous optically transparent specimen, sizing and counting the fibres using a phase contrast microscope. The results are expressed as fibres per cubic centimetre of air, calculated from the number of fibres on the filter and the measured volume of air sampled. Limitations of the method are stated.


This standard specifies a Reference method using transmission electron microscopy for the determination of the concentration of asbestos structures in ambient atmospheres and includes measurement of the lengths, widths and aspect ratios of the asbestos structures. The method allows determination of the types of asbestos fibres present.

The method cannot discriminate between individual fibres of the asbestos and non-asbestos analogues of the same amphibole mineral.
ISO 10397:1993 Stationary source emissions - Determination of asbestos plant emissions - Method by fibre count measurement

The principle of the method specified is isokinetically withdrawing a known volume from a moving gas stream, passing the sampled gas through a filter medium to remove particulate matter (including fibres), treating the filter to make it transparent when viewed under a microscope and counting the number of fibres in a precise number of fields viewed using a phase-contrast optical microscope. The method may be used to determine fibre concentrations in flowing gas streams in ducts, chimneys, or flues from a wide range of industrial processes.

iv) Basel Convention on the Control of Transboundary Movements of Hazardous Wastes and their Disposal

In the late 1980s, a tightening of environmental regulations in industrialized countries led to a dramatic rise in the cost of hazardous waste disposal. Searching for cheaper ways to get rid of the wastes, “toxic traders” began shipping hazardous waste to developing countries and to Eastern Europe. When this activity was revealed, international outrage led to the drafting and adoption of the Basel Convention.

This convention is a global agreement, ratified by several member countries and the European Union, for addressing the problems and challenges posed by hazardous waste. The Secretariat, in Geneva, Switzerland, facilitates the implementation of the Convention and related agreements. It also provides assistance and guidelines on legal and technical issues, gathers statistical data, and conducts training on the proper management of hazardous waste. The Secretariat is administered by UNEP.

The categories of hazardous waste covered by the convention are toxic, poisonous, explosive, corrosive, flammable, ecotoxic and infectious wastes.

The key objectives of the Basel Convention are:
- to minimize the generation of hazardous wastes in terms of quantity and hazardousness;
- to dispose them as close to the source of generation as possible;
- to reduce the movement of hazardous wastes.

v) International Labour Organization

The ILO is the international organization responsible for drawing up and overseeing international labour standards. It is the only 'tripartite' United Nations
agency that brings together representatives of governments, employers and workers to jointly shape policies and programmes.

**ILO issues a code of practice ‘Safety in the use of asbestos’**

The code is based on principles established by the following conventions and recommendations adopted by the international labour conference: the Occupational Cancer Convention, 1974 (No. 139), and Recommendation, 1974 (No. 147), the Working Environment (Air Pollution, Noise and Vibration) Convention, 1977 (No. 148), and Recommendation, 1977 (No. 156), and the Occupational Safety and Health Convention, 1981 (No. 155), and Recommendation, 1981 (No. 164).

The practical recommendations of this code of practice providing guidance of exposure limits, environmental monitoring, preventive methods, personal protection, plant cleaning, packaging-transport-storage, disposal of asbestos waste, supervision of health of workers, training, and control of asbestos exposure in specific activities.

**Chemical Safety Card, ICSC 0014 -Chrysotile**

The ICSC project is a joint undertaking between the International Labour Office (ILO) and the World Health Organization (WHO) which provide essential health and safety information on chemicals. The primary aim of the cards is to promote the safe use of chemicals in the workplace and the main target users are therefore workers and those responsible for health and safety in the workplace.

The Cards are made available free of charge via the Internet, in a searchable database, in as many languages as possible, and in a format which is easily displayed. The web-based database hosting the Cards can be searched by chemical name, common synonyms or CAS number.


**vi) European Union**

**Directive 2003/18/EC**

This directive has been amended from the Council Directive 83/477/EEC on the Protection of workers from the risks related to exposure to asbestos at work in March 2003.
This directive provides regulations including worker protection, training and medical surveillance; inspections for asbestos-containing materials; notification of asbestos work; air sampling; and new exposure limits of 0.1 fibres per cm³ (8-hr TWA) measured by Phase Contrast Microscopy – PCM. The main issue amended in Directive 2003/18/EC were as follows:

- reduces the limit value for occupational exposure of workers to asbestos. It repeals the two limit values established by Directive 83/477, setting a single maximum limit value for airborne concentration of asbestos of 0.1 fibres per cm³ as an eight-hour time-weighted average (TWA);
- abolishes the derogations applicable to the sea and air transport sectors;
- prohibits activities exposing workers to asbestos fibres, with the exception of the treatment and disposal of products resulting from demolition and asbestos removal;
- updates the practical recommendations on the clinical surveillance of exposed workers in the light of the latest medical expertise, with a view to the early detection of pathologies linked to asbestos.

Previous regulations (been amended as in Directive 2003/18/EC)

The Directives do not apply to sea or air transport.

"Asbestos" is taken to mean six fibrous silicates (actinolite, asbestos gruenerite, anthophyllite, chrysotile, crocidolite, and tremolite).

The limit values pertaining to in-air concentrations are corrected and Referred to are:

for chrysotile: 0.60 fibres per cm³ calculated or measured for an eight-hour Reference period;

for all other forms of asbestos: 0.30 fibres per cm³ calculated or measured for an eight-hour Reference period.

Any activity likely to entail risk of exposure to dust arising from asbestos or materials containing asbestos must be assessed in such a way as to determine the degree and nature of the workers’ exposure.

These activities are to be notified by the employer to the responsible authority of the Member State. The notification must include at least a description of the types and quantities of asbestos used the activities and processes involved, and the products
manufactured. Workers or their representatives are entitled to see the documents concerned.

The application of asbestos by means of the spraying process and working procedures that involve the use of low-density (less than 1g/cm3) insulating or soundproofing materials are prohibited.

Exposure to asbestos is reduced by limiting its use as far as possible, keeping to a minimum the number of persons exposed, and taking adequate measures to maintain buildings and ensure that materials are properly stored, transported and labeled.

In order to ensure compliance with the limit values, asbestos-in-air concentrations are to be measured regularly.

If these values are exceeded, the reasons must be identified and appropriate measures to remedy the situation must be taken before work is resumed.

The places in which activities giving rise to exposure risks are carried out must be clearly marked and indicated by warning signs. They are to be out of bounds to smokers and workers other than those who, by reason of work or duties, are required to enter such areas. Areas are to be set aside where workers can eat and drink without risking being contaminated by asbestos dust. Workers are to be provided with appropriate working or protective clothing.

Workers and/or their representatives must receive adequate information on health risks; the existence of limit values; the need for monitoring of the atmosphere; hygiene requirements and specific precautions to be taken.

Each worker's state of health must be assessed, including a specific chest examination, prior to exposure to dust arising from asbestos or materials containing asbestos and subsequently at least once every three years for the duration of the exposure. The employer is required to keep a register indicating the nature and duration of the activity and the exposure to which the worker is subjected; both the worker concerned and doctors must have access to the information in the register.

A plan of work setting out the necessary health and safety measures is to be drawn up before the commencement of any demolition work or work involving removal of asbestos.

Member States must keep a register of cases of asbestosis and mesothelioma. The employer will not be required to notify the authority, take atmospheric measurements, put up warning signs, carry out health assessment or inform workers if the assessment of the exposure risks shows that the asbestos-in-air concentration is as follows:

for chrysotile, lower than 0.20 fibres per cm³ for an eight-hour Reference period or
lower than a cumulative dose of 12.00 fibres over a three-month period,

For all other forms of asbestos, lower than 0.10 fibres per cm$^3$ for an eight-hour Reference period or lower than a cumulative dose of 6.00 fibres over a three-month period.

**Directive 98/24/EC**


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**Some national standards and regulations**

**i) United States of America**

**ASTM International**

ASTM International, formerly known as the American Society for Testing and Materials (ASTM), is a globally recognized leader in the development and delivery of international voluntary consensus standards established in 1898. All products produced and published by ASTM International are copyrighted and available on purchase.

This e-book will describe briefly the ASTM standard for asbestos removal procedures (E2356, E2394, E1368 and E2308) and for asbestos test method (D6281 and D7201) which are relevant to support an asbestos management program as follows:


This standard covers baseline surveys for management of ACM and includes assessment protocols to make and prioritize removal vs. maintenance decisions. ASTM E2356 provides information for long-term management of ACM in a Baseline Survey and for preparation of the plans and specifications for a removal project. It contains detailed procedures and equipment (mostly ordinary hardware items) needed to take bulk samples of common types of suspect ACM. Once materials have been identified as asbestos-containing, an assessment is made as to which can be left in place. Quantitative assessment of the Current Condition and Potential for Disturbance of all friable and non-friable materials allows removal
priorities to be tabulated and graphically displayed. Budgetary estimates for removal can be established on the basis of the quantitative assessments.

**E2394 Standard Practice for Maintenance, Renovation and Repair of Installed Asbestos Cement Products (October 2004).**

Describes materials, hazardous operations, necessary precautions and infrastructure requirements with detailed procedures in appendices. Not intended for installation of asbestos-cement products in new construction or renovation.

**E1368 Standard Practice for Visual Inspection of Asbestos Abatement Projects (May 2005).**

Provides an approach to managing a removal project to enhance prospects of passing final inspections and clearance air sampling. Describes preparation, removal and inspection procedures and criteria.

**E2308 Standard Guide on Limited Asbestos Screens of Buildings (2005).**

Provides the minimum amount of information needed to facilitate a real estate transaction.

**D6281 Standard Test Method for Airborne Asbestos Concentration in Ambient and Indoor Atmospheres as Determined by Transmission Electron Microscopy Direct Transfer (TEM).**

A method for distinguishing asbestos from non-asbestos fibers on an air sample filter and identifying and quantifying smaller and thinner fibers than Phase Contrast Microscopy

**D7201: Practice for Sampling and Counting Airborne Fibers, Including Asbestos Fibers, in the Workplace, by Phase Contrast Microscopy (with an Option of Transmission Electron Microscopy)**

Combines methodology of NIOSH 7400 and 7402
**Occupational Safety and Health Administration (OSHA), Department of Labor**

OSHA have adopted the standards and enforcement policies for asbestos both for general industry and shipyard available for free download and been used as the international guideline in many countries. The 3 regulations for occupational exposure to asbestos are 29 CFR 1926.1101 Asbestos Standard for Construction; CFR 1926.1101, 29 CFR 1910.1001 OSHA general industry regulations; CFR, and 29 CFR 1915.1001 OSHA Shipyard employment regulations.

29 CFR1926.1101 Asbestos Standard for Construction

The significant issues in the Asbestos Standard for Construction included:

- 1926.1101 App A - OSHA Reference Method - Mandatory
- 1926.1101 App B - Sampling and Analysis - Non-mandatory
- 1926.1101 App C - Qualitative and quantitative fit testing procedures - Mandatory
- 1926.1101 App D - Medical questionnaires; mandatory
- 1926.1101 App E - Interpretation and classification of chest X-ray - mandatory
- 1926.1101 App F - Work practices and engineering controls for Class I Asbestos Operations - non-mandatory
- 1926.1101 App G - [Reserved]
- 1926.1101 App H - Substance Technical Information for Asbestos - Non-Mandatory
- 1926.1101 App I - Medical surveillance guidelines for asbestos, non-mandatory
- 1926.1101 App J - Smoking cessation program information for asbestos, non-mandatory
- 1926.1101 App K - Polarized Light Microscopy of Asbestos - Non-Mandatory

According to this standard, the asbestos work is categorized into 4 classes.

Class I Asbestos Work -means activities involving the removal of thermal system insulation –TSI (TSI means ACM applied to pipes, fittings, boilers,
breeching, tanks, ducts or other structural components to prevent heat loss or gain) TSI and surfacing ACM and presumed asbestos containing material -PACM.

Class II Asbestos Work -means activities involving the removal of ACM which is not thermal system insulation or surfacing material. This includes, but is not limited to, the removal of asbestos-containing wallboard, floor tile and sheeting, roofing and siding shingles, and construction mastics.

Class III Asbestos Work -means repair and maintenance operations, where ACM, including TSI and surfacing ACM and PACM, may be disturbed.

Class IV Asbestos Work -means maintenance and custodial construction activities during which employees contact but do not disturb ACM or PACM and activities to clean up dust, waste and debris resulting from Class I, II and III activities.

29 CFR 1910.1001 OSHA general industry regulations

This regulation outlined reference method for:
- analyzing air samples for asbestos and specifies quality control procedures (Mandatory)
- detailed procedure for asbestos sampling and analysis (Non-Mandatory)
- Qualitative and quantitative fit testing procedures (Mandatory)
- Medical questionnaires (Mandatory); Interpretation and classification of chest roentgenograms (Mandatory)
- Work practices and engineering controls for automotive brake and clutch inspection, disassembly, repair and assembly (Mandatory)
- Substance technical information for asbestos (Non-Mandatory)
- Medical surveillance guidelines for asbestos (Non-Mandatory)
- Smoking cessation program information for asbestos (Non-Mandatory)
- Polarized light microscopy of asbestos (Non-Mandatory)

29 CFR 1915.1001 OSHA Shipyard employment regulations

This regulation is similar to 29 CFR 1910.1001 OSHA general industry regulations but add extended issue on work practices and engineering controls for automotive brake and clutch inspection, disassembly, repair and assembly (Mandatory).
OSHA Method ID 160 Asbestos in Air (1994) Phase Contrast Microscopy method\textsuperscript{33} similar to NIOSH 7400

**National Institute of Occupational and Health (NIOSH), Division of Central Disease Control (CDC), Department of Health and Human Services**

NIOSH recommendations for preventing occupational exposure to asbestos resources range from manuals to individual standards and a variety of work guidelines: sampling and analysis of airborne asbestos, biologic effects of exposure, environmental and medical surveillance, NIOSH B-Reader program, worker notification program, personal protection, protecting and reducing workers' families from take-home asbestos exposure, and asbestos abatement renovation, repair, removal, and disposal\textsuperscript{34}.

Specific NIOSH manual for asbestos 1\textsuperscript{st} prevention\&control was well described in ‘Asbestos bibliography, revised version (1997)\textsuperscript{35}. The issue outlined asbestos prevention:

- Occupational safety and health guideline for asbestos\textsuperscript{36}
- Revised recommended asbestos standard (partial text)
- Workplace exposure to asbestos, Review and recommendations
- Occupational respiratory diseases in relation to asbestos
- Statement of the National Institute for Occupational Safety and Health before the subcommittee on toxic substances, environmental oversight, research and development, committee on environment and public works, April 26, 1990
- Occupational exposure to chrysotile asbestos and cancer risk: A review of the amphibole hypothesis
- Work-related lung disease surveillance report, 1996 (partial text)
-Building air quality. A guide for building owners and facility managers
-Danger asbestos. Working with brakes?

Environmental Protection Agency
This EPA resource focused on basic information of environmental asbestos, management of asbestos in schools, management of asbestos in home including home mechanics, and laws and regulations.\(^\text{37}\)

EPA has issued publications on managing asbestos in products, buildings and schools\(^\text{38}\) as follows:

20T-2003 Managing asbestos in place: A building owner’s guide to operations and maintenance programs for asbestos-containing materials “Green book” (1990)\(^\text{39}\)

The guide’s purpose is: First, it offers building owners the more detailed and up-to-date instruction they need to carry out a successful operation and maintenance (O&M) program. Second, it informs building owners, lenders, and insurers that a properly conducted O&M program can in many cases be as appropriate an asbestos control strategy as removal. The ‘Green book’ covered mainly on organizing an O&M program, recognizing types of O&M, O&M regulations, training O&M workers, work practices, and precautions for O&M work.

How to manage asbestos in school buildings -AHERA designated person’s self–study guide\(^\text{40}\)

In 1986, Congress promulgated the Asbestos Hazard Emergency Response Act (AHERA), Public Law 99-519. AHERA mandated that EPA develop regulations to respond to asbestos in schools. EPA promulgated the asbestos-containing materials in schools rule (hereinafter referred to as the AHERA Rule), 40 CFR Part 763, Subpart E in 1987. This book focused on response actions consistent with the assessment of the Asbestos Containing Building Materials (ACBM), operations and maintenance (O&M) program, periodic surveillance, notification about asbestos activities to workers, students, parents, teachers, and short-term workers, recordkeeping, and warning label immediately adjacent to any friable and non-friable ACBM in the school building.
Furthermore, EPA stated the Code of federal regulations on Asbestos as follows:

40 CFR Part 763 –Asbestos, Subpart E, G, I

Subpart E -Asbestos Containing Materials in Schools. This regulation includes procedures for inspection and reinspections, analysis of bulk samples, assessment of friable ACM, response actions (removal, encapsulation, enclosure), operations and maintenance, training, surveillance, management plans, recordkeeping, and warning labels.

Subpart G -Asbestos Worker Protection. This regulation protects certain State and local government employees in any state of U.S. who are not protected by the Asbestos standards of OSHA. This subpart applies the OSHA asbestos standards in 29 CFR 1910.1001 and 29 CFR 1926.1101 to these employees.

Subpart I –Prohibition of the manufacture, importation, processing, and distribution in commence of certain asbestos containing products; labeling requirements.

40 CFR Part 61, Subpart M -National Emission Standards for Asbestos

Regulations include: definitions of friable and non-friable asbestos-containing materials; notification requirements for renovation and demolition of buildings and facilities containing ACM; work practices to prevent visible emissions; disposal of ACM and waste material in approved landfills; and operation and closure of landfills.


This document provide all methods in identifying and quantifying asbestos fibers in bulk building materials such as Polarized Light Microscopy, Gravimetry, X-ray diffraction and Transmission Electron Microscopy. The analytical procedure is described and the equipment to perform the analyses is required including quality control and proficiency testing programs.

ii) United Kingdom
**The Health and Safety Executive –HSE**

The Health and Safety Executive (HSE) is a non-departmental public body in the United Kingdom. It is the body responsible for the encouragement, regulation and enforcement of workplace health, safety and welfare, and for research into occupational risks in England and Wales and Scotland. The HSE was created by the Health and Safety at Work etc. Act 1974 and sponsored by the Department for Work and Pensions.

**SI 2006/2739 -Control of Asbestos Regulations 2006**

This regulation came into enforce in 2006. The outline included general requirement for asbestos control: identification the presence of asbestos, work assessment, licensing and notification of work with asbestos, training, prevention and reducing of exposure, use and maintenance of control measures, emergencies, cleanliness of premises and plant, air monitoring, standards of air testing and analysis, medical surveillance, recordkeeping, storage/distribution/labeling of raw asbestos and asbestos waste.

Prohibitions and related provisions: prohibitions of asbestos exposure, prohibition of asbestos importation, prohibitions of asbestos supply, prohibition of asbestos use, labeling of products containing asbestos.

**Asbestos Essentials**

This sections include practical guideline of asbestos control for task which need no asbestos license: work with asbestos cement, work with textured coatings containing asbestos, minor work with asbestos insulating board, work with undamaged asbestos materials, removal and replacement of other asbestos containing materials, fly-tipped or friable waste that contained asbestos, equipment and method sheets.

**Asbestos Licence Assessment Guide –ALAG**

This guide is object to explain the asbestos licensing regime and the standards required by applicants. It is intended to help HSE inspectors and the Asbestos Licensing Unit (ALU) ensure that assessments and license reviews are conducted fairly, consistently and transparently. It will also be a useful guide for potential applicants, or those preparing for assessments. The issues stated are: the namelist of company which HSE has granted asbestos license, role of Asbestos Licensing Unit (ALU), industrial standards for the licensed company, information for workers in the licensed company, and classification of license work. Furthermore, the namelist of company which holds license to work with
asbestos is established and updated approximately every 2 weeks on HSE on this section.

**Enforcement Management Model – EMM**

EMM is a framework which helps inspectors make enforcement decisions in line with the Health and Safety Commission’s. EMM help setting out the principles inspectors should apply when determining what enforcement action to take in response to breaches of health and safety legislation.

Some interesting HSE publications for safety in working with asbestos and its webpage for downloading:

1. A comprehensive guide to managing asbestos in premises
2. Work with materials containing asbestos
   http://www.hse.gov.uk/pubns/books/l143.htm
3. Asbestos: The analysts’ guide for sampling, analysis and clearance procedures
4. Health and safety in roof work
5. Asbestos: The survey guide
6. The management of asbestos in non-domestic premises
7. Health and safety in construction
8. Managing health and safety in construction
   http://www.hse.gov.uk/pubns/priced/l144.pdf

**iii) Australia**

**Safe work Australia**

Safe Work Australia is an Australian Government statutory agency established in 2009, with the primary responsibility of improving work health and safety and workers’ compensation arrangements across Australia. The agency is jointly funded by the Commonwealth, state and territory governments facilitated through an intergovernmental agreement signed in 2008. Safe Work Australia represents a partnership between governments, unions and industry. Since 1988, Australian national codes of practice for safe removal of asbestos -

*Note: NOHSC stands for National Occupational Health and Safety Commission (Australia)*


This code included responsibilities of asbestos removal customer and removalists, planning for ACM removal, method and equipment for removal in details (determination the asbestos removal boundaries, security-signs-barriers, electrical and lighting installations, wet and dry methods for removing ACM, removal equipment, personal protective device, air monitoring, decontamination, waste removal-disposal-recycling), additional requirements for the removal of friable ACM (negative pressure exhaust units, enclosure for large-scale asbestos removal work, mini-enclosures for small-scale asbestos removal work, glove bag removal method as shown in Figure 2.1, wrap and cut removal method), clearance to reoccupy an asbestos work area (visual inspection, clearance monitoring, settled dust sampling), and the examples of specific asbestos removal procedures.

![Figure 2.1 Glove bag removal method](image_url)

**Code of Practice for the management and control of asbestos in workplaces [NOHSC: 2018 (2005)]**

This code elaborated on responsibilities (consultation, training of workers, contractors and others), principle of management plan, identification of ACM in the workplace (material sampling and analysis, presuming that materials contain asbestos, register of ACM, warning signs and labels), risk assessment, control
measures (implementing, controlling maintenance, safe maintenance techniques, tools, personal protective device, vacuum cleaners, decontamination, clearance inspections, waste removal and disposal).

National Hazardous Substances Regulatory Package: Substances Subject to Limitations on Exposure (National Exposure Standards); Amendment to update standards – chrysotile asbestos

The objective of this amendment is to update the National Exposure Standard maintained by the National Occupational Health and Safety Commission by replacing the existing standard for chrysotile asbestos. This regulation replaced the TWA (f/ml) value for chrysotile in the Adopted National Exposure Standards for Atmospheric Contaminants in the Occupational Environment [NOHSC: 1003(1995)] with the revised TWA (f/ml) value by decreasing chrysotile TWA from 1 f/cc to 0.1 f/cc.


This guidance note has been developed to provide laboratories and analysts with a consistent methodology for the sampling and analysis of airborne asbestos fibres in workplaces. It elaborated on exposure monitoring (control, total sample duration, flow rate and sample volume), reporting, limitations of the method and presentation of results, laboratory techniques and analysis (sampling equipment and procedures, sample preparation, optical requirements, counting and sizing fibers, quality assurance and quality control), sampling and analytic uncertainty.

Australian Standard Institute

Standards Australia is an independent, not-for-profit organization, recognized by the Australian Government as the peak non-government Standards body in Australia. Standards Australia develops internationally aligned Australian Standards that deliver net benefit to Australia and is the Australian member of ISO and IEC. The standards of asbestos issued are:
Determination of asbestos concentration in air ONORM M 9405:1993 1001
Asbestos-free fibre-cement flat sheets with light inorganic aggregates

Requirements, testing, marking of conformity ONORM B 3216:2002 1001

Handling of products containing weakly bound asbestos ONORM M 9406:2001 0801

All this documents is for sales and no free download.

iv) Canada
Ministry of Labour
Ontario regulation 278/05 under the occupational health and safety act (2005)
Designated substance – Asbestos on construction projects and in buildings and repair operations  

This regulation covers application and adoption of standard, restrictions re-sprayed material/insulation/sealants, demolition, asbestos management in buildings, responsibilities of employers and owner, type of operation with asbestos, information, training, sampling and analysis of asbestos, exposure limit of 0.01 fiber/cc, measures and procedures of operations for friable/non-friable asbestos (separation, negative closures, clearance air testing requirements, glove bag method, etc.), respiratory protection, asbestos abatement training, asbestos work notice and report, worker registration, and inspection.

Ontario regulation 490/09 under the occupational health and safety act (2009)
Designated substance  

This regulation covers application, employer duties, assessment and control program of each hazardous substance, and medical examination and clinical tests.

Some interesting Canadian guideline and publications for safety in working with asbestos:
1) A Guide to the Regulation Respecting Asbestos on Construction Projects and in Buildings and Repair Operations
2) Construction sector plan 2010-2011
3) Guideline C-6 Handling, Transportation and Disposal of Asbestos Waste in Bulk

**Chrysotile Institute**

The Chrysotile Institute, a registered lobby group for the Quebec asbestos mining industry, takes the position that chrysotile can be handled safely.

Of note is that the Canadian Medical Association, the Canadian Cancer Society, and Canada’s leading health experts oppose the export of asbestos to developing countries. The National Public Health Institute of Quebec (INSPQ) has published fifteen reports, all of them showing a failure to achieve “controlled use” of asbestos in Quebec itself.

**Guideline for a regulation on the safe and responsible use of chrysotile asbestos**

This online guideline covered briefly the activities involving a risk of occupational exposure to asbestos, permissible exposure limit, work clothing and respiratory equipment, work education and training, labeling, waste handling and disposal, transportation, prevention and environmental pollution, medical surveillance, inspection and substitution.

**Safe use of chrysotile asbestos manual**

This manual covered chrysotile health effect, basic chrysotile regulations, dust control, personal protective equipment, waste disposal, installation and maintenance of chrysotile-cement products, working with friable materials, air monitoring, medical surveillance, and worker information and training.

This manual, however, misled by using old WHO permissible exposure limit in 1989 of 1 fiber/cc as standard exposure limit including inadequate respiratory protection. Of note is that this manual though mainly referred to ILO convention and WHO, completely ignored the clear and present evidence that WHO and ILO has recently declared no safe exposure level for chrysotile and call for universal ban.

**v) Singapore**
Ministry of Manpower, Occupational Safety and Health Division
Factories Act (chapter 104, section 68, 69, 77 and 102) Factories (Asbestos) Regulations

The asbestos prevention and control regulations in Singapore grounded on the Factories (Asbestos) Regulations, 1980 and The Factory (Asbestos) (Amendment) Regulations, 1989 which provided issues on obligations of employers and contractors, notification to chief inspectors, exhaust ventilation and protective equipment, cleanliness of premises and plant, storage and distribution, accommodation for and cleaning of protective equipment, and restriction on employment of young employees.

Factories Act (chapter 104, section 69) Factories (Medical examinations) Regulations

This section included medical examination of persons employed in hazardous occupations (pre-employment medical examination and certified fit before employment, periodic medical examination, other medical examinations, medical expenses, reporting, registers of employees in hazardous occupations, recommendation of work suspension, inspection workplace by designated doctor, exemption), designated factory doctors (application as designated factory doctor, refusal to register, appeal against refusal, cancellation of registration).

Guidelines on the handling of asbestos materials

This guideline elaborated on identification and notification for asbestos involving work, handling of asbestos-based materials in the building and engineering construction industries, removal of asbestos-based insulating lagging, removal of asbestos materials from buildings, handling of raw asbestos and products containing asbestos in plants and factories, protective clothing and equipment, changing and sanitary facilities, waste disposal, personal hygiene, dust monitoring, and medical examinations.

Guidelines on the removal of asbestos materials in buildings

The use of asbestos in buildings in Singapore has been banned by the National Environmental Agency since 1989. Special precautions are needed in removal, repair, dismantling, demolition, renovation, maintenance and alteration.
of structures in old buildings containing asbestos and ACM. This guideline prepared by the Occupational Safety and Health Division, Ministry of Manpower included sources of asbestos, identification asbestos, notification to authorized organization, medical examinations, engineering and work practice control (preparation and demarcation of asbestos work area, isolation of asbestos work area, wet method for safe work, personal protective device, washing/changing facilities, housekeeping, waste disposal, transportation of asbestos waste).

vi) Thailand

Thailand does not have an integrated legislative structure for the control and management of hazardous substances and waste of Asbestos. Legislation is fragmented and the jurisdiction and authority to implement these laws is spread out in several ministries, e.g., Ministry of Industry, Ministry of Public Health, Ministry of Labor, Ministry of Science, Technology and Environment, and the Ministry of Agriculture and cooperatives (vermiculite in fertilizer).

No law and regulations on asbestos abatement and removal in Thailand.

Ministry of Industry

Toxic and hazardous substances control Act 1992

According to this act, asbestos is classified as type 3 hazardous substances which are that the productions, import, export, or having in possession must obtain a permit.

The authority directly concerned with industrial hazardous waste is the Hazardous Waste Disposal Subdivision of the Office of Industrial Services and Waste Management in the Ministry of Industry. Despite the country's rapid industrial growth, this subdivision has not been allocated more manpower to deal with escalating hazardous waste problems. Moreover, the Hazardous Waste Management Action Plan 1992 was made inactive following the reorganization of the Office of the National Environment Board-the government agency directly responsible for the country's environmental problems. This inactive status has dashed hopes for a systematic approach to hazardous waste management in Thailand.

Concerning pollution control, Ministry of Industry has issued several ministerial regulations, as follows: Ministerial regulation No. 25 (1988), which
decrees that all factories have to carry out proper treatment of polluting and discarded materials; Ministerial regulation No. 57 (1990), which stipulates that all waste materials specified in the Basel Convention are toxic wastes that have to be under the control of the laws.

**Public Health Act 1992: Ministry of Public Health**

This act determined asbestos-related activity to be hazardous to health as work with automobile brake and clutch; work with asbestos containing materials in roof tiles, floor tiles, ceilings tile, and water pipelines; construction.

**Ministry of Labour**


This notification specifies the ambient air TLV-TWA of asbestos (unspecific) and tremolite at 5 fiber/cc.

There are other notifications of Ministry of Labor on Determination of category and type of chemicals 1992, Safety report and Chemical surveillance report 1992, regulations on hazardous substance transportation, keeping, moving, packaging, utensils 1991. However, these notifications did not mention on Asbestos.

**Ministry of Science and Technology**


This act elaborated the organization and its partners, financial resources, standard, planning, environmental restriction and protection zone, environmental impact assessment, pollution prevention and control, promotion measures, and penalty.

**The Secretariat of the Cabinet**


This notification specified the label of ACM in details including the tag applied to ACM as below (Figure 2.2).
vii) South Africa


This regulations covered notification of asbestos work; duties of persons who may be exposed; risk assessment, air monitoring, training; medical surveillance; respirator zoning; control of exposure to asbestos; occupational exposure limit of 0.2 fiber/cc for 4 hr TWA measured by PCM; cleanliness of premise and plant; control of exposure to persons other than employees; control of asbestos in part of workplace, buildings, plants and premises; control of asbestos cement sheeting and related products; recordkeeping, personal protective equipment and facilities; maintenance and control measures; labeling, packaging, transportation and storage; disposal of asbestos; demolition; prohibition; offences and penalties.
2.3 Some national occupational exposure limits (OEL) of asbestos in the ambient air

<table>
<thead>
<tr>
<th>Country</th>
<th>Control Limit</th>
</tr>
</thead>
<tbody>
<tr>
<td>USAa</td>
<td>1. OSHA: PEL 0.1 f/cc in 8 hours (fibers &gt;5 µm long); Excursion limit 1 fiber/cc in 30 minutes; carcinogen&lt;br&gt;2. NIOSH: REL TWA 0.1 f/cc (fibers &gt;5 µm long/400 L); carcinogen&lt;br&gt;3. ACGIH: TLV TWA 0.2 (crocidolite), 0.5 (amosite), 2 (chrysotile and other asbestos) f/cc; carcinogen&lt;br&gt;Definition:&lt;br&gt;- PEL Permissible Exposure Limit. This is the term OSHA uses for the exposures limits it publishes and all of OSHA’s PELs are actually TWA limits.&lt;br&gt;- REL Recommended Exposure Limit, also called NIOSH REL), is an exposure limit recommended by NIOSH scientists to OSHA. RELs are science-based recommendations rather than legal standards. They are based on animal and human studies. A REL is defined in up to three ways:&lt;br&gt;  - A time-weighted average (TWA) concentration that NIOSH recommends not be exceeded for up to a 10-hour workday during a 40-hour workweek.&lt;br&gt;  - A ceiling value, which NIOSH recommends not be exceeded at any time during the workday (unless noted otherwise).&lt;br&gt;  - A short-term (STEL) value, which NIOSH recommends not be exceeded for longer than 15 minutes during a workday (unless noted otherwise).&lt;br&gt;4. TLV Threshold Limited Value. This is a term ACGIH uses for permissible concentrations, to which workers may be exposed continuously, day after day, without adverse effects, for a normal eight-hour workday and a forty-hour work week.&lt;br&gt;- TWA Time Weighted Average. This is the level of exposure that a person has been exposed to on average over some period of time (usually 8 hours).&lt;br&gt;Excursion Limit - An ACGIH term that refers to the ceiling limit for a short period of time (typically 15 - 30 minutes). This limit is used when no STEL is published, and is defined as 5 times the 8-Hour TWA limit.</td>
</tr>
<tr>
<td>United Kingdomb</td>
<td>Control limit: 0.1 f/cc in 4 hours; Short term exposures: 0.6 f/cc in 10 minute</td>
</tr>
<tr>
<td>Canadae</td>
<td>OEL 0.1 fibres/cc</td>
</tr>
<tr>
<td>Australiad</td>
<td>OEL 0.1 fibres/cc</td>
</tr>
<tr>
<td>South Africae</td>
<td>OEL: 0.2 fibres/cc in 4 hours; short term exposure limit: 0.6 f/cc of air in 10 minutes</td>
</tr>
</tbody>
</table>
China

<table>
<thead>
<tr>
<th>OEL 2 fibers/cc</th>
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</thead>
</table>

Japan

<table>
<thead>
<tr>
<th>OEL 2 fibers/cc; asbestos ban in 2005</th>
</tr>
</thead>
</table>

Korea

<table>
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<tr>
<th>OEL 2 fiber/cc since 1982; decreased to 0.1 f/cc in 2003; asbestos ban in 2009</th>
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Malaysia

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<tr>
<th>OEL 0.1 fibers/cc</th>
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Philippines

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<tr>
<th>OEL 2 fibers/cc</th>
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Singapore

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<tr>
<th>OEL 0.1 fibers/cc</th>
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Taiwan

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<tr>
<th>OEL 1 fibers/cc</th>
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Thailand

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<th>OEL 5 fibers/cc</th>
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</table>

Vietnam

<table>
<thead>
<tr>
<th>OEL 1 fibers/cc</th>
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Sources:

aNIOSH method #7400
bhttp://www.hse.gov.uk/asbestos/regulations.htm
chttp://www.labour.gov.on.ca/english/hs/pubs/oel_table.php#a
fTakahashi K, karialainen A. A cross-country comparative overview of the asbestos situation in ten Asian countries. Int J Occup Environ Health 2003;9:244-8

2.4 Alternatives to Asbestos

2.4.1 Man-made fibers (MMF) as substitution in general

Non-Asbestos fibrous materials, both man-made and extracted from natural deposits, are used and/or proposed as substitutes for asbestos. There are wide variations in competitiveness according to price, availability, technical performance, ease of handling and mixing, compatibility with other materials in composites, durability, etc.

There is no single fibrous alternative that could replace asbestos in all of its many varied applications. On the other hand, some fibrous materials are really not alternatives for asbestos, as they are used in areas where asbestos cannot be used (example: very high temperature refractory materials).

Compared to asbestos, evidence of biological activity of non-asbestos fibrous materials has been reported sparsely. The as alternatives man-made fibers (MMF) for asbestos are as follows:
1) Cellulose fibers

This MMF is a subset of man-made fibers, regenerated from natural cellulose. The cellulose comes from various sources. Modal is made from beech trees, bamboo fiber is a cellulose fiber made from bamboo, seacell is made from seaweed, etc.

Exposure limits$^{64,65}$

**USA:** TLV (ACGIH) total dust 10 mg/m$^3$; PEL (OSHA) total dust 15 mg/m$^3$; PEL (OSHA) respiratory dust 5 mg/m$^3$

**Canada:** OEL (British Columbia) total dust 10 mg/m$^3$; OEL (British Columbia) 3 mg/m$^3$

**British:** OEL total dust 10 mg/m$^3$; OEL respiratory dust 4 mg/m$^3$; STEL 20 mg/m$^3$

2) Mineral fibers (glass wool, rock wool, slag wool)

The mineral wool was at one time the most common type of insulation; its market share was largely lost to glass fiber in the 1960s and 1970s. In the past few years, however, the product appears to have begun a comeback. "Mineral wool" actually refers to two different materials: slag wool and rock wool. Slag wool is produced primarily from iron ore blast furnace slag, an industrial waste product. Rock wool is produced from natural rocks. Slag wool accounts for roughly 80 percent of the mineral wool industry, compared with 20 percent for rock wool. Given the relative use of these two materials, mineral wool has, on average, 75 percent post-industrial recycled content.

The glass fiber is a soft wool-like material made from molten glass that is usually pink or yellow. Glass wool is composed of relatively short cylindrical glass fibers that are produced by drawing, centrifuging, or blowing molten glass. Silicon dioxide is the primary chemical component in all glass types; however, many other metal oxides are present. Glass wool is resistant to chemical corrosion by mineral acids. It is used as insulation, in weatherproofing, and as textile material. It was originally used as a "safe" substitute for asbestos. Glass fiber was used as a liner inside air supply ducts and air handler compartments of the ventilation system of homes and buildings built from the early 1960s through the late 1980s. It was used in ventilation systems as an insulator to prevent loss of hot or cold air and to reduce the noise from the blower fan.
Improvements in glass fiber manufacturing technology and new markets in textiles fueled much of the growth and in the 1950s and 1960s, glass wool began to replace rock wool and slag wool products used in thermal insulation.

ILO has issued code of practice for safe work with synthetic vitreous fibre insulation wools (glass wool, rock wool, slag wool). This code was adopted unanimously by a meeting of experts on safety in the use of insulation wools, held in Geneva in 2000 and also provided the examples of exposure limits (EL) and related comments in various countries for glass wool, rock wool and slag wool as shown in the table 2.3.

Table 2.3 Exposure limits in various countries and related comments for glass wool, rock wool and slag wool

<table>
<thead>
<tr>
<th>Country</th>
<th>EL&lt;sub&gt;1&lt;/sub&gt; f/cc</th>
<th>EL&lt;sub&gt;2&lt;/sub&gt; mg/m³</th>
<th>Related comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Australia</td>
<td>0.5</td>
<td>2.0</td>
<td>Exposure standard: a TWA exposure standard of 0.5 f/ml (respirable fibres) for all forms of synthetic mineral fibres and a secondary exposure standard of 2 mg/m³ (TWA) for inspirable dust in situations where almost all the airborne material is fibrous.</td>
</tr>
<tr>
<td>Austria</td>
<td>0.5</td>
<td>-</td>
<td>EL: 0.5 f/ml for respirable fibres measured by the WHO method.</td>
</tr>
<tr>
<td>Denmark</td>
<td>1.0</td>
<td>-</td>
<td>Classified as a carcinogen due to IARC 2B, and included in the general environmental list of hazardous substances with designations according to Commission Directive 97/69/EC. Specific health and safety regulations, on installation and demolition of insulation materials containing synthetic vitreous fibres, state that: – insulation wools are not considered hazardous in the health and safety regulations on hazardous substances, meaning that there are no obligations for substitution by other products; – insulate on wools which generate the least dust should be used; and – general and specific provisions for preventive measures are to be followed.</td>
</tr>
<tr>
<td>Finland</td>
<td>-</td>
<td>10.0</td>
<td>Insulation wools are classified according to rules based on Commission Directive 97/69/EC. EL: Inhalable dust as eight-hour average (EN 481: 1993 CEN/TC 137)).</td>
</tr>
<tr>
<td>France</td>
<td>1.0</td>
<td>-</td>
<td>EL: 1.0 f/ml for glass wool, rock wool and slag wool, measured as an eight-hour TWA value.</td>
</tr>
<tr>
<td>Country</td>
<td>EL&lt;sup&gt;1&lt;/sup&gt; f/cc</td>
<td>EL&lt;sup&gt;2&lt;/sup&gt; mg/m³</td>
<td>Related comments</td>
</tr>
<tr>
<td>--------------</td>
<td>----------------------</td>
<td>----------------------</td>
<td>--------------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Germany</td>
<td>-</td>
<td>6.0</td>
<td>Exemption criteria according to the Dangerous Substances Ordinance (Gefahrstoffverordnung), Annex V, No. 7.1(1): – a suitable intraperitoneal test has not shown indications of significant carcinogenicity; or – the half-life time after intratracheal instillation of 2 mg of a fibre suspension of fibres with a length greater than 5 μm, a diameter smaller than 3 μm and a length-to-diameter ratio greater than 3:1 (respirable fibres measured by the WHO method) is less than or equal to 65 days (40 days from 1 October 2000); or – the carcinogenicity index K&lt;sub&gt;I&lt;/sub&gt;, which is calculated from the difference between the sum of the mass content (as a percentage) of the oxides of sodium, potassium, boron, calcium, magnesium, barium and twice the mass content (as a percentage) of aluminium oxide, is greater than or equal to 40.</td>
</tr>
<tr>
<td>Germany</td>
<td>0.25</td>
<td>-</td>
<td>EL: 0.25 f/ml for non-exonerated insulation wool fibres.</td>
</tr>
<tr>
<td>Italy</td>
<td>&lt;1.0</td>
<td>5.0</td>
<td>EL: total dust: 5 mg/m³; fibre diameter less than 3 μm: less than 1 f/ml.</td>
</tr>
<tr>
<td>Japan</td>
<td>-</td>
<td>2.9</td>
<td>The Ministry of Labour guidelines for glass wool and rock wool recommend measuring the airborne fibres or respirable dust concentration. The administrative control level (ACL)&lt;sup&gt;5&lt;/sup&gt; is 2.9 mg/m³ for respirable dust, but no fibre concentration has been set. Fibre counting method: JIS K3850.</td>
</tr>
<tr>
<td>Netherlands</td>
<td>2.0</td>
<td>-</td>
<td>EL: 2 f/ml eight-hour TWA. No occupational exposure limit for non-respirable fibres with a diameter greater than 4-5 μm.</td>
</tr>
<tr>
<td>Norway</td>
<td>1.0</td>
<td>-</td>
<td>No official classification, but the Directorate of Labour Inspection cites the IARC 2B classification. In the TLV list, wool insulation is labeled with a K, which Refers to IARC 2B. EL: 1 f/ml.</td>
</tr>
<tr>
<td>Sweden</td>
<td>1.0</td>
<td>-</td>
<td>Insulation wools are classified according to the National Chemicals Inspectorate rules based on Commission Directive 97/69/EC, and Sweden has issued specific rules for handling synthetic vitreous fibres.</td>
</tr>
<tr>
<td>Switzerland</td>
<td>0.5</td>
<td>-</td>
<td>The EL of 0.5 f/ml is for respirable fibres measured by the WHO method.</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>2.0</td>
<td>5.0</td>
<td>EL: 5 mg/m³ total inhalable dust eight-hour TWA, or 2 f/ml eight hour TWA. Both are maximum exposure limits. The 2 f/ml eight hour TWA applies when fibres are measured or calculated by a method approved by the Health and Safety Executive.</td>
</tr>
</tbody>
</table>
Country | EL$^1$ f/cc | EL$^2$ mg/m$^3$ | Related comments
--- | --- | --- | ---
United States | 1.0 | - | Manufacturers are required to identify fibre glass as a potential carcinogen on warning labels and provide information in the form of Material Safety Data Sheets, under the US Occupational Safety and Health Administration (OSHA) Hazard Communication Standard, based on epidemiological studies which demonstrated an increased mortality rate for lung cancer. The US OSHA also cites the IARC 2B classification, as well as the listings of the US National Toxicology Program (NTP). EL: 1 f/ml eight-hour TWA. This non-statutory limit has been agreed to in a partnership programme between the US OSHA, the North American Insulation Manufacturers’ Association (NAIMA) and the users. The Health and Safety Partnership Programme (HSPP) established a 1.0 f/ml eight-hour TWA exposure limit for respirable synthetic vitreous fibre insulation wools. “Where worker exposures can readily be reduced below 1 f/cc, NAIMA recognizes that it is prudent to do so.”

Notes:
1 Exposure limit for the airborne concentration of respirable fibres expressed as fibres per millilitre of air (f/ml).
2 Exposure limit for the airborne mass of dust expressed as milligrams per cubic metre (mg/m$^3$).
3 Time-weighted average.
4 For production and use of exempted insulation wool fibres, appropriate hygiene measures (“good industrial practice”) have to be applied; see “Technische Regeln für Gefahrstoffe: TRGS 500 – Schutzmassnahmen: Mindeststandards”, in Bundesarbeitsblatt, No. 3, 1998, p.57.
5 The administrative control level (ACL), according to the Japanese Government, has a different concept from exposure limits, even though it was developed on that basis. The ACL is the concentration of an airborne hazardous substance providing a standard for judging the condition of the working environment, and assumes the implementation of engineering control measures. Taking account of the technical feasibility to secure the workplace, the work environment is evaluated in three categories safe zone, grey zone and unsafe or hazardous zone – by statistical comparison of the measured concentration of an airborne substance with an ACL.
6 The NTP has listed “glass wool (respirable size)”, which includes special-purpose glass fibres, as “reasonably anticipated to be a human carcinogen”. Mineral wools (rock wool and slag wool) have not been classified by the NTP.

3) Polymeric man-made organic fibers

Polymeric man-made organic fibers are synthesized from organic polymers that are derived from petroleum-based chemicals. Some examples of man made organic fibers -MMOF are: polyamides (nylon, aramid), polyester, polyolefins (polyethylene, polypropylene), and polyvinyls. Petroleum-based MMOFs have been utilized in the production of textiles for carpets, clothing,
bedding, curtains, draperies, and upholstery. In addition, some MMOF fiber-types are used for tire cords (e.g., p-aramid, nylon), protective clothing (e.g., m-aramid) industrial fabrics, ropes and cables, and friction materials (brake pads and gaskets).

   Exposure Limits\(^67\):

   USA: TLV (ACGIH) : None established; PEL (OSHA) : None established

   The company Dupont proposed 2 respirable fibers/cc (8-hr. TWA, < 3-micron diameter) on its MSDS\(^68\).

2.4.2 European Union Consideration of a Ban on Chrysotile Asbestos and Evaluation of Substitute Organic Fiber types\(^69,70\)

   The European Union recently considered a ban on the use of chrysotile asbestos fibers. Such a consideration requires an evaluation of the health effects of substitute materials. The main organic fiber substitutes that were evaluated for the residual uses of chrysotile were para-aramid (p-aramid), polyvinyl alcohol (PVA), and cellulose fibers.

   Much of the risk consideration was based upon hazard assessment, including fiber dimensions and durability (as discussed above) and potential exposure assessment, i.e., the likelihood that respirable fiber aerosols would be generated. The EU committee paper specifically addresses the main substitutes for the remaining residual uses of chrysotile, i.e., p-aramid, polyvinyl alcohol (PVA), and cellulose, and does not cover substitute materials already widely used for thermal and sound insulation, such as glass and other man-made mineral fibers. Finally, the paper focuses only on health impacts and does not attempt a cost benefit analysis.

   Here is a brief summary of their conclusions:

1) Polyvinyl alcohol (PVA) fibers

   It was concluded that the diameter of most manufactured PVA fibers is approximately 10–16 μm, and therefore exceeds the criteria for respirable size (i.e., generally considered to be 3 μm for fiber counting purposes). There is evidence that PVA fibers can fibrillate (longitudinal breakage); however, most of the dust particles measured in the working atmosphere appear to be of a nonfibrous particulate nature. Although the toxicological data base for PVA fibers is sparse, the results of generally negative epidemiology and exposure assessment studies indicate that, relative to asbestos, there are significantly reduced human exposures to PVA fibers.
Morinaga and colleagues recently conducted a retrospective cohort study of male workers exposed to PVA fibers. A total of 447 exposed and 2416 non-exposed male workers were evaluated. Lung cancer SMR rates were 0.86 for the workers with 20 or more years of employment. The authors concluded that there was no difference in lung cancer risk between workers exposed to PVA fibers when compared to non-exposed workers.

2) Para-aramid fibers and respirable-sized, fiber-shaped particulates (RFP)

Para-aramid (p-aramid) RFP forms the respirable component of para-aramid fibers in pulp, and generally are used in friction products such as gaskets and brake linings. As discussed above, RFP is an acronym for respirable-sized, fiber-shaped particulates and is the new nomenclature used for identifying respirable-sized organic fibers. Para-aramid RFP (also referred to herein as fibrils) generally have diameter dimensions of 0.3–0.7 μm and are produced under conditions of abrasion of p-aramid fibers, which are considered to be nonrespirable, having diameters in the range of 12–15 μm.

Recent inhalation toxicity studies with rats comparing the biopersistence of p-aramid RFP with asbestos fibers have demonstrated that the fibrils were less biopersistent than chrysotile asbestos. The longer p-aramid RFP were shortened in the lungs of rats while the longer chrysotile asbestos fibers were preferentially retained. Significant differences were also measured in cell proliferation parameters, with p-aramid producing a transient increase in terminal bronchiolar cell proliferative responses, while chrysotile asbestos fibers produced a sustained cell proliferative response in the airways, lung parenchyma, and subpleural regions of the lung.

3) Cellulose fibers

Cellulose fibers are produced from natural sources and have historically been used in the paper industry. Although epidemiological data for cellulose is sparse, there appears to be little evidence of disease in workers, even at high exposure levels in the workplace. Exposures to hardwood-associated wood dust are linked with development of sinonasal cancer; however, exposure to softwoods seems to be significantly less potent in producing similar effects, indicating that cellulose was not the causative agent.

With regard to experimental studies, Muhle and colleagues recently reported that cellulose RFP were more biopersistent than chrysotile in the lungs or rats, however, this pulmonary toxicokinetic study likely was conducted at
overload concentrations. There exists a paucity of data regarding the pulmonary toxicity of inhaled cellulose RFP. Harrison et al.\(^69\) noted that there exist surprisingly few data on cellulose despite the fact that this fiber is associated with products with rather wide commercial applications. The few \textit{in vitro} and \textit{in vivo} experimental studies that have been conducted suggest that cellulose RFP may be biopersistent in the lung and may produce pulmonary inflammation. Cullen and coworkers recently conducted a 3-week inhalation study with one form of cellulose RFP (i.e., mechanical wood pulp) at 1000 f/ml. It was reported that cellulose induced an early pulmonary inflammatory response in rat lungs, as assessed by bronchoalveolar lavage, which peaked at 1 day following the start of inhalation and thereafter declined. These investigators concluded that the cellulose material studied was less inflammagenic than crocidolite and that the extent of the inflammatory response within the lung was reduced with continued inhalation exposure. It is unclear whether the type of cellulose utilized in these studies is a representative form of cellulose that is widely used in the paper industry.

In summary, the few \textit{in vitro} and \textit{in vivo} studies that have been conducted suggest that cellulose RFP may be biopersistent in the lung and may produce pulmonary inflammation. Since cellulose represents a family of materials, there is a great need to assess the toxicity of various respirable forms of cellulose fibers. In conclusion, the European Commission Health and Consumer Protection Directorate Scientific Committee pointed that chrysotile asbestos fibers are fundamentally more hazardous than p-aramid, PVA, or cellulose fibers. As a consequence, they have endorsed the opinion that the continued use of chrysotile asbestos in cement products and friction materials is not justifiable, given the availability of less hazardous organic fiber substitutes.

2.4.3 Alternatives to Asbestos containing products (ACM)

The Building and Wood workers International (BWI)

The Building and Wood workers International (BWI) is the Global Union Federation grouping and democratic unions with members in the building, building materials, wood, forestry and allied sectors. The BWI groups together around 328 trade unions representing around 12 million members in 130 countries.

The Headquarters is in Geneva, Switzerland. Regional Offices and Project Offices are located in Panama and Malaysia, South Africa, India, Burkina Faso, Bosnia Herzegovina, Curaçao, Chile, Kenya, South Korea, Russia, Peru, Brazil and Thailand. The BWI mission is to promote the development of trade unions
in our sectors throughout the world and to promote and enforce workers rights in the context of sustainable development.

The BWI works closely with the European Federation of Building and Wood Workers (EFBWW), the Nordic Federation of Building and Wood Workers (NFBWW), the International Trade Union Confederation (ITUC) and the Global Union Federations (GUFs). The BWI has a special consultative status to the economic and social committee of the United Nations and is engaged with international organizations such as the International Labour Organization (ILO), the International Tropical Timber Organization (ITTO), the Food and Agricultural Organization (FAO), the international employers' organizations, such as the Confederation of International Contractors' Associations (CICA) and the regional and international financial institutions such as the World Bank and World Trade Organization (WTO)\textsuperscript{71}.

BWI stated that 90% of world asbestos consumption goes into asbestos-cement products and 7 percent into friction materials and suggested a number of substitutes for asbestos-cement products as in the following table 2.4\textsuperscript{72}.

Table 2.4 Alternatives to Asbestos-containing products according to BWI

<table>
<thead>
<tr>
<th>Asbestos product</th>
<th>Substitute products</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asbestos-cement corrugated roofing</td>
<td>-Fiber-cement roofing using: synthetic fibers (polyvinyl alcohol, polypropylene) and vegetable/cellulose fibers (softwood kraft pulp, bamboo, sisal, coir, rattan shavings and tobacco stalks, etc.); with optional silica fume, fly ash, or rice husk ash.</td>
</tr>
<tr>
<td></td>
<td>-Microconcrete (Parry) tiles</td>
</tr>
<tr>
<td></td>
<td>-Galvanized metal sheets</td>
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<tr>
<td></td>
<td>-Clay tiles</td>
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<tr>
<td></td>
<td>-Vegetable fibers in asphalt</td>
</tr>
<tr>
<td></td>
<td>-Slate</td>
</tr>
<tr>
<td></td>
<td>-Coated metal tiles (Harveytile)</td>
</tr>
<tr>
<td></td>
<td>-Aluminum roof tiles (Dekra Tile)</td>
</tr>
<tr>
<td></td>
<td>-Extruded uPVC roofing sheets</td>
</tr>
<tr>
<td></td>
<td>-Recycled polypropylene and high-density</td>
</tr>
<tr>
<td></td>
<td>-Polyethylene and crushed stone (Worldroof)</td>
</tr>
<tr>
<td></td>
<td>-Plastic coated aluminum/ Plastic coated galvanized steel.</td>
</tr>
<tr>
<td>Asbestos product</td>
<td>Substitute products</td>
</tr>
<tr>
<td>---------------------------------------------------------------------------------</td>
<td>---------------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
</tbody>
</table>
| Asbestos-cement flat sheet (ceilings, facades, partitions)                       | -Fiber-cement using vegetable/cellulose fibers (see above), wastepaper, optionally synthetic fibers  
- Gypsum ceiling boards (BHP Gypsum)  
- Polystyrene ceilings, cornices, and partitions  
- Façade applications in polystyrene structural walls (coated with plaster)  
- Aluminum cladding (Alucabond)  
- Brick  
- Galvanized frame with plaster-board or calcium silicate board facing  
- Softwood frame with plasterboard or calcium silicate board facing. |
| Asbestos-cement pipe                                                            | **High Pressure:**  
- Cast iron and ductile iron pipe  
- High-density polyethylene pipe  
- Polyvinyl chloride pipe  
- Steel-reinforced concrete pipe (large sizes)  
- Glass-reinforced polyester pipe  

**Low Pressure:**  
- Cellulose-cement pipe  
- Cellulose/PVA fiber-cement pipe  
- Clay pipe  
- Glass-reinforced polyester pipe  
- Steel-reinforced concrete pipe (large diameter drainage) |
| Asbestos-cement water storage tanks                                             | - Cellulose-cement  
- Polyethylene  
- Fiberglass  
- Steel  
- Galvanized iron  
- PVA-cellulose fiber-cement |
| Asbestos-cement rainwater gutters; open drains (mining industry)                | - Galvanized iron  
- Aluminum  
- Hand-molded cellulose-cement  
- PVC |
**German**

**Table 2.5 German Type of substitute material in according to group of products**

<table>
<thead>
<tr>
<th>Type of substitute material</th>
<th>Group of products</th>
<th></th>
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</thead>
<tbody>
<tr>
<td>textile glass fibre</td>
<td>Occup. safety</td>
<td>fire protection</td>
<td>heat isolation</td>
<td>electric isolation</td>
<td>sealing</td>
<td>Filtration</td>
<td>breaks/clutch</td>
<td>Construction</td>
</tr>
<tr>
<td>SiO2 fibre</td>
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<td>carbon fibre</td>
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<tr>
<td>non textile glass fibre</td>
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<td>gypsum fibre</td>
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<td>polyacrylnitrile</td>
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<tr>
<td>thermal stabilized polyacrylnitrile</td>
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<td>Flax and hemp</td>
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<td>+</td>
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</tr>
</tbody>
</table>

Source: paiboon choungthong. Safety management for chrysotile. (Unpublished document in the meeting on Safety management on chrysotile 2/2554, 11 February 2011, Department of industrial works, Ministry of industry73)
2.5 Smoking cessation

A number of epidemiologic studies of lung cancer have investigated whether there is interaction between asbestos exposure and cigarette smoking. Most of the studies involved populations exposed to amphiboles as well as chrysotile. The data are best described by a multiplicative (synergistic) interaction between asbestos and cigarette smoke. The composite effect may range from less than additive to supramultiplicative has been accepted by many authorities for about the last 30 years. Moreover, the population-based studies from various European regions on occupational asbestos exposure, mesothelioma, and lung cancer are reviewed in 1999. This study assessed information among European countries on national asbestos consumption, proportions of the population exposed, and exposure levels in is summarized. Asbestos consumption in 1994 ranged, per capita, between 0.004 kg in northern Europe and 2.4 kg in the former Soviet Union. Studies on mesothelioma combining occupational history with biologic exposure indices indicate occupational asbestos exposure in 62 to 85% of the cases. Population attributable risks for lung cancer among males range between 2 and 50% for definite asbestos exposure. After exclusion of the most extreme values because of methodological aspects, most of the remaining estimates are within the range of 10 to 20%. The combination of a current high asbestos consumption per capita, high exposure levels and high underlying lung cancer rates in Central Europe and the former Soviet Union suggests that the lung cancers will arise from the smoking and its interaction with asbestos should be of a major concern.

Conversely, most epidemiological evidences supported no interaction between cigarette smoking and asbestos exposure in the development of mesothelioma. The smoking reduction strategy on the contrary might then be ineffective for mesothelioma, for which asbestos is the only known causative factor.\textsuperscript{74-77}

In view of the synergistic effect of smoking and asbestos exposure solely on lung cancer risk, smoking cessation should be recommended to effectively reduce that risk for both current as well as previously asbestos exposed workers. There is additional benefit in preventing passive smoking among family members and neighbours. In view of its importance, smoking cessation programs for all currently and previously exposed should be covered by public and/or private health insurance systems or employers.
2.6 Some considerations for the key issues according to review of primary prevention for Thailand

2.6.1 General key elements in asbestos prevention and control techniques

1. Introduction:
   Health aspects

2. General management:
   Specific laws and regulation for asbestos work;
   Notification of asbestos work to competent authority;
   Consultation with Health & Safety organization at each step of work, e.g.,
   identification of asbestos, evaluation, and control process;
   Registration of employers for asbestos work - contractors, agencies
   engaged in asbestos removal and maintenance work, whether incorporated or
   self-employed shall be registered under authorized state organization;
   Registration for employees;
   Inspection at worksite for worker’s health - organization, function

3. Responsibilities:
   All parties involved with asbestos, e.g., governments, property owners,
   employees, health & safety representatives, have obligatory role in establishing
   and maintaining safe practices with asbestos.

4. Hazard identification:
   Material or bulk samples;
   Analysis of material or bulk samples

5. Risk evaluation:
   Assessment of exposure by air sampling (area/ personal sampling);
   Exposure standards or limits

6. Hazard control:
   Alternative materials;
   method of controls – engineering control such as restricted area/ enclosure,
   wet method, general ventilation, local ventilation; safe work practice such as
   follows the instruction required for safe work, appropriate damping before
   processing, handling, cleaning, stripping or removing, regular cleaning of
   machinery and work areas, proper use of PPE;
   Control program;
   Local and exhaust ventilation;
Selected safe operation procedure and maintenance for specific asbestos work, e.g., work with part of structure of building, plant or premises, cement sheet, spraying, textile, friction materials, handling asbestos at ports and container terminals, construction, removal/demolition etc

7. Removal/Demolition work:
   - Planning - training, certified employers, supervisory personnel;
   - Preparation of the removal area – site preparation (total enclosure, floor coverings, closing down all ventilation and air-conditioned of the removal area, exhaust extraction equipment installed, compliance testing of removal area contaminant before starting the removal);
   - Asbestos removal equipment and facilities – cutting tool, vacuum cleaning, appropriated removal techniques (spraying method, dry method, removing asbestos from hot metal, small removals job using glove-bag method, etc);
   - Decontamination method – zoning for dirty and clean area, showering facilities, cloth removal area, etc);
   - Environmental monitoring of removal site

8. Personal protective device and equipment

9. Medical surveillance of exposed worker

10. Information, education, training, labeling/ warning signs

11. Packaging, storaging, transportation:
   - Initial packing;
   - Packing for transport;
   - Transport;
   - Warehousing

12. Asbestos waste disposal:
   - Certified contractor;
   - Container of waste;
   - Waste transportation;
   - Decontamination

13. Cleaning of premises and plant:
   - Clearance testing of the work area after finishing asbestos work

14. Offences and penalties
2.6.2 Specific area of consideration for work with asbestos materials in existing structure in the perspective of World Bank

A. Evaluation of alternatives

1. Determine if the project could include the installation, replacement, maintenance or demolition of:
   - Roofing, siding, ducts or wallboard
   - Thermal insulation on pipes, boilers, and ducts
   - Plaster or fireproofing
   - Resilient flooring materials
   - Other potentially asbestos-containing materials

2. If the use of asbestos-containing materials (ACM) has been anticipated for new construction or renovation, provide information about alternative non-asbestos materials and their availability. For new construction, determine the expected difference for the entire project - on initial and operating costs, employment, quality, expected service life, and other factors - using alternatives to ACM (including consideration of the need for imported raw materials).

3. In many cases, it can be presumed that ACM are part of the existing infrastructure that must be disturbed. If there is a need to analyze samples of existing material to see if it contains asbestos, provide information on how and where can that be arranged.

4. Once the presence of ACM in the existing infrastructure has been presumed or confirmed and their disturbance is shown to be unavoidable, incorporate the following requirements in tenders for construction work in compliance with applicable laws and regulations.

B. Understanding the regulatory framework

1. Review the host country laws and regulations and the international obligations it may have entered into (e.g., ILO, Basel conventions) for controlling worker and environmental exposure to asbestos in construction work and waste disposal where ACM are present. Determine how the qualifications of contractors and workers who maintain and remove ACM are established, measured, and enforced.

2. Determine whether licensing and permitting of the work by authorities is required.
3. Review how removed ACM are to be disposed of to minimize the potential for pollution, scavenging, and reuse.
4. Incorporate the following requirements in tenders involving removal, repair, and disposal of ACM.

C. Considerations and possible operational requirements related to works involving asbestos

1. Contractor qualification:
   Require that contractors demonstrate having experience and capability to observe international good practice standards with asbestos, including training of workers and supervisors, possession of (or means of access to) adequate equipment and supplies for the scope of envisioned works, and a record of compliance with regulations on previous work.

2. Related to the technical requirements for the works:
   Require that the removal, repair, and disposal of ACM shall be carried out in a way that minimizes worker and community asbestos exposure, and require the selected contractor to develop and submit a plan, subject to the engineer’s acceptance, before doing so.

   Describe the work in detail in plans and specifications prepared for the specific site and project, including but not limited to the following:
   - Containment of interior areas where removal will occur in a negative pressure enclosure;
   - Protection of walls, floors, and other surfaces with plastic sheeting;
   - Construction of decontamination facilities for workers and equipment;
   - Removing the ACM using wet methods, and promptly placing the material in impermeable containers;
   - Final clean-up with special vacuums and dismantling of the enclosure and decontamination facilities;
   - Disposal of the removed ACM and contaminated materials in an approved landfill;³⁹³⁹
   - Inspection and air monitoring as the work progresses, as well as final air sampling for clearance, by an entity independent of the contractor removing the ACM.
Other requirements for specific types of ACM, configurations and characteristics of buildings or facilities, and other factors affecting the work shall be enumerated in the plans and specifications. Applicable regulations and consensus standards shall be specifically enumerated.

3. Related to the contract clauses

Require that the selected contractor notifies the relevant authorities of the removal and disposal according to applicable regulations as indicated in the technical requirements and cooperates fully with representatives of the relevant agency during all inspections and inquiries.

4. Related to training and capacity building

Determine whether specialist industrial hygiene expertise should be hired to assure that local contractors learn about and apply proper protective measures in work with ACM in existing structures.

2.6.3 Air sampling, bulk sampling and the analysis of asbestos

The role of laboratory testing

The risk of exposure is not simply a function of the properties of asbestos containing materials, but also the type of work being done and the control measures. For example, though ACM presents less risk to asbestos exposure than fire-proofing materials, cutting dry ACM with a power saw can release greater amounts of airborne fibers than scraping wet, saturated fireproofing off. Moreover, the control used to control the release of fibers and debris also plays important roles.

As a result, compliance to exposure limits is demonstrated by bulk samples of ACM at the preparation phase and the ongoing monitoring using both area and personal sampling at the operation and maintenance phase.

Air sample method for asbestos

Air sampling is used to test for the concentration of airborne asbestos in and around the workplace and consisted of 2 types – area sampling and personal sampling.

Regarding area sampling, it should collect at pre-abatement, during abatement and post-abatement period as follow:

a) pre-abatement or backgrounds samples
- collect from both inside and outside the proposed work area.
- Air samples collected prior to commencement of abatement activities to represent fiber concentrations which occur in the air during normal activities.

b) During abatement

- These samples are collected during the preparation or set-up of the work area and decontamination units until the completion of the removal and cleaning activities.
- The collection of air samples during abatement is important to all parties involved. The documentation of fiber concentrations determines if the contractor provided adequate engineering controls, work practices, and maintained barriers in order to prevent the release of fibers to outside the work area.
- These are obtained daily from a variety of locations; outside critical barriers, decontamination units, and floors above/below. The Locations often change daily to make sure all areas outside the containment have been checked for increased fiber levels, if any.
- If air samples collected outside the regulated abatement work area indicate airborne fiber concentrations at or above 0.01 fibers per cubic centimeter (f/cc), or the established background level, whichever is greater, work shall stop immediately for inspection and repair of barriers and negative air ventilation systems.
- At no time during the project should airborne levels be higher than the levels acceptable for work area re-occupancy.
- If the work stoppage criteria is exceeded, State and City regulations mandate the cleanup of surfaces outside of the regulated abatement work area using HEPA-vacuums and wet-cleaning methods be performed prior to resumption of preparation, abatement or cleaning activities.

c) Post-abatement or clearance testing.

- Final clearance sampling is conducted at the completion of abatement and cleanup activities; and after visual inspections are conducted, but before any isolation and critical barriers are removed.
- Final clearance sampling is conducted at the conclusion of abatement procedures and after at least three separate cleanings of the work area has been performed.
- This sampling will help to determine if the contractor removed the asbestos and cleaned the area properly, and if the area is acceptable for building occupants to reenter.

Regarding personal sampling, there’s no specific suggestion for personal sampling in asbestos work. However, OSHA technical manual of personal
sampling for air contaminants provided 2 approaches: The first approach is to sample what the compliance officer believes to be the worst continuous 8-hour work period of the entire extended work shift; and the second approach is to collect multiple samples over the entire work shift. Sampling is done so that multiple personal samples are collected during the first 8-hour work period and additional samples are collected for the extended work shift.

In general, air sampling involves 2 steps as a) capturing air borne fibers on a filter; b) a laboratory analysis of the fiber samples to determine the quantity and/or types of fibers. The method for performing asbestos air sampling includes:

1. **Phase Contrast Microscopy (PCM)**

   A calibrated pump is used to draw in a steady amount of air through a filter, which collects airborne fibers. The filter is then sent to a laboratory and examined using PCM. PCM technique operates at magnifications of 400X and fiber of 0.25 um in diameter could not be detected. Result will be expressed in the number of fibers per cubic centimeter (f/cc).

   This method counts all fibers (e.g. a cotton fiber, a fiberglass fiber, a carpet fiber, a wood fiber, etc) and will not distinguish between asbestos and non-asbestos fiber.

   The techniques in details were described in NIOSH method 7400.

2. **Transmission Electron Microscopy (TEM)**

   TEM samples are collected in a similar manner to PCM. This method uses magnifications of 20000x and can distinguish between asbestos and non-asbestos fiber and determine the type of asbestos fibers. This method reported in units of fibers per square millimeter on the filter (f/mm2). PCM and TEM result then could not be directly comparable. The clearance limit by the TEM method is 70 asbestos fibers (asbestos structures) per square millimeter, usually written S/mm2. If the result is <70 S/mm2, it mean the result is not beyond clearance limit.

   This method is expensive and not widely accessed.

   This technique is well elaborated in NIOSH method 7402.

3. **Fibrous Aerosol Monitor (FAM)**

   The FAM is a portable device that instantaneously analyses the fiber content in the air. The device counts all fibers, includes asbestos and non-asbestos and will not distinguish fiber types. This device is used in the industry when continuous measurement may be useful, e.g., monitoring the integrity of an enclosure by placing FAM machine outside the enclosure; immediate
checking for fiber contamination level; determining area of evacuation and seal-up, etc.

This method is not officially address in any nation elsewhere.

**Bulk sample method for asbestos**

A bulk sample is a solid quantity of insulation, floor tile, building material, etc. suspected of containing asbestos fibres that will be analyzed for asbestos content and quantity. This method help identifying asbestos in structure at the commencement of asbestos work and help planning for the work or in evaluating percent of asbestos in suspected materials.

For EPA method for bulk sampling of asbestos, please see at

http://www.epa.gov/asbestos/pubs/2003pt763.pdf,
http://www.epa.gov/ne/info/testmethods/pdfs/EPA_600R93116_bulk_asbestos_part2.pdf

**1. Polarized Light Microscopy (PLM)**

PLM is the most popular technique for bulk building materials analysis. The light microscopy method uses the unique quality of polarized light to observe mineral specific optical properties. PLM can differentiate asbestos from non-asbestos fibres and further classify the various types that compose the asbestos mineral family. The limit of detection of the PLM is below 1% but not higher than 0.1% asbestos.

However, as with PCM, there are limitations to light microscopy testing due to the magnification employed and due to other interferences present in the building material matrix (ex: tar and petroleum binding components, sub-micron particulate adhering to the surface of asbestos mineral, etc.). The limitation of PLM analysis include: Asbestos is not detectable at low concentrations; Very fine asbestos fibres, such as those in brake dusts may not be detectable; Analysis may not be representative for small heterogeneous samples; Accuracy of analysis is dependent on experience of analyst. Where necessary, alternative laboratory services are available. These include transmission electron microscopy (TEM) and scanning electron microscopy (SEM).

The procedures for sample analysis are fully described by the US Occupational Safety and Health Administration (OSHA) as analytical method ID-181 and by the US Environmental Protection Agency (EPA) as analytical method 600/R93-116, including NIOSH method 9002.
For NIOSH method 9002, please see at http://www.cdc.gov/niosh/docs/2003-154/.

2. Transmission Electron Microscopy (TEM)

Because of the limitations mentioned above, some regulatory bodies such as EPA\textsuperscript{80} have recommended further analysis of bulk building materials by TEM. Using magnifications routinely at 20,000X or greater and employing powerful chemical (energy-dispersive X-ray analysis -EDXA) and mineralogical (Selected area electron diffraction pattern -SAEDP) tools, the TEM can differentiate not only asbestos from non-asbestos fibres, but also can classify the several species of different asbestos minerals.

However, the sample preparation and analysis process requires much longer than PLM or PCM and the equipment involved is extremely expensive. For this reason, TEM costs substantially more.

3. X-Ray Diffraction (XRD)

The principle of x-ray diffraction (XRD) analysis is that solid crystalline material will diffract an incident beam of parallel, monochromatic x-rays. By appropriate orientation of a sample relative to the incident x-ray beam, the diffraction pattern can be generated that will be uniquely characteristic of the structure of the crystalline present. XRD cannot determine crystal morphology, so in asbestos analysis, XRD techniques can not differentiate between fibrous and non-fibrous forms of serpentine minerals.

XRD is therefore partially successful in determining chrysotile fiber because it could be interfered from nonasbestiform polymorphs of serpentine, leading to overestimation of chrysotile. Also, the minimum detection limit for asbestos analysis by X-ray diffraction (XRD) is about 1%.

The below flow charts (Figure 2.3) are easy-to-understand diagram showing the step by step process on how to select the appropriate air and bulk sampling and analysis.
At the start of handling or abatement of suspected asbestos materials, do you know for sure whether it contained asbestos,

considered valid document such as SDS and official declared documents, etc.

Yes, it’s ACM.

Don’t know

No, it’s not ACM.

Bulk sample, analysis by PLM w/s SEM, TEM for asbestos

Yes, it’s ACM.

No, it’s not ACM.

No need for air sampling for asbestos

1. Area/ personal air sampling at worksite at pre-abatement, during abatement, and post-abatement
2. Sample analysis using PCM w/s SEM, TEM for asbestos

Figure 2.3 Flow chart for selecting the appropriate asbestos air and bulk sampling and analysis.
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Secondary prevention: Early diagnosis and treatment

3.1 Diagnostic criteria and treatment of non-malignant asbestos-related diseases


Diagnostic criteria

The early diagnosis of non-malignant asbestos-related disease requires knowledge of the presenting disease sign, knowledge of the occupations, circumstances associated with exposure risk and insight into the pathophysiology of asbestos in the body.

According to the revised guidelines of the individual patient developed by the American Thoracic Society in 2004, which is slightly modified from that presented in 1986, the diagnostic criteria of non-malignant asbestos-related disease formulated are:

1) Evidence of structural pathology consistent with asbestos-related disease as documented by imaging or histology.
2) Evidence of causation by asbestos as documented by the occupational and environmental history (with plausible of latency), markers of asbestos exposure (usually pleural plaques), recovery of asbestos bodies, or other means.
3) Exclusion of alternative plausible causes for the findings.

Demonstration of functional impairment is not required for the diagnosis of a non-malignant asbestos-related disease, but where present should be documented as part of the complete evaluation.

Marker of asbestos in lung tissue

Marker of asbestos in lung tissue included asbestos fibers and asbestos bodies which can be identified and quantified in lung tissue specimen from needle biopsy, transbronchial biopsy or open lung biopsy, and bronchoalveolar lavage (BAL). Transbronchial lung biopsy is less reliable than BAL or open
lung biopsy since it could not recover sufficient tissue to demonstrate elevated asbestos body or fiber counts when they do occur.

*Asbestos fibers* are rarely seen by light microscopy and must be analyzed by scanning/transmission electron microscopy. There is considerable variation among laboratories in procedures to quantify asbestos fibers in tissue, which has led to efforts to standardize procedures. Asbestos mineralogical types can be identified by energy-dispersive X-ray analysis -EDXR, in which detection of magnesium and silicon is characteristic of most forms of asbestos and the presence of a large iron peak signifies an amphibole (with the exception of tremolite). Fiber analysis can be helpful in assessment of exposure and provides information about intensity, duration, and latency (e.g., uncoated fibers may reflect recent heavy exposure). However, because some fibers dissolve over time, the absence of a high fiber count does not necessarily mean that there has been no exposure, especially when chrysotile is the predominant exposure. Mineralogic analysis of asbestos fibers is largely a research technique and is not widely available.

*Asbestos bodies* are asbestos fibers that have been coated with an iron-rich, proteinaceous concretion. Amphibole asbestos forms the majority of asbestos bodies and is more persistent in lung tissue than chrysotile. Asbestos bodies are larger than asbestos fibers and can be identified and quantified by light microscopy. An iron stain is helpful to identify fibrous bodies coated by iron, hence the general name “ferruginous bodies”. Ferruginous bodies generally form on fibers at least 10 µm in length, and more than 90% of all coated fibers have asbestos cores. Demonstration of an elevated body burden of asbestos confirms past exposure. Levels of at least one or two asbestos bodies per field of a tissue section on a slide under light microscopy are consistent with occupational exposure.

Transbronchial lung biopsies are usually too small to analyze for asbestos bodies. The absence of observable asbestos bodies is not reliable in excluding significant exposure in transbronchial biopsy tissue.

Bronchoalveolar lavage recovers more material and therefore provides a better indicator of tissue burden. Some experienced clinicians have found that identification of six or more bodies in bleach-digested samples from at least two biopsies is characteristic of patients with occupational exposure.

These indicators of fiber burden (both asbestos bodies and asbestos fibers) are sufficient but not necessary to identify occupational exposure and to diagnose asbestos related disease. Beyond clinical research, the method has applications in litigation and exposure assessment for epidemiology.
Asbestos bodies and fibers can be identified and quantified in bronchoalveolar lavage (BAL) specimens. There is considerable variation among laboratories in these tests. The count of asbestos bodies in BAL fluid appears to correlate with the presence or degree of fibrosis in some studies but not others\textsuperscript{3-5}.

BAL in patients with asbestosis has demonstrated an alveolar macrophage alveolitis associated with a modest increase in neutrophils. This neutrophilia correlates with the finding of crackles (rales) on physical examination and disturbances in oxygenation and is apt to be more pronounced in patients with advanced disease. Clinically apparent asbestosis occurs only after a significant latent period. However, studies using BAL, computed tomography (CT) scanning, and gallium-67 scanning have demonstrated that inflammatory events occur well before the onset of clinical disease. Thus, it is likely that the initial exposure induces inflammation and injury that persist through the latent or subclinical phase and later develop into the clinical disease, which is typically diagnosed by chest imaging.

**Clinical evaluation of non-malignant asbestos-related diseases**

Asbestos fibers are deposited at airway bifurcations and in respiratory bronchioles and alveoli primarily by impaction and interception. Fibers migrate into the interstitium, in part via an uptake process involving type I alveolar epithelial cells (see figure 3.1). Asbestos fibers stimulate macrophages to produce a variety of mediators. Oxygen radicals contribute to tissue injury. Granulocytes are recruited to sites of disease activity and they in turn release mediators that contribute to tissue fibrosis by stimulating fibroblast proliferation and chemotaxis and ultimately promoting collagen synthesis.
Inhaled asbestos fibers can also result in pleural inflammation. Asbestos fibers are transported to the pleural surface along lymphatic channels by macrophages and/or direct penetration. The degree of fibrosis is dose dependent.

The non-malignant asbestos-related diseases refers to the following conditions: asbestosis, non-malignant pleural abnormalities associated with asbestos (pleuritis, pleural effusion, circumscribed pleural thickening (plaques), diffuse pleural thickening), and chronic airflow obstruction.

ATS guideline 2004 has elaborated each disease in details as follows:

(i) Asbestosis
Diagnosis

Asbestosis is the diffuse interstitial pneumonitis and fibrosis caused by the deposition of asbestos fibers in the lung. It does not refer to visceral pleural fibrosis, the subpleural extensions of fibrosis into the interlobular septae or lesions of the membranous bronchioles.

Neither the clinical features nor the architectural tissue abnormalities sufficiently differ from those of other causes of interstitial fibrosis to allow confident diagnosis without a history of significant exposure to asbestos dust in...
the past or the detection of asbestos fibers or bodies in the lung tissue greatly in excess of that commonly seen in the general population.

*Note: membranous bronchioles are the term described airways < 2 mm of internal diameter, without cartilage in walls, and non-alveolated.*

Asbestosis is commonly associated with prolonged exposure, usually over 10 to 20 years. However, short, intense exposures to asbestos, lasting from several months to 1 year or more, can be sufficient to cause asbestosis. For example, shipyard workers who applied or removed insulation in confined spaces have developed asbestosis after brief periods of heavy exposure. Insulation workers have had similarly intense exposures during their apprenticeship when they unloaded asbestos-containing sacks into troughs for mixing asbestos cement. Such occupational exposures are now rare but were common around 1970s-1980s in developed country. Adequate industrial hygiene controls were absent or not widely applied. Protective regulations were inadequate and only partially enforced during much of that period. However, the occupational exposure in developing countries is still going on especially in Asia and Eastern Europe.

Asbestosis becomes evident only after an appreciable latency period, often two decades. In a study by Ehrlich (1992) of former workers from an amosite asbestos insulation factory that had high levels of asbestos dust, employment for as little as 1 month resulted in a prevalence of 20% of parenchymal opacities 20 years after exposure ceased. The duration and intensity of exposure probably influence the length of the latency period. Relatively short-term, high-intensity exposure may be associated with a shorter latency than prolonged, lower intensity exposures⁶. Asbestosis is usually associated with dyspnea, bibasilar rales, and, less commonly, clubbing of the fingers.

Functional disturbances can include gas exchange abnormalities, a restrictive pattern, and mixing between restrictive and obstructive pattern due to small airway disease. The characteristic change in pulmonary function observed in asbestosis is a restrictive impairment, characterized by reduction in lung volumes (especially the FVC and total lung capacity), decreased diffusing capacity, and arterial hypoxemia. Large airway function, as reflected by the FEV1/FVC ratio, is generally well preserved. In one of the earliest studies conducted, about 50% of asbestos workers presented with FVC below 80% predicted. The frequency of abnormal vital capacity increased, and the mean vital capacity decreased by 18% over the subsequent 10 years. The frequency
and magnitude of the restrictive defect increased with ILO category (i.e.,
increased profusion of irregular opacities) and the presence of pleural changes.

The predominantly parenchymal and restrictive pattern of the disease,
airway obstruction can also be observed and can be seen alone in nonsmokers
who have asbestosis. These patients usually have a restrictive pattern of lung
function, but clinically they also feature an obstructive component characterized
physiologically by increased isoflow volume, and increased upstream resistance
at low lung volumes. These obstructive findings may be due to asbestos-induced
small airway disease. Thus, mixed restrictive and obstructive abnormalities do
not rule out asbestosis or necessarily imply that asbestos has not caused an
obstructive functional impairment.

Note: Definition of disease

**Small airway disease:** this disease refers to abnormality of respiratory bronchioles
which are small airways with alveolated walls, extending in 3 generations from terminal
membranous bronchiole to alveolar ducts.

The airway remodeling processes are similar to larger airways involving goblet cell
metaplasia with mucus plugging, inflammation, smooth muscle hyperplasia, and fibrosis.
Smoking leads to a predominantly mononuclear inflammatory process in the small airways
and lung parenchyma. Destruction of lung parenchyma may lead to loss of alveolar
attachments, predisposing to small airway collapse.

**Chronic bronchitis:** a chronic lung disease which the main manifestation is of large
airway and is not associated with airflow obstruction. The symptoms presentation is chronic
sputum production.

**Empysema:** a chronic, irreversible disease of the lungs characterized by abnormal
enlargement of air spaces in the lungs accompanied by destruction of the tissue lining the
walls of the air spaces.

**Chronic Obstructive Pulmonary Disease (COPD):** a chronic lung disease
characterized by a mixture of small airway disease (obstructive bronchiolitis) and
parenchymal destruction (emphysema), of which the relative contributions of the mixture
varies from person to person.

The abnormal PA chest film and its interpretation remain the most
important factors in establishing the presence of pulmonary fibrosis. Asbestosis
is generally associated with relatively high exposure levels with radiological
signs of parenchymal fibrosis which is characteristically appears earliest in
bilateral lower lung field. However, it is possible that mild fibrosis may occur at
lower exposure levels, and the radiological criteria need not always be fulfilled
in cases of histologically detectable parenchymal fibrosis. The recognition of
asbestosis by chest radiography is best guided by standardized methods such as
the classification of the International Labour Organization (ILO) and its
modifications. Standard films must always be used. For research and screening purposes, radiological findings of small opacities, grade 1/0, are usually regarded as an early stage of asbestosis. Inspiratory basilar sales, restrictive impairment, small airway obstruction, and gas exchange disturbances in pulmonary function are considered valuable information for clinical diagnosis, for occupational health practice, and for attribution purposes. HRCT can confirm radiological findings of asbestosis and show early changes not seen on chest X-rays, but should be performed only in selected cases.

The College of American Pathologists has developed histological criteria for asbestosis grading system to describe the severity and extent. The mildest (Grade I) form of asbestosis involves the alveolated walls of respiratory bronchioles and the alveolar ducts. More severe histologic grades involve greater proportions of the acinus (Grade II) until the whole acinar structure is involved (Grade III asbestosis) and some alveoli are completely obliterated. Alveolar collapse, with fibrosis and honeycomb remodeling resulting in new dilated spaces in the parenchyma, results in the most severe grade of asbestosis (Grade IV). These patterns of acinar fibrosis together with the demonstration of asbestos bodies in standard histologic sections are diagnostic of asbestosis as shown in the table 3.1.

Table 3.1 Histologic grades of asbestosis

<table>
<thead>
<tr>
<th>Grade</th>
<th>change</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No fibrosis associated with bronchioles</td>
</tr>
<tr>
<td>1</td>
<td>Early fibrosis involving walls of at least one respiratory bronchioles, with or without extension into septa of adjacent alveoli; fibrosis confined to alveolated walls of respiratory bronchioles and ducts and not present to more distant alveoli. Alveolitis and inflammation similar to that caused by cigarette smoking</td>
</tr>
<tr>
<td>2</td>
<td>More severe fibrosis involving acinus ; alveolar ducts and/ or two or more layers of adjacent alveoli. Normal lung remains in a zone between adjacent bronchioles</td>
</tr>
<tr>
<td>3</td>
<td>Fibrosis advanced and coalescent, involves entire acinus; all lung between at least two adjacent bronchioles is affected. Some alveoli are completely obliterated</td>
</tr>
<tr>
<td>4</td>
<td>Honeycomb remodeling and large (up to 1 cm) dilated spaces grossly visible in parenchyma</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Grade of extent</th>
<th>change</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Only occasional bronchioles are involved. Most appear normal</td>
</tr>
<tr>
<td>B</td>
<td>“More than occasional” but less than half of the bronchioles are</td>
</tr>
</tbody>
</table>
More than half of bronchioles are involved

Note: See also Figure 3.2 showing anatomy and dimensions of secondary lobule and pulmonary acinus to make the readers understand clearly the histologic grading of asbestosis. This diagram illustrates 2 secondary pulmonary lobules in the lung periphery and 1 acinus.

![Figure 3.2 Secondary lobule and pulmonary acinus](http://http://radiology.rsna.org/content/239/2/322.full)

Regarding its prognosis, asbestosis may remain static or progress but regression is rare. Progression, after cessation of exposure or reduction to current permissible exposure levels, is considerably more common in persons who already have radiographic abnormalities and appears to be associated with level and duration of exposure and therefore cumulative exposure.

Asbestosis is more prevalent and more advanced for a given duration of exposure in cigarette smokers, presumably because of reduced clearance of asbestos fibers in the lung. Some studies suggest that smokers without dust exposure may show occasional irregular radiographic opacities on chest film, but if so the profusion is rarely as high as 1/0; smoking alone therefore does not result in a chest film with the characteristics of asbestosis. Both smokers and ex-smokers have a higher frequency of asbestos-related irregular opacities on their chest radiographs than do nonsmoking asbestos-exposed workers in all profusion categories.
Smoking alone does not affect the presentation of asbestos-related pleural fibrosis.

Differential diagnosis

Although lung biopsy is not usually necessary for the diagnosis of asbestosis when a significant exposure history is obtained, it may be warranted to exclude other, potentially treatable diseases. Biopsy material may be helpful in identifying the nature of a disease in an indeterminate case or one lacking an adequate exposure history.

The presence of asbestos bodies in tissue sections should be sufficient to differentiate asbestosis from other forms of interstitial fibrosis. The chance of finding one asbestos body from background exposure alone has been shown to be about 1 per 1,000\(^7\). Conversely, the presence of interstitial fibrosis in the absence of asbestos bodies is most likely not asbestosis. Idiopathic pulmonary fibrosis (IPF in clinical terms or usual interstitial pneumonitis in terms of pathology) has an acinar pattern of fibrosis different from that of asbestosis and is not associated with asbestos bodies in tissue sections. On occasion, asbestosis is seen in conjunction with an unrelated interstitial lung disease (such as sarcoidosis) or in association with another pneumoconiosis, for example, silicosis. In the absence of fibrosis, asbestos bodies are an indication of exposure, not disease.

Asbestosis resembles a variety of other diffuse interstitial inflammatory and fibrotic processes in the lung and must be distinguished from other pneumoconioses, IPF, hypersensitivity pneumonitis, sarcoidosis, and other diseases of this class. The clinical features of asbestosis, although characteristic, are not individually unique or pathognomonic, but the characteristic signs of the disease are highly suggestive when they occur together. The presence of pleural plaques provides useful corollary evidence that the parenchymal process is asbestos related.

Diagnostic uncertainty is most likely in certain groups of patients. Patients may have a heavy cigarette-smoking history and concurrent emphysema (which also reduces the diffusing capacity). In such cases, one expects a history of asbestos exposure commensurate with the degree of disease. On occasion, a patient with another interstitial lung disease, such as IPF, will have a history of asbestos exposure. Rapid progression, with a visible, year-to-year increase in symptoms, progression of radiographic findings, and loss of pulmonary function in the absence of intense asbestos exposure, suggests the diagnosis of IPF rather than asbestosis.
Treatment

Fibrotic-scarred lung tissue cannot be repaired and the disease could remain static or progress but regression is rare. Once the exposure to asbestos has stopped the disease will progress to the level dictated by the amount of asbestos fiber in the lungs and stabilize. Treatment for the disease is focused on relieving the symptoms caused by reduced oxygen availability and avoiding other medical problems that may be caused by asbestosis.

One of the primary treatment modalities is putting an end to smoking. The primary concern with the combination of asbestosis and smoking is the onset of emphysema, which will further reduce breathing capability. It may be the most difficult of all the treatment steps.

Avoiding pulmonary disease is critical with reduced lung function. It is important to avoid the onset of flu or pneumonia, which may require periodic vaccination. The only way to avoid a cold is avoid exposure to people who are contagious.

Medication may be in order if the reduced oxygen supply is leading to high blood pressure. A blood thinner and/or medication to relax constricted blood vessels may be prescribed by the treating physician.

Pleural effusion may develop as the result of asbestosis. Accumulation of fluid between the lungs and the ribs or lungs and the diaphragm may be relieved by draining the fluid with a thoracentesis procedure.

Oxygen therapy may be an option for periodic treatment if the lungs have reached an advanced state of deterioration.

(ii) Non-malignant pleural abnormalities associated with asbestos (pleuritis, pleural effusion, circumscribed pleural thickening (pleural plaques), diffuse pleural thickening)

Asbestos-related pleural abnormalities are divided into pleural plaques, mainly involving the parietal pleura, sometimes with calcification, and diffuse pleural thickening, which is a collective name for pleural reactions involving mainly the visceral pleura. These include benign asbestos-related pleural effusion, blunted costophrenic angle, crow's feet or pleuroparenchymal fibrous strands, and rounded atelectasis.

Acute pleural effusion
Asbestos may cause an acute pleural effusion, often lasting several months, that is exudative and often hemorrhagic, with variable numbers of erythrocytes, neutrophils, lymphocytes, mesothelial cells, and often eosinophils. It may occur early (within 10 years, unlike other asbestos-related diseases) or late after the onset of asbestos exposure. It may be superimposed on long-standing pleural plaques.

Although it is usually asymptomatic, the acute pleural effusion due to asbestos may also be exuberant, with fever and severe pleuritic pain. It is sometimes detected only incidentally on a radiograph taken for another purpose. The effusion may persist for months, present bilaterally, or recur on the same or the opposite side. A friction rub may be present. The traces of pleural effusion may be observed years later as a blunted costophrenic angle or as diffuse pleural thickening. Acute pleuritis is thought to underlie many cases of diffuse pleural thickening. Of 20 insulators with a past history of definite pleural effusion, diffuse pleural thickening was detected on radiograph in 16. Dose–response relationships or characteristic features of exposure associated with effusion have not been described.

Chronic severe pleuritic pain is rare in patients with asbestos related pleural disease. Vague discomfort appears to be more frequent. Studies examining the frequency of atypical chest pain in asbestos-exposed patients have not been performed. In the few cases described, it was present for many years, disabling, and often bilateral. Radiographic evidence of pleural disease ranged from plaques to extensive diffuse and circumscribed pleural thickening; several cases followed pleural effusions. The diagnosis of acute asbestos-related pleural effusion is by exclusion of other causes of acute pleuritis, and most often is not arrived at until the pleural space is fully explored and biopsied, generally by thoracoscopy.

Differentiation from Dressler’s syndrome is difficult in asbestos-exposed patients who have undergone recent cardiac surgery. Differentiation from mesothelioma or pleural extension of a pulmonary malignancy is critical, and may be difficult on clinical grounds (including positive gallium and positron emission scan). Pleural fluid cytology is useful for distinguishing benign from malignant effusions. It is not unusual for nonspecific effusions to precede mesothelioma by several years. If a malignancy has not manifested itself within 3 years, the effusion is generally considered benign.

Note: Dressler’s syndrome is a secondary form of pericarditis that occurs in the setting of injury to the heart or the pericardium. It is believed to result from an autoimmune inflammatory reaction to myocardial neo-antigens. Dressler's syndrome is associated with
myocardial infarction (heart attack). A similar pericarditis can be associated with any pericardiotomy or trauma to the percardium or heart surgery.

The diagnosis of chronic pleuritis manifested by pleuritic pain is reached by excluding malignancies, because most other causes of acute pleuritis do not result in chronic pain. Malignancy is unlikely when pain persists for years with little or no clinical or radiographic change.

Circumscribed pleural thickening (Pleural plaques)

Pleural plaques are indicators of exposure to asbestos. They are clearly the most common manifestation of the inhalation, retention, and biologic effect of asbestos. Their prevalence is most directly related to duration from first exposure; they are rare within less than 20 years. Pleural plaques consistent with asbestos exposure appear in chest films of 2.3% of U.S. males, a percentage that has been remarkably stable both for the general population in the early 1970s and veterans in the 1990s. Calcification is similarly related to duration. Smoking plays no role in the prevalence of pleural plaques.

Pleural plaques are bilateral, but not symmetric, lesions of the parietal pleura. Characteristically, they are found following the ribs on the lower posterior thoracic wall and over the central tendons of the diaphragm as shown in figure 3.2 and 3.3. As seen, pleural plaques are raised, sharply circumscribed with a smooth or with a rounded knobby surface, and range in color from white to pale yellow. They generally spare the costophrenic angles and apices of the thoracic cavity.
Microscopically, they consist of mature collagen fibers arranged in an open basket-weave pattern and are covered by flattened or cuboidal mesothelial cells. They are relatively avascular and acellular and show minimal inflammation. They are sharply demarcated from subpleural tissues and central calcification is common.
Asbestos bodies are not seen in or adjacent to the pleural plaque lesions. Isolated plaques may be associated with tuberculosis, trauma, and hemothorax; however, multiple lesions having the classic appearances described above are almost invariably associated with asbestos exposure.

The conventional chest film is a sensitive and appropriate imaging method for plaques, although it may identify abnormalities that resemble plaques but are not. In the PA radiograph, they are best seen in profile on the midlateral chest walls and on the diaphragm or face on, and show serrated borders.

HRCT is not a practical screening method for demonstrating plaques because of the separation between sections, the high radiation exposure, and the lack of access to the test in some locations. HRCT is useful to identify questionable abnormalities and to resolve questions about structures that resemble plaques. Typical pleural plaques are easily identified on plain films by sharp, often foliate, borders (face on) and by a raised straight surface with clear, cut-off edges when seen face on and as irregular margins (sometimes almost rectangular) when seen in profile on the chest wall or diaphragm.

Apparent pleural thickening with gradually tapering or indistinct edges is often due to subpleural fat or superimposed soft tissue; fat pads below the parietal pleura typically occur in the midthoracic wall, between the fourth and eighth ribs, as do pleural plaques. Proper penetration is important on plain film; differentiation of fat from pleural plaques may still be difficult but is readily made by HRCT.

Less typical plaques on the diaphragm may be difficult to detect and should be distinguished from atelectatic streaks, visceral folds, or diaphragmatic straightening caused by bullae. Calcification is helpful but may not be apparent in an underpenetrated film. Axial CT scans often fail to image diaphragmatic plaques.

The burden of asbestos fibers in lung tissue and of asbestos bodies in bronchoalveolar lavage fluid is greatly increased in patients with diffuse pleural thickening or asbestosis and moderately increased in patients with pleural plaques compared with unexposed subjects. The presence of pleural plaques is correlated with parenchymal disease, in particular fibrotic bands and both peribronchiolar and alveolar fibrosis. However, peribronchiolar fibrosis is absent in many cases with pleural plaques and present in many cases without them.

Slow progression of plaques is typical. Approximately 85% of heavily exposed workers showed pleural thickening (predominantly plaques) on plain film more than 40 years from first exposure, as did up to 17% of environmentally
exposed populations. More than half the cases were bilateral. The presence of plaques is associated with a greater risk of mesothelioma and of lung cancer compared with subjects with comparable histories of asbestos exposure who do not have plaques\textsuperscript{9,10}. This is thought to be due to greater exposure or retained body burden, not malignant degeneration. Therefore, the presence of pleural plaques should be interpreted as a marker for elevated risk of malignancy, which may be higher than the occupational history alone might suggest.

**Diffuse pleural thickening**

Diffuse pleural thickening affects the visceral pleural surface and is quite different in appearance from the parietal pleural plaque. It consists of pale gray diffuse thickening that blends at the edges with the more normal pleura. It may be extensive and cover a whole lobe or whole lung and obliterate lobar fissures. It ranges in thickness from less than 1 mm up to 1 cm or more. Adhesions to the parietal pleura are common, particularly opposite to pleural plaques. The lesion may show a gradient with immature granulation tissue and fibrin at the surface, progressing to mature collagen adjacent to the lung. The fibrosis may extend for a few millimeters into the lung parenchyma and into the lobular septae. The latter features do not constitute asbestosis.

Diffuse pleural fibrosis or thickening extends continuously over a portion of the visceral pleura, often causing adhesions to the parietal pleura, involving the fissures and obliterating the costophrenic angle. The newly revised ILO classification\textsuperscript{11} recognizes pleural thickening as diffuse “only in the presence of and in continuity with, an obliterated costophrenic angle”. Localized subpleural parenchymal fibrosis is often present without diffuse interstitial fibrosis. Calcification of the pleura occurs with the passage of time, and may involve fissures. A rare variant of visceral pleural fibrosis is progressive apical thickening associated with fibrosis of the upper lobe.

Diffuse pleural thickening may have a significantly greater impact on pulmonary function than circumscribed plaques. A reduction of 270 ml of FVC has been associated with diffuse pleural thickening. Workers with diffuse pleural thickening have a significantly greater decrement in FVC (by a factor of two or more) than those with circumscribed pleural thickening. This effect is unrelated to the radiographic extent of pleural thickening; a similar reduction in FVC was seen with little more than costophrenic angle blunting as with extensive involvement. Decrements associated with diffuse pleural thickening reflect pulmonary restriction as a result of adhesions of the parietal with the visceral pleura. Restrictive
impairment is characteristic, with relative preservation of diffusing capacity (pattern of entrapped lung). Ventilatory failure leading to hypercapnia and cor pulmanale, decortications may be considered.

*Rounded atelectasis.*

Rounded atelectasis, also known as shrinking pleuritis, contracted pleurisy, pleuroma, Blesovsky’s syndrome, or folded lung, presents radiographically as a mass and may be mistaken for a tumour.

The condition may result from pleuritis of any cause. The lesion is thought to develop from infolding of thickened visceral pleura with collapse of the intervening lung parenchyma. The classic “comet sign” is pathognomonic and is often more readily seen on an HRCT than on plain films. Clues to its identity are a band connecting the mass to an area of thickened pleura and a slower evolution than that of a lung cancer, so that previous films will show a similar finding. Rounded atelectasis may be multiple and bilateral. Asbestos bodies and/or evidence of asbestosis should be carefully sought.

Histologic examination shows folded and fibrotic visceral pleura with atelectasis and variable amounts of chronic inflammation in the adjacent lung parenchyma. The sudden appearance of rounded atelectasis may follow acute pleuritis with effusion.

Rounded atelectasis is important for the diagnostic pathologist to recognize as it is frequently removed surgically as a suspected peripheral lung cancer.

*Differential diagnosis of non-malignant pleural abnormalities including rounded atelectasis and apical thickening.*

Acute pleuritis of any cause can result in diffuse pleural thickening that is indistinguishable from that associated with asbestos, although such causes are usually unilateral. The most likely causes, empyema, tuberculosis, and trauma, including surgery, are likely to be identified in the medical history. Empyema in childhood or an infected pleural effusion associated with pneumonia may not be.

The major differential diagnostic consideration with diffuse pleural thickening is mesothelioma, which is progressive and more likely to be symptomatic at the time of detection. On occasion, when fibrosis and mesothelial proliferation are exuberant, The distinction is difficult clinically, radiographically, and histologically. Apical thickening must also be distinguished from mesothelioma and tuberculosis, which may be suggested by history and (previous) bacteriologic findings.
(iii) **Chronic airway obstruction**

In early asbestosis, the fibrosing process is limited to the walls of alveoli immediately around the bronchioles. Consequently, fibrosis extends outward until it ultimately links adjacent bronchioles; at which time, the initial, predominantly peribronchiolar pattern of fibrosis may no longer be evident. Regarding that, asbestos exposure has traditionally been considered to cause predominantly restrictive lung.

The role of asbestos as a cause of airway obstruction, however, has not been well clarified but more researches elaborated mainly through asbestos effect on small airway. Histologically, inflammation and airway fibrosis caused by asbestos was found at membranous and respiratory bronchioles and then extends into the alveolated portions of the walls and alveolar ducts. Differently, small airway effect caused by cigarette smoking primarily involves mainly the nonalveolated portions of the first generation of respiratory bronchioles. Additionally, asbestos bodies are not present in the walls of the membranous bronchioles, although inflammatory changes are present, but are commonly seen in the walls of the respiratory bronchioles and/or adjacent alveoli. Some researchers consider it appropriate to describe these lesions as true asbestosis while others consider the small airway lesions as distinct from asbestosis and refer to the lesions of both membranous and respiratory bronchioles as asbestos-induced small airway disease. These small airway lesions are the likely anatomic basis for airflow obstruction limitation in asbestos-exposed individuals. In general, the magnitude of the asbestos effect on airway function is relatively small. This effect, by itself, is unlikely to result in functional impairment or the usual symptoms and signs of chronic obstructive pulmonary disease.

**ii) Comments on ATS 2004 “Diagnostic and initial management of nonmalignant diseases related to asbestos”**

The main argument to ATS 2004 focused on the conflict of interest on using plain chest film at profusion level 1/0 instead of 1/1 in asbestosis diagnosis as in the previous ATS 1986 as shown. The original letter of the argument which was not published was shown in the box below.

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**Original Letter to the editor of American Journal of Respiratory Critical Care Medicine, e-mailed 10/25/04 and rejected.**

*2004 Asbestos Disease Guidelines Ignore Mass Screening Abuse*

I had hoped that the long-awaited ATS update on diagnosis of non-malignant asbestos diseases would be thorough and point out the diagnostic abuse of mass asbestos claims. Instead, key references are omitted and some of the statements seem slanted toward supporting these claims. This is unfortunate when one considers the growing evidence...
that most of these claims are medically specious.

1) The authors provide no reference for their assertion that the difference between 1/0 and 0/1 profusion readings "is generally taken to separate films that are considered to be positive for asbestosis from those that are considered to be negative." It is well known that a B-reading of 1/0 is non-specific and non-diagnostic, as it is commonly found in middle-aged smokers and in ex-factory workers never exposed to asbestos.

2) The authors do not reference their assertion that "the sensitivity of the plain chest film for identifying asbestosis at a profusion level of 1/0 has been estimated at or slightly below 90%. The corresponding specificity has been estimated at 93%." Is this information from plaintiff-attorney-hired B-readers (PAHP)? The authors do not acknowledge the fact that most ILO readings by PAHP are over-interpreted, or that PAHP are paid more for a positive diagnosis than a negative one. This is crucial information, as it should invalidate all medical conclusions based on "diagnoses" generated by PAHP.

3) The authors provide no explanation of why ATS lowered the profusion score for diagnosing asbestosis from 1/1 (in 1986) to 1/0 ("presumptively diagnostic").

4) The disclaimer that the 2004 criteria "are intended for the diagnosis of nonmalignant asbestos-related disease in an individual in a clinical setting for the purpose of managing that person's current condition and future health" is naive at best, disingenuous at worst. Just like the 1986 article, the new ATS review will be quoted in the legal arena. Unwittingly or not, the authors have published unsupported statements that can (and will) be taken out of context and quoted in court.

5) There is (incredibly) no Conflict of Interest Statement (CIS) for the authors, yet such a statement is provided in every other article in the same issue, including letters to the editor and studies where it would be hard to imagine any conflict. Furthermore, the website regarding manuscript submissions indicates the CIS is an ironclad requirement. Is ATS itself exempt? Considering the partisanship of asbestos litigation, each author's experience consulting for plaintiff vs. defense sides should have been spelled out in detail.

I have had the opportunity to examine hundreds of these mass asbestos claims on behalf of defendants, and am dismayed at the lack of scientific or medical merit for most of them. Solid legal and medical discourse is beginning to acknowledge this abuse of diagnosis. Now, sadly, ATS has squandered a golden opportunity to publish an above-suspicion review and champion science and objectivity in the diagnosis of non-malignant asbestos disease.

Lawrence Martin, M.D.
CWRU School of Medicine, Cleveland, Ohio

References
More arguments toward ATS 2004 besides the profusion score for diagnosing asbestosis are as follows:
1. Statement on airflow obstruction caused by asbestos is equivocal and is not conclusive as seen in the below ATS’s quote.

“...airway obstruction can also be observed and can be seen alone in nonsmokers who have asbestosis..... These obstructive findings may be due to asbestos-induced small airway disease.”

and then contradicted by

“In general, the magnitude of the asbestos effect on airway function is relatively small. This effect, by itself, is unlikely to result in functional impairment or the usual symptoms and signs of chronic obstructive pulmonary disease.”

It is also disputed that there is no strong evidence that asbestos inhalation alone, without smoking or other industrial pollutants, causes airflow obstruction.
2. The sensitivity and specificity of plain chest film at a profusion 1/0 might not satisfied considering the prevalence of disease in the screening population.

The sensitivity of the plain chest film for identifying asbestosis at a profusion level of 1/0 has been estimated in ATS statement at or slightly below 90%.
Likewise, the corresponding specificity has been estimated at 93%. Applied to populations with varying prevalence of disease, the positive predictive value of the minimally abnormal chest film alone in making the diagnosis of asbestosis may fall below 30% when exposure to asbestos has been infrequent and exceed 50% when it has been prevalent.

This suggests that screening programs based on the chest film alone may vary considerably in their yield of true cases depending on the characteristics of the population being screened. In the general population and for occupational groups with low levels of exposure they may be unreliable in identifying asbestosis. The application of multiple criteria, as outlined in this statement, is a preferable approach.

3. The Helsinki criteria referred by ATS was claimed as a completely unreferenced editorial in a European medical journal. It also did not acknowledge any of the mass-asbestos claim abuse evident at the time, nor did it provide any Conflict of Interest Statements for the authors.

4. ATS statement of “the risk of asbestos-related cancer may be elevated in a person exposed to asbestos without obvious signs of nonmalignant asbestos related disease” is objected because ATS have ignored a numerous of data either contradicts these statements. This ATS statement is so vague and broad especially with lung cancer of which prevalence is even highest among asbestos related cancer.

5. ATS statement of “Some studies suggest that smokers without dust exposure may show occasional irregular opacities on chest film, but if so the profusion is rarely as high as 1/0; smoking along therefore does not result in a chest film with the characteristics of asbestosis’ was refuted that small opacities could related to age, smokers and ex-smokers, and may be confused with asbestosis.

**iii) American College of Chest Physicians –ACCP¹⁶**

ACCP conducted a Delphi study to obtain consensus among 20 international outstanding experts to evaluate the asbestos-related disease impairment controversial after more than 20 years of research. The table 3.2, 3.3, and 3.4 below showed result of 32 statements under study: 17 statements with agreement consensus, 6 statements with disagreement consensus, and 9 statements without expert panel consensus.

Table 3.2 Consensus 17 statements of agreements (total 32 statements)
<table>
<thead>
<tr>
<th>Statement No.</th>
<th>Consensus Statement</th>
<th>Median</th>
<th>IQR</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Workers with asbestos exposure and pleural plaques or diffuse pleural thickening (in the absence of fibrosis) are at increased risk of mesothelioma</td>
<td>9.5</td>
<td>3</td>
<td>0.0001</td>
</tr>
<tr>
<td>2</td>
<td>Asbestos exposure can cause diffuse pleural thickening</td>
<td>10</td>
<td>0</td>
<td>0.0001</td>
</tr>
<tr>
<td>3</td>
<td>Asbestos exposure can cause pleural plaques</td>
<td>10</td>
<td>0</td>
<td>0.0001</td>
</tr>
<tr>
<td>4*</td>
<td>... a reliable history of exposure</td>
<td>10</td>
<td>1</td>
<td>0.0001</td>
</tr>
<tr>
<td>5*</td>
<td>... an appropriate time interval between exposure and detection</td>
<td>9</td>
<td>2</td>
<td>0.0001</td>
</tr>
<tr>
<td>6†</td>
<td>... chest roentgenographic evidence of “s,” “t,” “u” small irregular opacifications of a profusion of 1/1 or greater</td>
<td>6.5</td>
<td>4</td>
<td>0.0112</td>
</tr>
<tr>
<td>7†</td>
<td>... a restrictive pattern of lung impairment with a FVC below the lower limit of normal</td>
<td>7</td>
<td>3</td>
<td>0.0474</td>
</tr>
<tr>
<td>8†</td>
<td>... a diffusing capacity below the lower limit of normal</td>
<td>7</td>
<td>3</td>
<td>0.0074</td>
</tr>
<tr>
<td>9†</td>
<td>... bilateral late or pan inspiratory crackles at the posterior lung bases not cleared by cough</td>
<td>6</td>
<td>3</td>
<td>0.0471</td>
</tr>
<tr>
<td>10</td>
<td>A history of asbestos exposure of sufficient duration, dose and latency is likely the cause of interstitial fibrosis in the absence of other explanations</td>
<td>9</td>
<td>2</td>
<td>0.0001</td>
</tr>
<tr>
<td>11</td>
<td>Asbestos exposure causes other neoplasms in addition to lung cancer and mesothelioma</td>
<td>7</td>
<td>3</td>
<td>0.0114</td>
</tr>
<tr>
<td>12</td>
<td>Identification of asbestos fibers in lung specimens is integral to the histological diagnosis of asbestos</td>
<td>8</td>
<td>4</td>
<td>0.0175</td>
</tr>
<tr>
<td>13†</td>
<td>... chest radiographic changes of profusion 1/1 small irregular opacities or greater or high-resolution CT scanning images in the prone position at lung bases indicating interstitial fibrosis are of value in detecting asbestosis.</td>
<td>8</td>
<td>3</td>
<td>0.0001</td>
</tr>
<tr>
<td>14†</td>
<td>... chest radiographic changes of a profusion level 1/0 small irregular opacities are a good screening tool, but lack specificity for an accurate diagnosis of asbestosis. HRICT scanning should be performed to increase the specificity of these chest radiographic findings.</td>
<td>7</td>
<td>4</td>
<td>0.0091</td>
</tr>
<tr>
<td>15</td>
<td>In an asbestos-exposed worker without asbestosis and with lung cancer, the recognition of asbestosis among coworkers with similar exposures is sufficient to attribute the worker’s lung cancer to asbestos exposure</td>
<td>8</td>
<td>1</td>
<td>0.0037</td>
</tr>
<tr>
<td>16</td>
<td>Compared to the chest radiograph, an HRICT scan is a more sensitive method for detecting asbestos-related pleural and parenchymal disease</td>
<td>9</td>
<td>2</td>
<td>0.0001</td>
</tr>
<tr>
<td>17</td>
<td>Workers who have significant asbestos exposure (but who do not have asbestosis) are at increased risk of bronchogenic carcinoma</td>
<td>9</td>
<td>2</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

*Based on 1986 ATS guidelines. This statement was preceded by “In the absence of pathologic examination of lung tissue, the diagnosis of asbestosis is a judgment based on a careful consideration of all relevant clinical findings. In our opinion, it is necessary that there be.”
†This statement was preceded by “These clinical criteria are of recognized value.”
‡This statement was preceded by “With a reliable history of exposure and an appropriate time interval between exposure and detection [and in] the absence of pathologic examination of lung tissue.”
Table 3.3 Consensus 5 statements of disagreements (total 32 statements)

<table>
<thead>
<tr>
<th>Statement No.</th>
<th>Consensus Statement</th>
<th>Median</th>
<th>IQR</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Chest radiographs are a sensitive method to diagnose interstitial disease attributable to asbestos exposure</td>
<td>2</td>
<td>3</td>
<td>0.0009</td>
</tr>
<tr>
<td>2</td>
<td>Chest radiographs are a sensitive method to measure pleural abnormalities attributable to asbestos exposure</td>
<td>3</td>
<td>2</td>
<td>0.0001</td>
</tr>
<tr>
<td>3</td>
<td>Pleural plaques alter lung function to a clinically significant degree</td>
<td>2</td>
<td>3</td>
<td>0.0003</td>
</tr>
<tr>
<td>4</td>
<td>Workers with asbestos-induced pleural abnormalities are at increased risk for lung cancer compared to workers with similar exposures without those pleural abnormalities</td>
<td>1</td>
<td>2</td>
<td>0.001</td>
</tr>
<tr>
<td>5</td>
<td>Asbestos exposure (in the absence of interstitial fibrosis) leads to COPD</td>
<td>3</td>
<td>4</td>
<td>0.0001</td>
</tr>
<tr>
<td>6</td>
<td>A decline in small airway flow rates in a smoker can be attributed to asbestos exposure</td>
<td>2</td>
<td>3</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

Table 3.4 The 9 Statements without expert panel consensus (total 32 statements)

<table>
<thead>
<tr>
<th>Statement No.</th>
<th>Statement</th>
<th>Median</th>
<th>IQR</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>A heavy asbestos exposure (sufficient to cause asbestosis) with sufficient latency is necessary to establish asbestos exposure as causative for lung cancer (clarified from round 1)</td>
<td>2.5</td>
<td>7</td>
<td>0.0594</td>
</tr>
<tr>
<td>2</td>
<td>The extent of asbestos exposure correlates with the presence and extent of pleural abnormalities</td>
<td>6</td>
<td>4</td>
<td>0.325</td>
</tr>
<tr>
<td>3</td>
<td>A reasonable scheme can be developed to apportion the individual attributability of smoking and exposure in a cigarette smoking asbestos-exposed worker with lung cancer</td>
<td>5</td>
<td>5</td>
<td>0.5907</td>
</tr>
<tr>
<td>4</td>
<td>A decline in small airway flow rates in a nonsmoker can be attributed to asbestos exposure</td>
<td>6</td>
<td>6.5</td>
<td>0.7637</td>
</tr>
<tr>
<td>5</td>
<td>BAL is a technique for accurately establishing lung fiber burden</td>
<td>5</td>
<td>4</td>
<td>0.252</td>
</tr>
<tr>
<td>6</td>
<td>CT scanning of the chest should be used to screen populations at risk for asbestos-related diseases</td>
<td>5</td>
<td>3</td>
<td>0.2445</td>
</tr>
<tr>
<td>7</td>
<td>There should be initiatives to develop protocols to attempt therapy for asbestosis</td>
<td>5</td>
<td>5</td>
<td>0.0206</td>
</tr>
<tr>
<td>8</td>
<td>Nonsmoking workers with significant asbestos exposure (without asbestosis) have at least double the risk of bronchogenic carcinoma compared to nonsmoking workers with low-level exposure</td>
<td>7.5</td>
<td>4</td>
<td>0.0600</td>
</tr>
<tr>
<td>9</td>
<td>Workers who smoke cigarettes and have significant asbestos exposure (without asbestosis) have at least double the risk of bronchogenic carcinoma compared to nonexposed smokers</td>
<td>9</td>
<td>5</td>
<td>0.0031</td>
</tr>
</tbody>
</table>

iv) European Commission: Information notices on occupational diseases: a guide to diagnosis

Asbestosis

Bilateral, diffuse, interstitial pulmonary fibrosis caused by exposure to asbestos. Asbestosis is similar to many other fibroses and the diagnostic criteria below must be used with a history suggestive of asbestos exposure.

Diagnostic criteria:

There are no specific anatomo-pathological criteria for the diagnosis of asbestosis. The following criteria, together with a history of asbestos exposure, suggest the diagnosis of asbestosis and provide a basis for assessing its severity:
• Symptoms and signs: breathlessness; persistent bilateral late inspiratory basal crepitations; clubbing
• Chest X-ray: diffuse interstitial opacities (usually reticular or reticulonodular), mainly in the lower lung fields
• Computerized tomography: diffuse interstitial opacities mainly in the lower lung fields
• Lung function tests: restriction, reduction in gas transfer, decrease of the flow rates at low volume (flow-volume curve).

These features do not necessarily appear simultaneously, and the order in which they occur may differ from one subject to another. At present in industrialized countries, most cases of asbestosis show up only on radiological examinations without progression to respiratory insufficiency. Early disease that is only visible on CT scanning requires expert radiological assessment.

Exposure criteria:

Minimum intensity of exposure: confirmed occupational exposure, assessed by history and study of working conditions, providing evidence of prolonged and repeated heavy exposure to asbestos, and by (where feasible):

• Estimation of a cumulative exposure index from exposure times, type of occupational activity and concentrations in the air which might have been measured at the place of work. There is evidence that the risk of developing asbestosis at cumulative exposures of <25 fiber-year is low.

Note:

fiber-year is a unit of measurement equivalent to level of exposure in f/cc multiplied by the length of time of exposure in years or fraction therefore 25 fiber-years could be 25 f/cc x 1 yr or 2.5 f/cc x 10 years or 1 f/cc x 25 years.

• significant concentrations of asbestos bodies or fibres in the sputum, fluid from bronchoalveolar lavage or lung parenchyma.

Minimum duration of exposure: 5 years. This may be shorter in the event of heavy exposure.

Maximum Latent Period: not applicable

Minimum induction period: 5 years

Thickenings of parietal pleura

These are localized, usually focal, bilateral hyaline thickenings (fibrosis) of the parietal pleura; they are sometimes (partially) calcified. Their presence does not imply the existence of other asbestos related diseases. On their own they do not usually cause symptoms or deficits in lung function.
Exposure criteria:

Minimum intensity of exposure: confirmed occupational exposure, assessed by history and study of working conditions providing evidence of exposure to asbestos. This exposure may be confirmed by the presence of asbestos bodies or fibres in biological samples (sputum, fluid from bronchoalveolar lavage or lung biopsy).

Minimum duration of exposure: unknown

Maximum latent period: not applicable.

Minimum induction period: usually more than 10 years. The onset of pleural plaques is related to the time since first exposure.

Other benign lung diseases

Asbestos pleural effusions: Diffuse exudative pleural reaction, with or without symptoms and often recurrent.

Diffuse pleural thickening: Diffuse thickening mainly of the visceral pleura, accompanied by parenchymal strips or atelectasis caused by twisting or deterioration of the bottom of the psilateral pleural sac. It often follows asbestos pleurisy. It may be accompanied by a restrictive syndrome or a decline in total lung capacity.

Rounded atelectasis: Twisting of a segment of lung parenchyma in contact with an area of visceral pleural fibrosis.

Exposure criteria:

Minimum intensity of exposure: confirmed occupational exposure, if possible assessed by history and study of working conditions providing evidence of prolonged or repeated exposure to asbestos

Minimum duration of exposure: unknown

Maximum latent period: not applicable.

Minimum induction period: usually more than 10 years. With high exposures it may be less.

v) The Helsinki criteria

The ‘Helsinki criteria’ was the name of the document resulting from the international expert meeting on asbestos, asbestosis, and cancer convened in Helsinki on 20-22 January 1997. The expert panel has discussed on the disorders of the lung and pleura in relation to asbestos and agreed upon state of the art criteria for their diagnosis and attribution with respect to asbestos. The meeting was attended by 19 participants from 8 countries not producing asbestos. The chairmen were Professor Douglas W Henderson (Flinders Medical Centre, Australia) and Professor Jorma Rantanen (Finnish Institute of Occupational Health, Finland). The group was a multidisciplinary gathering of pathologists, radiologists, occupational and
pulmonary physicians, epidemiologists, toxicologists, industrial hygienists, and clinical and laboratory scientists specializing in tissue fiber analysis. Collectively, the group has published over 1000 articles on asbestos and associated disorders.

Some interesting point regarding asbestos fibers in lung tissues in ‘Helsinki criteria’ was that a histological diagnosis of asbestosis requires the identification of diffuse interstitial fibrosis in well inflated lung tissue remote from a lung cancer or other mass lesion, plus the presence of either 2 or more asbestos bodies in tissue with a section area of 1 cm$^2$ or a count of uncoated asbestos fibers that falls into the range recorded for asbestosis by the same laboratory. The meeting was scientifically supported by leading institutions in the field of asbestos research, and it was funded by the Ministry of Social Affairs and Health and the Finnish Work Environment Fund.

**vi) ICOH Scientific Committee for Respiratory Disorders on Secondary prevention: early diagnosis and treatment**

*Non-malignant asbestos-related diseases*

The early diagnosis of asbestos-related disease requires knowledge of the presenting disease signs, recording of complete occupational histories, knowledge of the relevant occupations and their related exposures and hazards, and of the pathophysiology of asbestos in the body. The recognition of the role of asbestos in causing disease is important for early diagnosis and disease surveillance. When populations are being studied, the relative contribution of a specific cause or risk factor is called “attribution”. In individual cases, where the most likely cause is determined for the exposed worker the process and is called “apportionment”.

The ICOH Scientific Committee on Respiratory Disorders recognizes the basic elements of the revised set of guidelines for evaluation of individual patients developed by the American Thoracic Society in 2004, namely:

- Evidence of structural lesion consistent with asbestos-related disease,
- Evidence of causation by asbestos, and
- Exclusion of alternative diagnoses

Evidence of structural lesions can be demonstrated by imaging and histology. The International Labour Organisation’s (ILO) International Classification of Radiographs of Pneumoconiosis is the recommended radiographic diagnostic tool. The International Classification of HRCT for Occupational and Environmental Respiratory Disease (ICOERD) should be added, particularly when the diagnosis is uncertain. When appropriate and feasible, and when the risk to the worker is
acceptable, tissue or bronchoalveolar lavage may be obtained for histologic and cytologic studies, respectively.

Evidence of plausible causation by asbestos should be based on demonstrating one or more of the following: an appropriate occupational or environmental asbestos exposure history with a plausible latency time, markers of exposure (pleural plaques), or recovery of asbestos bodies or fibres from appropriate tissue or fluid samples.

Exclusion of alternative diagnoses: Other causes of pleural changes or fibrotic lung disease should be carefully investigated and reasonably excluded.

Notes: Regarding ICOH scientific committee for respiratory disorders, non-malignant asbestos-related diseases include asbestosis, pleural thickening and calcification, benign pleural effusions, and rounded atelectasis.

3.2 Diagnostic criteria and treatment of malignant asbestos-related diseases

3.2.1 Malignant pleural mesothelioma (MPM)

This article has collected several clinical guidelines for MPM diagnosis and treatment available in MEDLINE as follows:

i) The European Society for Medical Oncology (ESMO) guideline

Incidence

MPM is considered a rare tumour by ESMO of the incidence of 1.25/100,000 in Great Britain and of 1.1/100,000 in Germany. However, the incidence is estimated to double in many countries within the next 20 years. Exposure to asbestos is a well-established etiological factor for MPM, with occupational exposure being documented in 70%–80% of those affected.

Diagnosis

Patients typically present with shortness of breath due to pleural effusion or chest pain in a more advanced stage. The diagnosis is usually suggested by imaging studies (unilateral pleural thickening; pleural effusion). An occupational history must be obtained. Cytological examination of the effusion can be diagnostic, but often shows equivocal results. Therefore, histology, including immunohistochemistry, is the gold standard. Pleuroscopy, a video-assisted surgical procedure or open pleural biopsy in a fused pleural space may be necessary to provide sufficient material for accurate histological diagnosis.
There are three main histological types (epithelial, sarcomatous and mixed) with 60% being epithelial. Data suggest the possible contribution of serum mesothelin-related proteins and osteopontin as useful markers to support the diagnosis of mesothelioma; however, the precise role of these markers is yet to be defined.

**Staging**

Clinical staging is based on the CT scan of the chest. However, the translation of the images into TNM stages is often not conclusive. Mediastinoscopy and video-assisted thoracoscopy may be useful in determining the stage. Accurate initial staging is essential to provide both prognostic information and guidance on the most appropriate therapeutic options. Several different staging systems exist, among them the International Mesothelioma Interest Group (IMIG) staging system for MPM which emphasizes the extent of disease post-surgery in a traditional TNM system and stratifies patients into prognostic categories similar to those shown in Table 3.5.

The European Organization for Research and Treatment of Cancer prognostic scores may be used. They include performance status, gender, and certainty of histology, histological type and white blood count.

MPM rarely metastasizes to distant sites but most patients present with locally advanced disease. The use of PET scan to rule out extra-thoracic metastasis in patients considered for radical treatment is under investigation and findings seem promising.
Table 3.5 TNM staging system for MPM

<table>
<thead>
<tr>
<th>Stage</th>
<th>TNM</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ia</td>
<td>T1a N0 M0</td>
<td>Primary tumour limited to ipsilateral parietal pleura</td>
</tr>
<tr>
<td>Ib</td>
<td>T1b N0 M0</td>
<td>As stage Ia plus focal involvement of visceral pleura</td>
</tr>
<tr>
<td>II</td>
<td>T2 N0 M0</td>
<td>As stage Ia or Ib plus confluent involvement of diaphragm or visceral pleura or involvement of the lung</td>
</tr>
<tr>
<td>III</td>
<td>Any T3 M0</td>
<td>Locally advanced tumour</td>
</tr>
<tr>
<td></td>
<td>Any N1 M0</td>
<td>Ipsilateral, bronchopulmonary or hilar lymph node involvement</td>
</tr>
<tr>
<td></td>
<td>Any N2 M0</td>
<td>Subcarinal or ipsilateral mediastinal lymph node involvement</td>
</tr>
<tr>
<td>IV</td>
<td>Any T4</td>
<td>Locally advanced technically unresectable tumour</td>
</tr>
<tr>
<td></td>
<td>Any N3</td>
<td>Contralateral mediastinal, internal mammary, and ipsilateral or contralateral supraclavicular lymph node involvement</td>
</tr>
<tr>
<td></td>
<td>Any M1</td>
<td>Distant metastases</td>
</tr>
</tbody>
</table>

**Primary Tumour (T)**

T1

T1a  Tumour limited to the ipsilateral parietal pleura, including mediastinal and diaphragmatic pleura; no involvement of the visceral pleura

T1b  Tumour involving the ipsilateral parietal pleura, including mediastinal and diaphragmatic pleura; scattered foci of tumour also involving the visceral pleura
T2  Tumour involving each of the ipsilateral pleural surfaces (parietal, mediastinal, diaphragmatic, and visceral pleura) with at least 1 of the following features:
- Involvement of diaphragmatic muscle
- Confluent visceral pleural tumour (including the fissures) or extension of tumour from visceral pleura into the underlying pulmonary parenchyma

T3* Tumour involving all of the ipsilateral pleural surfaces (parietal, mediastinal, diaphragmatic, and visceral pleura) with at least 1 of the following features:
- Involvement of the endothoracic fascia
- Extension into the mediastinal fat
- Solitary, completely resectable focus of tumour extending into the soft tissues of the chest wall
- Nontransmural involvement of the pericardium

* T3 describes locally advanced but potentially resectable tumour.

T4† Tumour involving all of the ipsilateral pleural surfaces (parietal, mediastinal, diaphragmatic, and visceral pleura) with at least 1 of the following features:
- Diffuse extension or multifocal masses of tumour in the chest wall with or without associated rib destruction
- Direct transdiaphragmatic extension of tumour to the peritoneum
- Direct extension of tumour to the contralateral pleura
- Direct extension of tumour to 1 or more mediastinal organs
- Direct extension of tumour into the spine
- Tumour extending through to the internal surface of the pericardium with or without a pericardial effusion; or tumour involving the myocardium

† T4 describes locally advanced technically unresectable tumour.

**Regional Lymph Nodes (N)**
NX  Regional lymph nodes cannot be assessed
N0  No regional lymph node metastasis
N1  Metastasis in the ipsilateral bronchopulmonary or hilar lymph nodes
N2  Metastasis in the subcarinal or the ipsilateral mediastinal lymph nodes, including the ipsilateral internal mammary nodes
N3  Metastasis in the contralateral mediastinal, contralateral internal mammary, ipsilateral or contralateral supraclavicular lymph nodes
Distant Metastasis (M)
MX  Distant metastasis cannot be assessed
M0  No distant metastasis
M1  Distant metastasis present

Treatment
Note: Levels of Evidence [I–V] and Grades of Recommendation [A–D] as used by the American Society of Clinical Oncology are given in square brackets. Statements without grading were considered justified standard clinical practice by the expert authors and the ESMO faculty.

Levels of Evidence
Level I evidence is reserved for meta-analyses of randomized controlled trials or randomized trials with high power.
Level II evidence includes randomized trials with lower power.
Level III evidence includes nonrandomized trials, such as cohort or case-controlled series.
Level IV evidence includes descriptive and case studies.
Level V evidence includes case reports and clinical examples.

Grading of evidence
Grade A is reserved for Level I evidence or consistent findings from multiples studies of Level II, III, or IV evidence.
Grade B is for Level II, III, or IV evidence with generally consistent findings.
Grade C is similar to grade B but with inconsistencies.
Grade D implies little or no evidence.

Surgery: Various surgical procedures have been studied with varying degrees of success.
Extra-pleural pneumonectomy (EPP) with resection of the hemi-diaphragm and the pericardium en bloc has the potential for a radical treatment and this approach is generally combined with neoadjuvant or adjuvant chemotherapy and/or adjuvant radiotherapy.
Surgery, the appropriateness of which is still under consideration, should only be performed on selected patients by experienced thoracic surgeons in the context of a multidisciplinary team and preferably as part of a clinical trial [III, A].

Selection criteria include good performance status, and earlier stage disease with not more than localized involvement of the thoracic wall, and adequate cardiopulmonary function. The inclusion of patients with N2 or sarcomatoid disease is controversial. Pleurectomy/decortication may be indicated for elderly patients, at early stages or when EPP would leave macroscopic tumour behind.

To optimally palliate patients from dyspnea and pain, local procedures to control pleural effusion include parietal pleurectomy or talc pleurodesis.

Radiotherapy: The use of curative intent hemithoracic radiotherapy has been limited because of the difficulty of irradiating such a large target volume to high doses without exceeding the tolerance of the adjacent normal tissues, especially the (homolateral) lung. The exact role of definitive radiotherapy in the multimodality approach of MPM is currently under investigation. Nevertheless, in an attempt to improve local control after extra-pleural pneumonectomy, it has been shown feasible to deliver radiotherapy doses of >45 Gy with both 3D conformal (3D-CRT) and intensity-modulated radiotherapy (IMRT). However, caution must be exercised regarding the exposure of the contralateral lung to low-dose irradiation, especially when using IMRT [III, B].

In the palliative setting, radiotherapy can be delivered locally in view of pain control or prevention of obstructive symptoms [IV, C]. As MPM invades the tracts made by chest instrumentation, prophylactic irradiation to the intervention tracts (PIT) has been advocated to reduce the incidence of port metastases. In the absence of unambiguous prospective data, the consequence of randomized trials with small patient numbers, different results according to histology and highly variable RT techniques—however, it remains impossible to draw definitive conclusions regarding its efficacy [II, C].

Chemotherapy: Platinum analogues, doxorubicin and some antimetabolites (methotrexate, raltitrexed, pemetrexed) have shown modest single-agent activity [III, B].

The combinations of both pemetrexed/cisplatin, and to a smaller extent raltitrexed/cisplatin, have been shown to improve survival as well as lung function and symptom control in comparison with cisplatin alone in randomized trials [II, A]. The combination of pemetrexed/carboplatin is an alternative effective therapy [III, A].

A phase III trial evaluated second-line pemetrexed versus best supportive care in patients not previously exposed to this agent and found a longer time to disease
progression in the chemotherapy arm. Since vinorelbine or gemcitabine have first-line activity they might be a reasonable choice in second-line therapy. One study on 63 patients treated with vinorelbine reported a 16% response rate and median survival of 9.6 months [III, A].

If extrapleural pneumonectomy is planned, platinum-based neoadjuvant or adjuvant combination chemotherapy should be considered. Response evaluation using CT scan is recommended after two to three chemotherapy cycles and the modified RECIST criteria should be applied. Volumetric measurements are under investigation.

Follow-up

Follow-up consists of clinical evaluation, with particular attention to symptoms or chest wall recurrence, and chest CT as needed.

ii) British Thoracic Society - BTS 20

Diagnostic strategy

It is essential to use the combination of history, examination, radiology and pathology to reach a diagnosis of malignant mesothelioma. All the above elements are needed, and the overall strategy for diagnosis in a case of suspected mesothelioma is therefore to ensure that the patient has the relevant investigations rapidly and efficiently.

In a clear-cut case it is possible to inform a patient of the diagnosis immediately when a biopsy result is available, but in many cases it is usually wiser to defer this until the case has been discussed in detail at the local multidisciplinary team meeting and a diagnosis agreed. This also enables a preliminary view about management strategy to be given.

History

The history of asbestos exposure is very important but is often not recalled by the patient at presentation. An occupation may strongly suggest that exposure has occurred, although it is important to recognize less obvious occupations such as teacher, decorator and assembly worker. The possibility of neighborhood or para-occupational exposure needs to be considered. Further history at other stages of the patient’s pathway is often much more informative after the patient has been able to think over his or her employment history. It has to be borne in mind that many patients will be attempting to recall working conditions up to 50 years earlier.

Physical examination
Physical examination does not usually aid the differential diagnosis. Occasionally tumour tissue may be felt between the ribs.

**Investigations**

Plain chest radiographic abnormalities may strongly suggest a malignant process.

The key investigations subsequently are a pleural tap if an effusion is present and a contrast-enhanced CT scan, together with an appropriate biopsy procedure (see later sections). A pleural tap can be performed in the outpatient clinic and the fluid should be sent for cytology and immunocytochemistry on a cell block. The risk of seeding from a pleural tap site is thought to be low, but the site of a puncture should be recorded.

If the clinical, radiological and cytological results subsequently support a diagnosis of mesothelioma, then this can be accepted. However, although immunocytochemistry can reliably show that cells are mesothelial in origin, it may be difficult to distinguish malignant from highly reactive cells.

A biopsy is recommended if there is doubt about the diagnosis on radiological or clinical grounds as cytology may be unreliable. In general medical practice it is not uncommon for a patient to have an undiagnosed pleural effusion despite a pleural tap and a CT scan. A biopsy is required if the diagnosis is not clear after the pleural tap and a CT scan. The choices of technique are an ultrasound or CT-guided percutaneous pleural biopsy, or a thoracoscopic biopsy. Blind biopsy techniques are quick to perform and inexpensive, and are thus still used in some centres. However, a recent study has shown that a blind Abrams’ punch biopsy is less effective at reaching a diagnosis for pleural thickening than a CT-guided biopsy, and the latter is therefore preferable.

A potential diagnosis of mesothelioma may not have been considered by the managing team. For this reason, institutions are recommended to have a policy of prompt referral of such cases for a respiratory opinion.

Thoracoscopy is appropriate where there is pleural fluid and the technique facilitates not only complete drainage of the fluid and biopsy, but also immediate talc pleurodesis where appearances are clearly malignant. Where there is doubt about the macroscopic appearance, pleurodesis should be deferred. Biopsies are essential even if the appearances seem to be those of normal pleura.
Figure 3.5 Diagnostic algorithm: suspected MPM
MPM = malignant plural mesothelioma; CT = computed tomogram of thorax; US = ultrasound; PET = positron emission tomography; MDT = multidisciplinary team meeting

Diagnostic imaging
(i) Imaging at presentation

There should be a clear rapid referral mechanism in place if either a chest radiograph or a CT scan suggests malignant pleural disease. A second copy of the radiologist’s report should ideally be sent electronically or by facsimile to a designated member of the lung cancer multidisciplinary team, usually the chest physician.

Ultrasound can be very useful in identifying pleural abnormalities. The presence of a pleural effusion acts as an acoustic window, enabling the detection of intrapleural and intrapulmonary processes. Pleural effusions and thickening can be readily appreciated by ultrasound and discrete malignant nodules may be seen.
Ultrasound-guided biopsy of pleural thickening and drainage of effusions are well-established safe techniques.

**(ii) Computed tomography (CT)**

Contrast-enhanced CT is the primary imaging modality used for the evaluation of suspected malignant pleural disease. Malignant or inflammatory pleural disease enhances strongly, and the contrast allows differentiation between thickened pleura, effusion and underlying aerated or collapsed lung. Multi-detector CT allows a scan of the entire chest to be performed in <10 seconds.

A scan delay of 60 seconds allows optimal visualization of pleural disease while still allowing assessment of the mediastinal nodes and liver in the portal venous phase of enhancement. A standard protocol includes the liver and adrenal glands.

CT features used to distinguish malignant from benign pleural disease were 1) circumferential pleural thickening; 2) nodular pleural thickening; 3) parietal pleural thickening >1 cm; and 4) mediastinal pleural involvement. Coincidental pleural plaques are found on the CT scan in approximately 20% of patients with malignant mesothelioma and there may be other features of asbestos exposure.

The specificities of these findings were 100%, 94%, 94% and 88% respectively. The sensitivities were 41%, 51%, 36% and 56%, respectively. While the positive predictive value of these signs is high, their absence does not exclude a diagnosis of pleural malignancy and CT cannot reliably differentiate malignant mesothelioma from other malignancy.

**(iii) Magnetic resonance imaging (MRI)**

MRI has a limited role in the evaluation of malignant mesothelioma. Pleural malignancy enhances avidly with use of gadolinium-based contrast material. Anatomical and morphological MRI features are similar to those seen at CT. MRI, with its ability to scan in any plane, has been used to accurately assess resectability prior to radical surgery. Multi-detector CT scanning is able to provide detailed reconstructions, thus giving MRI only a limited role in evaluating patients with questionable areas of local tumour extension at CT or in whom intravenous administration of iodinated contrast material is contraindicated.

**(iv) 18F-fluorodeoxyglucose positron emission tomography (FDG PET)**

In a limited number of patients where conventional imaging and biopsy have been either unhelpful or equivocal, FDG PET may be useful in differentiating benign from malignant pleural disease and might guide choice of biopsy site.
The study by Duysinx of 63 patients with FDG PET found a sensitivity for detecting malignancy of 96.8% and a specificity of 88.5%. False positive results may be seen in cases of parapneumonic effusion and both tuberculous and uraemic pleural disease. Care should be taken with patients who have previously undergone talc pleurodesis, as the inflammatory process caused by this procedure can also cause a false positive result. It is not known how long the scan remains positive after pleurodesis.

The standardized uptake value (SUV) is used as a semiquantitative measure of the metabolic activity of a lesion. The SUV is significantly higher in malignant mesothelioma than in benign pleural diseases such as inflammatory pleuritis and asbestos-related pleural plaques. However, some cases of malignant mesothelioma are low-grade tumours and may not be avid on FDG PET. SUV can be taken at any time following injection of the tracer. There is neither an accepted time at which SUV should be measured in patients with malignant mesothelioma nor a particular threshold able to differentiate between benign and malignant disease. Volume measurements can be taken using SUV, and this offers the potential for assessing disease response following either chemotherapy or other novel treatment.

(v) Imaging and staging

The TNM staging system proposed by the International Mesothelioma Interest Group (IMIG) is used for assessing patients with potentially resectable disease (Table 2.5). This staging system was designed as a surgical tool and may not be completely applicable to imaging.

CT and MRI overall have fairly similar accuracies for staging malignant mesothelioma, but both techniques may underestimate the stage of the disease. Mediastinal nodes are commonly involved by mesothelioma and, as with the staging of lung cancer; CT has limited accuracy for detecting mediastinal node involvement.

FDG PET also appears to be relatively poor at distinguishing mediastinal nodal metastases from adjacent mediastinal pleural involvement, although a high SUV seems to correlate with the presence of N2 disease. Co-registration of CT with PET images, ‘CT-PET’, may have a role in assessing these N2 disease patients but studies are limited at present. Currently, mediastinoscopy is normally performed before radical surgery to exclude patients with N2 disease.

CT-PET may have a complementary role aiming to detect occult metastatic or N3 disease.

Pathology

Pathological diagnosis may be obtained from cytology or histology. Cytological diagnosis is based either on sampling of effusion fluid or by
percutaneous fine needle aspiration cytology of a region of pleural thickening. In specialist centers the sensitivity of the former technique can be up to 76% and the latter 78%. Immunocytochemistry can be applied to the cytological material (including cell blocks), which can fairly reliably identify that the cellular content is mesothelial.

However, where there is poor clinical and radiological correlation, the pathological diagnosis should be based on tissue biopsy due to difficulties in distinguishing malignant mesothelioma cells from reactive mesothelial cells and other pleural malignancies in fluid.

Percutaneous core biopsy may provide sufficient material on which to confirm a diagnosis of malignant mesothelioma and to perform ancillary studies. This is reported to have a higher yield (86% sensitivity and 100% specificity) than closed Abrams’ or Cope needle biopsy which only offers a sensitivity of 21–43%.

Thoracoscopy has a sensitivity of over 90% with a low complication rate (10%).

**NOTE:** A percutaneous core needle biopsy is an image-guided biopsy using x-ray, computed tomography (CT), ultrasound or magnetic resonance imaging (MRI). It allows a physician to obtain a large sample of tissue and is usually performed on an outpatient basis. The standard technique for pleural biopsy uses a reverse bevel needle without image guidance, such as the Abrams’ needle and cope needle. The standard technique yields a small sample of tissue while is associated with a substantial incidence of complications, including pneumothorax, haemothorax, and empyema.

(i) **Histopathological classification**

The precise cell of origin of malignant mesothelioma is unclear, but it is now suggested that tumours arise from submesothelial cells that have the ability to differentiate along diverse lines. Numerous histopathological subtypes of diffuse malignant mesothelioma have been described (table 3.6). It is important for the pathologist to be aware of these alternative forms but the WHO classification advises that, as these various subtypes have no particular prognostic significance, tumours should be classified into one of three main types: epithelioid, sarcomatoid (with desmoplastic mesothelioma being a particularly aggressive form of the latter) and biphasic. Classification into these three main groups is important as it may alter management.
(ii) Ancillary tests

Despite the numerous publications describing the usual morphological features of mesothelioma, confirmation requires support from additional studies which may include histochemical, immunohistochemical and electron microscopic analysis.

Unfortunately, no single stain or test can unequivocally confirm or exclude a diagnosis of mesothelioma and a panel of tests is performed, particularly when trying to differentiate mesothelioma from adenocarcinoma. Epithelioid mesothelioma can mimic (and be mimicked by) several other tumours, most frequently metastatic adenocarcinoma.

The most useful differentiating histochemical stains are those for mucins (table 2.4). Two recent publications have reviewed the immunohistochemical profile of mesothelioma compared with metastatic adenocarcinoma, which most commonly spreads from the lung. These confirm that a panel of antibodies is required and the most useful are listed in table 3.7.

*NOTE* Mucins are a family of high molecular weight, heavily glycosylated proteins (glycoconjugates) produced by epithelial tissues.

<table>
<thead>
<tr>
<th>Epithelial</th>
<th>Sarcomatoid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tubulopapillary</td>
<td>Fibrosarcomatoid</td>
</tr>
<tr>
<td>Solid variant</td>
<td>Chondrosarcomatoid</td>
</tr>
<tr>
<td>Adenomatoid</td>
<td>Osteosarcomatoid</td>
</tr>
<tr>
<td>Small cell</td>
<td>Leiomyosarcomatoid</td>
</tr>
<tr>
<td>Clear cell</td>
<td>Malignant fibrous histiocyтома-like</td>
</tr>
<tr>
<td>Deciduoid</td>
<td>Lymphohistiocyтома</td>
</tr>
<tr>
<td>Adenoidystic</td>
<td>Desmoplastic</td>
</tr>
<tr>
<td>Pleomorphic</td>
<td>Biphasic (= mixed)</td>
</tr>
<tr>
<td>Mucin-positive</td>
<td>Any combination across the above</td>
</tr>
<tr>
<td></td>
<td>groups</td>
</tr>
</tbody>
</table>
Table 3.7 Histochemical and immunohistochemical methods used to differentiate mesothelioma from adenocarcinoma

<table>
<thead>
<tr>
<th>Histochemistry</th>
<th>Epithelioid mesothelioma</th>
<th>Adenocarcinoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>PAS</td>
<td>+ (glycogen)</td>
<td>+ (small amount of glycogen with mucin)</td>
</tr>
<tr>
<td>plus diastase</td>
<td>– (almost always)</td>
<td>+</td>
</tr>
<tr>
<td>A1cian blue plus hyaluronidase</td>
<td>+</td>
<td>May be +</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Usually still +</td>
</tr>
<tr>
<td>Immunohistochemistry</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Calretinin</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>CK5/6</td>
<td>+</td>
<td>–</td>
</tr>
<tr>
<td>WT-1</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>Thrombomodulin</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>HBME-1</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>N-cadherin</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>CEA</td>
<td>–</td>
<td>+</td>
</tr>
<tr>
<td>MOC-31</td>
<td>–</td>
<td>+</td>
</tr>
<tr>
<td>Ber EP4</td>
<td>–</td>
<td>+</td>
</tr>
<tr>
<td>B72.3</td>
<td>–</td>
<td>+</td>
</tr>
<tr>
<td>LeuM1 (CD15)</td>
<td>–</td>
<td>+</td>
</tr>
<tr>
<td>E-cadherin</td>
<td>–</td>
<td>+</td>
</tr>
<tr>
<td>Lewisy (BG8)</td>
<td>–</td>
<td>+</td>
</tr>
<tr>
<td>TIF-1</td>
<td>–</td>
<td>+ (lung and thyroid)</td>
</tr>
<tr>
<td>Others</td>
<td>Either</td>
<td>Or</td>
</tr>
</tbody>
</table>

Note that all may give aberrant or unexpected results occasionally and need to be assessed in combination, and also that adenocarcinomas from non-pulmonary sites may show different expression (for sensitivities and specificities see King et al.23 and Ordonez24).

Most pathologists employ a limited combination of these markers with a mixture of positive and negative results indicating the diagnosis. Immunohistochemistry is useful in differentiating between reactive and neoplastic mesothelial proliferations, particularly in cytological preparations or superficial biopsies. The usual markers, however, are of much less value when trying to confirm the diagnosis of sarcomatoid malignant mesothelioma, where the sensitivity and specificity is much lower.

Immunohistochemistry is useful in differentiating mesothelioma from tumours other than adenocarcinoma (whether primary or metastatic). Table 3.8 lists most of the important differential diagnoses of diffuse malignant mesothelioma with antibodies that may aid diagnosis. EMA is more likely to be positive in a neoplastic process, with more extensive p53 expression, while desmin decorates reactive mesothelial cells preferentially.
Electron microscopy can play a role in the diagnosis by demonstrating the long slender microvilli of mesothelioma that contrast with the broader, blunt microvilli of adenocarcinoma.

Table 3.8 Differential diagnosis of diffuse malignant mesothelioma

<table>
<thead>
<tr>
<th>Differential diagnosis</th>
<th>Immunohistochemistry that may help</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary pleural tumours</td>
<td>CD34, CD31, FVIIIA</td>
</tr>
<tr>
<td>Angiosarcoma</td>
<td>CD34, CD31, FVIIIRA</td>
</tr>
<tr>
<td>Epithelioid haemangioendothelioma</td>
<td>Cytokeratins, CD99, bcl-2, cytogenetics</td>
</tr>
<tr>
<td>Synovial sarcoma</td>
<td></td>
</tr>
<tr>
<td>Sarcomas (various)</td>
<td>Various depending on type</td>
</tr>
<tr>
<td>Localised malignant mesothelioma</td>
<td>None</td>
</tr>
<tr>
<td>Solitary fibrous tumour</td>
<td>CD34, bcl-2, CD99</td>
</tr>
<tr>
<td>Well-differentiated papillary mesothelioma</td>
<td>None (needs macroscopic appearance and usually peritoneum)</td>
</tr>
<tr>
<td>Adenomatoid tumour</td>
<td>None (needs macroscopic appearance)</td>
</tr>
<tr>
<td>Califying tumour of the pleura</td>
<td>Cytokeratins, desmin, EMA, WT-1, NSE</td>
</tr>
<tr>
<td>Desmoplastic small round cell tumour</td>
<td></td>
</tr>
<tr>
<td>Thymic tumours</td>
<td>Cytokeratins, EMA, occasionally CD5</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>Lymphoid markers</td>
</tr>
<tr>
<td>Metastatic tumours</td>
<td></td>
</tr>
<tr>
<td>Carcinomas</td>
<td>Cytokeratins</td>
</tr>
<tr>
<td>Sarcomas</td>
<td>Various depending on type</td>
</tr>
<tr>
<td>Lymphomas</td>
<td>Lymphoid markers</td>
</tr>
<tr>
<td>Malignant melanoma</td>
<td>S-100, HMB45, melan-A</td>
</tr>
<tr>
<td>Thymic tumours</td>
<td>Cytokeratins, EMA, occasionally CD5</td>
</tr>
<tr>
<td>Non-neoplastic mimics</td>
<td>Rarely cytokeratins</td>
</tr>
<tr>
<td>Pleural fibrosis</td>
<td>Desmin, EMA, p53</td>
</tr>
<tr>
<td>Reactive mesothelial cells</td>
<td></td>
</tr>
</tbody>
</table>

Management

1. General management

Patients with mesothelioma should be discussed by a lung cancer and mesothelioma multidisciplinary team, be under the care of a specialist (usually a respiratory physician) and have a specialist nurse allocated to them. The multidisciplinary team should include core professionals as defined in the National Institute for Health and Clinical Excellence (NICE) guidelines and Department of Health Framework document. Where there is diagnostic difficulty or a possibility of radical treatment, the patient should be discussed at a specialist multidisciplinary team meeting.

The specialist nurse (usually a lung cancer or mesothelioma specialist nurse) should facilitate the pathway of care for the patient and the family throughout the illness, ensure good liaison between hospital services and primary care, and ensure
access to specialist palliative care services as required. Patients should be advised who to contact in case of need. Further details are provided in a later section. The diagnosis should be communicated skillfully and sympathetically. A clear picture of the disease and what to expect, including a realistic prognosis, should be given to the patient and, if appropriate, to families and carers. It is important to avoid a nihilistic approach. A copy record of the consultation could be offered to the patient. Immediate communication with the general practitioner should include the known extent of the disease, what was said to the patient and the management plan.

Ongoing follow-up by a member of the multidisciplinary team (usually the respiratory physician) is recommended, even if there is no change in treatment, as it provides an opportunity for further discussion including issues of compensation and benefits, symptom control and provision of support. There should be continuing close liaison with the general practitioner and primary health care team. The patient should have access to a specialist nurse, usually the nominated key worker.

The relatives or carers and the general practitioner should be warned, at an appropriate stage, that a Coroner’s post mortem examination will nearly always be required after the death of a patient with mesothelioma, and all deaths have to be reported to the Coroner (in Scotland the Procurator Fiscal).

2. Surgery

The role of surgical resection in malignant mesothelioma is very uncertain. Two approaches can be taken. The more radical is extrapleural pneumonectomy (EPP) (sometimes referred to as pleuropneumonectomy). The less radical approach is a debulking operation (sometimes known as cytoreductive surgery), which is either performed at open thoracotomy or by video-assisted thoracic surgery (VATS). Both are being tested in randomized controlled trials (see below). Radical treatment should only be considered for patients with epithelioid tumours (although the Mesothelioma and Radical Surgery (MARS) trial has not made this distinction owing to unreliability of sampling techniques).

Extrapleural pneumonectomy (EPP)

This procedure was first described in the 1970s and its aim is to eradicate all macroscopic disease, ideally with good clearance margins. The nature, extent, pattern of growth and proximity to major organs makes mesothelioma impossible to eradicate completely without resection of all the parietal and visceral pleura, the underlying lung, the diaphragm and the pericardium. Even then there are
often doubts about resection margins. Operative mortality is 4–9%, but significant complications from EPP occur in over 60% of patients.

A median survival of 19 months following this radical operation with adjuvant chemotherapy and radiotherapy has been reported in the largest series, but this is based on highly selected patients reported with no indication of the denominator from which they were drawn and no control or comparative group. There have been further series reporting “improved” outcomes following EPP with multi-modality therapy, but again with no control group.

The absence of randomized controlled trials on the role of EPP for mesothelioma led a recent systematic review of surgical management to conclude that the role of EPP could not be defined. Currently, the MARS trial is recruiting in the British Isles in its pilot phase. This is a randomized study comparing EPP against no EPP surgery within the context of trimodality therapy (neoadjuvant chemotherapy and postoperative radical hemithoracic radiotherapy). The aim is to randomize 50 patients to determine the feasibility and acceptability of performing an adequately powered randomized trial. The primary outcomes of the main trial will be survival and quality of life. Patients being considered for EPP should be treated within the context of the MARS trial.

With potentially high mortality and morbidity, patients must undergo rigorous preoperative assessment before being considered for EPP. Fitness for surgery should be assessed according to standard BTS guidelines for pneumonectomy in lung cancer and should also include preoperative echocardiography to assess pulmonary artery systolic pressure.

Preoperative staging with a CT scan, PET scan and mediastinoscopy are important to assess resectability (T1–3, N0–1, and M0). Together with positive resection margins and non-epithelioid subtypes, involvement of mediastinal lymph nodes has been shown to be a negative predictor of survival following EPP. A PET scan, particularly integrated CT-PET imaging, identifies distant metastasis but is less good at identifying positive N2 lymph nodes owing to the proximity of the mediastinal pleura. Accurate staging of the mediastinum by mediastinoscopy is therefore required in the MARS trial in all patients for whom randomisation is being considered for possible EPP.

As most patients who present are usually already in advanced stages of the disease, only a minority may be eligible for EPP. Of these, it is likely that only a few will benefit from radical treatment with or without EPP. Until there is clear evidence for EPP, it cannot be recommended as the treatment of choice.
**Debulking/cytoreductive surgery**

This less radical approach, which can be performed by VATS or thoracotomy, involves removal of as much of the tumour burden as possible without removing the underlying lung, diaphragm or pericardium. Where the underlying lung is trapped by the diseased pleura, re-expansion of the lung may be possible following decortication, thereby offering symptom control with less morbidity. VATS pleurectomy/cytoreductive surgery has been reported to be effective in preventing fluid recurrence and may also be associated with increased survival although, like EPP, it has not yet been tested in a randomised trial.

MesoVATS is an ongoing randomized study in the UK comparing VATS cytoreductive surgery against bedside talc pleurodesis in patients with a pleural effusion secondary to proven or suspected mesothelioma. Survival and quality of life re-outcome measures, as well as clinical and cost effectiveness.

Patients who present with a pleural effusion and have been deemed ineligible for the MARS trial should be considered for the MesoVATS trial. Patients referred for radical surgery should be aware that it is likely to be either preceded or followed by chemotherapy and followed by hemithorax radiotherapy (“trimodality therapy”). Patients should be given realistic information about the perioperative risks and the chances of long-term survival.

3. **Management of pleural effusion**

One of the central aims in the management of patients with symptomatic pleural effusions caused by mesothelioma is to achieve an early and successful pleurodesis. This helps symptom control and a trapped lung is less likely to occur if the procedure is performed promptly. Given the low diagnostic yield of bedside procedures, early thoracoscopy also gives an opportunity to obtain a definitive histological diagnosis.

Thoracoscopy is an extremely useful technique in the evaluation and management of undiagnosed exudative pleural effusions. As well as providing a high diagnostic yield, it allows complete drainage of the pleural space followed by talc poudrage. Thoracoscopy can be performed under conscious sedation (usual for medical thoracoscopy) or under general anesthesia (VATS). Complications are uncommon but include pleural space infection and surgical emphysema.

If the patient is either too frail to undergo thoracoscopy or a firm diagnosis has already been made, talc slurry pleurodesis may be performed via an intercostal drain. Occasionally, simple repeated pleural aspirations without pleurodesis may be
appropriate for very frail patients with advanced disease. Small-bore indwelling catheters and drainage systems are an alternative in these circumstances.

Chemical pleurodesis should be performed via a small bore (16–18F) that should be flushed regularly with normal saline to maintain its patency. Lignocaine (3 mg/kg; maximum 250 mg) should be administered intrapleurally just before sclerosant administration. In addition, premedication should be considered to alleviate anxiety and pain associated with pleurodesis. Satisfactory apposition of the parietal and visceral pleura should be confirmed radiographically. There are no data to suggest that suction improves the success rate, or that frequently changing the position of the patient improves either dispersion of the sclerosant or the success of pleurodesis.

Currently the most effective freely available pleurodesis agent is sterile talc. The dose of the talc should not exceed 4 g, and it should be calibrated to avoid the rare risk of the development of adult respiratory distress syndrome. The intercostal tube should be clamped for 1 h after sclerosant administration and, in the absence of excessive fluid drainage (250 ml/day), removed 24–48 h later. Recent data showed no difference in success rates between talc poundage and talc slurry.

Pleuroperitoneal shunts have been used where pleurodesis has failed and for trapped lung. However, there is a high complication rate, including shunt occlusion and infection. Their use is therefore diminishing.

Unfortunately, a minority of patients will have a trapped lung at presentation or develop the problem during the course of their disease. If asymptomatic, partial entrapment and little fluid production then no action are required. However, if there are symptoms due to rapid re-accumulation of pleural fluid, an indwelling pleural catheter may be inserted. Catheters may be inserted as day case procedures and, with nursing support, allow patients and their carers to drain their effusions at home. They have been shown to significantly improve the quality of life and, with regular drainage, up to 45% of effusions undergo spontaneous pleurodesis. Complications are rare but include pleural infection.

None of the available techniques designed to control pleural effusion in malignant mesothelioma is universally successful. Patients and their carers should therefore be made aware of the risk of re-accumulation of pleural fluid and the methods of accessing the secondary care team—for example, via the cancer nurse specialist.

4. **Radiotherapy**

Radical radiotherapy as a single modality irradiation of the pleura is limited by its toxicity to the lung and adjacent organs, particularly the bowel and stomach.
(for left-sided lesions). A retrospective review of 123 patients treated with hemithoracic radiation after surgical debulking of tumour (pleurectomy/decortication) showed actuarial local control at 1 year of 42% and median survival of 13.5 months. The lung is sensitive even to small (palliative) doses of radiation and, in the same study; severe pulmonary toxicity was found in 10% with 1.5% treatment-related mortality at 1 month. Hemithoracic irradiation with the lung in situ is therefore not indicated for mesothelioma.

**Palliative radiotherapy**

Retrospective and uncontrolled series suggest that radiotherapy can help relieve pain from mesothelioma in around half of patients treated. Although there are no controlled trials evaluating the effect of field size on pain relief, retrospective studies suggest that palliation of pain can be achieved by treating relatively small volumes of symptomatic disease and using short schedules (1–5 fractions) of radiotherapy. Such schedules have been shown to be effective and well tolerated in palliating pain from both thoracic and non-thoracic malignancy. Large-volume radiotherapy has been used, but its effect is usually short-lived and the need to treat bulky disease (necessitating long treatment times) limits its usefulness. Patients with symptoms from mediastinal infiltration such as superior vena caval obstruction have a poor response to radiotherapy and generally have a short survival. Other means of palliation are more appropriate.

**Radiotherapy as an adjunct to surgery**

When extrapleural pneumonectomy is performed, radical radiotherapy is viewed as an integral part of management and can result in local control in 60–90% of patients, albeit with significant (though acceptable) morbidity. Radiotherapy can be delivered with conventional techniques or with the aid of sophisticated planning and treatment hardware and software known as intensity modulated radiotherapy (IMRT). Preliminary evidence suggests that this technique does result in improved local control over more traditional ways of delivering radiotherapy. However, no improvement in overall survival has yet been observed as most patients develop progressive disease outside the hemithorax.

**Prophylactic radiotherapy**

There is a risk of seeding of malignant cells in the scar produced by biopsy and/or pleural drainage, resulting in an uncomfortable subcutaneous tumour (although ulceration is rarely a problem). A randomized trial has shown that the risk of this happening can be reduced from 40% to 0% by the administration of three
fractions of radiotherapy to scars. Observational studies and first principles suggest that such treatment should be given promptly (i.e., as soon as the wound has healed).

However, a recent randomized trial showed that the use of a single dose of radiotherapy was ineffective for prophylaxis, with recurrences occurring in 10% of sites not given radiotherapy compared with 7% of sites irradiated. However, this study did show a trend for a lower prevalence of seeding with less invasive procedures. The overall rates of drain site disease were 22% for Abrams’ needles, 9% for thoracic drains and 4% for fine needle aspirates. Similarly, a randomized study of 61 patients given three fractions of radiotherapy showed no difference in the prevalence of wound seeding at 1 year with 23% of treated patients and 10% of controls developing scar-related nodules.

The current recommendation is that patients of good performance status (and therefore longer survival) who have chest wall wounds should be referred for radiotherapy promptly and treated with a three-fraction schedule. If the patient is of poor performance status and/or has had a minimally invasive procedure, radiotherapy may be unnecessary. Tumour seeding can also occur in the abdominal wall after paracentesis for secondary thoracic malignant mesothelioma or primary peritoneal mesothelioma; however, the potential need for either

5. **Chemotherapy**

In general, palliative chemotherapy should be considered for all patients with performance status 0–2. The objective response rate that should be expected is of the order of 20–40%, and two randomized controlled trials have shown significant differences in survival between regimens, implying that chemotherapy may extend the life expectancy of some patients with mesothelioma. This benefit is not dependent on age, stage or histology.

However, there is no randomized trial evidence showing that chemotherapy confers better quality of life and survival than supportive care without chemotherapy. These questions continue to be addressed by the BTS study MSO-1 which compares two alternative chemotherapy regimens (single agent vinorelbine and the combination of mitomycin, vinblastine and cisplatin) with active symptom control alone. This trial closed to recruitment with 409 patients randomised and the results are expected by late 2007.

A number of phase II studies of various chemotherapy regimens have demonstrated both objective response rates comparable to those seen in advanced non-small cell lung cancer and worthwhile palliation of symptoms in
half or more of the patients treated. Symptom relief may occur in patients whose
tumours have not shown radiological response as defined by conventional criteria.

There has been considerable interest in a new chemotherapeutic agent for
malignant mesothelioma, pemetrexed (Alimta; Eli Lilly). The main evidence
supporting its use consists of a randomised study which compared a combination of
pemetrexed and cisplatin (PC) with cisplatin (C) alone in patients with
mesothelioma. The trial showed that the combination regimen extended
median survival by nearly 3 months. On the basis of this study, the US Food
and Drug Administration (FDA) approved pemetrexed for the treatment of
mesothelioma and it has also been licensed for this indication in Europe, including
the UK. Inclusion criteria included Karnofsky performance status (PS) >70
corresponding to WHO or ECOG PS 0–1. Part way through the trial folic acid and
vitamin B12 supplementation was introduced to reduce toxicity resulting in
three patient subgroups: never supplemented (NS), partially supplemented (PS)
and fully supplemented (FS). The sample size was substantially increased to
ensure adequate statistical power of the FS subgroup; 456 patients were
randomised but eight who did not receive chemotherapy were excluded
from analysis. Patients in the PC arm received a median of six cycles while those in
the C arm received a median of four cycles. NS patients received a median of two
cycles on each arm. Median survival in the whole group was 12.1 months with PC
and 9.3 months with C (p = 0.02). Among 331 FS patients, median survival was 13.3
months with PC compared with 10.0 months with C (p = 0.05). The investigators
reported a tumour partial response rate of 41.3% in the PC arm, but a review by the
FDA confirmed only half of these. Quality of life data, published in abstract form in
2003, reported a significant improvement in quality of life and symptom relief when
compared with cisplatin alone. However, full quality of life data have not been
published.

The subsequent paper reported that 84 patients from the PC arm and 105 from
the C arm received second-line chemotherapy which was associated with significant
prolongation of survival after adjustment for baseline prognostic factors and
treatment received. This strengthened the conclusion that first-line pemetrexed
prolonged survival since the survival advantage was seen despite the fact that
more patients in the C arm had received second-line chemotherapy. The subset
analyses performed in this study mean that the results should be interpreted with caution. It is important to note borderline significance in survival advantage in the FS group, as well as the fact that the patients were younger and fitter than most with mesothelioma.
Two phase II studies have suggested that efficacy may be approximately similar when carboplatin (in a dose of area under the curve 5) is used instead of cisplatin in combination with pemetrexed. The substitution of carboplatin for cisplatin is associated with reduced symptomatic toxicity (particularly nausea and vomiting) and increased ease of administration with less need for prolonged hydration with intravenous fluids. This has the potential to improve quality of life.

Support for the efficacy of antifolates is provided by similar results from a smaller study of cisplatin with or without raltitrexed (another antifolate) in 250 patients with mesothelioma. Median overall and 1 year survival with cisplatin vs raltitrexed was 8.8 (CI 7.8 to 10.8) months vs 11.4 (CI 10.1 to 15) months and 40% vs 46%, respectively (p = 0.05). There was no detriment to quality of life from raltitrexed. Unfortunately, the manufacturers do not intend to continue development of raltitrexed for treatment of mesothelioma and may stop production for economic reasons, leaving only pemetrexed in this class in the short to medium term.

The message from the randomised studies of pemetrexed and raltitrexed is that, unless cisplatin alone actually shortens survival—which seems unlikely—these drugs probably do confer a small median survival advantage and, as with any chemotherapy, patients whose tumours respond well to therapy are likely to gain more than average in terms of survival. The effects on quality of life are not yet fully evaluated but appear to be beneficial. Despite the need for caution in interpretation of the data, pemetrexed is an agent with demonstrable clinical efficacy in the treatment of mesothelioma and, as such, it is to be welcomed. It is less toxic than alternatives, particularly when used with carboplatin rather than cisplatin, and easily administered with a 3-weekly outpatient treatment schedule. Pemetrexed is the only drug licensed for the treatment of mesothelioma on the basis of randomised trial evidence and therefore may be considered the drug of first choice, used in combination with cisplatin or carboplatin. Other cheaper agents with useful activity include vinorelbine, gemcitabine, irinotecan and mitomycin, but none has yet been shown to confer a survival advantage in a randomised trial.

All patients who are fit enough to receive chemotherapy (all PS 0–1 and some PS 2 patients) should therefore be given accurate information and should have the opportunity to discuss chemotherapy with a specialist experienced in its use for mesothelioma. Patients who prefer to receive chemotherapy after a discussion of the merits of this form of treatment should be offered it.
iii) *The European Respiratory Society –ERS and the European Society of Thoracic Surgeons -ESTS* 22

Note: Grading/recommendations from the American College of Chest Physicians (ACCP) from 1A-2C used in this article are:

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1A/ Strong recommendation, High-quality evidence:</td>
<td>Benefit vs Risk and Burdens: Benefits clearly outweigh risk and burdens, or vice versa. Methodological Quality of Supporting Evidence: Randomized controlled trials (RCTs) without important limitations or overwhelming evidence from observational studies. Implications: Strong recommendation, can apply to most patients in most circumstances without reservation.</td>
</tr>
<tr>
<td>1B/ Strong recommendation, moderate quality evidence</td>
<td>Benefit vs Risk and Burdens: Benefits clearly outweigh risk and burdens, or vice versa. Methodological Quality of Supporting Evidence: RCTs with important limitations (inconsistent results, methodological flaws, indirect, or imprecise) or exceptionally strong evidence from observational studies. Implications: Strong recommendation, can apply to most patients in most circumstances without reservation.</td>
</tr>
<tr>
<td>1C/ Strong recommendation, low-quality or very low quality evidence</td>
<td>Benefit vs Risk and Burdens: Benefits clearly outweigh risk and burdens, or vice versa. Methodological Quality of Supporting Evidence: Observational studies or case series. Implications: Strong recommendation but may change when higher quality evidence becomes available.</td>
</tr>
<tr>
<td>2A/ Weak recommendation, high quality evidence</td>
<td>Benefit vs Risk and Burdens: Benefits closely balanced with risks and burden. Methodological Quality of Supporting Evidence: RCTs without important limitations or overwhelming evidence from observational studies. Implications: Weak recommendation, best action may differ depending on circumstances or patients’ or societal values.</td>
</tr>
<tr>
<td>2B/ Weak recommendation, moderate-quality evidence</td>
<td>Benefit vs Risk and Burdens: Benefits closely balanced with risks and burden. Methodological Quality of Supporting Evidence: RCTs with important limitations (inconsistent results, methodological flaws, indirect, or imprecise) or exceptionally strong evidence from observational studies. Implications: Weak recommendation, best action may differ depending on circumstances or patients’ or societal values.</td>
</tr>
<tr>
<td>2C/ Weak recommendation, low quality or very low-quality evidence</td>
<td></td>
</tr>
</tbody>
</table>
Benefit vs. Risk and Burdens: benefits, risks, and burden may be uncertain; benefits, risk, and burden may be closely balanced

Methodological Quality of Supporting Evidence: Observational studies or case series

Implications: Very weak recommendations; other alternatives may be equally reasonable

Diagnosis of MPM

1. Available methods to evaluate exposure to asbestos

Several methods and tools exist to evaluate cumulative exposures, such as occupational questionnaires and the use of job/exposure matrices. Due to the long latency period of the disease and the lack of precise data on airborne fibre levels, the exact evaluation may be difficult.

Mineral analyses of biological samples (bronchoalveolar lavage and lung tissue) by light or electron microscopy can provide information about the retained asbestos dose, mainly for amphiboles which have a longer pulmonary biopersistence than chrysotile. Due to the long latency periods of MPM and the fact that MPM can be associated with low dose exposures, mineral analyses will not always show high levels of asbestos fibers or asbestos bodies. Thus, it might be useful in revealing high levels of fibers in case that exposure history is unknown or difficult to assess.

Most MPM cases are linked to past occupational exposure, and MPM is recognized as an occupational disease in most, if not all, national worker’s compensation schemes. Similar with other occupational cancer, MPM are under-reported, it is then advisable to systematically assess the past exposure history of MPM patients according to the practices of the national workers’ compensation or other relevant social security schemes.

Exposure assessment is also important in specific scientific purposes. However, it has no therapeutic relevance and may be difficult to perform without the help of occupational hygienists or occupational physicians.

These principles also apply for mineralogical analysis of biological samples (quantification of asbestos bodies or asbestos fibres in BAL fluid or lung tissue samples). Such mineralogical analyses are not required in the clinical management of mesothelioma.

Evaluation of asbestos exposure (mainly through specific occupational and environmental questionnaire) is relevant and should be performed for social security and medico-legal purposes according to relevant national practices, but not for clinical management (grade 1A).

2. From a clinical point of view
The clinical manifestation of MPM are usually nonspecific and insidious and should not be used alone as diagnostic criteria, even in case of previous asbestos exposure (grade 1A).

Chest radiographs usually show a unilateral pleural effusion or thickening. Chest radiographs alone should not be used for the diagnosis of MPM (grade 1A).

A chest CT scan is unsuitable for definite diagnosis of MPM, but diffuse or nodular pleural thickening are suggestive of the disease (grade 1A).

MRI is not relevant for the diagnosis of mesothelioma (grade 1B).

PET scanning is currently not useful for the diagnosis of MPM (grade 1C).

It is recommended to perform thoracoscopy for the diagnosis of MPM, except in the case of pre-operative contraindication or pleural symphysis (grade 1A).

3. From a pathological point of view

The accurate diagnosis of MPM, a malignant tumour that arises from mesothelial cells that line the serosal cavities, is made on histopathological examination. However, diagnosis can be difficult because MPM is a very heterogeneous cancer which creates various misleading histopathological pitfalls. Moreover, the pleura are a common site for metastatic disease. Gross appearance of advance mesothelioma becomes more suggestive of MPM, but other malignant tumours may have a pseudomesotheliomatous aspect such as thymoma, lymphomas, angiosarcomas, etc.

Microscopically, MPM has a varied and deceptive appearance in a high percentage of cases and may resemble benign pleural lesions or metastatic lesions, which are much more common that MPM in the general populations. Thus, the most frequent metastatic pleural tumours are from lung cancer (7-15%) and breast cancer (7-11%), whose morphology can be mistaken for MPM on standard sections stained with haematoxylin-eosin-saffron. Diagnostic problems also occur with frequent benign inflammatory or reactive lesions of the pleura that may occur in patients at approximately the same age as in MPM (pleural effusion during cardiac failure, collagen disease, pneumonia, digestive disease such as cirrhosis, etc). These lesions are often secondary and lead to atypical mesothelial hyperplasia which can result in diagnostic error. Such errors represent about 13% of initially diagnosed cases.

Which pathological specimens for which clinical presentation

Pleural effusion is usually the first clinical sign of MPM; cytology is often the first diagnostic examination to be carried out. However, it is not recommended to make a diagnosis of mesothelioma based on cytology alone because of the high risk of diagnostic error (grade 1B).
It is recommended that a cytological suspicion of mesothelioma is followed by tissue confirmation (grade 1B).

Disease recurrence and metastases can be ascertained on cytology alone. This recommendation is in agreement with that proposed by the International Mesothelioma Panel (grade 1B).

Diagnosis of mesothelioma from fine needle biopsies (Abrams or Castelain needles) is associated with the same problems as cytology. A conclusive diagnosis can only be made if the material is representative of the tumour, in sufficient quantity to allow immunohistochemical characterisation and in the context of appropriate clinical, radiological and/or surgical findings.

Thoracoscopy should be preferred for diagnostic investigation, allowing complete visual examination of the pleura, multiple, deep and large biopsies (preferably including fat and/or muscle to assess tumour invasion) and providing a diagnosis in >90% of cases (grade 1A).

Fine needle biopsies are not primarily recommended for the diagnosis of mesothelioma because they are associated with low sensitivity (~30%) (grade 1A).

It is recommended to take biopsies of both normal and seemingly abnormal pleura (grade 1C). It is not recommended to make a diagnosis of MPM solely on frozen tissue sections (grade 1B).

**What classification should be used for MPM?**

The updated classification from the International Mesothelioma Interest Group 2009 is recommended as shown in table 3.5 above (grade 1A). This provides a comparative basis for diagnosis, prognosis and patient management.

**Should a complementary immunohistochemical examination be carried out in addition to morphological examination, and which immunohistochemical markers and how many antibodies should be used for which histological variants?**

It is recommended that a diagnosis of MPM always be based on immunohistochemical examination (grade 1A).

The International Mesothelioma Panel has put forward various recommendations. The immunohistochemical approach depends on whether the tumour subtype of mesothelioma is epithelioid or sarcomatoid.

To separate epithelioid mesothelioma from adenocarcinoma, it is recommended that two markers with positive diagnostic value for mesothelioma (nuclear markers such as anti-calretinin and anti-Wilms tumour antigen-1 or the membrane marker anti-epithelial membrane antigen (EMA); for epithelioid mesothelioma, anti-cytokeratin (CK)5/6, antiD2-40 (podoplanin) or anti-mesothelin,
etc.) and two markers with negative diagnostic value (anti-Ber-EP4, a membrane marker; anti-thyroid transcription factor-1, a nuclear marker; or monoclonal anti-carcinoembryonic antigen, anti-B72-3, anti-MOC-31, anti-oestrogen/progesterone, anti-EMA, cytoplasmic staining) are used to validate the diagnosis (grade 1A). Among the various sources of antibodies, it is mandatory to use those presenting at a minimum of 60–70% sensitivity. It is not recommended to use anti-CK7/anti-CK20 to make the diagnosis of mesothelioma (grade 1A). The antibodies requirements are summarised in Table 3.9.

**Table 3.9 Immunohistochemistry to separate epitheloid mesothelioma from adenocarcinoma**

<table>
<thead>
<tr>
<th>Antibody</th>
<th>Current value</th>
<th>Mesothelioma</th>
<th>Positivity</th>
<th>Adenocarcinoma</th>
<th>Positivity</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mesothelioma</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Calretinin</td>
<td>Essential</td>
<td>Positive</td>
<td>80–100%</td>
<td>Usually negative</td>
<td>5–10% cytoplasmic positivity of lung adenocarcinoma</td>
</tr>
<tr>
<td>Keratin CK5/6</td>
<td>Useful</td>
<td>Positive</td>
<td>60–100%</td>
<td>Usually negative</td>
<td>2–10% focal positivity</td>
</tr>
<tr>
<td>WT-1</td>
<td>Useful</td>
<td>Positive</td>
<td>43–93%</td>
<td>Lung adenocarcinoma are negative</td>
<td>0%</td>
</tr>
<tr>
<td>EMA</td>
<td>Useful</td>
<td>Positive</td>
<td>60–100%</td>
<td>Positive (cytoplasmic)</td>
<td>70–100%</td>
</tr>
<tr>
<td>Podoplanin</td>
<td>Useful</td>
<td>Positive</td>
<td>80–100%</td>
<td>Usually negative</td>
<td>7% focal positivity</td>
</tr>
<tr>
<td><strong>Lung adenocarcinoma</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CEA monoclonal</td>
<td>Very useful</td>
<td>Almost invariably negative</td>
<td>0%</td>
<td>Positive (cytoplasmic)</td>
<td>50–90%</td>
</tr>
<tr>
<td>CD15</td>
<td>Useful</td>
<td>Never expressed in mesothelioma</td>
<td>0%</td>
<td>Positive (membranous)</td>
<td>50–70% focal positivity</td>
</tr>
<tr>
<td>Ber-EP4</td>
<td>Very useful</td>
<td>Positive or negative (membranous)</td>
<td>Up to 20% can be focally positive</td>
<td>Positive (membranous)</td>
<td>95–100%</td>
</tr>
<tr>
<td>TTF-1</td>
<td>Very useful</td>
<td>Never expressed</td>
<td>0%</td>
<td>Positive (nuclear)</td>
<td>70–89% of lung adenocarcinoma</td>
</tr>
<tr>
<td>B72.3</td>
<td>Very useful</td>
<td>Rarely positive</td>
<td>&lt;1%</td>
<td>Positive (cytoplasmic)</td>
<td>70–89% of lung adenocarcinoma</td>
</tr>
<tr>
<td><strong>Breast carcinoma</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ER</td>
<td>Very useful</td>
<td>Never expressed in mesothelioma</td>
<td>0%</td>
<td>Positive nuclear staining</td>
<td>~70%</td>
</tr>
</tbody>
</table>

To separate sarcomatoid mesothelioma from squamous and transitional cell carcinoma (Table 3.10), it is recommended to use two broad-spectrum anti-cytokeratin antibodies and two markers with negative predictive value (such as anti-CD34 and anti-B-cell lymphoma 2 marker, anti-desmin, anti-S100) to confirm the diagnosis (grade 1A). Negative immunostaining with a single antibody does not exclude the diagnosis (grade 1C).
Table 3.10 Immunohistochemistry for separating sarcomatoid mesothelioma from squamous and transitional cell carcinoma

<table>
<thead>
<tr>
<th>Antibody</th>
<th>Current value</th>
<th>Mesothelioma</th>
<th>Positivity</th>
<th>Squamous and transitional cell carcinoma</th>
<th>Positivity</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mesothelioma</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Calretinin</td>
<td>Useful</td>
<td>Positive (strong nuclear and cytoplasmic)</td>
<td>80–100%</td>
<td>Usually cytoplasmic positivity</td>
<td>5–40%</td>
</tr>
<tr>
<td>Keratin CK5/6</td>
<td>Not useful</td>
<td>Positive (cytoplasmic)</td>
<td>60–100%</td>
<td>Cytoplasmic positivity</td>
<td>100%</td>
</tr>
<tr>
<td>WT-1</td>
<td>Very useful</td>
<td>Positive (nuclear)</td>
<td>43–93%</td>
<td>Negative</td>
<td>0%</td>
</tr>
<tr>
<td><strong>Squamous cell carcinoma</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>p63</td>
<td>Very useful</td>
<td>Almost always negative</td>
<td>0%</td>
<td>Positive (nuclear)</td>
<td>~100%</td>
</tr>
<tr>
<td>Ber-EP4</td>
<td>Useful</td>
<td>Positive or negative</td>
<td>Up to 20% are positive</td>
<td>Positive (cytoplasmic)</td>
<td>80–100%</td>
</tr>
<tr>
<td>MCC 31</td>
<td>Useful</td>
<td>Positive or negative (focal membranous staining)</td>
<td>2–10%</td>
<td>Positive (membranous)</td>
<td>97–100%</td>
</tr>
</tbody>
</table>

With regard to atypical mesothelial hyperplasia (superficial mesothelial proliferations), there are currently no commercially available immunohistochemical markers that identify the benign or malignant nature of the cells observed.

**Should electron microscopic examination and molecular biology be performed**

Electron microscopy and molecular biology should not be carried out routinely to confirm the diagnosis of mesothelioma (grade 1A).

There are no diagnostic or therapeutic reasons for freezing pleural tumour tissue (grade 1A).

**Should the advice of an expert panel be sought faced with a suspicion of MPM?**

An independent expert panel should be asked to confirm the diagnosis particularly in clinical trials, or in any case where there is doubt about the diagnosis (grade 1B).

**Staging, pre-therapeutic investigations and prognostic factors**

**Which staging classification is used?**

Staging describes the anatomical extent of a tumour. There are at least five staging systems available in pleural mesothelioma, the latest one devised by members of the International Mesothelioma Interest Group and approved by the Union International Contre le Cancer (UICC) as shown in table 3.5. The main drawback of the classifications is the inaccuracy in describing T- and N-extent by
current imaging techniques. Because of this, an international panel of experts could not agree on a common staging classification in pleural mesothelioma and strongly advocated the development of a new robust and uniform clinical staging system that should be prospectively validated, TNM-based and include the existing surgical–pathological staging systems.

In the absence of a uniform, robust and validated staging system as mentioned, the experts advocate the use of the most recent TNM-based UICC classification (grade 1C).

**What are the minimal pre-treatment staging examinations?**

A three-step pre-treatment assessment is recommended based on empirical observation, good clinical practice and the fact that the treatment intent differs between patients (grade 1C).

The pre-treatment assessment is empirically split into three steps which are, to some degree, overlapping. Whether a patient goes through all three steps strongly depends on the results of the procedures and the consequences for the choice of treatment with radical or palliative intent only.

Step I is to be considered in all patients at presentation or diagnosis (table 3.11).

**Table 3.11 Parameters to be considered in all patients at presentation/ diagnosis.**

<table>
<thead>
<tr>
<th>Investigations</th>
<th>Including</th>
<th>Confirmatory tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographics</td>
<td>Sex and age, asbestos exposure</td>
<td>As appropriate</td>
</tr>
<tr>
<td>Clinical history</td>
<td>Performance status, comorbidities, presence/absence of chest pain, dyspnoea, change in body weight or BMI</td>
<td>As appropriate</td>
</tr>
<tr>
<td>Physical examination</td>
<td>Presence or absence of “shrinking hemithorax”, cutaneous nodules</td>
<td>As appropriate</td>
</tr>
<tr>
<td>Radiological investigations</td>
<td>Chest radiograph, PA lateral</td>
<td>Chest radiograph, inspiration/expiration, pre-/post-drainage of pleural fluid</td>
</tr>
<tr>
<td>Blood tests</td>
<td>Haemoglobin, leukocytes, platelets, basic biochemistry</td>
<td></td>
</tr>
</tbody>
</table>

BMI: body mass index; PA: postero-anterior.

Step II is to be considered in patients who are candidates for any kind of active treatment (table 3.12).
Table 3.12 Investigations performed in patients likely to receive some form of active treatment

<table>
<thead>
<tr>
<th>Investigations</th>
<th>Including</th>
<th>Confirmatory tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary tumour</td>
<td>Adequate biopsy for histology confirmation</td>
<td></td>
</tr>
<tr>
<td>CT scan of chest and upper abdomen</td>
<td>Spiral technique, with i.v. contrast, including at least level of both kidneys after drainage of pleural fluid</td>
<td></td>
</tr>
<tr>
<td>Pulmonary function tests</td>
<td>Forced vital capacity, forced expiratory volume in 1 s</td>
<td></td>
</tr>
<tr>
<td>Bone scan</td>
<td>Not routine, to be considered on clinical suspicion only</td>
<td>CT/MRI to confirm dubious findings</td>
</tr>
<tr>
<td>Brain CT/MRI</td>
<td>Not routine, to be considered on clinical suspicion only</td>
<td></td>
</tr>
</tbody>
</table>

CT: computed tomography; MRI: magnetic resonance imaging.

Step III is the final process of patient selection for combined modality or radical locoregional treatment (table 3.13).

Table 3.13 Investigations to be considered in patients who are candidates for surgery or multimodal treatment

<table>
<thead>
<tr>
<th>Area</th>
<th>Investigation</th>
<th>Comment</th>
<th>Confirmatory tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulmonary function tests</td>
<td>DLco in addition to PVC and FEV1</td>
<td>Assessment similar to the one for lung cancer</td>
<td>Lung scintigraphy probably performed as for any pneumectomy</td>
</tr>
<tr>
<td>Primary tumour</td>
<td>Adequate biopsy for histological subtyping</td>
<td>CT scan or MRI</td>
<td></td>
</tr>
<tr>
<td>Diaphragm</td>
<td>FDG-PET/CT</td>
<td>According to institutional practice</td>
<td>Biopsy of suspected extrathoracic lesions</td>
</tr>
<tr>
<td>Extra-thoracic, to exclude &quot;occult&quot; M1</td>
<td>Laparoscopy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mediastinum, excluding T4, N2/3 involvement</td>
<td>Cervical mediastinoscopy</td>
<td>According to institutional practice</td>
<td></td>
</tr>
<tr>
<td></td>
<td>VATS, contra lateral VATS</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>MRI of the chest, gadolinium enhanced</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>E(B)US-FNA</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

DLco: diffusing capacity of the lung for carbon monoxide; PVC: forced vital capacity; FEV1: forced expiratory volume in 1 s; CT: computed tomography; MRI: magnetic resonance imaging; FDG-PET: 18-Fluor-2-deoxy-glucose positron emission tomography; VATS: video-assisted thoracic surgery; E(B)US-FNA: enobronchial ultrasound-fine needle aspiration.

It is the opinion of the experts that this last step will only considered in a minority of patients with pleural mesothelioma. This is reflected in the paucity of evidence, reflecting different institutional practice. Among the investigations to be considered are mediastinoscopy, MRI of the chest, video-assisted thoracoscopy (VATS), enobronchial ultrasound-fine needle aspiration (E(B)US-FNA), FDG-PET scan and laparoscopy. In the absence of comparative trials, no formal advice regarding their respective efficacy can be given.
The experts further agree that in patients proceeding to step II or higher: 1) a diagnosis of mesothelioma should be confidently established, preferably on a biopsy specimen with adequate immunohistochemistry and subtyping; 2) the interval within which the pre-treatment assessment has to be finalised should be as short as possible; and 3) recent (<1 month) imaging studies should be available prior to invasive procedures. Further research should be performed with regard to the comparative efficacy of different intrathoracic techniques (mediastinoscopy, VATS, and EUS-FNA) and the value of the new techniques (PET-CT, EBUS-FNA).

Which prognostic factors are of importance?

Several prognostic factors have been described in large multicenter series and have been independently validated. Among these, the Surveillance, Epidemiology and End Results (SEER) Program review is a landmark retrospective series of 1,475 patients with histological confirmed mesothelioma and showing that age, sex, tumour stage, treatment and geographic area of residence were important prognostic factors. A number of factors, such as performance status, stage and weight loss, are common to other tumours; others factors, such as age and sex have not been confirmed in all series. Symptoms and quality of life are increasingly being investigated as prognostic factors. Nonepitheloid subtype is consistently associated with a poorer prognosis. Of the numerous biological factors studied, low haemoglobin level, high lactose dehydrogenase (LDH), a high white blood cell count and a high thrombocyte count have been repeatedly associated with a poor prognosis. New serum biomarkers with potential prognosis significance (e.g. soluble mesothelin and osteopontin) are currently under investigation. Based on these various factors, three prognostic scores have been developed and prospectively validated; the CALGB (Cancer and Leukaemia Group B) and two EORTC (European Organization for Research and Treatment of Cancer) prognostic scoring systems (Table 3.14). The latter was later adapted according to the results of the multivariate analysis of prognostic factors of a large randomised chemotherapy trial in good performance patients.
Performance status of the patient and histopathological subtype are currently the only prognostic factors of clinical importance that may routinely be used in the management of patients with malignant mesothelioma (grade 2A).

Other parameters with prognostic capacity, such as age, sex, stage, presence or absence of certain symptoms and haematological factors, should be recorded at baseline and reported in clinical trials (grade 2A).

**Treatment of MPM**

1. **Surgery for MPM**

   *What is the evidence for debulking decortication/pleurectomy for symptom control?*

   Debubling pleurectomy/decortication can be defined as significant but incomplete macroscopic clearance of pleural tumour. The objective of the operation is to relieve an entrapped lung by removing the visceral tumour cortex. Removal of the parietal tumour cortex may relieve a restrictive ventilatory deficit and reduce chest wall pain. The operative procedure may be performed by either open thoracotomy or closed VATS.

   There is limited evidence supporting debulking surgery. At present there is an absence of randomised trials, but a national study is ongoing in the UK which is being supported by the National Cancer Research Institute comparing VATS debulking with chemical pleurodesis (MesoVATS). There are a small series of

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**Table 3.14 Prognostic scoring systems in malignant mesothelioma**

<table>
<thead>
<tr>
<th>First author [ref.]</th>
<th>Subjects n</th>
<th>Parameter</th>
<th>Good prognostic group</th>
<th>Poor prognostic group</th>
</tr>
</thead>
<tbody>
<tr>
<td>CALGB</td>
<td>337</td>
<td>Performance status</td>
<td>Good&lt;br&gt;Age&lt;br&gt;Chest pain&lt;br&gt;Platelet count&lt;br&gt;LDH</td>
<td>Poor&lt;br&gt;&gt; 75 yrs&lt;br&gt;Absent&lt;br&gt;&lt;400 × 10^9-L^{-1}&lt;br&gt;&lt;500 IU-L^{-1}</td>
</tr>
<tr>
<td>EORTC</td>
<td>204</td>
<td>Performance status histological subtype sex certainty of diagnosis WBC count</td>
<td>Epithelioid&lt;br&gt;FEMALE&lt;br&gt;DEFINITATE&lt;br&gt;&lt;8.3 × 10^9-L^{-1}</td>
<td>Nonepithelioid&lt;br&gt;male&lt;br&gt;possible&lt;br&gt;&gt;8.3 × 10^9-L^{-1}</td>
</tr>
<tr>
<td>EORTC</td>
<td>250</td>
<td>Stage histology interval since diagnosis platelet count Haemoglobin difference Pain Appetite loss</td>
<td>I-II&lt;br&gt;Epithelioid&lt;br&gt;&lt;50 days&lt;br&gt;&lt;350 × 10^9-L^{-1} &lt;1&lt;br&gt;Absent&lt;br&gt;Absent</td>
<td>III-IV&lt;br&gt;Nonepithelioid&lt;br&gt;&gt;60 days&lt;br&gt;&gt;350 × 10^9-L^{-1} &gt;1&lt;br&gt;Present&lt;br&gt;Present</td>
</tr>
</tbody>
</table>

CALGB: Cancer and Leukaemia Group B; EORTC: European Organization for Research and Treatment of Cancer; LDH: lactate dehydrogenase; WBC: white blood cell.

&superscript;1: performance status 0–1 was an inclusion criterion for this series; &superscript;2: difference between actual value and 16 g-dL^{-1} and 14 g-dL^{-1} in males and females, respectively.
retrospective studies which provide low-grade evidence for debulking pleurectomy. The associated morbidity of thoracotomy may diminish the benefits; however there is limited but emerging evidence that VATS can provide good symptom control and may have a beneficial effect on survival.

Pleurectomy/decortication should not be proposed in a curative intent but can be considered in patients to obtain symptom control, especially symptomatic patients with entrapped lung syndrome who cannot benefit from chemical pleurodesis (grade 2C). The VATS approach is preferred (grade 1C).

What is the evidence for radical surgery in MPM?

Radical surgery may be defined as an attempt to remove all macroscopic tumours from the hemithorax. These objectives are usually achieved by extrapleural pneumonectomy (EPP) with *en bloc* resection of pleura, lung, pericardium and diaphragm and systematic nodal dissection.

There is limited evidence for the efficacy of radical surgery for mesothelioma. Among resected mesothelioma patients, the only published long-term survivors have undergone radical surgery (EPP) as part of a multimodality programme. There have been a number of subsequent prospective and retrospective series which have all demonstrated a similar median survival of 20-24 months. Operative mortality has fallen to an acceptable level of 5% in experienced centers but mortality remains high at 50%.

Radical surgery (EPP) should only be performed in clinical trials, in specialised centres, as part of multimodal treatment.

2. Radiotherapy in MPM

What is the role of “palliative” radiotherapy aimed at pain relief?

Palliative radiotherapy aimed at pain relief may be considered in cases of painful chest wall infiltration or nodules (grade 2C).

What is the role of radiotherapy in the prevention of parietal seeding along the drainage channels?

The value of prophylactic radiotherapy is questionable. Therefore, the experts were not able to draw any recommendation.

What is the role of post-operative radiotherapy?

Radiotherapy should not be performed after pleurectomy or decortication (grade 1A). Post-operative irradiation after EPP should only be proposed in clinical trials, in specialised centres, as a part of multimodal treatment (grade 1A).
In the absence of phase III randomised trials, the establishment of a prospective controlled study evaluating the efficacy and tolerability of adjuvant radiotherapy post-EPP (minimum dose of 50 Gy with daily fraction size of 1.8 to 2 Gy) is recommended (grade 1C). A randomised multicenter European study is ongoing to answer this question (SAKK study).

What is the place for intensity-modulated radiotherapy in MPM after EPP?

Preliminary results of intensity-modulated radiotherapy in the adjuvant setting after EPP seem particularly promising as they provide good local control and protect organs at risk, such as the heart or liver. However, severe pulmonary toxicity has been reported in recent studies so it should not be recommended outside of clinical trials; six out of 13 patients developed fatal pneumonitis.

Further studies are needed to better establish the role of radiotherapy. Recent studies have underlined the importance of radiotherapy technique both in terms of local control and toxicity.

Therefore, it is recommended to carry out this radiotherapy in specialised centres only (advice of experts).

3. Chemotherapy of MPM

Has the benefit of chemotherapy been demonstrated?

First-line combination chemotherapy including cisplatin and pemetrexed or raltitrexed demonstrated greater activity than cisplatin alone in phase III trials (level 1), with higher response rates and improved survival. However, in the BTS study, there was no survival advantage of chemotherapy (vinorelbine alone or mitomycin C, vinblastin and cisplatin combination) over best supportive care alone (level 2). Other studies, including potentially active combination, such as cisplatin plus gemcitabine or etoposide or doxorubicin, could be conducted (versus best supportive care or cisplatin/pemetrexed or raltitrexed) (expert opinion). The role of nonplatinum regimens remains to be elucidated (level 2).

No randomised study has demonstrated the benefit of second-line chemotherapy on survival (except on survival without disease progression in a phase III study (23) or quality of life after failure of primary chemotherapy.

Every patient should receive at least best supportive care (grade 1A). When a decision is made to treat patients with chemotherapy, subjects in a good performance status (performance status >60% on the Karnofsky scale or <3 on the Eastern Cooperative Oncology Group scale) should be treated with first-line combination chemotherapy consisting of platinum and pemetrexed or raltitrexed (grade 1B). Alternatively, patients could be included in first- and second-line clinical trials.
In the light of limited evidence of efficacy of chemotherapy, the decision to administer chemotherapy should be discussed with the patients and their relatives on a case-by-case basis, like all other treatment modalities without curative purposes (advice of experts).

When should chemotherapy be started, and for how long should chemotherapy be continued?

Administration of chemotherapy should not be delayed and should be considered before the appearance of functional clinical signs (grade 1C).

Chemotherapy should be stopped in case of progressive disease, grade 3–4 toxicities or cumulative toxic doses (grade 1A), or following up to six cycles in patients who respond or who are stable (grade 2C).

What cytotoxic drugs are effective as second-line treatment?

No drug has been validated in second-line chemotherapy and patients in a good performance status should be recommended to enter clinical trials instead.

Patients demonstrating prolonged symptomatic and objective response with first-line chemotherapy may be treated again with the same regimen in the event of recurrence (grade 2C).

In other cases, inclusion of the patients in clinical trials is encouraged (grade 2C).

What is the role of biotherapies in the treatment of MPM?

Results of studies assessing the efficacy of drugs modulating the activity of the immune system or having a “specific” action on the tumour (targeted therapies) are summarised in this article (see table in supplementary tables and references part of reference 22 at http://www.ersj.org.uk/content/35/3/479/suppl/DC1).

**Immunomodulators**

Interferons and interleukins (ILs) are the principal drugs being tested in the treatment of malignant mesothelioma. Dose, method of administration (intrapleural, sub-cutaneous, intramuscular and intravenous), type of drug and disease stage varied from one study to another, therefore, interpretation of the results must be performed cautiously. Monotherapy with interferons or IL-2 did not seem to effective and is not recommended outside of a clinical trial.

Interesting preliminary results were observed after administration of *Mycobacterium vaccae* in a limited number of patients. This treatment needs to be
confirmed before its use can be recommended. Ranpirnase has not demonstrated its effectiveness.

**What assessment criteria should be used to determine the efficacy of chemotherapy in MPM?**

The activity of a treatment can be assessed on clinical criteria (symptoms control and quality of life), imaging criteria (CT scan or PET) and survival criteria (time to progression and overall survival). The evaluation of response by thoracoscopy was never reported.

**Imaging evaluation criteria of tumour response**

Response evaluation criteria are vary from one study to another and are not always reported. The systematic practice of a referential CT scan after pleural symphysis and before beginning chemotherapy was not mandatory, distorting response evaluation. The timing for evaluation is also lacking most of the time. Today, it can be considered that standard chest radiography is not a valuable method by which to assess response to chemotherapy (refer to Diagnosis section).

There are different methods for objective response assessment depending on the type of criteria, WHO (product of two perpendicular measures) or RECIST (one dimension measure). Neither of these methods is adapted to malignant mesothelioma in which development is essentially circumferential on the gross pleural surface 85. It is currently proposed to use modified “RECIST criteria” (measure of the short diameter perpendicular to the chest wall court) to assess objective response in MPM.

**Tumour response evaluation according to PET criteria**

Differentiating tumour tissue from post-chemotherapy scar lesions is difficult with CT scanning. PET allows assessment of both tumour sizes and captation intensity. The combination of PET and CT scan, with both examinations performed on the patient in the same position, allows a better correlation of these two techniques. The contribution of this new imaging modality in response evaluation still needs to be validated. For clinical trials, in the absence of standardisation in response evaluation with PET in malignant mesothelioma, the use of the PET response criteria proposed by EORTC 88 can be considered as show in table 3.15.
Table 3.15 EORTC guidelines for therapeutic response assessment with PET

<table>
<thead>
<tr>
<th>Complete metabolic response</th>
<th>Partial metabolic response</th>
<th>Stable metabolic disease</th>
<th>Progressive metabolic disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete resolution of uptake within the tumour volume so that it was indistinguishable from surrounding normal tissue</td>
<td>Reduction of $^{18}$-FDG (SUV) tumoural uptake of at least 15-25% after one cycle of chemotherapy and of more than 25% after more than one cycle</td>
<td>Increase in SUV of less than 25% or a decrease of less than 15% and no visible extent of tumour uptake (&lt;20% in the longest dimension)</td>
<td>Increase in SUV greater than 25% or a visible increase in the extent of tumour uptake (&gt; 20% in the longest dimension) or the appearance of a new metastatic lesion</td>
</tr>
</tbody>
</table>

5. Combined modality approach

Surgery alone for MPM is not curative since no oncological resection margins can be obtained. Pleural lining, especially on the pericardium and mediastinum, cannot be resected with a 1-2 cm margin. Thus, all surgical procedures are considered R1 resections.

The use of radiation therapy to the full hemithorax is limited by critical organs, such as contralateral lung and heart most particularly, as well as spinal cord and esophagus. In addition, it is difficult to administer a total dose of >54 Gy. The multi-modality approach oriented by findings from surgeons and pathologist, are then in need.

Which patient is suitable for this approach?

For potential patients, the work-up should consist of at least the following: 1) Physical examination: shrinkage of the afflicted hemithorax is considered a sign of advanced disease. No signs of growth through the ribs or in the abdomen. 2) Pulmonary function tests: post-pneumonectomy values should be sufficient for normal daily life functioning. 3) Adequate cardiac reserve with the absence of elevated pulmonary pressure or rhythm disorders (level of evidence: weak/moderate-quality evidence). 4) Radiological examinations to rule out spread of the disease beyond the rib cage through the diaphragm; contra-lateral extension and multiple node involvement (level of evidence: weak/moderate-quality evidence). 5) Histological examination: the best results have been obtained with MPM of the epithelial type (level of evidence: weak/high-quality evidence). 6) Sex: there are no solid data that there is a difference in response to treatment between the different sexes (level of evidence: strong/low-quality evidence).
What is the best combination?

A body of literature that deals with the combination of surgical resection followed by radiation therapy. The procedures vary with regard to the extent of resection (removal of complete diaphragm, pericardium, placement of patches, etc.). The bi-modality approach has recently been extended with pre- and post-operative chemotherapy.

In conclusion, there are limited and weak data available on the best combination treatment.

Patients who are considered candidates for the multimodal approach should be included in a prospective randomized trial in specialised centres.

iv) European Commission: Information notices on occupational diseases: a guide to diagnosis

This included primary malignant tumour of the pleura, primary malignant tumour of the peritoneum, and primary malignant tumour of the pericardium. About 80-90% of pleural mesotheliomas are attributable to occupational exposure to asbestos. Smoking does not increase the risk. The risk of mesotheliomas increases considerably in relation to time since first exposure. Exposure to amphibole asbestos fibres carries a far higher risk of mesothelioma than does chrysotile asbestos exposure.

Diagnostic Criteria

The diagnosis of mesothelioma is a pathological diagnosis. Its presence may be suggested by:

- Characteristic clinical features including chest pain, pleural effusion, breathlessness and weight loss
- Standard radiology and computed tomography
- Histological examination of biopsy specimen
- Immunocytochemistry may be helpful in distinguishing the chief differential diagnosis of secondary adenocarcinoma.

Exposure criteria

Minimum intensity of exposure: confirmed occupational exposure, if possible assessed by history and study of working conditions providing evidence of exposure to asbestos. Some occupations (for example those involved with the refurbishment of office buildings) may incur unrecognized exposure to asbestos, in which case a history of occupational exposure may be unreliable.

Minimum duration of exposure: usually a few years but shorter exposures (as low as 3 months) have been described.
Minimum induction period: usually more than 20 years but rarely, cases associated with high exposure have been described with shorter induction periods

2.2.2 Lung cancer

The epidemiologic evidence dates to the 1950s supported that asbestos causes lung cancer. Whether asbestos acts directly as a carcinogen or through indirect mechanisms, such as causing chronic inflammation that eventually leads to cancer development, remains uncertain. In addition, both asbestos and cigarette smoking are independent causes of lung cancer, but in combination they act synergistically to increase the risk for lung cancer in a manner that is compatible with a multiplicative effect. It is postulated that cigarette smoking may increase the lung cancer risk by enhancing retention of asbestos fibers.

However, up to this search, there is only few documents on diagnostic criteria for asbestos-related lung cancer regarding academic perspective. The diagnostic criteria available focused on compensation criteria. Thus it will be elaborated in the next chapter of 3rd prevention.

i) The Helsinki criteria for lung cancer

The Helsinki Criteria state that the risk of developing lung cancer is materially increased (by a factor of 2), even without asbestosis, under the following conditions:
1. One year of heavy exposure (e.g., manufacturing of asbestos products, asbestos spraying, insulation work with asbestos materials, demolition of old buildings) or 5 to 10 years of moderate exposure (e.g., construction, shipbuilding).
2. Estimated cumulative exposures to mixed (amphibole plus chrysotile) asbestos fibers of 25 fibers per milliliter per year (fiber-years).
3. A lung fiber burden within the range recorded for asbestosis in the same laboratory.
4. Retained fiber levels of 2 million amphibole fibers (>5 µm) per gram of dry lung tissue or 5 million amphibole fibers (>1 µm) per gram of dry lung tissue, as determined by electron microscopic analysis.
5. Asbestos body concentrations determined by light microscopic analysis greater than 10 000 per gram of dry lung tissue.
Criteria 1 and 2 can be considered as clinical or anecdotal assessments of cumulative asbestos exposure and 3 through 5 as mineralogical estimates of exposure.
However, Gibbs (24) argued that it’s anecdotal estimates due to many difficulties as follows:

Firstly, it implies a false precision concerning the estimate. There are many methodological problems related to determination of the fiber-years level. Many of the estimates have been based on inadequate sampling techniques that have changed in the course of the years;

Secondly, the measurements of airborne fiber levels have been conducted by optical microscopic techniques. Direct comparisons between fiber levels determined by optical and transmission electron microscopic techniques have shown approximately a 10-fold greater amount for amosite and a 40- to 200-fold greater amount for crocidolite with the latter. It can be seen that equivalent optical counts obtained for amosite and crocidolite would in fact be 4 to 20 times higher for crocidolite than for amosite if transmission electron microscopy (TEM) techniques had been used;

Thirdly, the document states that the relative risk of lung cancer is estimated to increase 0.5% to 4% for each fiber-year of cumulative exposure and then proceeds to use the upper level of this boundary range for stating that the increase of lung cancer is 2-fold, with a cumulative exposure of 25 fiber-years. If, on the other hand, one took the lower boundary level of 0.5%, this would translate into an equivalent of 200 fiber-years. Even this is debatable because there are industries with substantial exposure to asbestos where no increase in lung cancer risk has been detected. In fact, the published estimated percent increases in relative lung cancer risk for different industries has been much wider, namely from 0.01% to 9.1%, with consequent doubling of relative risk at 10000 fiber-years to 11 fiber-years exposure.

**ii) European Commission: Information notices on occupational diseases: a guide to diagnosis**

Asbestos may cause a primary bronchial cancer. The presence of asbestosis increases the likelihood of causal association between asbestos and primary bronchial cancer. However, asbestosis is not essential for the development of primary bronchial cancer arising from asbestos exposure. The risk is increased considerably by smoking. Since tobacco smoke is the main risk factor for bronchial cancer, it must be considered carefully alongside workplace exposures in attributing an occupational cause.

**Diagnostic Criteria**

All histological types of bronchial cancer have been linked to asbestos exposure. The diagnosis is pathological. Its presence may be suggested by:
Characteristic clinical features including haemoptysis, cough, weight loss, and pleural effusion.

Standard radiography and computed tomography. PET scanning may be helpful.

Cytological examination of sputum, bronchial aspiration or bronchial lavage

Histological examination of biopsy specimen

**Exposure criteria**

*Minimum intensity of exposure:* confirmed occupational exposure, assessed by history and study of working conditions, providing evidence of prolonged and repeated heavy exposure to asbestos, and by (where feasible):

- Estimation of a cumulative exposure index from exposure times, type of occupational activity and concentrations in the air which might have been measured at the place of work.
- There is evidence that the risk of developing bronchial cancer at cumulative exposures of <25 fibres.ml-1.year is low.
- Significant concentrations of asbestos bodies or fibres in the sputum, fluid from bronchoalveolar lavage or lung parenchyma.
- The presence of asbestosis (the presence of pleural plaques suggests exposure to asbestos but does not reflect the exposure level).

*Minimum duration of exposure:* usually a few years.

*Minimum induction period:* usually more than 15 years.

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**iii) ICOH Scientific Committee for Respiratory Disorders on Secondary prevention: early diagnosis and treatment**

*Malignant asbestos-related diseases*

Lung cancer is a known consequence of asbestos exposure. Among non-smokers, lung cancer is sufficiently rare that an association with asbestos can be assumed if asbestos exposure has occurred. Powerful biological interactions between cigarette smoking and asbestos have been clearly demonstrated. Asbestos increases the risk of lung cancer among smokers up to a factor of 6. Thus, for purposes of apportioning cause, or for eligibility for compensation, asbestos exposure almost invariably contributes to risk among smokers to the extent that a relationship to work can be presumed.

Objective indicators of sufficient asbestos exposure to cause lung cancer include a chest film classified by the ILO system as 1/0 or greater, or demonstration
of pleural plaques or an exposure history roughly equal to or greater than 25 fibre/cm$^3$-year. The histology of asbestos-related and unrelated lung cancers does not differ significantly.

Mesothelioma should be deemed causally related to asbestos in all cases when there is evidence of exposure to asbestos.

3.3 Disease surveillance

i) Screening tools from some international and national organization

Chest X-ray

Sensitivity and Specificity of the Chest Radiograph in asbestosis: The chest radiograph is problematic, when trying to diagnose minimal or mild disease (ILO grade, 1/0 and 1/1). Abnormal chest radiographic findings in patients with asbestosis could be interpreted normal or false negative about 10 to 15% which yields a sensitivity of 85 to 90% while the specificity is around 75-95% among qualified readers. Some factors other than asbestos exposure, such as radiographic technique, aging, obesity, smoking, presence of COPD, and exposure to various other fibrogenic and nonfibrogenic dusts, can lead to a mildly abnormal chest radiographic finding, affecting its specificity.

Positive predictive value of chest x-ray in asbestosis: Using a prevalence of 5%, a sensitivity of 90%, and a specificity of 93%, the positive predictive value of a positive chest radiograph alone (ILO grades, 1/0 and 1/1) is about 40%. If the prevalence of asbestosis is lowered to 3%, the positive predictive value of the chest radiograph alone is only 28%. It should be mentioned that in cohorts with less exposure to asbestos, the prevalence of asbestosis will be even lower, and so the positive predictive value of an abnormal chest radiograph will also be lower. On the other hand, for cohorts with a high prevalence of asbestosis, such as the insulators studied by Selikoff and coworkers, a radiograph with an ILO reading of 1/0 or 1/1 may have a positive predictive value 50%.

Interobserver variation in asbestosis: In addition, the radiologic diagnosis of mildly abnormal has a rather large interobserver variation. For example, in one study in which 23 “B-readers” certified by the National Institute of Occupational Safety and Health evaluated 105,029 chest radiographs for the assessment of asbestosis among naval personnel, there was a 20 fold difference in the prevalence of positives findings (ILO grade $\geq$ 1/0) between the extreme readers, and the average prevalence was 2.4%.

Another study reviewed the interobserver variation in chest radiograph interpretation of pneumoconiosis, finding that among the same 119 chest
radiographs that were read by six qualified readers, the number that were read as being positive for asbestosis (ILO grade ≥ 1/0) varied from 24 to 91%. **Interobserver variation, thus, significantly affects sensitivity and specificity.**

If, in fact, 91% of the group actually had asbestosis, the individual who found it in only 24% would exhibit a very poor sensitivity of, at best, 24 of 91 patients (true positive rate or sensitivity of 26%). Conversely, if 24% were the correct figure, the individual who diagnosed it in 91% of the people would exhibit very poor specificity of, at best, 9 of 76 patients (true negative rate or specificity of 12%).

Although CXR is a highly valuable tool in the evaluation of asbestos-related disease, there are ongoing controversies regarding the sensitivity and specificity of the plain film in diagnosing asbestos-related disorders. Autopsy series indicate that at least 60% of **pleural plaques** may be overlooked using chest radiographs. Conversely, such series indicate that up to 20% of plaques are false positive. The significance of visceral pleural thickening and the definition and positive predictive value of diffuse pleural thickening as they relate to asbestos exposure are unresolved issues. Data suggest that the CXR may fail to reflect significant asbestosis in 10% to 20% of cases. On the other hand, the presence of overlying pleural abnormalities as well as technical factors may contribute to overreading of interstitial disease. Data on the rate of false positive readings for asbestosis are limited. In practice, an ILO radiographic reading system of profusion less than 1/0 implies that the diagnosis is unlikely.  

**High-resolution CT (HRCT)**

HRCT of the chest is better than chest radiographs for the evaluation of asbestosis. The sensitive and specificity increased to more than 95%. Even if the sensitivity and specificity is quite increased, the positive predictive value of the HRCT scan alone would be only 50% if the prevalence of asbestosis were 5%, and 37% if the prevalence were 3%.

Recent study in German in a cohort of 636 asbestos-exposed subjects found more often ‘‘positive’’ parenchymal and pleural findings in the HRCT scans as compared to the X-rays and conclude HRCT scans to be superior to CXR in recognizing manifest lung and pleura alterations at an early stage as in figure 3.5. The inter-observer variability, however, did not differ between CXR and HRCT in this study. This was probably due to the only discrete asbestos-related lung or pleura alterations of this cohort and to the unfamiliar CT classification.  

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Pitchaya Phakthongsuk, Occupational Health Unit, Community Medicine Department, Faculty of Medicine, Prince of Songkla University, Songkhla province, Thailand  

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Fig 3.6 Parenchymal and pleural positive/borderline findings of CXR and CT scans (CXR: positive s/t/u C 1/1; borderline s/t/u 1/0; HRCT: positive s0/t0/u0 C 1; borderline s0/t0/u0 = 1/0)

Regarding lung cancer, low-dose CT play important role. Recent study suggested the superior sensitivity of low-dose CT of the chest compared with conventional CXR for lung cancer according to the size of detected nodules. This 2-year screening trial consisted of biennial CXR and chest CT among 972 subjects aged 50-75 years at the date of recruitment and had worked in various professions dominated by asbestos-based textiles, friction lining, metallurgy and naval construction. Altogether 24 cases of bronchopulmonary cancer were diagnosed. The sensitivity of CXR was only 33% while that of CT was 83%, regarding that lesions measuring over 2 mm in diameter being considered as suspect. The specificity of CXR was 95% while that of CT was 78%. The detected primary bronchopulmonary cancers according to histological type, staging and clinical presentation under study was shown in table 3.16.

Table 3.16 the detected primary brochopulmonary cancers according to histological type, staging and clinical presentation

<table>
<thead>
<tr>
<th>Histological type</th>
<th>R− Sc− (n)</th>
<th>R+ Sc+ (n)</th>
<th>R− Sc+ (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epidermoid carcinoma</td>
<td>5</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Adenocarcinoma</td>
<td>5</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>Anaplastic small cell cancer</td>
<td>0</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Large-cell neuro-endocrine carcinoma</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Carcinoid</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Stage</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IA</td>
<td>5</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>IB</td>
<td>1</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>IIA</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>IIB</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>III</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>IIIA</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>IV</td>
<td>2</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Stage yet to be confirmed</td>
<td>2</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Clinical characteristics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Symptomatic</td>
<td>0</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>Asymptomatic</td>
<td>12</td>
<td>8</td>
<td>0</td>
</tr>
</tbody>
</table>

R- negative CXR, R+ positive CXR; Sc- negative low-dose CT, Sc+ positive low-dose CT

The receiver operating characteristic curve (ROC) performed of both CXR and CT according to the suspected mass diameter was shown in figure 3.6.

Figure 3.6 False positive (1-specificity) vs. true positive rate (sensitivity) of CXR and low-dose CT according to suspected pulmonary nodules.
Disease surveillance

Disease surveillance should be considered for individuals or groups of workers with previous or current asbestos exposure. The majority of previously exposed are found among the general population.

There are no specific international guidelines for recommended asbestos-related disease surveillance. Thus establishing a surveillance program is presently based on an appropriate evaluation of the particular situation. Individuals with current asbestos exposure or previous estimated exposure to or greater than 25 fibre/cm$^3$–years may be included. The ILO classification of radiographs, standard respiratory questions and lung function tests should be included. Surveillance can be repeated annually or at other reasonable intervals.

Due to the powerful biological interaction between cigarette smoking and asbestos, it is imperative that smoking cessation be strongly encouraged among asbestos-exposed workers as well as ex-workers previously exposed. Transferring of workers with more than 25 fibre/cm$^3$-years exposure to non-exposed work areas should be considered.
Bibliography
1. Diagnosis and initial management of nonmalignant diseases related to asbestos. Am J Respir Crit Care Med 2004;170:691-715.


4 Tertiary prevention: limit disease progression and disability

4.1 Patient notification

The objective of patient notification is to inform patient of work-related illness, to report the case to appropriate authority as occupational disease, as required by law and to guided the patient for their rights on compensation.

*The ILO Convention no. 155 and Recommendation no. 164* calls for action in essential areas pertaining to occupational health and safety implementation, namely for the formulation, implementation and periodical review of a national occupational health policy; the full participation at all levels of employers, workers and their respective organizations, as well as other stakeholders. These ILO convention and recommendation provide a blueprint for setting up and implementing comprehensive national occupational safety and health (OSH) systems based on prevention and continuous improvement including patient notification as follows:

Conventions: C155 Occupational Safety and Health Convention, 1981, III. Action at the national level, article 11(c) has stated as shown1.

> c) the establishment and application of procedures for the notification of occupational accidents and diseases, by employers and, when appropriate, insurance institutions and others directly concerned, and the production of annual statistics on occupational accidents and diseases.


> II. SYSTEMS FOR RECORDING AND NOTIFICATION
> Article 2
> The competent authority shall, by laws or regulations or any other method consistent with national conditions and practice, and in consultation with the most representative organizations of employers and workers, establish and periodically review requirements and procedures for:
> (a) the recording of occupational accidents, occupational diseases and, as appropriate, dangerous occurrences, commuting accidents and suspected cases of occupational diseases; and
> (b) the notification of occupational accidents, occupational diseases and, as
appropriate, dangerous occurrences, commuting accidents and suspected cases of occupational diseases.

Article 3
The requirements and procedures for recording shall determine:
(a) the responsibility of employers:
   (i) to record occupational accidents, occupational diseases and, as appropriate, dangerous occurrences, commuting accidents and suspected cases of occupational diseases;
   (ii) to provide appropriate information to workers and their representatives concerning the recording system;
   (iii) to ensure appropriate maintenance of these records and their use for the establishment of preventive measures; and
   (iv) to refrain from instituting retaliatory or disciplinary measures against a worker for reporting an occupational accident, occupational disease, dangerous occurrence, commuting accident or suspected case of occupational disease;
(b) the information to be recorded;
(c) the duration for maintaining these records; and
(d) measures to ensure the confidentiality of personal and medical data in the employer's possession, in accordance with national laws and regulations, conditions and practice.

Article 4
The requirements and procedures for the notification shall determine:
(a) the responsibility of employers:
   (i) to notify the competent authorities or other designated bodies of occupational accidents, occupational diseases and, as appropriate, dangerous occurrences, commuting accidents and suspected cases of occupational diseases; and
   (ii) to provide appropriate information to workers and their representatives concerning the notified cases;
(b) where appropriate, arrangements for notification of occupational accidents and occupational diseases by insurance institutions, occupational health services, medical practitioners and other bodies directly concerned;
(c) the criteria according to which occupational accidents, occupational diseases and, as appropriate, dangerous occurrences, commuting accidents and suspected cases of occupational diseases are to be notified; and
(d) the time limits for notification.

Article 5
The notification shall include data on:
(a) the enterprise, establishment and employer;
(b) if applicable, the injured persons and the nature of the injuries or disease; and
(c) the workplace, the circumstances of the accident or the dangerous occurrence and, in the case of an occupational disease, the circumstances of the exposure to health hazards

In addition, the database of labour legislation of ILO member states in the English and Dutch-speaking Caribbean also provided their legislations on patient
notifications available online. Some examples of legislations on this source were shown in the box below.

Example 1: Barbados
Accidents and Occupational diseases Notification
chapter 338, Sections 5

5. Notification of occupational diseases and other diseases.
5. (1) Every registered medical practitioner attending on or called in to visit a patient whom he believes to be suffering from any occupational disease contracted in the course of his employment as a worker shall, unless such a notice has been previously sent, forthwith send addressed to the Chief Labour Officer a notice stating the name and full postal address of the patient and the disease from which, in the opinion of such medical practitioner, the patient is suffering and the name and address of the place at which, and of the employer by whom, he is or was last employed.

5. (2) Any registered medical practitioner who fails to send any notice in accordance with the requirements of this section shall be guilty of an offence against this Act and liable to a fine of ten dollars.

5. (3) Any employer who believes or suspects, or has reasonable grounds for believing or suspecting, that a case of occupational disease has occurred among the workers employed by him shall forthwith send written notice of such case in the form, and accompanied by the particulars, set out in the Second Schedule to the Chief Labour Officer and to the Chief Medical Officer, and the provisions of this Act with respect to the notification of accidents shall apply to any such case in like manner as to any such accident as is mentioned in those provisions.

5. (4) The Minister may, as respects any class or description of place where workers are employed, by regulations, apply the provisions of this section to any disease other than an occupational disease.

Example 2: Republic of Trinidad and Tobago
Occupational Safety and Health Act, 2004
Act No. 1 of 2004, Part 5, Section 48

Notification of occupational diseases
48. (1) Where a medical practitioner who, having attended to a patient, forms the opinion that the patient is suffering from an occupational disease contracted in any
industrial establishment or in the course of his employment, he shall within forty-eight hours of having formed that opinion send to the Chief Medical Officer a notice stating the disease from which the medical practitioner is of the opinion that the patient is suffering and the industrial establishment in which the patient is and was last employed.

48. (2) The Chief Medical Officer shall send forthwith to the Chief Inspector any notice that he receives under subsection (1).

48. (3) If an employer is advised by or on behalf of an employee that the employee suffers from a disease referred to in Schedule 1, he shall give notice in writing to the Chief Inspector within four days of being so advised.

48. (4) Where a notice is sent to the Chief Inspector under this section, he shall arrange, within two weeks of having received the notice, for a medical inspector to investigate and submit to him a report on the case of occupational disease referred to in the notice within two weeks.

48. (5) The Chief Inspector, upon receiving the report referred to in subsection (3), shall conduct the necessary enquiries.

48. (6) Every employer who contravenes subsection (3) commits an offence and is liable on summary conviction to a fine of five thousand dollars and to imprisonment for three months.

48. (7) Every medical practitioner who contravenes subsection (1) commits an offence and is liable, on summary conviction, to a fine of five thousand dollars, and to imprisonment for three months if it is proven that he ought reasonably to have formed the opinion that the patient was suffering from an occupational disease contracted in an industrial establishment or in the course of his employment.

Regarding patient notification, ICOH Scientific Committee for Respiratory Disorders on Secondary prevention: early diagnosis and treatment suggested two points as follows:

1. Inform the patient about the disease
   The patient should be fully informed about the disease and its prognosis. In the case of asbestosis, survival following the diagnosis varies with the stage of the
disease and accompanying conditions. Since the disease often requires decades to develop, there should be no time limit on recognition of the disease and qualification for compensation. The prognosis for mesothelioma is more predictable. Survival past five years is uncommon. Because mesothelioma in the absence of asbestos exposure is extremely rare, recognition of mesothelioma should be accepted grounds for qualification for compensation in every case.

2. Report the disease

Systems should be in place to report the disease to the appropriate authorities and public health registries, and promote its inclusion in death certificates. Information captured by registries, on the other hand, should guide timely and appropriate interventions to support disease prevention initiatives.

4.2 Impairment and disability assessment

4.2.1 Definition

According to the World Health Organization (WHO), impairment refers to "any loss or abnormality of psychological, physiological, or anatomical structure or function". Impairment is assessed by medical means after diagnosis has been made and appropriate treatment given.

It is also important to recognize that “no impairment” is not an absolute and could vary with age, sex and other factors such as vision and hearing. Interpretation of “no impairment” that is too strict can result in overestimation the degree of impairment.

Disability refers to any resulting alteration in the individual's capacity to perform activities. It was defined by the WHO as “any restriction or lack of ability to perform any activity within the range considered normal for a human being”. The American Medical Association (AMA) defined disability as an “alteration of an individual's capacity to meet or perform personal, social, or occupational demands or statutory or regulatory requirements because of an impairment”. ATS’s definition is less specific that “impairment” is purely medical concept and that disability is the total effect of the impairment on the person’s life.

Whereas impairment evaluation is a medical perspective, disability assessment is a legal one. It is of note that impairment is not necessarily a disability. In assessing disability, the extent of a person’s impairment has to be judges in the context of the job function. Though the degree of impairment frequently correlates
with the degree of disability, it is not always the case. The classic example of this is the loss of the fifth finger of the non-dominant hand. Under the typical impairment rating system, the loss of this finger for the average person would be associated with a very disability of the whole person. For a concert pianist, this small impairment would be associated with significant disability, particularly in the context of work activities.

The disease should be objectively evaluated. Standard lung function testing should be performed. Impairment should be evaluated according to an appropriate standardized severity scale. Chest radiographs should be classified with ILO´s standard radiographs adding the International Classification of HRCT for Occupational and Environmental Respiratory Disease (ICOERD) when appropriate. The ILO classification contributes to making the diagnosis and is used to classify disease stage.

### 4.2.2 Impairment/Disability assessment

#### i) Diagnostic approach for impairment/disability

The impairment rating itself is considered a part of what should be a comprehensive medical evaluation as shown in table 3.1.

The physician must first fully understand the purpose and the requirements of the program for which the evaluation is being conducted.

The initial goal of the impairment evaluation should be to confirm the medical diagnosis using a thorough, detailed patient history, physical examination, and review of diagnostic testing results that established the diagnosis. The diagnosis should be clearly stated, along with extrapulmonary conditions that may be contributory to symptoms, limitations in ADLs, and/or impairment.

A statement of maximum medical improvement (MMI) is often required.

Factors important to the impairment rating itself include items from history, physical examination, and diagnostic testing results that reflect disease severity, including impact on normal ADLs, and current treatment requirements. The physician may be asked to make a statement on causation or apportionment to the patient’s occupation. An outline of reasonably anticipated future medical course and treatment requirements should be given (Table 4.1).
Table 4.1 Clinical approaches for impairment rating

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
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<tbody>
<tr>
<td>1.</td>
<td>Clear understanding of the rules and specific requirements of the program under which the individual is being evaluated.</td>
</tr>
<tr>
<td>2.</td>
<td>Complete medical history</td>
</tr>
<tr>
<td></td>
<td>a. Complete occupational and environmental exposure history</td>
</tr>
<tr>
<td></td>
<td>b. Limitations in activities of daily living (ADLs)</td>
</tr>
<tr>
<td>3.</td>
<td>Physical examination</td>
</tr>
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<td>4.</td>
<td>Diagnostic examination</td>
</tr>
<tr>
<td></td>
<td>a. Test that establish the diagnosis</td>
</tr>
<tr>
<td></td>
<td>b. Tests that identify extra-pulmonary conditions contributing to impairment</td>
</tr>
<tr>
<td></td>
<td>c. Results used in the assessment of impairment</td>
</tr>
<tr>
<td></td>
<td>i. Pulmonary function tests – spirometry, single-breath diffusing capacity (DL_CO)</td>
</tr>
<tr>
<td></td>
<td>ii. Cardiopulmonary exercise test -CPET (when indicated)</td>
</tr>
<tr>
<td></td>
<td>iii. Arterial blood gas measurement (when indicated)</td>
</tr>
<tr>
<td>5.</td>
<td>Diagnosis - assessment of causation and its relationship to work (when indicated)</td>
</tr>
<tr>
<td>6.</td>
<td>Impairment assessment</td>
</tr>
<tr>
<td></td>
<td>a. Statement of maximum medical improvement (MMI)</td>
</tr>
<tr>
<td></td>
<td>b. Impairment rating</td>
</tr>
<tr>
<td></td>
<td>c. Ability to work/work restrictions (when indicated)</td>
</tr>
<tr>
<td></td>
<td>d. Apportionment (if requested)</td>
</tr>
<tr>
<td></td>
<td>e. Future medical treatment</td>
</tr>
</tbody>
</table>

Notes:
Diffusion capacity of the lung for carbon monoxide (DL_CO) or Transfer factor (TL_CO) or is a test measuring the extent to which oxygen passes from the air sacs of the lungs into the blood. After a single breath of carbon monoxide inhaled, the partial pressure difference between inspired and expired carbon monoxide is measured. This test demonstrates gas uptake by the capillaries that is less dependent on cardiac output.

ii) Respiratory diagnostic methods for impairment

Respiratory impairment can be objectively measured through several tests such as spirometry, measuring the carbon monoxide diffusing capacity (DL_co) or transfer factor (TL_CO), the arterial blood gas analysis (ABGA) and the cardiopulmonary exercise test (CPET).

The disability in asbestos-related disease requires that chest x-rays (CXR) be read by a National Institute of Occupational Safety and Health (NIOSH) certified B-reader in United States and AIRPneumo in Asia which both were classified
according to the International Labour Organization's (ILO's) classification system\(^7\). Differentiation of benign pleural complications such as hyaline and calcified plaques, acute pleuritic reactions, and diffuse pleural fibrosis from each other and from parenchymal fibrosis is largely dependent on CXR. The pattern of calcification in plaques is characteristic and both hyaline and calcified plaques can usually be well discriminated.

Asbestos related parenchymal fibrosis is a well recognized cause of disability for which compensation can be claimed.

Circumscribed pleural thickening or pleural plaques have little effect on lung function and seldom cause disability, whereas diffuse pleural thickening, particularly when extensive and bilateral, causes functional impairment and disability (7). The British study aimed to find the effect of diffuse pleural thickening on PFT. This study use costophrenic angle and the extent of the pleural thickening on the chest wall in CXR for scoring as:

a) For CPA scored 1 or 0 as presence or absence of costophrenic angle obliteration and

b) extent of pleural thickening on chest wall scored 1, 2 and 3 when 1 = if the thickening extended for less than 25% of the total height of the lung; 2 = if it was 25-50%; 3 = if it was greater than 50%.

This score then gives a maximum of 4 for each side of the chest and of 8 for each film. Scores above 4 imply bilateral disease but some men with scores below 4 also had bilateral disease of lesser severity. The main result of this study demonstrated that diffuse pleural thickening, particularly when extensive and bilateral, causes functional impairment and disability as shown in table 4.2\(^8\).

### Table 4.2 Radiographic scores and results of lung function tests

<table>
<thead>
<tr>
<th>Radiographic score</th>
<th>n</th>
<th>Lung function values (mean % predicted)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>FEV(_1)</td>
</tr>
<tr>
<td>1-4</td>
<td>15</td>
<td>90</td>
</tr>
<tr>
<td>5-6</td>
<td>12</td>
<td>87</td>
</tr>
<tr>
<td>7-8</td>
<td>10</td>
<td>72</td>
</tr>
</tbody>
</table>

FEV\(_1\), forced expiratory volume at 1 second; FVC, forced vital capacity; TLC, total lung capacity; RV, residual volume; TLCO, transfer factor

Of note is that the CXR interpretation serves, however, mainly to raise suspicion for diagnosis of asbestos-related disease not for disability assessment. None of the disability rating systems uses CXR findings in the assessment of disability because the variability in the extent of radiographic findings and the degree of physiologic impairment.

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Pitchaya Phakthongsuk, Occupational Health Unit, Community Medicine Department, Faculty of Medicine, Prince of Songkla University, Songkhla province, Thailand
**Pulmonary function test (PFT),** on the other hand, is the most important test to determine impairment for asbestos-related pulmonary diseases. Both the ATS and the AMAGuides, specify the use of forced vital capacity (FVC), FEV₁, FEV₁/FVC, and single-breath diffusing capacity (DL_{CO}).

The ATS specifies that individuals should be evaluated only after they have received an accurate diagnosis and while they are receiving optimal therapy which is consistent with the AMA Guides’ requirement.

Both ATS and the AMA Guides emphasize only using test results that meet the quality standards defined in the latest ATS statement “Standardization of lung function testing.”

American Thoracic Society guidelines for evaluation of impairment or disability recommends that impairment due to most lung diseases be rated based on PFT results. The results of the ATS impairment system, based on PFTs, places individuals into four impairment categories associated ability to perform job demands as shown in table 4.3. ATS assessment, however, does not apply to use in compensation systems and not derived percentage of whole-person impairment as AMA guidelines.⁹⁻¹².
Table 4.3  American Thoracic Society impairment categories, with corresponding description of ability to perform job demands.\textsuperscript{11}

<table>
<thead>
<tr>
<th>Category</th>
<th>Criteria</th>
<th>Ability to Perform Job Demands</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>FVC $\geq$ 80% of predicted, and FEV\textsubscript{1} $\geq$ 80% of predicted, and FEV\textsubscript{1}/FVC $\geq$ 75%, and DL\textsubscript{CO} $\geq$ 80% of predicted</td>
<td>-</td>
</tr>
<tr>
<td>Mildly impaired</td>
<td>FVC 60%-79% of predicted, or FEV\textsubscript{1} 60%-79% of predicted, or FEV\textsubscript{1}/FVC 60%-74%, or DL\textsubscript{CO} 60%-79% of predicted</td>
<td>Usually not correlated with diminished ability to perform most jobs</td>
</tr>
<tr>
<td>Moderately impaired</td>
<td>FVC 51%-59% of predicted, or FEV\textsubscript{1} 41%-59% of predicted, or FEV\textsubscript{1}/FVC 41%-59%, or DL\textsubscript{CO} 41%-59% of predicted</td>
<td>Progressively lower levels of lung function correlated with diminishing ability to meet the physical demands of many jobs</td>
</tr>
<tr>
<td>Severely impaired</td>
<td>FVC $\leq$ 50% of predicted, or FEV\textsubscript{1} $\leq$ 40% of predicted, or FEV\textsubscript{1}/FVC $\leq$ 40%, or DL\textsubscript{CO} $\leq$ 40% of predicted</td>
<td>Unable to meet the physical demands of most jobs, including travel to work</td>
</tr>
</tbody>
</table>

DL\textsubscript{COsb}, single-breath diffusing capacity; FEV\textsubscript{1}, forced expiratory volume in 1 second; FVC, forced vital capacity.

American Medical Association (AMA) guides, the fifth edition is the widely used methods for calculating a percentage of permanent partial impairment of the whole person. The recent sixth edition of AMA guides has been available since 2008 but has not yet adopted in the US compensation systems. Thus, the AMA Guides, fifth edition, delineate methodology similar to ATS by which to place individuals into one of four impairment categories, as shown in table 4.4 and also provide an associated range of percentage whole-person impairment as:

- Class 1 impairment is equal to 0% whole-person impairment,
- Class 2 impairment ranges from 10% to 25% impairment,
- Class 3 ranges from 26% to 50% impairment, and
- Class 4 ranges from 51% to 100% whole-person impairment.
Table 4.4 American Medical Association classification of respiratory impairment

<table>
<thead>
<tr>
<th>Class 1, 0%–9%: No impairment of the whole person</th>
<th>Class 2, 10%–25%: Mild Impairment of the Whole Person</th>
<th>Class 3, 26%–50%: Moderate impairment of the Whole Person</th>
<th>Class 4, 51%–100%: Severe Impairment of the Whole Person</th>
</tr>
</thead>
<tbody>
<tr>
<td>FVC ≥ lower limit of normal*, and FEV₁ ≥ lower limit of normal†, and FEV₁/FVC ≥ lower limit of normal, and DŁCO ≥ lower limit of normal, or VO₂max &gt; 5 mL/kg/min</td>
<td>FVC between 60% and lower limit of normal or FEV₁ between 60% and lower limit of normal or VO₂max between 20-25 mL/kg/min</td>
<td>FVC between 51% and 59% of predicted, or FEV₁ between 41% and 59% of predicted, or VO₂max between 15-20 mL/kg/min</td>
<td>FVC ≤ 50% of predicted, or FEV₁ ≤ 40% of predicted, or DŁCO ≤ 40% of predicted, or VO₂max &lt; 15 mL/kg/min</td>
</tr>
</tbody>
</table>

DLCO, Diffusing Capacity for Carbon monoxide; FVC, Forced Vital Capacity; VO₂max, Maximal Oxygen Consumption.

*Lower limit of normal FVC for men is predicted normal FVC 1.115 L; Lower limit of normal FVC for women is predicted normal FVC 0.676 L

†Lower limit of normal FEV₁ for men is predicted normal minus 0.842 L; Lower limit of normal FEV₁ for women is predicted normal minus 0.561 L

‡Lower limit of normal DLCO from men is predicted normal 8.2 mL/min/mm Hg; Lower limit of normal DLCO for women is predicted normal 5.74 mL/min/mm Hg

Maximal voluntary ventilation (MVV) and FEF_{25-75} are not recommended for use by ATS or the AMA Guides in impairment evaluation.

Although ATS defines a restrictive ventilatory defect as a reduction in total lung capacity (TLC) below the fifth percentile of the predicted value, with a normal FEV₁/FVC ratio. TLC is not included in the standard rating criteria in either the ATS or the AMA Guides.

Regarding Cardiopulmonary exercise testing (CPET), neither the ATS nor the AMA Guides recommend a routine use of CPET in the determination of
permanent impairment, but do note that maximal exercise test results, specifically \( \text{VO}_2\text{max} \), should be used in specific circumstances.

Notes: CPET is an objective method of evaluating both cardiac and pulmonary function. Cardiac function is evaluated in terms of aerobic capacity and respiratory function is evaluated by dynamic flow volume loops and Ventilation-Perfusion (VQ) measurements actually performed during exercise.

The subject is exercised preferably on a bicycle ergometer or failing that a treadmill. During exercise he breathes through a mouthpiece which is in fact a miniaturized pressure differential pneumotachygraph. The inspired and expired gas is continuously sampled and both oxygen uptake and carbon dioxide elimination is computed.

Not only is maximal aerobic capacity calculated but also the point during exercise where anaerobic metabolism is used to supplement aerobic metabolism as a source of energy. That point is very accurately measured via gas exchange data and is termed the anaerobic threshold or AT.

ATS recommended that CPET results be used in cases where the static PFTs do not reflect the true impairment present. For example, studies have demonstrated that alveolar-arterial oxygen pressure difference during exercise is a better reflection of impairment due to gas exchange abnormality than DL\(_{CO}\). By the way, there are no details provided on how these criteria should be met for disability and the AMA Guides do not delineate a specific methodology regarding CPET in term of %permanent partial impairment of the whole person\(^{14}\).

To determine work capacity, and thus impairment, ATS requires use of \( \text{VO}_2\text{max} \) to place workers into one of three categories of work tolerance, assuming that workers can comfortably perform sustained work at 40% of \( \text{VO}_2\text{max} \) and that \( \text{VO}_2 \) requirements of the workers’ job are known in table 4.5 and 4.6 respectively\(^{11,15}\).
Table 4.5 American Thoracic Society Interpretation of Exercise Test Results Using VO\(_2\)\(_{\text{max}}\)

<table>
<thead>
<tr>
<th>VO(<em>2)(</em>{\text{max}})</th>
<th>METS</th>
<th>Estimated work ability</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥25 mL/kg/min</td>
<td>≥7.1</td>
<td>Continuous heavy exertion throughout an 8-hour day in all but the most physically demanding jobs</td>
</tr>
<tr>
<td>15–25 mL/kg/min and Metabolic demands of the work ≤ VO(<em>2)(</em>{\text{max}})</td>
<td>4.4-7.0</td>
<td>Able to perform that job comfortably, assuming there are no frequent or extended periods (5 min) requiring exertion substantially &gt;40% VO(<em>2)(</em>{\text{max}})</td>
</tr>
<tr>
<td>≤ 15 ml/kg/min</td>
<td>≤4.3</td>
<td>Unable to perform most jobs because they would be uncomfortable traveling back and forth</td>
</tr>
</tbody>
</table>

METS, the energy demand in liters of oxygen consumption per minute/basal oxygen consumption (3.5 mL/kg/min); VO\(_2\)\(_{\text{max}}\), maximal oxygen consumption.

Table 4.6 Energy Requirements Expressed as Oxygen Uptake (VO\(_2\)) of Various Types of Work

| Level of work | VO\(_2\) (Approximate) | |
|---------------|------------------------|
| | mL/kg/min | L/min | METS |
| Light to moderate work (sitting) | | |
| Clerical | 5.6 | 0.42 | 1.6 |
| Using repair tools | 6.3 | 0.47 | 1.8 |
| Operating heavy equipment | 8.8 | 0.66 | 2.5 |
| Heavy truck driving | 12.6 | 0.95 | 3.0 |
| Moderate work (standing) | | |
| Light work, own pace | 8.8 | 0.66 | 2.5 |
| Janitorial work | 10.5 | 0.79 | 3.0 |
| Assembly line (lifts ≥ 45 lb) | 12.3 | 0.92 | 3.5 |
| Paper hanging | 14.0 | 1.05 | 4.0 |
| Standing and/or walking (arm work) | | |
| General heavy labor | 15.8 | 1.19 | 4.5 |
| Using heavy tools | 21.0 | 1.58 | 6.0 |
| Lift and carry 60–80 lb | 26.2 | 1.97 | 7.5 |

METS, the energy demand in liters of oxygen consumption per minute (basal oxygen consumption 3.5 mL/kg/min); VO\(_2\)\(_{\text{max}}\), maximal oxygen consumption.
Major limitations to CPET include:

a. little published data that substantiate its use;
b. heterogeneous methods of assessing maximal oxygen uptake;
c. the fact that actual work performed by workers with the same job title can vary markedly from employer to employer or among employees with differing seniority at the same employer;
d. the questionable relationship between exercise tolerance on the treadmill or bicycle and performance on the job;
e. the lack of consideration of modifying factors such as the need to talk or use personal protective equipment (PPE) while performing the work.

The AMA Guides, fifth and sixth editions, both consider a VO$_2$max greater than 25 mL/kg/min to place one into the lowest (least) category of impairment (class 1 and class 0, respectively), and a VO$_2$max less than 15 mL/kg/min to place one into the highest (greatest) category of impairment (class 4).

The study of 38 asbestosis subjects report that radiographic profusion scores, number of affected lung parenchyma zones on CXR, categorizing according to the ILO radiographic classification of pneumoconiosis, correlated significantly with the percentage predicted values of DL$_{CO}$, FVC, TLC, arterial oxygen desaturation but not VO$_2$max as shown in table 4.7 and 4.8$^{16}$.

**Table 4.7 Correlation (Pearson’s coefficient) between ILO score, lung function, and symptom score.**

<table>
<thead>
<tr>
<th>Profusion score</th>
<th>Number of zones affected</th>
<th>Opacity type “Y” over “S”</th>
<th>Pleural thickening</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV$_1$, % pred</td>
<td>-0.34*</td>
<td>-0.27</td>
<td>-0.19</td>
</tr>
<tr>
<td>FVC, % pred</td>
<td>-0.52***</td>
<td>-0.38*</td>
<td>-0.41**</td>
</tr>
<tr>
<td>FEV$_1$/FVC ratio</td>
<td>0.38*</td>
<td>0.23</td>
<td>0.16</td>
</tr>
<tr>
<td>TLC, % pred</td>
<td>-0.60****</td>
<td>-0.40*</td>
<td>-0.33*</td>
</tr>
<tr>
<td>DLCO, % pred</td>
<td>-0.63*****</td>
<td>-0.42**</td>
<td>-0.15</td>
</tr>
<tr>
<td>KCO, % pred</td>
<td>-0.34*</td>
<td>-0.17</td>
<td>0.05</td>
</tr>
<tr>
<td>A-a gradient</td>
<td>0.35*</td>
<td>0.27</td>
<td>-0.09</td>
</tr>
<tr>
<td>Symptom score</td>
<td>0.26</td>
<td>-0.06</td>
<td>0.22</td>
</tr>
</tbody>
</table>

FEV$_1$, force expiratory volume in 1 second; FVC, force vital capacity; TLC, total lung capacity; DLco, single breath diffuse capacity of carbon monoxide; KCO, alveolar volume; A-a gradient, alveolar-arterial oxygen gradient
Table 4.8 Correlation (Pearson’s coefficient) between ILO score and ventilator response to exercise

<table>
<thead>
<tr>
<th></th>
<th>Profusion</th>
<th>Number of zones affected</th>
<th>Opacity type “d” over “s”</th>
<th>Pleural thickening</th>
</tr>
</thead>
<tbody>
<tr>
<td>VO2max, % pred</td>
<td>-0.38*</td>
<td>-0.30</td>
<td>-0.33*</td>
<td>-0.26</td>
</tr>
<tr>
<td>Desaturation</td>
<td>0.54***</td>
<td>0.55***</td>
<td>0.46**</td>
<td>0.20</td>
</tr>
<tr>
<td>Ve at 1 l/min</td>
<td>0.64****</td>
<td>0.28</td>
<td>0.44**</td>
<td>0.12</td>
</tr>
<tr>
<td>Ve at 50% of pred VO2max</td>
<td>0.32</td>
<td>0.31</td>
<td>0.08</td>
<td>-0.25</td>
</tr>
<tr>
<td>Vd/Vt at VO2max</td>
<td>0.62****</td>
<td>0.33*</td>
<td>0.38*</td>
<td>0.20</td>
</tr>
</tbody>
</table>

* p<0.05; ** p<0.01; *** p<0.001; **** p<0.0001.

VO2max, maximal oxygen uptake; desaturation, arterial oxygen desaturation% measured with pulse oximetry; Ve, minute ventilation at an oxygen uptake of 1 litre per minute; Ve at 50%, minute ventilation at 50% of maximal oxygen uptake; Vd/Vt, physiologic dead space.

Arterial blood gas analysis (ABGA) is not used for impairment rating purposes on a routine basis. Resting arterial PO2 does not correlate with exercise capacity. As a result, arterial hypoxemia at rest is, by itself, not evidence of severe impairment in exercise tolerance. ATS recommends it only be used in “selected patients” under “rigidly controlled laboratory conditions,” and should be documented on at least two occasions separated by at least 4 weeks. They consider hypoxemia to be evidence of severe impairment only when accompanied by evidence of cor pulmonale. ABGA analysis was also considered to be a test infrequently indicated in the evaluation of impairment in the AMA Guides, Fifth Edition. It is not included in the Sixth Edition.

4.2.3 Some examples of pulmonary disability assessment
i) United States Social Security Administration (SSA)

The United States Social Security Administration (SSA) also provided the Disability Evaluation Under Social Security criteria for respiratory system under topic 3.06 pneumoconiosis the as shown in the box below.

Notes: SSA is an independent agency of the United States federal government that administers Social Security, a social insurance program consisting of retirement, disability, and survivors' benefits. The Social Security Administration was established by a law currently codified at 42 U.S. Code 901. To qualify for these benefits, most American workers pay Social Security taxes on their earnings; future benefits are based on the employees' contributions.
Pulmonary disability evaluation of US Social Security criteria

3.06 *Pneumoconiosis* (demonstrated by appropriate imaging techniques). Evaluate under the appropriate criteria in 3.02.

The documents on 3.02 is elaborated as follows:

3.02 Chronic pulmonary insufficiency

A. Chronic obstructive pulmonary disease due to any cause, with the FEV$_1$ equal to or less than the values specified in table I corresponding to the person's height without shoes.

The pulmonary function tables in 3.02 are based on measurement of standing height without shoes. If an individual has marked spinal deformities (e.g., kyphoscoliosis), the measured span between the fingertips with the upper extremities abducted 90 degrees should be substituted for height when this measurement is greater than the standing height without shoes.

### Table I

<table>
<thead>
<tr>
<th>Height without Shoes (cm)</th>
<th>Height without Shoes (inches)</th>
<th>FEV$_1$ ≤ (L.BTPS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>154 or less</td>
<td>60 or less</td>
<td>1.05</td>
</tr>
<tr>
<td>155-160</td>
<td>61- 3</td>
<td>1.15</td>
</tr>
<tr>
<td>61-165</td>
<td>64-65</td>
<td>1.25</td>
</tr>
<tr>
<td>6-170</td>
<td>66-67</td>
<td>1.35</td>
</tr>
<tr>
<td>171-175</td>
<td>68-69</td>
<td>1.45</td>
</tr>
<tr>
<td>176-180</td>
<td>70-71</td>
<td>1.55</td>
</tr>
<tr>
<td>181 or more</td>
<td>72 or more</td>
<td>1.65</td>
</tr>
</tbody>
</table>

or

B. Chronic restrictive ventilatory disease, due to any cause, with the FVC equal to or less than the values specified in Table II corresponding to the person's height without shoes.

The pulmonary function tables in 3.02 are based on measurement of standing height without shoes. If an individual has marked spinal deformities (e.g., kyphoscoliosis), the measured span between the fingertips with the upper extremities abducted 90 degrees should be substituted for height when this measurement is greater than the standing height without shoes.
<table>
<thead>
<tr>
<th>Height without Shoes (cm)</th>
<th>Height without Shoes (inches)</th>
<th>FVC ≤ (L,BTPS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>154 or less</td>
<td>60 or less</td>
<td>1.2</td>
</tr>
<tr>
<td>155-160</td>
<td>61-63</td>
<td>1.35</td>
</tr>
<tr>
<td>161-165</td>
<td>64-65</td>
<td>1.45</td>
</tr>
<tr>
<td>166-170</td>
<td>66-67</td>
<td>1.55</td>
</tr>
<tr>
<td>171-175</td>
<td>68-69</td>
<td>1.65</td>
</tr>
<tr>
<td>176-180</td>
<td>70-71</td>
<td>1.75</td>
</tr>
<tr>
<td>181 or more</td>
<td>72 or more</td>
<td>1.85</td>
</tr>
</tbody>
</table>

or

C. Chronic impairment of gas exchange due to clinically documented pulmonary disease. With:
1. Single breath DLCO of less than 10.5 ml/min/mm Hg or less than 40 percent of the predicted normal value. (Predicted values must either be based on data obtained at the test site or published values from a laboratory using the same technique as the test site. The source of the predicted values should be reported. If they are not published, they should be submitted in the form of a table or nomogram);

or

2. Arterial blood gas values of PO2 and simultaneously determined PCO2 measured while at rest (breathing room air, awake and sitting or standing) in a clinically stable condition on at least two occasions, three or more weeks apart within a 6-month period, equal to or, less than the values specified in the applicable table III-A or III-B or III-C:
### Table III-A
(Applicable at test sites less than 3,000 feet above sea level)

<table>
<thead>
<tr>
<th>Arterial PCO$_2$ (mm Hg) and Arterial PO$_2$ ≤ (mm Hg)</th>
<th>Arterial PCO$_2$ (mm Hg) and Arterial PO$_2$ ≤ (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>30 or below</td>
<td>65</td>
</tr>
<tr>
<td>31 . . . . .</td>
<td>64</td>
</tr>
<tr>
<td>32 . . . . .</td>
<td>63</td>
</tr>
<tr>
<td>33 . . . . .</td>
<td>62</td>
</tr>
<tr>
<td>34 . . . . .</td>
<td>61</td>
</tr>
<tr>
<td>35 . . . . .</td>
<td>60</td>
</tr>
<tr>
<td>36 . . . . .</td>
<td>59</td>
</tr>
<tr>
<td>37 . . . . .</td>
<td>58</td>
</tr>
<tr>
<td>38 . . . . .</td>
<td>57</td>
</tr>
<tr>
<td>39 . . . . .</td>
<td>56</td>
</tr>
<tr>
<td>40 or above</td>
<td>55</td>
</tr>
</tbody>
</table>

### Table III-B
(Applicable at test sites 3,000 through 6,000 feet above sea level)

<table>
<thead>
<tr>
<th>Arterial PCO$_2$ (mm Hg) and Arterial PO$_2$ ≤ (mm Hg)</th>
<th>Arterial PCO$_2$ (mm Hg) and Arterial PO$_2$ ≤ (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>30 or below</td>
<td>60</td>
</tr>
<tr>
<td>31 . . . . .</td>
<td>59</td>
</tr>
<tr>
<td>32 . . . . .</td>
<td>58</td>
</tr>
<tr>
<td>33 . . . . .</td>
<td>57</td>
</tr>
<tr>
<td>34 . . . . .</td>
<td>56</td>
</tr>
<tr>
<td>35 . . . . .</td>
<td>55</td>
</tr>
<tr>
<td>36 . . . . .</td>
<td>54</td>
</tr>
<tr>
<td>37 . . . . .</td>
<td>53</td>
</tr>
<tr>
<td>38 . . . . .</td>
<td>52</td>
</tr>
<tr>
<td>39 . . . . .</td>
<td>51</td>
</tr>
<tr>
<td>40 or above</td>
<td>50</td>
</tr>
</tbody>
</table>
Table III-C
(Applicable at test sites over 6,000 feet above sea level)

<table>
<thead>
<tr>
<th>Arterial PCO₂ (mmHg) and</th>
<th>Arterial PO₂ ≤ (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>30 or below .</td>
<td>55</td>
</tr>
<tr>
<td>31 . . . . .</td>
<td>54</td>
</tr>
<tr>
<td>3 . . . . . .</td>
<td>53</td>
</tr>
<tr>
<td>33 . . . . . .</td>
<td>52</td>
</tr>
<tr>
<td>34 . . . . . .</td>
<td>51</td>
</tr>
<tr>
<td>35 . . . . . .</td>
<td>50</td>
</tr>
<tr>
<td>36 . . . . . .</td>
<td>49</td>
</tr>
<tr>
<td>37 . . . . . .</td>
<td>48</td>
</tr>
<tr>
<td>38 . . . . . .</td>
<td>47</td>
</tr>
<tr>
<td>39 . . . . . .</td>
<td>46</td>
</tr>
<tr>
<td>40 or a . . . . . . . .</td>
<td>45</td>
</tr>
</tbody>
</table>

or

3. Arterial blood gas values of PO₂ and simultaneously determined PCO₂ during steady state exercise breathing room air (level of exercise equivalent to or less than 17.5 ml O₂ consumption/kg/min or 5 METs) equal to or less than the values specified in the applicable table III-A or III-B or III-C above.

Table IV
(Applicable only for evaluation cystic fibrosis)

<table>
<thead>
<tr>
<th>Height without Shoes (cm)</th>
<th>Height without Shoes (inches)</th>
<th>FEV₁ ≤ (L,BTPS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>154 or less</td>
<td>60 or less</td>
<td>1.45</td>
</tr>
<tr>
<td>155-159</td>
<td>61-62</td>
<td>1.55</td>
</tr>
<tr>
<td>160-164</td>
<td>63-64</td>
<td>1.65</td>
</tr>
<tr>
<td>165-169</td>
<td>65-66</td>
<td>1.75</td>
</tr>
<tr>
<td>170-174</td>
<td>67-68</td>
<td>1.85</td>
</tr>
<tr>
<td>175-179</td>
<td>69-70</td>
<td>1.95</td>
</tr>
<tr>
<td>180 or more</td>
<td>71 or more</td>
<td>2.05</td>
</tr>
</tbody>
</table>
or
3. Arterial blood gas values of PO$_2$ and simultaneously determined PCO$_2$ during steady state exercise breathing room air (level of exercise equivalent to or less than 17.5 ml O$_2$ consumption/kg/min or 5 METs) equal to or less than the values specified in the applicable table III-A or III-B or III-C above.

**ii) Korea**

In Korea, the diagnostic criteria are specified in the Handicapped-person Welfare Law enacted in 2003. A *pulmonary disability* can be diagnosed when the duration of the disease is more than one year and the impairment of the pulmonary function is fixed after 2 or more months of treatment, and there is a decrease of the forced expiratory volume for 1 second (FEV$_1$) on the PFT or there is hypoxemia on the ABGA at a resting state, as well as dyspnea is present. Of note is that only two indices, that is, the FEV1 and the partial pressure of oxygen in arterial blood (PaO$_2$), are used to evaluate pulmonary disability in Korea.

The decision for diagnosing pulmonary disability according to the implementing regulation of the Handicapped person Welfare Law 2003 are as follows: the disability has to be judged by pulmonary subspecialists, and more than a year had elapsed since the first diagnosis as related with the present state, and the disability is fixed enough to show no improvement even after continuous treatment of 2 months or more.

The criteria for the diagnosis of pulmonary disability are
1) the pulmonary disability persists in spite of sufficient medical treatment.
2) before the disability decision is made, there should be objective testing for the patient through
   i) the decision on the degree of dyspnea,
   ii) the chest radiography,
   iii) the PFT,
   iv) and the ABGA.

In addition, if necessary, computerized tomography (CT) of the chest, bronchoscopy, pulmonary exercise testing, ventilation-perfusion scanning of the lungs and pulmonary arteriography should be done for a more accurate diagnosis according to the diseases,

3) of the repetitive test results for more than 2 months, the lowest level is chosen to represent the disease.

Through the above standards, the grade class of the pulmonary disability is decided as follows:

Pulmonary Disability Class 1 - Those who feel the dyspnea, even while resting, enough to receive oxygen treatment due to the chronic respiratory
insufficiency, and whose FEV$_1$ is lower than 25% of the predicted value in the resting state or the PaO$_2$ without an oxygen supply is lower than 55 mmHg in the stable state of disease.

Pulmonary Disability Class 2 - Those who feel dyspnea even while moving in the house due to chronic respiratory insufficiency, and whose FEV$_1$ is lower than 30% of the predicted value in the resting state or the PaO$_2$ without an oxygen supply is lower than 60 mmHg in the stable state of disease.

Pulmonary Disability Class 3 - Those who feel dyspnea, even while walking on flat ground, due to chronic respiratory insufficiency, and whose FEV$_1$ is lower than 40% of the predicted value in the resting state or the PaO$_2$ without an oxygen supply is lower than 65 mmHg in the stable state of disease.

Regarding impairment/disability evaluation, *ICOH Scientific Committee for Respiratory Disorders on Secondary prevention: early diagnosis and treatment* suggested as shown:

The disease should be objectively evaluated. Standard lung function testing should be performed. Impairment should be evaluated according to an appropriate standardized severity scale. Chest radiographs should be classified with ILO’s standard radiographs adding the international HRCT classification (ICOERD) when appropriate. The ILO classification contributes to making the diagnosis and is used to classify disease stage.

### 4.2.4 Apportionment

When multiple disease processes are present that may contribute to respiratory impairment, the physician may be asked to apportion, or make a statement of the relative contribution of each disease process to the total impairment. This is usually performed in the context of workers’ compensation in an effort to limit the amount of the monetary award to that specifically attributed to the workplace exposure or event. It does not typically reduce medical treatment benefits or wage compensation. Unfortunately, the scientific basis for this level of precision is rarely present and thus must be acknowledged as arbitrary even if required by the entitlement system.

Cigarette smoking and its sequelae is the most common condition taken into account when considering apportionment of respiratory impairment. For example, much has been written about the difference in symptoms and physical limitations in smoking compared with nonsmoking asbestos workers, and the observation that
the most common cause of exercise limitation in one group studied was the cardiovascular system rather than the respiratory system.

Specific methods for apportionment have been proposed, but none has been validated scientifically or considered generally accepted. If objective evidence of prior impairment exists, such as diagnostic testing results performed before the work-related exposure or development of disease, some states will allow apportionment to be performed by subtracting the preexisting impairment from the current total impairment\textsuperscript{19-21}.

4.3 Compensation on asbestos-related diseases

\textit{i) United States}

ATS recommendation in 2004 suggested chest radiograph findings of opacities with an ILO profusion score of at least 1/0 are “consistent with” asbestosis and will be accepted for compensation purposes by programs such as the Department of Labor for that condition. Of note was that previous ATS recommendation in 1986 used the profusion scores of 1/1. If the opacities are small and irregular (classified as “s” and “t”) and are found predominantly in the middle and lower lobes or are found in conjunction with pleural plaques, these findings are highly consistent with a diagnosis of asbestosis\textsuperscript{22}.

No data available on amount of compensation for asbestos-related diseases.

\textit{ii) England}\textsuperscript{23,32}

\textit{Industrial injuries benefit}

Industrial injuries benefit is governed by legislation under the terms of the Social Security Act (1975). This Act specifies that to qualify for industrial injuries benefit the following criteria must be met:

1. The person must be suffering from a "prescribed disease."
2. The person suffering from the disease must have been employed at some time since 5 July 1948 in one of the "prescribed occupations"-that is, occupations prescribed for the disease in question.

\textit{Prescribe diseases}

The categories relating to disease caused by asbestos are:

Pneumoconiosis -Defined as fibrosis of the lungs due to silica dust, asbestos dust, or other dust. The expression includes the condition of the lungs known as dust reticulation.

Diffuse mesothelioma (disease No 44) -Defined as primary malignant neoplasm of the mesothelium of the pleura or the peritoneum.
Prescribed occupations

In the case of asbestos the relevant occupations are obvious. Officially they are those where there is working or handling of asbestos or any admixture of asbestos, including the manufacture or repair of asbestos textiles or other articles containing or composed of asbestos; the cleaning of any machinery or plant used in any of the foregoing operations and of any chambers, fixtures, and appliances for the collection of asbestos dust; substantial exposure to the dust arising from any of the foregoing operations.

To qualify for benefit under the Social Security Act of 1975, the exposure must be occupational in origin and must have occurred at some time since 5 July 1948.

If the occupational exposure occurred before July 1948, however, the workman may be able to claim benefit under the provisions of the Pneumoconiosis, Byssinosis, and Miscellaneous Diseases Benefit Scheme.

Diagnosis criteria for asbestosis

Clinically:
Asbestosis during life should be diagnosed on clinical grounds. Lung biopsy for compensation purposes alone cannot be justified. The following features are usually present when asbestosis is diagnosed.
(a) A history of exposure to asbestos.
(b) Bilateral basal crepitations that are fine in quality, persistent, predominantly end-inspiratory, and best heard anterolaterally at the bases.
(c) Radiological changes of diffuse interstitial fibrosis in the lower halves of the lung fields.
(d) Lung function changes showing evidence of restriction and impairment of gas transfer.

Histologically:
In certain circumstances, especially after lung resection for carcinoma, lung tissue may be available for histological examination. Ideally, sections as large as 3 cm should be examined, and after postmortem examination similar sections should be taken from each lobe. The International Union against Cancer (UICC) recommends that at least three sections shall be examined—one from each lobe, including one from the lingula.

Apart from the presence of asbestos bodies; the changes seen do not have any features to distinguish them from several other types of interstitial fibrosis and thus an association is assumed on the basis of a history of exposure.
Diagnosis criteria for mesothelioma

The diagnosis of mesothelioma should be considered on clinical grounds when someone who has been exposed to asbestos presents with an irregular pleural opacity with or without a pleural effusion. The interval between the time of first exposure and the appearance of the disease is normally long and usually from 20 to 40 years.

Confirmation of the diagnosis is rare from cytological examination of pleural fluid and tissue is usually required, which may be obtained by pleural biopsy or thoracotomy.

If the diagnosis is strongly suspected on clinical grounds, however, histological confirmation should perhaps wait until after death as spread of the tumour on to the chest wall along the biopsy track has been reported.

In cases of peritoneal mesothelioma, laparotomy or laparoscopy is usually necessary to exclude more treatable causes of ascites. Histological diagnosis may be difficult as mesotheliomas have features in common with adenocarcinomas and alveolar cell carcinomas.

Histological confirmation of the diagnosis is not necessary to establish the presence of the condition during life, but it is desirable after death.

Diagnosis criteria for other asbestos-related conditions

Asbestos bodies

Asbestos bodies can be found in the sputum of people exposed does not in itself indicate the presence of any disease process. Confirmation of their presence is not essential before an asbestos-related condition is diagnosed. Cases have occurred where asbestos bodies have been found in the sputum, and on the basis of this information alone the patient has been wrongly informed by doctors that he has asbestosis. If asbestos bodies are found a clinical examination, chest radiography, and possibly lung function tests are indicated to exclude the presence of related disease.

Asbestos-related pleural changes

The term pneumoconiosis, in this case asbestosis, refers only to the diffuse pulmonary fibrosis that results from exposure and makes no reference to asbestos-related pleural changes. Pneumoconiosis medical boards are bound by the definition of pneumoconiosis in the Social Security (1975) Act. The person with evidence of asbestos-associated pleural changes alone is not eligible for compensation.
Pleural plaques of the hyaline and calcified variety occur almost exclusively in the parietal pleura and rarely give rise to any significant respiratory disability. There is evidence, however, that diffuse pleural thickening that affects both the parietal and visceral pleura can cause significant lung restriction producing disability. The Industrial Injuries Advisory Council intends to take the earliest opportunity to examine this evidence, and any other evidence submitted to them, with a view to advising the Secretary of State for Social Services on the case for making diffuse pleural thickening eligible for industrial injuries compensation.

Carcinoma of the lung

Carcinoma of the lung in people who have been exposed to asbestos has not been classified as a "prescribed disease" and therefore is not eligible for compensation as such. This is another question earmarked for early consideration by the Industrial Injuries Advisory Council.

Nevertheless, carcinoma of the lung is recognised as an important complication of asbestosis. Pneumoconiosis medical boards therefore accept carcinoma of the lung as a consequence of asbestosis and increase the assessment of disablement to cover the effects of both the asbestosis and the carcinoma.

Procedure of claiming benefit

A claim for industrial injuries disablement benefit is made by completing form Bi (100) Pn available from the local department of health and human services (DHSS) office, the address of which may be obtained at the post office. Occasionally the claimant may need some help with completing the form, and usually this can be obtained from the trade union, a social worker, a relative, the general practitioner, or the doctor advising the patient to make the claim. Once completed the form should be returned to the same DHSS office.

The claim is determined by the insurance officer at the local social security office, and he has the responsibility of ensuring that the claim satisfies the conditions relating to past employment.

If the claim does not fulfill the necessary criteria regarding prescription the insurance officer will disallow the claim. There is the right of appeal to a local tribunal and finally to a social security commissioner.

If the claim is satisfactory, it is passed to the pneumoconiosis medical panel for the area.

Pneumoconiosis medical panels are based at Cardiff, Glasgow, London, Manchester, Newcastle upon Tyne, Sheffield, Stoke-on-Trent, and Swansea. Once a claim is received by the panel, radiography, lung function tests, and examination by a pneumoconiosis medical board are arranged. The pneumoconiosis medical board
consists of two doctors of the pneumoconiosis panel and acts as an independent adjudicating authority. Once the diagnosis has been made it then has the duty of assessing the resulting degree of disablement.

If the medical board does not diagnose pneumoconiosis the claim is disallowed by the insurance officer. The following possibilities may then arise.

(a) The claimant may have a right of appeal to a medical appeal tribunal.
(b) The claimant may make a further claim at any time.
(c) The medical board may review its decision at any time if it is satisfied that fresh evidence is available.

The medical appeal tribunal is composed of a lawyer (as chairman) and two independent chest consultants with experience in occupational chest diseases. A claimant may appeal to a tribunal either disputing the diagnosis or questioning the assessment of disablement provided that certain conditions are fulfilled. These at present are as follows:

(a) Diagnosis—An appeal in cases of pneumoconiosis may be made provided that the claimant has been examined on at least two occasions by a pneumoconiosis medical board and found not to be suffering from the disease. This condition is under review, however, and a person wishing to appeal is advised to consult the local social security office. In cases of diffuse mesothelioma there is an unrestricted right of appeal on diagnosis.

(b) Assessment of disablement—At least two years must have elapsed since the case was referred to the medical board which diagnosed the disease and the period of assessment extends beyond those two years.

The two types of industrial injuries benefit available in cases of pneumoconiosis and mesothelioma are disablement benefit and death benefit.

Disablement benefit

In the case of these diseases benefit is paid as a weekly pension related to the assessment of the degree of disablement resulting from the disease. This type of payment is slightly different from that payable for other occupational diseases, where, if the disability is assessed at under 20% a gratuity (lump sum) rather than a pension is payable.

Assessment of disablement

Once it has made the diagnosis the pneumoconiosis medical board has to assess the degree of disablement. The assessment is made by comparing the condition of the claimant as a result of the disease with the condition of a normal healthy person of the same age and sex, taking into consideration the history, the
clinical and radiological examination, and the results of the full lung function tests.

Once the diagnosis has been made, there is a special provision that enables the claimant to receive a pension at the rate of at least 10% even though he does not appear to be appreciably disabled.

Normally, the assessment takes into account only the disablement resulting from the prescribed disease. Nevertheless, the effects of other conditions, notably chronic bronchitis and emphysema, may be taken into consideration in so far as they have made the pneumoconiosis more disabling. Special provisions operate if the assessment resulting from pneumoconiosis alone is 50% or more, when the full disablement arising is taken into account.

When pulmonary tuberculosis complicates pneumoconiosis the effects of tuberculosis are reckoned to be those of pneumoconiosis. The assessment is usually provisional and for a limited period of one or two years. The claimant is then re-examined and his disability reassessed.

Increase of disablement benefit

A person entitled to disablement benefit may qualify for one or more of the following increases.

- **Special hardship allowance** if, as a result of the disease, he is unable to continue in his regular job or to do work of an equivalent standard.
- **Constant attendance allowance** if his disablement is assessed at 100% and the disease handicaps him so seriously that he needs constant care and attention.
- **Exceptionally severe disablement allowance** if he is exceptionally severely disabled and already entitled to constant attendance allowance at a rate above the normal maximum, and if the need for such attendance is likely to be permanent.
- **Unemployability supplement** if, due to the disease, he is likely to be permanently unable to work or unable to earn more than a limited amount in a year.
- **Hospital treatment allowance** if he goes into hospital for treatment for the disease.

Leaflet NI 6 gives details of these increases and also how to claim them. A person entitled to disablement benefit may in addition claim sickness or invalidity benefit if he is incapable of work or a retirement pension if he is over pensionable age and retired.

Death benefit

Death benefit may be paid to a widow or other dependant only if death was caused or materially accelerated by a prescribed disease. Leaflet NI 10 gives full details of the conditions applying to this type of benefit.
In England and Wales any death known or suspected to have been caused by pneumoconiosis must be reported to HM Coroner, who is responsible for determining the cause of death for the purposes of registration.

The coroner normally arranges a postmortem examination and also the thoracic organs made available to the local pneumoconiosis medical panel. Two panel doctors then make their own independent examination of the organs. In Scotland, where there are no coroners, a postmortem examination may be carried out and the organs made available to the panel if the widow gives her consent.

Pathologists are encouraged to ensure that lungs that are to be examined by the panel are always perfused with formalin via the trachea as this facilitates examination.

The insurance officer makes his decision in the light of the postmortem and other reports and the report from the pneumoconiosis medical panel doctors on whether death was or was not caused or materially accelerated by the prescribed disease.

There is a right of appeal against this decision to a local tribunal and finally to a social security commissioner. The widow of anyone in receipt of disablement benefit in life will not automatically be entitled to death benefit as the death must be shown to have been caused or materially accelerated by pneumoconiosis. This may lead to much debate, but in giving their opinion the panel doctors advise on the balance of probability of the medical evidence and take into account the statutory definition of the disease and the case law established by the social security commissioners.

In a large proportion of the claims the cause of death is a malignancy. If a person dies from mesothelioma caused by exposure to asbestos at work there is no problem as death benefit is payable. Carcinoma of the lung is not a prescribed disease in asbestos workers, but where it occurs in the presence of asbestosis it is regarded as a consequence of the latter and for purposes of benefit it is treated as if it were asbestosis.

Rates of benefit

The rate of the basic disablement pension for an assessment of 100% is now £44.30 a week and for lower assessments the pension is roughly pro rata (£ = pound).

A widow entitled to an industrial death benefit pension will receive £38.00 a week for the first 26 weeks and will then be eligible for either the "higher permanent rate" of C27-70 a week or the "lower permanent rate" of C8-15 a week. Leaflet NI 10 outlines the various criteria for qualification for the higher rate. There is also an
allowance of £7.50 a week for each child. Full details of all benefit rates are given in DHSS leaflet NI 196. The benefits are all non-taxable.

**iii) Netherlands**

*Institute of Asbestos Victims (IAV)*

In November 1998, an agreement was made between the ministry of justice, social security, trade unions and the asbestos victims to ensure that future claims would be handled in a swift and socially acceptable way. For that purpose the Institute of Asbestos Victims (IAV) was founded. Its primary task is to support patients in this process, to provide cash advances and to organize a short track protocol to select patients who are entitled to additional compensation. In the latter case, it is assumed that the previous employer or his insurance company has a legal responsibility. One of the most important tasks is to help the patient to determine where and when the asbestos exposure has taken place and which employer is responsible.

This approach safeguards the victims from unwanted, time-consuming and expensive legal procedures. This arrangement only applies to patients with a mesothelioma, or their relatives, when occupational exposure to asbestos has occurred. It is therefore essential to obtain a definite diagnosis of malignant mesothelioma. Unfortunately it is not always possible to obtain representative tumour material for diagnosis.

*Application to the IAV*

Patients and their relatives can apply to the IAV for reimbursement. The IAV will collect the relevant medical information and obtain an occupational history (by interviewing the patient, if alive, or relatives or former colleagues if the patient is deceased).

Histo-pathological material will be requested from the local hospital and, when available, it will be reviewed by pathologists from “The Netherlands Mesothelioma Panel”.

If the diagnosis of a malignant mesothelioma is confirmed, the IAV will decide that the patients or their relatives are entitled to compensation. In cases where the diagnosis cannot be confirmed, the application is turned down.

*Unconfirmed cases*

The Netherlands Mesothelioma Panel cannot review all cases presented to the IAV. Tumour biopsies may not be representative or available, for example when no
diagnostic procedures have been performed due to the poor condition or death of the patient.

In such unclassified cases, the IAV requests the Mesothelioma Group of the Dutch Thoracic Society (DTS) to intervene. This group consists of 12 pulmonologists, who are specialized in the diagnosis and treatment of malignant mesothelioma. All available material on these unclassified cases, including radiological examinations, is sent to three independent panel members. Based on available information, each specialist must decide whether the diagnosis of malignant mesothelioma is considered probable or has to be rejected.

The above flow diagram shows the protocol for asbestos-related disease in Netherland. Patients first present their case to the IAV (Institute for Asbestos Victims) who collect data and pathology specimen which are sent to the NMP (Netherlands Mesothelioma Panel) for pathologic evaluation. When no diagnosis can be made based on the available histological or cytological specimen all available data are sent to the Mesothelioma Group (MG) of the Dutch Thoracic Society (DTS).

The common rate of disablement claim ranged from €15882 to €55000.

**iv) France**

*Occupational disease compensation in General*
According to compensation law for occupational injuries (since 1898) and for occupational diseases (since 1919), there are 3 characteristics of occupational compensation as follows:

The “presumption of imputability”: when the disease is on the official list of compensable occupational diseases, the victim does not need to prove a causal relationship between occupational exposure and the occurrence of the disease.

The “fixed-price compensation”: it is not necessary to assess the real harm to the worker, but rather to deliver a fixed amount of money as the result of an expert judgment of the extent of the disability.

The “loss of the gain capacity”: in cases that recognize the employer’s inexcusable fault, this allows “integral compensation” of the victim of the occupational disease.

The victims are to receive benefits even though the company is closed or in bankruptcy. The employers permanently supply a fund for compensation of victims of injuries and occupational diseases.

This system is managed by the Commission of Indemnity for the Victims of Criminal Acts (La Commission d’Indemnisation des Victimes d’Infraction (CIVI)) and all cases have to prove as employer’s inexcusable fault in court. The levels of compensation by CIVI are similar to the victims in cases of employer’s inexcusable fault. However, the process is time-consuming and many asbestos victims could not prove employer’s inexcusable fault.

Asbestos-related disease compensation

Though the asbestos-related diseases are occupational diseases and rise to the definition of accidents in the workers’ compensation system created in France by law since 1898, victims of asbestos exposure rarely received compensation for asbestos-related diseases before 1995.

From 1994-2001, the national movement in defense of the victims of asbestos has started. Victims’ groups created the Defense of the Asbestos Victims National Association (l’Association Nationale de Défense des Victimes de l’Amiante, ANDEVA), with three objectives: recognition of victims’ rights to compensation and of industry’s liability in civil and criminal courts; a complete ban on asbestos manufacture and use in France; and an effective public action to assess and remediate community asbestos hazards to prevent future cases of cancer. Now, ANDEVA has more than 7,000 members and is supported by a network of 25 local associations. They seek to obtain compensation for the victims of asbestos exposure and for their families, and to obtain responsible management of environmental asbestos in the community.
Since 1995, growth in asbestos compensation claims and awards in the civil courts has increased by enacting the Criminal Act Victims’ Commission (La Commission d’Indemnisation des Victimes d’Infraction, CIVI).

Finally, the French Parliament to enact a law creating in 2000 a Compensation Fund for Victims of Asbestos Exposure (Le Fonds d’Indemnisation des Victimes de l’amiante, FIVA). FIVA allows all asbestos victims to obtain, under control of the jurisdictions, an integral compensation of the prejudice due to an asbestos exposure. FIVA fund is financed 75% by the funds for occupational injuries and illnesses and 25% by the state. FIVA is part of a no-fault benefit system and provide the faster way to attain compensation, but in that case, this victim cannot claim the employer’s inexcusable fault.

Paradoxically, FIVA code of “Responsible but not guilty” is questioned as the protection by which the asbestos industry executives and the employers’ community prevailed against the penalty for manslaughter, poisoning, and causing danger to other people. The former asbestos industry workers prefer to demonstrate the guilt of the employers through insurance settlements and in the courts.

The amount of disablement claim in France was €4000 from FIVA while up to €45000 from court case (€ Euro).

v) Comparison between some countries in EU

Comparison with other countries indicates that there are many differences in the response to patients who request financial compensation for occupational diseases as shown in table 4.9.

In Germany, the claimant has much fewer possibilities compared with other countries. In most of the cases, the burden of proof lies with the patient and his family.

In Belgium, the situation is comparable with the Dutch situation as long as the disease is recognised as occupationally contracted.

In the UK and in Netherlands there is a general damage award, which covers the ‘pain, suffering and loss of amenity’, while additional compensation can be given for the loss of income or pension. In Netherlands, the Institute of Asbestos Victims was founded in 2000 to overcome most of the problems of patients with asbestos-related diseases. A covenant was made between involved groups: the government, industries, insurance companies, unions and patients group representatives.
Table 4.9 Guidelines for financial reimbursement for patients with occupational asbestos exposure

<table>
<thead>
<tr>
<th>Institution (year of foundations)</th>
<th>Belgium</th>
<th>France</th>
<th>German</th>
<th>Italy</th>
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<tr>
<td>FBZ, Fonds voor de beroepsziekten (1964)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>FIVA (2002) and Federation Francais de Societe´ d’Assuradeurs&lt;sup&gt;b&lt;/sup&gt;</td>
<td>Berufsgenossenschaften (1894)&lt;sup&gt;c&lt;/sup&gt;</td>
<td>INAIL, National Institute for Labour accidents&lt;sup&gt;d&lt;/sup&gt;</td>
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<td>Occupational exposure required</td>
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<td>Yes</td>
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<td>Environmental exposure included</td>
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<td>Proof of exposure lies with defendant or claimant</td>
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<td>Claimant (≥5 yr exposure)</td>
<td>claimant</td>
<td>Claimant (fibre count required)</td>
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<td>Reimbursement amount (commonly cited amounts)</td>
<td>50% of yearly income</td>
<td>FIVA €4000 Courts €45 000 FFSA open</td>
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<td>Age dependent</td>
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<td>Institution (year of foundations)</td>
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<td>UK</td>
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<td>Yes &gt;50%</td>
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<td>Reimbursement amount (commonly cited amounts)</td>
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<td>£100 000– open (age dependent)</td>
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</tr>
</tbody>
</table>

a) [http://fmp-fbz.fgov.be/](http://fmp-fbz.fgov.be/)
b) [http://www.senat.fr/rap/r05-037-1/r05-037-154.html](http://www.senat.fr/rap/r05-037-1/r05-037-154.html)
c) [http://www.hvbg.de/d/pages/](http://www.hvbg.de/d/pages/)
d) [http://www.inail.it/](http://www.inail.it/)
e) [http://www.asbestslachtoffers.nl/pages/welkom.html](http://www.asbestslachtoffers.nl/pages/welkom.html)
f) [http://andeva.free.fr/international/2003_0515_laurie_comparative%20review.htm](http://andeva.free.fr/international/2003_0515_laurie_comparative%20review.htm)
g) [http://www.asbestopfer.ch](http://www.asbestopfer.ch)
h) For the IAS a time limitation of 30 years is set; for cases beyond 30 years legal action is required.

vi) Japan

Japanese diagnosis criteria for compensation of asbestos-related lung cancer

The primary lung cancer with the following:

(i) asbestosis category I on chest radiography;
(ii) pleural plaques with more than 10 years’ occupational asbestos exposure;
(iii) asbestos particles or fibers on the lung tissues with more than 10 years’ occupational asbestos exposure;
(iv) more than 5000 asbestos particles per gram of dry lung tissue with occupational asbestos exposure.

The profusion of parenchymal opacities seen on the CT scans was graded with the same basic principles as the ILO 1980 system for grading pulmonary disease on the chest radiograph. The absence of opacities was graded as a score of the category 0 (profusion scores 0/-, 0/0, 0/1). The interpretation of definite presence of opacities allowed a category 1 or above grading of the opacities. If the opacities were not obliterating the vascular markings, they were read in the category 1 grade (1/0, 1/1, 1/2). Grouping of opacities obliterating some of the vascular masking were read in the category 2 (2/1, 2/2, 2/3).

vii) Korea

The Enforcement Ordinance describes three main conditions of asbestos-related diseases as follows:

A. diseases of workers who have been engaged in jobs related to asbestos exposure are recognized as occupational diseases;
B. asbestosis, primary lung cancer or mesothelioma which are accompanied by one among these three conditions
   (i) asbestosis,
   (ii) pleural thickening, pleural plaques, asbestos body or asbestos fiber,
   (iii) workers, even though they don’t have (1) or (2), exposed to asbestos more than 10 yr.

Also workers exposed to asbestos less than 10 yr may be recognized as occupational diseases, considering the history of smoking, asbestos exposure, and latency.

The Korean diagnosis criteria for compensation of asbestos-related lung cancer and MPM are.

For MPM:
1. Definite diagnosis of MPM with
2. pathology confirmation; if pathology unconfirmed (for example, patient’s condition is not allowed), clinical, radiological findings and history of asbestos exposure history can be considered

For asbestos-related lung cancer:
1. Primary lung cancer with latent period > 10 years
2. More than one of the following
   - asbestosis
pleural plaques
asbestos particles or fiber of more than 5000 f/dry lung 1 gm or asbestos bodies of more than 5/cc in BAL
asbestos fiber of 2 million f/dry lung 1 gm (length > 5 µm); of 5 million f/dry lung 1 gm (length > 1 µm)

4.4 Control of disease progression and palliative care
4.4.1 Non-malignant asbestos-related diseases

Though, the non-malignant asbestos-related diseases varied to many clinical conditions: asbestosis, non-malignant pleural abnormalities associated with asbestos (pleuritis, pleural effusion, circumscribed pleural thickening (plaques), diffuse pleural thickening), and chronic airflow obstruction, no specific guideline available in management non-malignant asbestos-related disease.

Generally, treatment of asbestosis is symptomatic and similar to that for other patients with chronic lung disease as shown in the box below. Lung transplantation should be considered in the setting of end-stage lung disease. Likewise, treatment of benign pleural disease is also symptomatic. Decortication is sometimes required for managing diffuse visceral pleural thickening depending on extent of disease.

Managing Patients with nonmalignant asbestos-related lung Disease
- Stop further exposure to asbestos.
- Stop smoking, avoid exposure to tobacco products.
- Provide early treatment of respiratory infections with antibiotics.
- Give pneumococcal and influenza vaccinations.
- Maintain a high index of suspicion and provide early evaluation of symptoms for lung, laryngeal, and ovarian cancers and mesothelioma in asbestos-exposed patients.
- Maintain a high index of suspicion for pulmonary infection with *Mycobacterium tuberculosis*, nontuberculous mycobacteria, and fungi. Skin test for latent tuberculosis infection with tuberculin skin test should be considered including treat latent infections with isoniazid (9 months) or rifampin (4 months).
- Provide empiric treatment with short- and long-acting inhaled bronchodilators and inhaled corticosteroids when they are found to provide symptomatic relief.
- Give supplemental oxygen therapy if pulmonary hypertension is present or
to prevent pulmonary hypertension if \(O_2\) saturation is less than 85% at rest, with exercise, or with sleep.

- Consider lung transplantation in the setting of end-stage lung disease.

### 4.4.2 Malignant asbestos-related disease

**i) Summarized important guidelines and recommendations for MPM**

Mesothelioma (MPM) may be treated with surgery, radiation, chemotherapy, or some combination of these. In general, prognosis is poor. Mesothelioma associated malignant pleural effusion can require palliation through procedures such as pleurodesis, pleurectomy, and decortication.

Asbestos-associated lung cancer is managed in the same fashion as lung cancer occurring without a history of exposure to asbestos. Similarly, other cancer in relation to asbestos are managed according specific guidelines available of each cancers.

A recent review has summarized guidelines and recommendations for the management of MPM of several international cancer organizations issued\(^{31}\): the British Thoracic Society –BTS\(^{32}\), the Societe de Pneumologie de Langue Francaise –SPLF\(^{33}\), The provincial Lung Cancer Disease Site Group of Ontario –CDN\(^{34}\), the European Society of Medical Oncology (ESMO)\(^{35}\), and the European Respiratory (ERS) with the European Society of Thoracic Surgeons (ESTS)\(^{36}\). These recommendations are summarized in table 4.4.10. More guidelines of the National Comprehensive Cancer Network (NCCN) which is an alliance of 21 leading cancer centers in USA, and of the alliance of several Italian scientific societies are also mentioned\(^{37,38}\). Some interesting practical guidelines and recommendations are also provided in this part.
Table 4.10 Summary recommendations from international organizations on the management of MPM

<table>
<thead>
<tr>
<th>Type of guideline</th>
<th>British Thoracic Society</th>
<th>French Speaking Society for chest Medicine (SPLF)</th>
<th>Provincial Lung Cancer Disease Site Group of Ontario (CDN)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Author(s)</td>
<td>Working Party of UK clinicians with an interest and experience in MPM management</td>
<td>Experts from different disciplines and institutions</td>
<td>Clinical practice guideline, based on a systematic review Lung cancer disease site group members</td>
</tr>
<tr>
<td>Supportive care</td>
<td>Early pleurodesis is a key aim for symptom control and prevention of the development of a trapped lung. Thoracoscopy is an extremely useful diagnostic and therapeutic tool. Calibrated talc is the pleurodesis agent of choice. Indwelling pleural catheters are useful for symptom control in cases of trapped lung or where chemical pleurodesis has failed. Several chemotherapeutic agents can reduce tumour bulk and help symptoms. The combination of pemetrexed and cisplatin significantly prolongs survival compared with cisplatin alone. All patients with mesothelioma and performance status 0–2 should have the opportunity to discuss the merits of chemotherapy with either an oncologist or a respiratory specialist experienced in the use of chemotherapy for malignant mesothelioma. Further clinical trials of chemotherapy should be encouraged.</td>
<td>P/D is considered as a palliative procedure. Therefore it is not a recommended surgical procedure for MPM. It is recommended that talc pleurodesis is early performed, if it does not compromise the oncological therapeutic strategy.</td>
<td>The association of cisplatin and an antimetabolite (pemetrexed or raltitrexed) is recommended as first line chemotherapy (A). It is nevertheless recommended that administration of chemotherapy not be delayed and not to wait for the appearance of functional signs (C). It is recommended that chemotherapy be stopped in cases of progressive disease, grades 3–4 toxicities, or cumulative toxic doses (A), and after six cycles in patients who respond or are stable (C). Chemotherapy cannot be recommended as second line after failure of chemotherapy including cisplatin. For patients who have not been given first line treatment including cisplatin, cisplatin-based chemotherapy can be proposed.</td>
</tr>
<tr>
<td></td>
<td>British Thoracic Society</td>
<td>French Speaking Society for chest Medicine (SPLF)</td>
<td>Provincial Lung Cancer Disease Site Group of Ontario (CDN)</td>
</tr>
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</tr>
<tr>
<td><strong>Palliative radiotherapy</strong></td>
<td>Palliative radiotherapy provides pain relief in about half of all patients. Palpable masses respond to radiotherapy in about half of all patients. Breathlessness and superior vena cava obstruction rarely respond to radiotherapy</td>
<td>Palliative radiotherapy aimed at pain relief is recommended in cases of painful parietal infiltration by MPM or subcutaneous metastasis (B)</td>
<td>-</td>
</tr>
<tr>
<td><strong>Prophylactic radiotherapy</strong></td>
<td>Prophylactic radiotherapy may reduce chest wall implantation following invasive procedures, but may be most applicable for patients with a better prognosis and after more invasive procedures</td>
<td>It is recommended that irradiation with 3–7 Gy for three consecutive days, in the 4 weeks following drainage or thoracoscopy, be performed to prevent subcutaneous metastasis developing along drainage channels or thoracocentis tracts, using electrons with an energy adapted for depth and a cutaneous bolus</td>
<td>-</td>
</tr>
<tr>
<td><strong>Radical radiotherapy</strong></td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><strong>Radical surgery</strong></td>
<td>There are no randomised control trials to establish the role of radical surgery. Radical surgery should only be considered within a randomised trial. Surgery should be concentrated in centres where there is experience in performing extrapleural pneumonectomies. The present claims for benefit are for surgery within multimodality therapy. Patients should be aware of the potential for trimodality treatment and be given realistic information about outcomes</td>
<td>Surgical treatment of MPM should only be considered as part of a multidisciplinary approach to management (A). It is recommended that surgical treatment of MPM be performed in a reference centre able to offer both a surgical team trained in this kind of surgery and a pulmonary-oncologist medical team (A). In the absence of results from randomised trials, it is recommended to perform this type of surgery only in clinical trials (A)</td>
<td>-</td>
</tr>
</tbody>
</table>
Table 4.10 Summary recommendations from international organizations on the management of MPM (cont.)

<table>
<thead>
<tr>
<th>Type of guideline</th>
<th>European Society of Medical Oncology (ESMO)</th>
<th>European Respiratory Society (ERS) and European Society of Thoracic Surgeons (ESTS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Author(s)</td>
<td>Single institutional experts</td>
<td>International experts from different disciplines, institutions and scientific societies</td>
</tr>
<tr>
<td>Supportive care</td>
<td>Palliative local procedures to control pleural effusion includes parietal pleurectomy or talk pleurodesis</td>
<td>Every patient should be offered supportive care. Plurectomy/decortication should not be proposed in a curative intent but can be considered in patients to obtain symptom control, especially symptomatic patients with entrapped lung syndrome who cannot benefit from chemical pleurodesis (2C)</td>
</tr>
<tr>
<td>Palliative chemotherapy</td>
<td>The combinations of both pemetrexed/ cisplatin and raltitrexed/cisplatin have been shown to improve survival as well as lung function and symptom control in comparison with cisplatin alone in randomised trials [II, A]. The combination of pemetrexed with carboplatin is an alternative effective therapy [III, A]</td>
<td>When a decision is made to treat patients with chemotherapy, subjects in a good performance status (PS &gt;60% on the Karnofsky scale or &lt;3 on the ECOG scale) should be treated with first line combination chemotherapy consisting of platinum and pemetrexed or raltitrexed (1B). Alternatively, patients could be included in first and second line clinical trials. Administration of chemotherapy should not be delayed and should be considered before the appearance of functional clinical signs (1C). Chemotherapy should be stopped in case of progressive disease, grade 3-4 toxicities, or cumulative toxic doses (1A), or following up to six cycles in patients who respond or are stable (2C)</td>
</tr>
</tbody>
</table>
Table 4.10 Summary recommendations from international organizations on the management of MPM (cont.)

<table>
<thead>
<tr>
<th>Approach</th>
<th>European Society of Medical Oncology (ESMO)</th>
<th>European Respiratory Society (ERS) and European Society of Thoracic Surgeons (ESTS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Palliative radiotherapy</td>
<td>Conventional radiotherapy dose can be delivered locally as a palliative measure for pain management</td>
<td>Palliative radiotherapy aimed at pain relief may be considered in cases of painful chest wall infiltration or nodules (2C)</td>
</tr>
<tr>
<td>Prophylactic radiotherapy</td>
<td>Conventional radiotherapy dose can be delivered locally as a palliative measure for pain management</td>
<td>Palliative radiotherapy aimed at pain relief may be considered in cases of painful chest wall infiltration or nodules (2C)</td>
</tr>
<tr>
<td>Radical radiotherapy</td>
<td>The use of hemithoracic radiotherapy has been limited because of severe side effects of irradiation of the underlying lung</td>
<td>Radiotherapy should not be performed after pleurectomy or decortication (1A)</td>
</tr>
<tr>
<td>Radial surgery</td>
<td>Extraleural pneumonectomy with resection of the hemi-diaphragm and the pericardium en bloc, the appropriateness of which is still under consideration, should only be performed on selected patients by experienced thoracic surgeons in the context of a multidisciplinary team [III, A]. This approach is generally combined with neoadjuvant chemotherapy and/or adjuvant radiotherapy</td>
<td>Postoperative irradiation after EPP should only be proposed in clinical trials, in specialised centres, as a part of multimodal treatment. Radical surgery (EPP) should be performed only in clinical trials, in specialised centres, as a part of multimodal treatment. Patients who are considered candidates for this multimodal approach should be included in a prospective randomised trial in specialised centres</td>
</tr>
</tbody>
</table>
**ii) ICOH Scientific Committee for Respiratory Disorders on tertiary prevention: Limit disease progression and disability**

The control of disease progression and palliative care was stated in no. 5-7 of ICOH recommendations as shown.

<table>
<thead>
<tr>
<th>Tertiary prevention: limit disease progression and disability</th>
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<tr>
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<td>..................</td>
</tr>
<tr>
<td>5. Prevent disease progression</td>
</tr>
<tr>
<td>Generally the worker with asbestos-related disease should be removed from further exposure. However, the worker may continue at his or her usual work if exposure is minimal, at or below permissible levels. This is important so as not to deprive the patient of his or her livelihood for no clinical benefit.</td>
</tr>
<tr>
<td>6. Immunization</td>
</tr>
<tr>
<td>Immunization against pneumococcal pneumonia and influenza should be provided to worker/patients with debilitating asbestos-related lung disease, because of the high risk of complications with these diseases.</td>
</tr>
<tr>
<td>7. Concurrent respiratory disorders and complications</td>
</tr>
<tr>
<td>The physician providing care for worker/patients with asbestos-related disease should effectively manage and treat concurrent diseases, like COPD, asthma, and respiratory infections when present, or secondary disorders like cor pulmonale, secondary polycythemia, and respiratory failure. Symptoms including breathlessness, pain, and psychological distress, should also be appropriately treated.</td>
</tr>
<tr>
<td>8. Pulmonary rehabilitation</td>
</tr>
<tr>
<td>Standard pulmonary rehabilitation may play a role in the management of individuals with non-malignant asbestos-related disease and related functional impairment and disability.</td>
</tr>
<tr>
<td>9. Coping with terminal cancer</td>
</tr>
</tbody>
</table>
As with other malignant diseases, healthcare providers should provide palliative and psychological support to the patient and family. The worker/patient should be made aware of the terminal nature of the disease. Disease management should include adequate pain management and maximize quality of life.

**iii) British Thoracic Society**

**Supportive and palliative care**

Supportive and palliative care of patients with mesothelioma and their families is very important, given that the disease has a poor and relatively well-defined prognosis and that most patients need symptom palliation from the time of diagnosis onwards. The patient, family and general practitioner may often have difficulty in accepting that palliative care is the only available treatment for the majority of cases. Anger and frustration are common, and there are particular issues in malignant mesothelioma concerning blame for the disease, obtaining benefits and litigation. In British, the National Institute for Clinical Health and Excellence describes supportive and palliative care as an umbrella term for services for mesothelioma.

Supportive care is encompassing information giving, self-help and support, user involvement, symptom control, psychological support, social support, spiritual support, rehabilitation, complementary therapies, palliative care, end-of-life and bereavement care.

Palliative care is described as the active holistic care of patients with advanced progressive illness. Management of pain and other symptoms and provision of psychological, social and spiritual support is paramount. The goal is achievement of the best quality of life for patients and their families.

Referral of the patient and/or their carers to specialist palliative care services is appropriate for a range of issues. These include unresolved symptoms and complex physical, psychosocial or spiritual needs, and end-of-life and bereavement issues.

Key points: Most patients need symptom palliation from the time of diagnosis onwards; Supportive and palliative care aims to provide relief from pain and other physical symptoms and to respond to emotional, psychological, social and spiritual needs.

**Communication**

It is usually the consultant that provides the patient with the diagnosis and an initial outline of management and prognosis, and support from a clinical nurse specialist is crucial at this stage.
The clinical nurse specialist should be promptly available for further discussion of these issues with patients and their families and carers, and offer supportive information. Rapid communication with the general practitioner should be ensured and should include details of the known extent of the disease, what was said to the patient and the management plan.

It is not unusual for several members of the lung multidisciplinary team and the general practitioner to be involved in providing medical care, resulting in complex communication pathways that need to be maintained. The clinical nurse specialist should ensure that the patient and/or carer are aware of the need for a Coroner’s post mortem examination and report to the Coroner or Procurator Fiscal and that this is confirmed in writing to the general practitioner.

Information

Patients with malignant mesothelioma and their families should have access to verbal and written information about the disease and its symptoms, end-of-life issues, treatments and the medicolegal implications. Regular contact with the clinical nurse specialist allows a steady flow of information according to the patient’s needs.

Lung cancer clinical nurse specialists have expressed concerns about obtaining up to date information and maintaining knowledge and expertise in the field of mesothelioma. Information and support for nurses to allow them to meet the needs of their patients with malignant mesothelioma is available from the organizations listed in Appendix 3 (available online at http://thorax.bmj.com/supplemental). The clinical nurse specialist should advise (or clarify) patients and their carers that, following a diagnosis of malignant mesothelioma, entitlement to some benefits and allowances is automatic.

Applying for benefits requires attention to detail and can be time-consuming. Patients and carers should be advised to make photocopies of everything they send to benefits centres for their own reference. The clinical nurse specialist should assist in directing or referring the patient and carer to an organization that can help with the completion of benefit applications. The lung cancer clinical nurse specialist will advise patients about what help is available locally and Macmillan Cancer Support (on free phone 0800 500 800) can also direct people to local benefits advisory organizations. National organizations offering a telephone benefits advice service, including help with completion of claim forms, are listed in Appendix 3 (available online at http://thorax.bmj.com/supplemental).
Coordinated care

The clinical nurse specialist facilitates the pathway of care for the patient and the family throughout the illness, ensuring good liaison between hospital services and primary care and access to specialist palliative care services as required. Patients should be made aware of whom to contact in case of need. The community nursing team (palliative care or district nurse) should be made aware of patients diagnosed with malignant mesothelioma within their area. A team approach should then be adopted to meet the nursing needs of the patient.

Nursing assessment

It is good practice to ensure that there is assessment of the needs of both the patient and the family or carers. Assessment of patients should include physical symptoms and physical functioning, psychological problems, social care needs and need for spiritual support.

Assessment of family members and carers includes their concerns and need for support, including eventually bereavement support. Such assessment may need to be repeated at key times during the illness.

Patient advocacy

The limited treatment options, variation in expert opinion and universally poor outcome means that patient preference is particularly relevant when making treatment decisions about malignant mesothelioma. The relationship between the clinical nurse specialist and patient should help elicit patient and carer hopes and expectations and ensure that treatment plans are mutually agreed upon.

Accessibility

Timely access to the health care team is vital to ensure rapid attention to symptoms. The clinical nurse specialist is often best placed to provide a contact point and should be aware of any other points at which the patient may contact the service.

Support

Patients should be directed to an appropriate cancer support group such as the Lung Cancer Support Group. Where there is a sufficient number of patients with malignant mesothelioma, the development of a local Mesothelioma Support Group is recommended. Patients’ carers should be offered information about carer support when required.
Symptom control

All symptoms need a working diagnosis, as some may be caused by concurrent non-cancer related problems. It is often helpful to record symptom severity on a simple scale to assess progress and response to treatment. Relief of pain, breathlessness and other symptoms can occur with response to chemotherapy.

For pain:

The treatment of pain in malignant mesothelioma follows the same principles as for any other cancer but can include more specific techniques where initial methods are inadequate. These may necessitate early referral to a specialist pain service.

Specific techniques include:
- Transcutaneous electrical nerve stimulation machines and acupuncture.
- Intercostal, paravertebral or brachial plexus nerve blocks.
- Interpleural, epidural or intrathecal analgesic infusions.
- Local thoracic spine neurolytic blocks.
- Percutaneous cervical cordotomy (particularly when the patient is still ambulant).

In pain from chest wall involvement the response to opioids is variable because of added inflammatory and neuropathic components. In this situation, the following adjuvant analgesics should be considered early: non-steroidal anti-inflammatory drugs (with gastric cover); steroids (with gastric cover); noradrenergic antidepressants such as amitriptyline; or anticonvulsants such as gabapentin or carbamazepine.

Pain control will be improved by attention to emotional, psychological, social and spiritual problems. Distraction and relaxation techniques and complementary therapies may also be helpful.

Pain associated with localised tumour invasion of the chest wall may respond to radiotherapy.

For dyspnoea:

The common causes of breathlessness in mesothelioma are pleural effusion, lung compression and chest wall stiffness. Weakness and malaise, and anxiety or panic will also contribute. Progressive breathlessness should be treated according to general palliative care guidelines that include pharmacological approaches such as opioids, benzodiazepines and oxygen, and non-pharmacological methods such as breathing exercises and relaxation combined with re-adaptation.
Cough, anorexia, weight loss, fatigue, excessive sweating and depression all occur in malignant mesothelioma and should be managed according to palliative care guidelines.

Key points: Early involvement of a pain is not controlled after initial measures; Dyspnea, cough and other symptoms should be managed according to palliative care guidelines.

**iv) Guidelines of the European Respiratory Society and the European Society of Thoracic Surgeons for management of Malignant Pleural Mesothelioma**

1. Management of pain
   a) How is pain in MPM evaluated?
   Pain in mesothelioma is frequently complex due to a combination of nociceptive, neuropathic and inflammatory factors.
   • Use of a visual analogue pain assessment tool improves cancer pain management (1C)
   • If the patient has cognitive impairment due to pain or advanced disease, pain may be assessed using a behavioral assessment tool such as the Doloplus scale (1C)
   b) What is the general principle of treatment of pain in MPM?
   Recommendations
   • Pain control in mesothelioma should follow the principles of cancer pain management (1C).
   • However, due to the complex nature of pain in mesothelioma, adjunct analgesia may frequently be required in addition to opiates. In cases of refractory pain unresponsive to the usual measures, a specialist pain management or specialist palliative medicine opinion should be sought (1C).
   • Occasionally neuroablative techniques may be required, depending on specialist advice, and with careful consideration of the risks and benefits (2C).
   • Palliative radiotherapy may be proposed and effective in treating pain due to tumour nodules (2C).

2. Management of dyspnea
   a) Is repeated pleural aspiration justified?
   Recommendations
   • This should be avoidable if pleurodesis is performed early in the disease and before effusions have become loculated and/or the lung has become fixed and unable to expand fully (1C).
   • Repeated aspiration or indwelling chest drain may occasionally be the most practical way to manage recurrent effusions in very frail patients (2C).
b) What is the place of pleurodesis?

Recommendation
• Pleurodesis is useful in preventing recurrent effusions. Sterile talc is preferred to other agents (1A).

c) When should talc pleurodesis be performed?

Recommendation
• Pleurodesis is most effective when performed early in the disease process (1C) but it should not be performed before sufficient tissue for diagnosis has been obtained (1A).

d) Are other treatments of value in the management of dyspnea?

Recommendations
• Low dose oral morphine may be useful in reducing the sensation of dyspnea and thus also reducing associated anxiety (1A).
• Oxygen may be helpful but should not be used unless there is evidence of reduced oxygen saturation (1C).

e) Can other measures be used to alleviate dyspnea?

A simple fan that creates a cool stream of air across the face may reduce the sensation of dyspnea via the trigeminal nerve. Self-help breathlessness management techniques, designed to increase patients’ sense of mastery over their breathlessness, have been shown to be effective in lung cancer but the work has not been conducted specifically in mesothelioma.

3. Management of other physical symptoms

This is a brief account of simple measures used to palliate common symptoms (advice of experts). Further information should be sought from expert texts on palliative medicine.

Statements
• Cough may respond to cough suppressants such as codeine linctus or pholcodine. It is important to exclude or treat co-morbidities such as chest infection or cardiac failure.
• Anorexia, weight loss, and fatigue constitute the anorexia/cachexia syndrome common to many malignant conditions. Attention to high-energy, small volume, frequent meals, treatment of oral candida if present, and avoidance of dehydration and constipation may help.
• Sweating may improve with avoidance of restrictive clothing, use of a fan, and medication such as cimetidine.
• Dysphagia may be due to oral candida or from external compression of the oesophagus due to tumour. Candida responds to treatment with oral fluconazole.
Stenting of the oesophagus may be effective in reducing dysphagia due to external compression.

- Ascites usually develops due to tumour extension through the diaphragm into the peritoneal cavity. Paracentesis may reduce discomfort due to large volume ascities but may need to be repeated.
- Constipation results from inactivity, poor oral intake and as an inevitable consequence of opiates. Laxatives should be prescribed proactively and taken regularly. This sign may suggest a tumour extension through the diaphragm into the peritoneal cavity.
- Vomiting may occur as a side effect of chemotherapy and responds to anti-emetics. It may also be a side-effect of opiate analgesics and changing to an alternative may be successful.

4. Management of psychological distress

Patients with mesothelioma may exhibit anger, depression or stoicism and resigned acceptance. Reports from specific mesothelioma telephone help-lines demonstrate that patients and their families request accurate information about the illness, treatment options, state benefits and medico-legal issues.

Recommendation

- Support may be offered by specialist nurses, psychological or psychiatric services and asbestos support groups (1C).
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