Environmental Health Criteria 53

ASBESTOS AND OTHER NATURAL MINERAL FIBRES

World Health Organization

INTERNATIONAL PROGRAMME ON CHEMICAL SAFETY

ENVIRONMENTAL HEALTH CRITERIA 53

ASBESTOS AND OTHER NATURAL MINERAL FIBRES

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NOTE TO READERS OF THE CRITERIA DOCUMENTS

Every effort has been made to present information in the criteria documents as accurately as possible without unduly delaying their publication. In the interest of all users of the environmental health criteria documents, readers are kindly requested to communicate any errors that may have occurred to the Manager of the International Programme on Chemical Safety, World Health Organization, Geneva, Switzerland, in order that they may be included in corrigenda, which will appear in subsequent volumes.

ENVIRONMENTAL HEALTH CRITERIA FOR ASBESTOS AND OTHER NATURAL MINERAL FIBRES

Following the recommendations of the United Nations Conference on the Human Environment held in Stockholm in 1972, and in response to a number of resolutions of the World Health Assembly and a recommendation of the Governing Council of the United Nations Environment Programme, a programme on the integrated assessment of the health effects of environmental pollution was initiated in 1973. The programme, known as the WHO Environmental Health Criteria Programme, has been implemented with the support of the Environment Fund of the United Nations Environment Programme. In 1980, the Environmental Health Criteria Programme was incorporated into the International Programme on Chemical Safety (IPCS), a joint venture of the United Nations Environment Programme, the

International Labour Organisation, and the World Health Organization. The Programme is responsible for the publication of a series of criteria documents.

A WHO Task Group on Environmental Health Criteria for Asbestos and Other Natural Mineral Fibres was held at the Fraunhofer Institute for Toxicology and Aerosol Research, Hanover, Federal Republic of Germany from 15-22 July 1985. Professor W. Stöber opened the meeting and greeted the members on behalf of the host institution, and Dr U. Schlottmann spoke on behalf of the Government. Professor F. Valic addressed the meeting on behalf of the three co-sponsoring organizations of the IPCS (WHO/ILO/UNEP). The Task Group reviewed and revised the draft criteria document and made an evaluation of the risks for human health from exposure to asbestos and other natural mineral fibres.

The first draft of the document was a combination of texts prepared by DR H. MUHLE and DR K. SPURNY of the Fraunhofer Institute for Toxicology and Aerosol Research, Hanover, Federal Republic of Germany, PROFESSOR F. POTT of the Medical Institute for Environmental Hygiene, Düsseldorf, Federal Republic of Germany, PROFESSOR J. PETO, of the Institute of Cancer, University of London, London, United Kingdom, PROFESSOR M. LIPPMANN, of the Institute of Environmental Medicine, New York University Medical Center, New York, USA, MS M.E. MEEK, Department of National Health and Welfare, Ottawa, Canada, and DR J.F. STARA and MS C. SONICH-MULLIN, of the US Environmental Protection Agency, Cincinnati, Ohio, USA.

A Working Group consisting of PROFESSOR C. McDONALD, MS M.E. MEEK, DR H. MUHLE, MS J. HUGHES, and PROFESSOR F. VALIC reviewed the first, and developed the second, draft.

The efforts of all who helped in the preparation and finalization of the document are gratefully acknowledged.

1. SUMMARY AND RECOMMENDATIONS FOR FURTHER RESEARCH

1.1. Summary

1.1.1. Identity; physical and chemical properties, methods of sampling and analysis

The commercial term asbestos refers to a group of fibrous serpentine and amphibole minerals that have extraordinary tensile strength, conduct heat poorly, and are relatively resistant to chemical attack. The principal varieties of asbestos used in commerce are chrysotile, a serpentine mineral, and crocidolite and amosite, both of which are amphiboles. Anthophyllite, tremolite, and actinolite asbestos are also amphiboles, but they are rare, and the commercial exploitation of anthophyllite asbestos has been discontinued. Other natural mineral fibres that are considered potentially hazardous because of their physical and chemical properties are erionite, wollastonite, attapulgite, and sepiolite.

Chrysotile fibres consist of aggregates of long, thin, flexible fibrils that resemble scrolls or cylinders. The dimensions of individual chrysotile fibres depend on the extent to which the sample has been manipulated. Amphibole fibres generally tend to be straight and splintery. Crocidolite fibrils are shorter with a smaller diameter than other amphibole fibrils, but they are not as narrow as fibrils of chrysotile. Amosite fibrils are larger in diameter than those of both crocidolite and chrysotile. Respirable fractions of asbestos dust vary according to fibre type and

manipulation.

Several methods involving optical phase contrast microscopy have been developed for determining levels of asbestos fibres in the air of work-places. Only fibres over 5 µm in length with an aspect ratio $\geq$ 3:1 and a diameter of less than 3 µm are counted. Thus, the resulting fibre count can be regarded only as an index of actual numbers of fibres present in the sample (fibres with diameters less than the resolution of the light microscope are not included in this assay). Fibres with diameters smaller than approximately 0.25 µm cannot be seen by light microscopy, and an electron microscope is necessary for counting and identifying these fibres. Electron microscopes that are equipped with auxiliary equipment can provide information on both structure and elemental composition.

The results of analysis using light microscopy can be compared with those using transmission or scanning electron microscopy, but only if the same counting criteria are used.

1.1.2. Sources of occupational and environmental exposure

Asbestos is widely distributed in the earth's crust. Chrysotile, which accounts for more than 95% of the world asbestos trade, occurs in virtually all serpentine rocks. The remainder consists of the amphiboles (amosite and crocidolite). Chrysotile deposits are currently exploited in more than 40 countries; most of these reserves are found in southern Africa, Canada, China, and the USSR. There are, reportedly, thousands of commercial and industrial applications of asbestos.

Dissemination of asbestos and other mineral fibres from natural deposits may be a source of exposure for the general population. Unfortunately, few quantitative data are available. Most of the asbestos present in the atmosphere and ambient water probably results from the mining, milling, and manufacture of asbestos or from the deterioration or breakage of asbestos-containing materials.

1.1.3. Environmental levels and exposures

Asbestos is ubiquitous in the environment because of its extensive industrial use and the dissemination of fibres from natural sources. Available data using currently-accepted methods of sampling and analysis indicate that fibre levels (fibres > 5 µm in length) at remote rural locations are generally below the detection limit (less than 1 fibre/litre), while those in urban air range from < 1 to 10 fibres/litre or occasionally higher. Airborne levels in residential areas in the vicinity of industrial sources have been found to be within the range of those in urban areas or occasionally slightly higher. Non-occupational indoor levels are generally within the range found in the ambient air. Occupational exposure levels vary depending on the effectiveness of dust-control measures; they may be up to several hundred fibres/ml in industry or mines without or with poor dust control, but are generally well below 2 fibres/ml in modern industry.

Reported concentrations in drinking-water range up to 200×10^6 fibres/litre (all fibre lengths).

1.1.4. Toxicological effects on animals

Fibrosis in many animal species, and bronchial carcinomas and

pleural mesotheliomas in the rat, have been observed following inhalation of both chrysotile and amphibole asbestos. In these studies, there were no consistent increases in tumour incidence at other sites, and there is no convincing evidence that ingested asbestos is carcinogenic in animals. Data from the inhalation studies have shown that shorter asbestos fibres are less fibrogenic and carcinogenic.

Few data are available concerning the pathogenicity of the other natural mineral fibres. Fibrosis in rats has been observed following inhalation of attapulgite and sepiolite; a remarkably high incidence of mesotheliomas occurred in rats following inhalation of erionite. Long-fibred attapulgite induced mesotheliomas following intrapleural and intraperitoneal administration. Wollastonite also induced mesothelioma after intrapleural administration. Erionite induced extremely high incidences of mesotheliomas following inhalation exposure and intrapleural and intraperitoneal administration.

The length, diameter, and chemical composition of fibres are important determinants of their deposition, clearance, and translocation within the body. Available data also indicate that the potential of fibres to induce mesotheliomas following intrapleural or intraperitoneal injection in animal species is mainly a function of fibre length and diameter; in general, fibres with maximum carcinogenic potency have been reported to be longer than 8 µm and less than 1.5 µm in diameter.

1.1.5. Effects on man

Epidemiological studies, mainly on occupational groups, have established that all types of asbestos fibres are associated with diffuse pulmonary fibrosis (asbestosis), bronchial carcinoma, and primary malignant tumours of the pleura and peritoneum (mesothelioma). That asbestos causes cancers at other sites is less well established. Gastrointestinal and laryngeal cancer are possible, but the causal relationship with asbestos exposure has not yet been firmly established; there is no substantial supporting evidence for cancer at other sites. Asbestos exposure may cause visceral and parietal pleural changes.

Cigarette smoking increases the asbestosis mortality and the risk of lung cancer in persons exposed to asbestos but not the risk of mesothelioma. Generally, cases of malignant mesothelioma are rapidly fatal. The observed incidence of these tumours, which was low until about 30 years ago, has been increasing rapidly in males in industrial countries. As asbestos-related mesothelioma became more widely accepted and known to pathologists in western countries, reports of mesothelioma increased. The incidence of mesothelioma prior to, e.g., 1960, is not known. Mesotheliomas have seldom followed exposure to chrysotile asbestos only. Most, but not all, cases of mesothelioma have a history of occupational exposure to amphibole asbestos, principally crocidolite, either alone or in amphibole-chrysotile mixtures.

There is strong evidence that one non-asbestos fibrous mineral (erionite) is carcinogenic in man. This fibrous zeolite is likely to be the cause of localized endemic mesothelioma in Turkey.

Non-malignant thickening of the visceral pleura is frequently associated with asbestosis. Thickening of the parietal pleura, sometimes with calcification, may occur in the absence of detectable asbestosis. It is seen in those occupationally exposed to asbestos and also occurs endemically in a number of countries,

but the causes have not been fully established. Tremolite fibre has been implicated as an etiological agent in some regions.

1.1.6. Evaluation of health risks

At present, past exposure to asbestos in industry or in the general population has not been sufficiently well defined to make an accurate assessment of the risks from future levels of exposure, which are likely to be low.

A simple risk assessment is not possible for asbestos. In making an assessment, the emphasis is placed on the incidence of lung cancer and mesothelioma, the principal hazards. Two approaches are possible, one based on a comparative and qualitative evaluation of the literature (qualitative assessment), the other based on an underlying mathematical model to link fibre exposure to the incidence of cancer (quantitative assessment). Attempts to derive the mathematical model have had limited success. Data from several studies support a linear relationship with cumulative dose for lung cancer and an exponential relationship with time since first exposure for mesothelioma. However, the derived "coefficients" within these equations cover a wide range of values from zero upwards. This numerical variability reflects the uncertainty of many factors including historical concentration measurements, fibre size distributions associated with a given fibre level, and variations in the activity of different fibre types. Furthermore, smoking habits are rarely well defined in relation to bronchial cancer. The variability may also reflect uncertainty in the validity of the models. These factors have complicated the quantitative extrapolation of the risk of developing these diseases to levels of exposure such as those in the general environment, which are orders of magnitude below levels of exposure in the populations from which the estimates have derived.

The following conclusions can be drawn on the basis of qualitative assessment:

(a) Among occupational groups, exposure to asbestos poses a health hazard that may result in asbestosis, lung cancer, and mesothelioma. The incidence of these diseases is related to fibre type, fibre dose, and industrial processing. Adequate control measures should significantly reduce these risks.

(b) In para-occupational groups including persons with household contact, those living in the vicinity of asbestos-producing and -using plants, and others, the risks of mesothelioma and lung cancer are generally much lower than for occupational groups. The risk of asbestosis is very low. These risks are being further reduced as a result of improved control practices.

(c) In the general population, the risks of mesothelioma and lung cancer, attributable to asbestos, cannot be quantified reliably and are probably undetectably low. Cigarette smoking is the major etiological factor in the production of lung cancer in the general population. The risk of asbestosis is virtually zero.

(d) On the basis of available data, it is not possible to assess the risks associated with exposure to the majority of other natural mineral fibres in the occupational or general environment. The only exception is erionite for

which a high incidence of mesothelioma in a local population has been associated with exposure.

1.2. Recommendations for Further Research

The molecular and cellular mechanisms associated with both the fibrogenic and carcinogenic action of asbestos are not known. In addition, precise epidemiological data and reliable exposure data to establish dose-response relationships for asbestos fibres are lacking. There should be further studies on:

(a) the significance of the physical and chemical properties of asbestos and other mineral fibres (fibre dimension, surface properties, and contaminants) with respect to their biological effects;

(b) the biological significance of the durability of mineral fibres in the body;

(c) the differences that exist between varieties of asbestos with respect to the induction of malignant tumours;

(d) the induction of malignant tumours by well-characterized samples of other natural mineral fibres, especially asbestos substitutes;

(e) immunological, cellular, and biochemical responses to natural mineral fibres (including their action as initiator and/or promotor);

(f) prevalence and incidence of disease in large cohorts of more recent workers with reliably-measured exposure; and

(g) improvement and international standardization of methods of monitoring exposure to asbestos and other fibrous materials.

2. IDENTITY, PHYSICAL AND CHEMICAL PROPERTIES, SAMPLING AND ANALYSIS

2.1. Identity; Physical and Chemical Properties of Asbestos Minerals

Asbestos is a collective name given to minerals that occur naturally as fibre bundles and possess unusually high tensile strength, flexibility, and chemical and physical durability. Fibre bundles may be several centimetres long. Bundle diameters may vary significantly, but tend to be in the millimeter range. This has given rise to a technical grading based on fibre bundles, lengths, and diameters. However, when these fibre bundles are manipulated, they may break down into smaller units, a portion of which have dimensions in the submicron range.

The asbestos minerals are not classified on a mineralogical basis, but rather on a commercial basis because of their unique properties. Therefore, the asbestos variety commercially known as crocidolite is referred to in the mineralogical literature as riebeckite. The asbestos variety called amosite is known mineralogically as grunerite. All other asbestos types are referred to by their proper mineral names.

The properties usually attributed to asbestos as controlling both its stability in the environment, and its biological behaviour, include fibre length and diameter, surface area, chemical nature, surface properties, and stability of the mineral within a biological host. The physical and chemical properties of

asbestos have been widely discussed in the literature (Allison et al., 1975; Selikoff & Lee, 1978; Michaels & Chissick, 1979; US NRC/NAS, 1984; Langer & Nolan, 1985).

Two basic mineral groups, serpentine and amphibole, contain important asbestos minerals including the 6 minerals of special interest listed in Table 1. These groups are hydrated silicates with complex crystal structures. The typical chemical composition of the individual types of asbestos within these groups is provided in Table 1.

2.1.1. Serpentine group minerals - chrysotile

Chrysotile is a sheet silicate composed of planar-linked silica tetrahedra with an overlying layer of brucite. The silica-brucite sheets are slightly warped because of a structural mismatch, resulting in the propagation of a rolled scroll that forms a long hollow tube. These tubes form the composite fibre bundle of chrysotile.

Table 1. Physical and chemical properties of common asbestos minerals[a]

Characteristic	Chrysotile	Crocidolite[b]	Amosite[c]	Antho-phyllite[d]	T
Theoretical formula	$Mg_3(Si_2O_5)(OH)$	$Na_2Fe^{II}_3Fe^{III}_2(Si_8O_{22})(OH)_2$	$(Fe, Mg)_7(Si_8O_{22})(OH)_2$	$(Mg, Fe)_7(Si_8O_{22})(OH)_2$	Ca (Si_8O
Chemical analysis (range of major consitutents (%))					
SiO_2	38 - 42	49 - 56	49 - 52	53 - 60	5
Al_2O_3	(0 - 2)[e]	(0 - 1)	(0 - 1)	(0 - 3)	(
Fe_2O_3	(0 - 5)	13 - 18	(0 - 5)	(0 - 5)	(
FeO	(0 - 3)	3 - 21	35 - 40	3 - 20	
MgO	38 - 42	(0 - 13)	5 - 7	17 - 31	
CaO	(0 - 2)	(0 - 2)	(0 - 2)	(0 - 3)	
Na_2O	(0 - 1)	4 - 8	(0 - 1)	(0 - 1)	(
N_2O^+	11.5 - 13	1.7 - 2.8	1.8 - 2.4	1.5 - 3.0	1
Colour	usually white to pale green yellow[f], pink[f]	blue	light grey to pale brown	white to grey pale brown	
Decomposition temperature[g] (°C)	450 - 700	400 - 600	600 - 800	600 - 850	
Fusion temperature of residual material (°C)	1500	1200	1400	1450	

Table 1 (contd).

Characteristic	Chrysotile	Crocidolite[b]	Amosite[c]	Antho-phyllite[d]	T
Density (g/cm^3)	2.55	3.3 - 3.4	3.4 - 3.5	2.85 - 3.1	2
Resistance to acids	undergoes fairly rapid attack	good	attacked slowly	very good	
Resistance to alkalis	very good	good	good	very good	
Mechanical properties of fibre as taken from rock samples					
Tensile strength (10^3 kg/cm^2)	31	35	17	(< 7)	
(Average) (10^3 psi)	(440)	(495)	(250)	(< 100)	
Young's modulus (10^3 kg/cm^2)	1620	1860	1620	-	
(Average) (10^4 psi)	(23)	(27)	(23)		
Texture	usually flexible, silky, and tough	flexible to brittle and tough	usually brittle	usually brittle	

Table 1 (contd).

Characteristic	Chrysotile	Crocidolite[b]	Amosite[c]	Antho-phyllite[d]	T
Main producing countries	Canada, China, Italy, South Africa, Swaziland, USA, USSR, Zimbabwe	South Africa	South Africa	Mozambique USA	

[a] From: CEC (1977).

[b] Mineralogical name of crocidolite is riebeckite.

[c] Mineralogical name of amosite is grunerite.

[d] Anthophyllite asbestos is the proper term, as with tremolite and actinolite.

[e] Bracketed figures denote common elemental substitution found in asbestos miner

[f] From serpentinized dolomite deposits.

[g] Dehydroxylation or dehydrogenation accompanied by disruption of crystal lattic strength.

[h] Commercial exploitation of anthophyllite discontinued.

The chemical composition is uniform in contrast to that of the amphibole asbestos varieties. Some trace oxides (Table 1) are always present as a result of contamination during the formation of the mineral in the host rock. Some of these trace elements may be structurally accommodated within the tetrahedral site of the silica

layer (as in the case of aluminum substituting for silicon), or the octahedral site of the brucite layer (as in the case of nickel or iron substituting for magnesium), or may exist as major elements within minor concentrations of discrete mineral phases intercalated in the fibre bundle (e.g., magnetite). Organic impurities have not been observed in virgin chrysotile (Harington, 1962).

Chrysotile fibrils are long, flexible, and curved, and they tend to form bundles that are often curvilinear with splayed ends. Such bundles are held together by hydrogen bonding and/or extrafibril solid matter. Chrysotile fibres naturally occur in lengths varying from 1 to 20 mm, with occasional specimens as long as 100 mm. Some of the physical properties of chrysotile are shown in Table 1.

Exposure to acid results in the liberation of magnesium ions and the formation of a siliceous residue. Chrysotile fibres are almost completely destroyed within 1 h when placed in 1 N hydrochloric acid at 95 °C (Speil & Leineweber, 1969). Chrysotile is highly susceptible to acid attack, yet is more resistant to attack by sodium hydroxide than any of the amphibole fibres.

Chrysotile dehydroxylates partially and gradually; dehydroxylation mainly occurs at approximately 600 - 650 °C followed by recrystallization to fosterite and silica at about 810 - 820 °C.

2.1.2. Amphibole group minerals

The amphibole minerals are double chains of silica tetrahedra, cross-linked with bridging cations. The hollow central core typical for chrysotile is lacking.

Magnesium, iron, calcium, and sodium have been reported to be the principal cations in the amphibole structure (Speil & Leineweber, 1969). Some physical properties are summarized in Table 1.

The amphibole structure allows great latitude in cation replacement, and the chemical composition and physical properties of various amphibole asbestos fibres cover a wide range. Only rarely does the composition of a field sample coincide with the assigned theoretical or idealized formula. However, theoretical compositions are used for identifying the various fibres as a matter of convenience (Table 1).

Whereas the comminution of chrysotile fibres may produce separated unit fibrils (which are bound by weak proton forces and/or interfibril amorphous magnesium silicate material), the breakage (both parting and cleavage) of amphiboles occurs along

defined crystallographic planes. Parting along some of these surfaces may result in fibrils of amphibole, 4.0 nm in diameter (Langer & Nolan, 1985).

These mechanisms of amphibole breakage are important biologically with regard to resultant particle number, surface area, and general respirability (all of which control penetration to target cells and delivered dose), and also with regard to expressed chemical information contained on the fibre surface (Harlow et al., 1985). In a crystallographic study of amosite asbestos and its physically-different counterpart, grunerite, size distributions were different when they were comminuted in an identical manner. This factor controls both quantity and quality

of dose (Harlow et al., 1985).

2.1.2.1 Crocidolite (Riebeckite asbestos)

Crocidolite is represented by the "idealized" empirical formula provided in Table 1. Iron can be partially substituted by Mg^{2+} within the structure. Typical crocidolite fibre bundles easily disperse into fibres that are shorter and thinner than other amphibole asbestos fibres, similarly dispersed. However, these ultimate fibrils are generally not as small in diameter as fibrils of chrysotile. In comparison with other amphiboles or chrysotile, crocidolite has a relatively poor resistance to heat, but its fibres are used extensively in applications requiring good resistance to acids. Crocidolite fibres have fair to good flexibility, fair spinnability, and a texture ranging from soft to harsh. Unlike chrysotile, crocidolite is usually associated with organic impurities, including low levels of polycyclic aromatic hydrocarbons such as benzo(*a*)pyrene (Harington, 1962). Only about 4% of asbestos being mined at present is crocidolite.

2.1.2.2 Amosite (Grunerite asbestos)

The characteristics of amosite are given in Table 1. The Fe^{2+} to Mg^{2+} ratio varies, but is usually about 5.5:1.5. Amosite fibrils are generally larger than those of crocidolite, but smaller than particles of anthophyllite asbestos similarly comminuted. Most amosite fibrils have straight edges and characteristic right-angle fibre axis terminations.

2.1.2.3 Anthophyllite asbestos

Anthophyllite asbestos is a relatively rare, fibrous, orthorhombic, magnesium-iron amphibole (Table 1), which occasionally occurs as a contaminant in talc deposits. Typically, anthophyllite fibrils are more massive than other common forms of asbestos.

2.1.2.4 Tremolite and actinolite asbestos

The other fibres mentioned in the text include tremolite asbestos, a monoclinic calcium-magnesium amphibole, and its iron-substituted derivative, actinolite asbestos. Both rarely occur in the asbestos habit, but are common as contaminants of other asbestos deposits; actinolite asbestos occurs as a contaminant fibre in amosite deposits and tremolite asbestos as a contaminant of both chrysotile and talc deposits. Tremolite asbestos fibrils range in size but may approach the dimensions of fibrils of crocidolite and amosite.

2.2. Identity; Physical and Chemical Properties of Other Natural Mineral Fibres

Many minerals, other than asbestos, exist in nature with a fibrous habit. Still others comminute to produce particles with a fibrous form. Some enter the environment through human activities and others through natural erosion processes. These have become increasingly important because they have been linked with human disease in a limited number of instances (as with the case of erionite associated with mesothelioma in Turkey) and because they have been suggested as substitutes for asbestos.

2.2.1. Fibrous zeolites

Zeolites are crystalline aluminosilicates in which the primary "building blocks" are tetrahedra consisting of either silicon or aluminium atoms surrounded by four oxygen atoms. These tetrahedra combine, linked together by oxygen bridges and cations, to yield ordered three-dimensional frameworks. Although there are more than 30 known natural zeolites, only part of them are fibrous, including erionite, mesolite, mordenite, natrolites, scolecite and thomsonite (Table 2) (Wright *et al.*,1983;Gottardi & Galli, 1985).

Erionite fibres are similar in dimension to asbestos fibres, though they are probably shorter in length on average (Suzuki, 1982; Wright et al., 1983).

Table 2. Typical formulae of some fibrous zeolites[a]

Erionite	$(Na_2K_2CaMg)_{4.5}(Al_9Si_{27}O_{72}) \times 27\ H_2O$
Mesolite	$Na_2Ca_2Al_6Si_9O_{30} \times 8H_2O$
Mordenite	$(Ca,Na_2,K_2)Al_2Si_{10}O_{24} \times 7(H_2O)$
Natrolite	$Na_2Al_2Si_3O_{10} \times 2H_2O$
Paranatrolite	$Na_2Al_2Si_3O_{10} \times 3H_2O$
Tetranatrolite	$Na_2Al_2Si_3O_{10} \times 2H_2O$
Scolecite	$CaAl_2Si_3O_{10} \times 3H_2O$
Thomsonite	$NaCa_2Al_5Si_5O_{20} \times 6H_2O$

[a] From: Mumpton (1979).

2.2.2. Other fibrous silicates (attapulgite, sepiolite, and wollastonite)

The chemical composition of these minerals is:

palygorskite (attapulgite):
$Mg_5Si_8O_{20}(OH)_2(H_2O)_4 \times 4H_2O$ (Barrer, 1978);

sepiolite:
$Mg_8Si_{12}O_{30}(OH)_4(H_2O)_4 \times 8H_2O$ (Barrer, 1978);

wollastonite:
$CaSiO_3$ (Ullmann, 1982).

Certain clay minerals, such as sepiolite and, especially, attapulgite, may occur in forms that are similar to both chrysotile and amphibole asbestos fibrils. Under the electron microscope, they may appear to have a hollow tube structure, or have an appearance of an amphibole lath. Meerschaum represents a massive form of fibrous sepiolite. The surface of attapulgite resembles that of chrysotile in that it is hydrated and protonated. Attapulgite consists principally of short fibres of the mineral palygorskite (Bignon et al., 1980).

Wollastonite has received considerable attention as a possible substitute for asbestos. The basic structure of this mineral is an infinite silicon oxygen chain (SiO_3). Calcium cations link the infinite chains together (Leineweber, 1980). The properties of wollastonite as well as its biological effects have been discussed

in several papers (Korhonen & Tossavainen, 1981; Huuskonen et al., 1983a,b).

Relevance of physical and chemical properties to biological effects

For respirability, the most important single property of both asbestos and other fibrous minerals appears to be fibre diameter. The smaller the fibre diameter, the greater the particle number per unit mass of dust; the more stable the dust aerosol, the greater the inhalation potential and penetration to distal portions of the lung. Once within the tissue, fibre length, surface chemistry, and physical and chemical properties are the likely factors controlling biological activity (Langer & Nolan, 1985).

2.3. Sampling and Analytical Methods

Collection and preparation of samples from the environment and subsequent analysis of asbestos and other natural mineral fibres or application of direct measuring methods are required for the assessment of human exposure, evaluation of control measures, and control of compliance with regulations. Sampling strategies and analytical procedures must be adequately planned and conducted. Calibration of instruments and quality control are essential to ensure accuracy and precision. Detailed descriptions of the collection and preparation of samples and of analytical procedures are beyond the scope of this document (Asbestos International Association, 1982, 1984; EEC, 1983; ILO, 1984).

2.3.1. Collection and preparation of samples

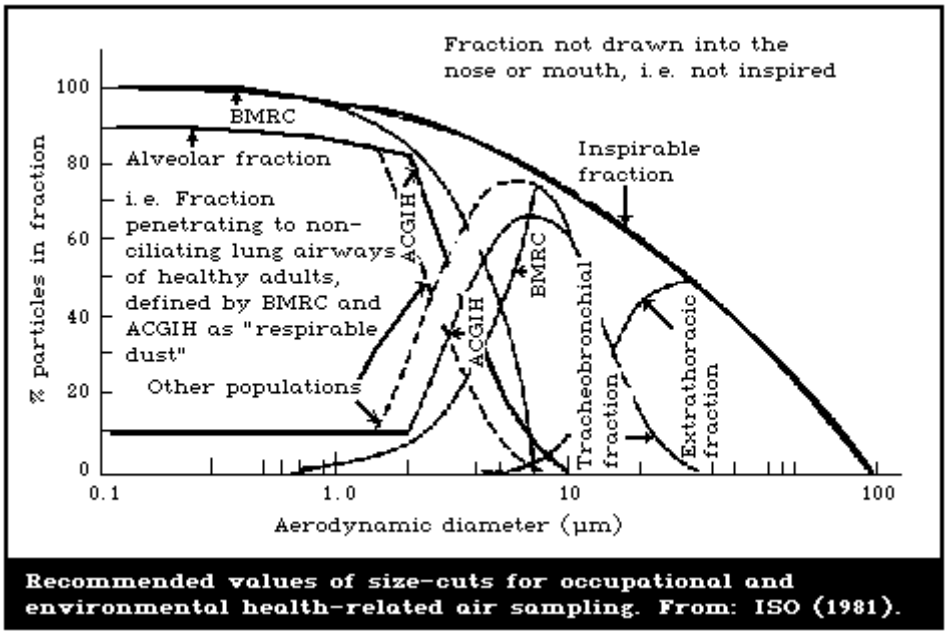
The collection and preparation of samples from air, water, and biological and geological media require different strategies and specimen preparation techniques. However, once in a suitable form for analysis, the instrumental methods required are virtually identical.

2.3.1.1 Air

The identity of fibres in the work-place is usually known. This is not true in the general environment, where fibre identification is generally necessary. The ratio of asbestos fibres to total respirable particles varies widely, ranging from $1:10^3$ to $1:10^7$ (Nicholson & Pundsack, 1973; Lanting & den Boeft,1979).

In addition to fibre identification and concentration, it is important to focus on fibre size and its relation to inspirability and respirability (Fig. 1).

The upper limit of the geometric diameter of respirable asbestos fibres is 3 µm, obtained from the cut-off of the alveolar fraction of spherical particles (aerodynamic diameter of 10 µm; specific gravity 1 g/cm^3) (Fig. 1) and the average specific gravity of asbestos (3 g/cm^3). While, in some countries, the inspirable fraction as a whole is covered when measuring the concentration of airborne asbestos, only the alveolar fraction (termed "respirable dust") is used in the majority of countries (ILO, 1984).



Recommended values of size-cuts for occupational and environmental health-related air sampling. From: ISO (1981).

The concentration of airborne fibres is expressed either as fibre number concentration, i.e., fibres/ml, fibres/litre, or fibres/m^3 (alveolar fraction) in the work-place and/or general environment, or as mass concentration, i.e., mg/m^3, in the work-place environment and for emission control (inspirable or alveolar fraction) (EEC, 1983; ILO, 1984), or ng/m^3 in the general environment (alveolar fraction).

When fibre number concentrations are determined by optical microscopy, particles having a diameter of less than 3 µm, a length-to-diameter ratio greater than 3:1, and a length greater than 5 µm are counted, since they are thought to be the most biologically-relevant part of the alveolar fraction (EEC, 1983; ILO, 1984). However, this conclusion is based mainly on studies on animals involving intrapleural or intraperitoneal administration of fibres, or intratracheal administration. In addition, alveolar deposition is relevant for the induction of pleural and peritoneal mesotheliomas and interstitial fibrosis, but not for the production of bronchial carcinomas in man, most of which develop in the large bronchi.

In the past, sampling strategies have not always been representative of workers' exposures. As an initial step, an inventory of the work-place exposure conditions should be undertaken. The sampling strategy should be determined by the nature of probable exposure at different work locations. An adequate sampling strategy can, and must be, designed and strictly followed, and should include decisions on "where", "when", and "for how long" to sample, as well as on the acceptable number of samples. The sampling procedure must also be considered so that a sampling plan can be established. Details of sampling strategies and procedures can be found in the literature (US NIOSH, 1973, 1977; Robock & Teichert, 1978; Rajhans & Sullivan, 1981; Asbestos International Association, 1982, 1984; Robock, 1982; Valic, 1983; ILO, 1984; WHO, 1984).

Specific procedures for the evaluation of airborne asbestos have been developed and some have been standardized and used in different countries (US EPA, 1978; US NIOSH, 1984; Asbestos International Association, 1982, 1984; EEC, 1983; ILO, 1984; ISO, 1984; OECD, 1984). These procedures usually provide guidelines for

sampling strategy in addition to collection and analytical procedures.

Samples are collected by drawing a given volume of air through a filter for a given length of time, using pumps that are able to provide a constant and measureable rate of flow. The concentration of the fibres deposited on the filter is subsequently determined.

Personal sampling within the worker's breathing zone, as well as static sampling at fixed locations, can be conducted, depending on the purpose of the evaluation. Personal sampling should be used to assess a worker's exposure (e.g., for compliance control and for epidemiological studies). Static sampling is widely applied for the evaluation of engineering control.

Basically, the same principles should be applied in collecting samples for the determination of airborne fibre concentrations in ambient-air (Asbestos International Association, 1984; VDI, 1984). However, the sampling strategy (e.g., location of sample collection points, duration of sampling, etc.) varies from that in the occupational environment (VDI, 1984).

The same principles should also be applied in the collection of samples at the work-place to determine mass concentrations (mg/m^3) by gravimetric methods (ILO, 1984).

2.3.1.2 Water

Available technology for determining asbestos in water is described in a US EPA report (US EPA, 1983). The water sample to be analysed is initially treated with ozone and ultraviolet radiation to oxidize suspended organic material. A capillary pore polycarbonate filter (0.1 μm pore size) is then used to filter the water sample. The filter is prepared by carbon extraction replication and then examined with a transmission electron microscope (TEM).

Since some problems may require less sophisticated instrumentation, depending on fibre size, type, and concentration, and to minimize expenditure, a more inexpensive rapid method has been developed to evaluate the need for the detailed analysis of water samples suspected of containing asbestos fibres. This method is not yet in common use. Details of both the full method and the rapid method are given in US EPA (1983).

2.3.1.3 Biological tissues

Many techniques have been developed for the recovery of mineral dust from human tissues (Langer et al., 1973; Gaudichet et al., 1980; Pooley & Clark, 1980). These include wet chemistry methods (e.g., formamide, glacial acetic and other acids, enzyme, alkali, and sodium hypochloride digestion), and physical methods (e.g., ashing using both low and high temperatures) for tissue destruction. The recovered residues can be assayed gravimetrically, by light microscopy or by electron beam instrumentation (Langer et al., 1973). In addition, with the development of the carbon-extraction replication technique, it is possible to analyse, *in situ,* minerals in tissue slides (Langer et al., 1972).

2.3.1.4 Geological samples

The preparation of geological specimens (rocks, soils, powdered mineral specimens, etc.) for fibre analysis follows standard

geological techniques for sample selection, splitting, and chemical-physical mineral separation. Detailed descriptions of the many techniques available is beyond the scope of this document (Bowes et al., 1977).

2.3.2. Analysis

In general, the analytical procedures for fibre quantification and identification are applicable to all types of samples.

2.3.2.1 Light microscopy

Several versions of a method for counting respirable fibres on filters, based on phase contrast light microscopy, have been developed (Asbestos Research Council, 1971; Asbestos International Association, 1982; US NIOSH, 1984). These are most appropriate for analysis in the occupational environment, where fibre identification is unnecessary. The most widely recommended procedure is the Membrane Filter Method, based on the Asbestos

International Association/RTMI method, which has also been adopted by the European Economic Communities (EEC, 1983) and the International Labour Office (ILO, 1984). The same principles are now under discussion for acceptance by the International Standards Organization (ISO, 1984). The determination of fibres by phase contrast microscopy has been widely discussed in the literature (Rooker et al., 1982; Walton, 1982; ILO, 1984; Taylor et al., 1984).

Mineral fibres down to about 0.25 µm in diameter (lower for amphiboles than for chrysotile) are visible and countable by this method. Identification of specific fibre types is not possible using this technique and, therefore, every fibre is counted as "asbestos". The detection limit of the method, defined as the minimum fibre concentration that can be detected above the background fibre count, is usually 0.1 fibre/ml. Theoretically, the detection limit can be lowered by increased sampling time, but this cannot normally be achieved in industrial situations because ambient dust levels lead to overloading of the filter.

Large systematic and random observer differences in optical fibre counts have been reported using the Membrane Filter Method. These can be reduced by selection of the proper equipment, training of personnel, and inter-laboratory comparisons.

Improvement in the counting of fibres can be effected by the automatic evaluation of filter samples. In principle, such evaluations can be conducted using image analysing systems (Dixon & Taylor, 1979) or magnetic alignment combined with scattered light measurements (Gale & Timbrell, 1980).

Finally, it must be stressed that the development, improvement, and refinement of the Membrane Filter Method in recent years have led to higher sensitivity and thus to more reliable assessment of levels in the work-place.

2.3.2.2 Electron microscopy

Asbestos fibres may represent a very small part of the total number of particles in the general environment, water, and biological and geological samples. Moreover, the types of fibres may not be known, and the diameters of asbestos fibres found may be smaller than those found in the work-place environment. Thus, an electron microscopic technique is preferred for the analysis of

these filter samples. For example, scanning electron microscopy (SEM), transmission electron microscopy (TEM, STEM) with energy dispersive X-ray analyser (EDXA), and selected area electron diffraction (SAED) (so-called analytical electron microscopy) can be applied. Analytical electron microscopy has been discussed in the specialized literature (Clark, 1982; Lee et al., 1982; Steel et al., 1982).

In order to establish a correlation with the results obtained by phase contrast microscopy, the results of any fibre count

(aspect ratio $\geq$ 3:1) must contain the following size fraction:

- fibres greater in length than 5 µm with diameters between 0.25 µm and 3 µm, which represent the size fraction recommended for counting by phase contrast microscopy.

When required, the following size fractions can also be considered:

- fibres greater in length than 5 µm with diameters of less than 0.25 µm; and

- fibres shorter in length than 5 µm with diameters greater than and/or smaller than 0.25 µm.

The results obtained by the electron microscopic assessment of concentrations of total fibrous particles and/or asbestos particles have often only been published for an aspect ratio greater than 3:1, independent of length and diameter. These results cannot be compared, since there are few data on the lower visibility limit (magnification) and identification limit with regard to the diameter, and since no correlation with the evaluation criteria for measurements in work-place environments can be established.

(a) *Scanning electron microscopy*

Fibres with diameters as small as 0.03 - 0.04 µm may be visible with this instrument, depending on preparation and instrumentation techniques (Cherry, 1983). The scanning electron microscope can be used routinely to identify fibres down to a diameter of 0.2 µm, when equipped with an energy dispersive X-ray spectrometry system (EDXA) in environments where fibres are known. Limitations may be encountered in environments where different minerals have identical elemental ratios; in this case, selected area electron diffraction (SAED) is required for identification.

One advantage of SEM is that the filter (membrane or Nuclepore) can be examined directly within the microscope, without the generation of preparation artifacts.

(b) *Transmission electron microscopy*

A modern Transmission Electron Microscope has a resolution of about 0.0002 µm, which is more than adequate for resolving unit fibrils of any mineral. The TEM, if equipped with EDXA, can chemically characterize fibres down to a diameter of 0.01 µm. In addition, SAED permits the determination of structural elements of crystalline substances. When samples containing large fibres are analysed under similar conditions, the detection limits are comparable for TEM and SEM. As the sensitivity of analytical instruments increases, so does the possibility of error in measurement, e.g., the incorporation of adventitious mineral

grains. This may result in erroneous fibre counts, especially in the analysis of samples with a low mineral fibre content.

The application of the TEM is very advantageous because of the possibility of structural characterization by means of SAED, which increases identification accuracy (Beaman & Walker, 1978).

2.3.2.3 Gravimetric determination

Various generally-known methods are available for the gravimetric evaluation of filter samples (mg/m^3) from the work-place environment and exhaust emissions, including the weighing of the filter before and after dust sampling or absorption of ionizing radiation. Qualitative and quantitative infrared spectrometry or X-ray diffraction analysis (Taylor, 1978; Lange & Haartz, 1979), to determine the composition of dust, can be carried out on such filter samples. These filters must contain a relatively large mass of dust. The disadvantage of gravimetric determination is that there is no discrimination between fibrous and non-fibrous dusts, and therefore, it is thought to provide a poor index of the health hazards posed by asbestos-containing dust.

2.3.3. Other methods

Optical dust-measuring instruments, such as the Tyndallo-meter, the Fibrous Aerosol Monitor, and the Royco particle counter (ACGIH, 1983), apply the light scattering principle for measuring dust concentrations in the work-place environment and in stacks of central dust collectors. They are direct-reading instruments to which a recorder can be connected.

The advantages of these instruments are:

(a) immediate location of dust sources;

(b) instant determination of the efficiency of dust-suppression measures;

(c) recording of fluctuations of dust concentrations; and

(d) determination of short-time peak concentrations.

However, these techniques are limited by dust concentration, particle morphology, and the lack of specificity in terms of particle identity.

These direct-reading instruments are used mainly for static monitoring, and for the evaluation of engineering control measures. For reliable evaluation of work-place air levels, these instruments should be calibrated with work-place dust samples of known concentration.

2.3.4. Relationships between fibre, particle, and mass concentration

There is no general relationship between the results of fibre counts and mass measurements in the assessment of the concentration of asbestos and other natural mineral fibres in the various types of environmental media.

Several attempts have been made to establish conversion factors between mass measurements and fibre counts (Bruckman & Rubino, 1975; Gibbs & Hwang, 1980). Although relationships for individual work-places and specific work practices have been determined, these factors cannot be applied generally. The very wide range of numbers

of fibres per unit weight for a given density as a function of fibre size has been calculated by Pott (1978) on a theoretical basis (Table 3). In early analyses for asbestos using electron microscopy, the sample-preparation technique artificially increased the number of fibres, and therefore, the authors usually reconverted fibre counts to mass units. However, using electron microscopy, it is now possible to measure asbestos fibres unchanged and, thus, the conversion is not warranted.

Conversion of the results of measurements of number of particles per unit volume (mppcf - millions of particles per cubic foot) obtained with the Midget Impinger into number of fibres per unit volume (F/ml) has presented similar problems (Robock, 1984). While the calculated mean ratios (F/cm^3/mppcf) for various industrial settings varied only between 3 and 8, there were large variations within each industry; for example, in the textile industry, the experimentally-determined ratio varied from 1.2 to 11.6 and, in mines, between 0.5 and 47.4 (Robock, 1984).

Table 3. The numbers of fibres per ng for different size categories (cylindrical fibre shape, density 2.5); diameter/length ratios in the second line[a]

Diameter	Length (µm)							
(µm)	0.625	1.25	2.5	5	10	20	40	80
0.031	819 200 1:20	409 600 1:40	204 800 1:80	102 400 1:160				
0.0625	204 800 1:10	102 400 1:20	51 000 1:40	25 600 1:80	12 800 1:160			
0.125	51 200 1:5	25 600 1:10	12 800 1:20	6400 1:40	3200 1:80	1600 1:160		
0.25	12 800 1:2.5	6400 1.5	3200 1.10	1600 1:20	800 1:40	400 1:80	200 1:160	
0.5		1600 1:2.5	800 1:5	400 1:10	200 1:20	100 1:40	50 1:80	25 1:160
1.0			200 1:2.5	100 1:5	50 1:10	25 1:20	12.5 1:40	6.25 1:80
2.0				25 1:2.5	12.5 1:5	6.25 1:10	3.2 1:20	1.6 1.40

[a] From: Pott (1978).

3. SOURCES OF OCCUPATIONAL AND ENVIRONMENTAL EXPOSURE

Once liberated into the environment, asbestos persists for an unknown length of time. The release of free fibres into the air through both natural and human activities is the most important mode to be considered. The main potential exposure sources are the handling, processing, and disposal of dry asbestos and asbestos-containing products. Fibres can also be released through the weathering of geological formations in which asbestos occurs or as a result of the disturbance of these formations by man.

3.1. Natural Occurrence

Asbestos is widely distributed throughout the lithosphere, and is found in many soils. Chrysotile, the most abundant and economically-important form, is present in most serpentine rock formations in the earth's crust and workable deposits are present

in over 40 nations; however, Canada, South Africa, the USSR, and Zimbabwe, have 90% of the established world reserves (Shride, 1973). On the other hand, the various amphibole asbestos mineral types have a comparatively limited geographical distribution, principally in Australia and South Africa.

The presence of asbestos minerals as accessory minerals in geological formations is quite common throughout the world. However, only a few of these deposits are commercially exploitable. In Europe, the serpentine belt of the Alpine mountain chain contains chrysotile as well as other mineral fibres. These rocks can be disturbed by weathering, land-slides, or by man during such activities as mining, road construction, and tilling of the soil.

The total amount of asbestos emitted from natural sources is probably greater than that emitted from industrial sources. However, no measurements concerning the extent of release of airborne fibres through natural weathering processes are available.

A study of the mineral content of the Greenland ice cap showed that airborne chrysotile existed long before it was used commercially on a large scale. The earliest dating in the ice cores showed the presence of chrysotile in 1750 (Bowes et al., 1977).

There are also some data on levels of asbestos in water supplies due mainly to erosion from natural sources (e.g., drinking-water in areas such as San Francisco, California; Sherbrooke, Quebec; and Seattle, Washington).

Increases in the incidence of asbestos-related diseases (e.g., pleural calcification and mesothelioma) in areas in Bulgaria, Czechoslovakia, Finland, Greece, and Turkey have served as a surrogate indicator of exposure to other natural mineral fibres (e.g., anthophyllite, tremolite, sepiolite, and erionite). The results of such studies are discussed more fully in section 8 (Burilkov & Michailova, 1970; Constantopoulos et al., 1985).

In the Federal Republic of Germany and the USA, asbestos emissions have been detected in quarries (Carter, 1977; Spurny et al., 1979b), and from quarried rocks used as road gravel (Rohl et al., 1977).

3.2. Man-Made Sources

3.2.1. Asbestos

Activities resulting in potential asbestos exposure can be divided into four broad categories. The first category is the mining and milling of asbestos. The second is the inclusion of asbestos in products that are currently being developed or manufactured such as brake shoes, thermal insulation, floor tiles, and cement articles, and the manipulation of these products (e.g., replacement of brake shoes and insulation materials). The third potential source includes construction activities (cutting and other manipulations), particularly the removal (e.g, tear-out or stripping) or maintenance of previously-installed asbestos in buildings or structures, and the demolition of asbestos-containing buildings or structures. The fourth is the transportation, use, and disposal of asbestos or asbestos-containing products. In each case, appropriate work practices and control measures to prevent or control the release of asbestos must be implemented (ILO, 1984).

3.2.1.1 Production

The world production of asbestos increased by 50% between 1964 and 1973, when it reached a level of nearly 5 million tonnes. The projected world demand for asbestos, based on historical consumption figures and usage patterns through the mid-1970s, indicates more than a doubling by the year 2000. However, world production figures for the period 1979-83 showed a decline in production (Table 4). Fig. 2 shows a drastic decline in major asbestos uses in the USA in the period 1977-83. The only substantial increase in asbestos demand seems to be occurring in developing countries (Clifton, 1980), and in some European countries. Industrial Minerals (1978) reported that the market for some natural mineral fibres, other than asbestos, is growing rapidly as a result of the constant search for asbestos substitutes. This is, in part, a result of the legislative restrictions on asbestos in some countries.

Table 4. World production figures on asbestos (tonnes)[a]

Country	1979	1980	1981	1982	1983
Afghanistan	4000				
Argentina	1371	1261	1280	1218	1350
Australia					
Chrysotile	79 721	92 418	45 494	18 587	20 000
Brazil	138 457	170 403	138 417	145 998	158 855
Bulgaria	600	700	400	600	700
Canada					
Chrysotile	1 492 719	1 323 053	1 121 845	834 249	820 000
China	140 000	131 700	106 000	110 000	110 000

Table 4 (contd.)

Country	1979	1980	1981	1982	1983
Cyprus					
Chrysotile	35 472	35 535	24 703	18 997	17 288
Czechoslovakia	564	617	388	342	325
Egypt	238	316	325	310	325
India					
Amphibole	32 094	33 716	27 521	19 997	17 288
Italy	143 931	157 794	137 000	116 410	139 054
Japan					
Chrysotile	3362	3897	3950	4135	4000
Korea, Republic of	14 804	9854	14 084	15 933	12 506
Mozambique	789	800	800	800	800
South Africa					
Amosite	39 058	51 646	56 834	43 457	40 656
Crocidolite	118 301	119 148	102 337	87 263	87 439
Chrysotile	91 828	106 940	76 772	81 140	93 016
Swaziland					
Chrysotile	34 294	32 833	35 264	30 145	28 287
Taiwan	2957	683	2317	2392	2819
Turkey	38 967	8882	2833	23 283	22 596
USA[b]	93 354	80 079	75 618	63 515	69 906
USSR	2 020 000	2 070 000	1 105 000	2 180 000	2 250 000
Yugoslavia	9959	10 468	12 206	10 748	9663
Zimbabwe					
Chrysotile	259 891	250 949	247 503	197 682	153 221
World Total	4 800 000	4 700 000	4 300 000	4 000 000	4 100 000

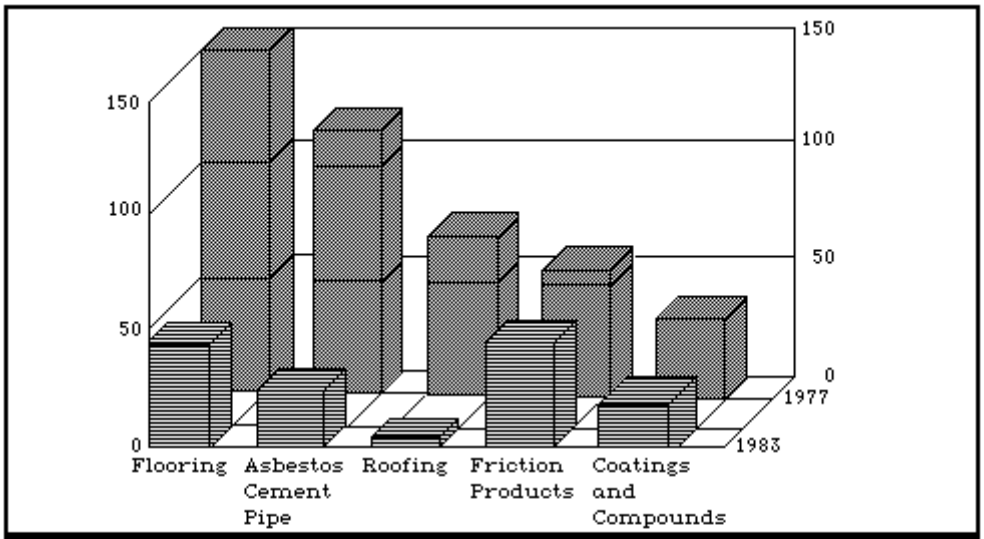
[a] From: BGS (1983).
[b] Sold or used by producers.

Note: In addition to the countries listed, the Democratic Peoples Republic of Korea and Romania are also believed to produce asbestos.

3.2.1.2 Mining and milling

Asbestos ore is usually mined in open-pit operations. Possible sources of particulate (asbestos) emissions include: drilling, blasting, loading broken rock, and transporting ore to the primary crusher or waste to dumps. Subsequently, the ore is crushed and may lead to exposure from the following emission sources: unloading ore from the open pit, primary crushing, screening, secondary crushing, conveying and stockpiling wet ore. A drying step follows, which involves conveying the ore to the dryer building, screening, drying, tertiary crushing, conveying ore to dry-rock storage building, and dry-rock storage. The next step is the milling of the ore. In well-controlled mills, this is largely confined to the mill building and presents very little emission to the air because the mill air is collected and, usually, ducted through some particulate matter control device.

Few attempts have been made to quantify fibre emissions from mining and milling operations.



Year	Flooring	Asbestos Cement Pipe	Roofing products	Friction products	Coatings and compounds
1977	150	115	70	57	36
1978	138	106	64	53	33
1979	125	96	58	48	30
1980	70	42	24	52	11
1981	67	42	16	51	13
1982	49	38	7	53	25
1983	45	26	6	48	23

Trend showing the decline of major asbestos uses in the USA during the 1977–83 period. From: Clifton (1985). Table gives end-use data in thousands of metric tonnes.

3.2.1.3 Uses

Asbestos has been used in thousands of applications (Shride, 1973). The way in which asbestos has been incorporated into various end-products is illustrated in Fig. 3. There are wide variations in the pattern of use of asbestos in various countries. For example, in some countries, the production and application of some of these asbestos products has been discontinued, in part,

because of serious health risks associated with their production. In some countries, there are also secular trends in the pattern of usage, i.e., decrease in the production of insulation and increase in the manufacture of friction materials. The products in group I cannot all be regarded as end-products but are generally used in conjunction with water as insulating plasters, cement, or spray mixtures. The greatest use of asbestos fibres lies in the manufacture of composites (group II). The cement variety, i.e., asbestos cement, constitutes a major component of this group. Other products of major importance are friction materials, insulation boards, millboard and paper, reinforced plastics, and vinyl tiles and sheets. Asbestos can be spun into yarn and woven into cloth. The resulting textile products (group III) can be used for further processing into friction materials, packings, and laminates, or may find direct applications such as insulation cloth, protective clothing, fire protection, and electrical insulation.

A list of the most important asbestos-containing products and their approximate fibre contents is given in Table 5. The references in the right-hand column refer to Fig. 3.

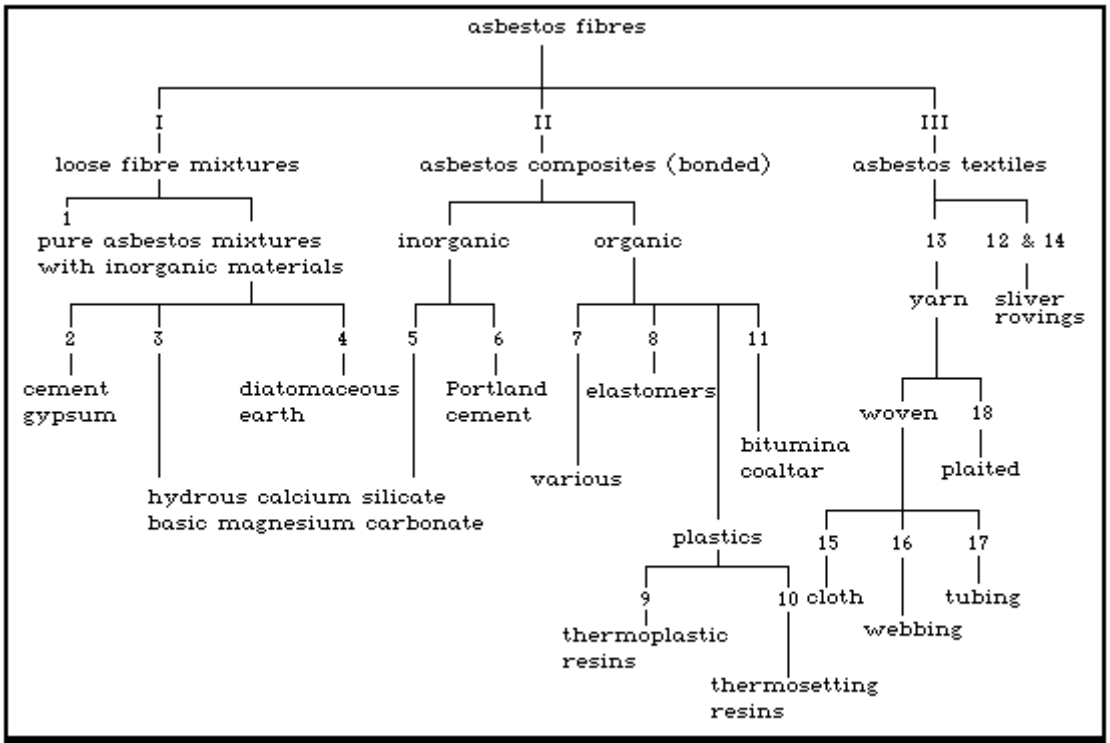
It should be noted that the extent to which respirable fibres are produced depends on the type of asbestos product and how it is manipulated.

3.2.2. Other natural mineral fibres

Other natural mineral fibres may be present in air in respirable form or may become respirable as a result of manipulation. The dimensions of these fibres are comparable with those of asbestos.

(a) *Fibrous zeolites*

Erionite has been mined in the USA for use in ion-exchange processes, for the retention of nitrogen in fertilizers, and for use in concrete aggregate or road surfacing. Some of these applications, as well as natural weathering, may lead to significant fibre concentrations in the local air (US NRC/NAS, 1984). Fibres may also be found in drinking-water as a result of natural weathering.



Applications of asbestos fibres. From: CEC (1977).

Table 5. Asbestos products and asbestos contents[a]

	Approximate asbestos content (% weight)	Asbestos fibre type[b]	Reference to Fig. 3
1. Asbestos-cement building products	10 - 15	C, A, Cr	II-6
2. Asbestos-cement pressure, sewage, and drainage pipes	12 - 15	C, Cr, A	II-6
3. Fire-resistant insulation boards	25 - 40	A, C	II-6, II-5
4. Insulation products including spray	12 - 100	A, C, Cr	I-1, I-2, I-3, I-4, II-5
5. Jointings and packings	25 - 85	C, Cr	II-8, III-18
6. Friction materials	15 - 70	C	II-10
7. Textile products not included in (6)	65 - 100	C, Cr	III
8. Floor tiles and sheets	5 - 7.5	C	II-9
9. Moulded plastics and battery boxes	55 - 70	C, Cr	II-9, II-10
10. Fillers and reinforcements and products made	25 - 98	C, Cr	II-7, II-11

	thereof (felts, millboard, paper, filter pads for wines and beers, underseals, mastics, adhesives, coatings, etc.	

[a] From: CEC (1977).
[b] A = amosite (not used in all countries); C = chrysotile; Cr = crocidolite (not used in all countries).

(b) *Palygorskite (attapulgite)*

Available data on the production of attapulgite in various countries are presented in Table 6.

Table 6. World production of attapulgite and sepiolite[a]

Country	Annual production of attapulgite (tonnes)	Annual production of sepiolite (tonnes)
France	unknown	2500
India	10 000	
Senegal	16 700	
Spain	50 000	236 000
USA	700 000	

[a] Modified from: Bignon et al. (1980).

The USA is the biggest producer and consumer of attapulgite; consumption currently exceeds 700 000 tonnes and is almost triple that of asbestos. The consumption figures for various uses of attapulgite in the USA are listed in Table 7. An additional 100 000 tonnes is exported from the USA each year (US Bureau of Mines, 1982). Similar data for other countries are not available.

Table 7. Uses of attapulgite in the USA[a]

Use	1981 consumption (1000 tonnes)
Drilling mud	173.5
Fertilizers	50.2
Filtering (oil and grease)	18.7
Oil and grease adsorbents	178.2
Pesticides and related products	106.5
Pet waste adsorbent	105.8
Medical, pharmaceutical, cosmetic ingredients	0.06
Other uses	79.5
Total	712.46

[a] From: US Bureau of Mines (1982).

In France, attapulgite is used in drugs for the treatment of gastrointestinal diseases (Bignon et al., 1980); in the USA, it is a component of non-prescription antidiarrhoeal drugs (Physicians'

Desk Reference, 1983).

The potential environmental effects of attapulgite were reviewed by the US NRC/NAS (1984). It was stated that, when used in such products as pet waste adsorbents, fertilizers, and pesticides, substantial amounts of attapulgite could be released into the air. Attapulgite has also been found in water supplies (Millette et al., 1979b).

(c) *Sepiolite*

Available data on the production of sepiolite in several countries are presented in Table 6.

Minerals that contain sepiolite are used as cat litter.

3.2.3 Manufacture of products containing asbestos

3.2.3.1 Asbestos-cement products

Throughout the world, the asbestos-cement industry is the largest user of asbestos fibres. Asbestos-cement products contain 10 - 15% asbestos, mostly in the form of chrysotile, though limited amounts of crocidolite may be used in large-size asbestos-cement pipes, to give the required strength as well as to increase the speed of production. The most important products are asbestos-cement pipes and sheets. Products are primarily manufactured in wet processes.

Possible emission sources are: (a) the feeding of asbestos fibres into the mix; (b) blending the mix; and (c) cutting or machining end products. Emissions may range from negligible to significant according to the dust control measures and technology. Emissions can also occur from sources other than processing operations, such as the improper handling and/or shipment of dry materials containing asbestos and during the cutting or machining of end-products. Recently, control measures have been developed and approved in the Federal Republic of Germany (Berufsgenossenschaftliches Institut für Arbeitssicherheit, 1985), which have reduced airborne levels in the immediate vicinity by 1 - 2 orders of magnitude, generally, to less than 1000 fibres/litre.

3.2.3.2 Vinyl asbestos floor tiles

The second largest user of asbestos fibres in the USA is the asphalt and vinyl floor tile manufacturing industry. This type of tile has found increased use in many countries because of its durability and impermeability to water.

3.2.3.3 Asbestos paper and felt

Products classified as asbestos paper and felt range from thin paper to 1 cm thick millboard, which contains up to 97% asbestos. The feed for paper machines is prepared by mixing short chrysotile fibres with water and binders. Since papermaking is a wet process, little asbestos dust is generated during manufacture. However, finishing operations, such as slitting and calendering, may be sources of dust emission. The use of asbestos paper and felt is declining in some countries.

3.2.3.4 Friction materials (brake linings and clutch facings)

Moulded brake linings are used on disc and drum-type car brakes. Woven brake linings and clutch facings for heavy use are

made from high-strength asbestos yarn and fabric reinforced with wire; this material is dried and impregnated with resin. In the moulding process, the asbestos fibres and other constituents are combined with the resin, which is thermoset. Final treatment involves curing by baking, and grinding to customer specifications. Emissions may range from negligible to significant depending on dust control measures and technology.

3.2.3.5 Asbestos textiles

Asbestos textiles are used in the manufacture of fire-resistant garments, sealing materials, wicks, and thermal insulation, or as an intermediate product in brake linings, clutch facing, insulation, and gaskets. Asbestos textile manufacturing is the dustiest of all asbestos-manufacturing processes, and dust emanating from this process is more difficult and costly to control. However, during the past decade, emissions have been substantially reduced in countries in which improved control measures and technology have been implemented.

3.2.4 Use of products containing asbestos

Few data are available on fibre emissions during the use of products containing asbestos or other mineral fibres. In most construction materials and consumer products, the fibres are firmly bound or encased in a solid matrix and are not expected to be released under normal conditions, but may be emitted during manipulation or renovation of such materials or products (e.g., fibre levels measured by light microscopy in the vicinity of such activities as removal of pipe lagging containing asbestos or the sanding of asbestos-containing drywall topping and spackling compounds may approach or exceed current occupational exposure limits) (Fischbein et al., 1979; Sawyer & Spooner, 1979).

4. TRANSPORT AND ENVIRONMENTAL FATE

4.1 Transport and Distribution

Once in the environment, fibres are mainly transported and distributed via air and water.

4.1.1 Transport and distribution in air

Airborne mineral fibres are stable and may travel significant distances from the site of origin. Airborne asbestos fibres, for example, have aerodynamic diameters that are generally less than 0.3 µm and, therefore, their sedimentation velocities are very low. Measurements concerning the transport and distribution of specific mineral fibres have been made under certain environmental conditions and at specific locations (Laamanen et al., 1965; Heffelfinger et al., 1972; Harwood & Blaszak, 1974; US EPA, 1974).

Calculations using a dispersion model from a point source (Harwood & Blaszak, 1974) indicated that concentrations of airborne fibres of small dimension decreased very slowly with increasing distance. This study underscores two important characteristics of ambient air fibre burden:

(a) fibres are transported great distances from point sources; and

(b) fibres in ambient air are small in size, requiring electron beam instrumentation for detection.

4.1.2 Transport and distribution in water

Long-range transport of asbestiform fibres in water has been reported. Cooper & Murchio (1974) concluded that chrysotile fibres present in tap-water in San Francisco, California, were actually introduced at a reservoir many km south of the city. Nicholson (1974) attributed the presence of amphibole fibres in the municipal water supply of Duluth, Minnesota, to the transport, over 96 km, of taconite tailings from a Silver Bay mining operation. In this instance, transport resulted from bottom currents in Lake Superior.

4.2 Environmental Transformation, Interaction, and Degradation Processes

Mineral fibres are relatively stable and tend to persist under typical environmental conditions. However, asbestos fibres may undergo chemical alteration as well as changes in dimension. For example, chrysotile, and to a lesser extent amphibole, asbestos fibres are capable of chemical alteration in aqueous media. The magnesium hydroxide content of chrysotile is partially or wholly removed by solution, depending on time, temperature, and pH. An insoluble silica skeleton of the fibre remains. Grunerite fibres, of which amosite is the known commercial form, have been reported to react with water, losing some iron on extended exposure to lake water; the fibres appeared partially degraded and broken when examined microscopically (Kramer et al., 1974).

The comparative solubility of selected mineral fibres has been studied and a general trend determined: chrysotile > amosite > actinolite > crocidolite > anthophyllite > tremolite (US NRC/NAS, 1977). Because of their high adsorption properties, it is thought that some mineral fibres may adsorb and carry various organic agents present in the environment.

5. ENVIRONMENTAL EXPOSURE LEVELS

Asbestos is ubiquitous in the environment because of its extensive industrial use and its dissemination through erosion from natural sources. Other natural mineral fibres also occur in the environment and may, at times, be present at similar or even higher concentrations than asbestos, depending on local conditions. Since the size distributions of such fibres are often similar to those of asbestos, it is likely that distribution patterns in the environment will also be similar.

It is difficult to compare available data on airborne fibre levels because of inconsistencies in both the methods of sampling and analysis, and the expression of results. In most countries, for instance, airborne fibre concentrations in the work-place are expressed as fibre/ml or mg/m^3. For concentrations in ambient air, fibre/litre, fibre/m^3, and ng/m^3 are commonly used. Fibre concentrations in biological materials are usually expressed in fibre/g or in µg/g of the dry tissue.

In this section, the available data will be discussed in terms of occupational, para-occupational (household and neighbourhood), and general environmental (air and other media) exposure.

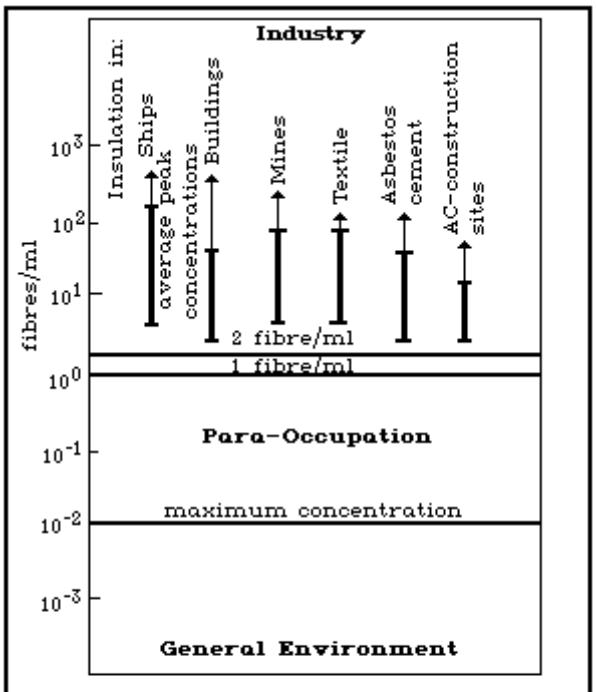
5.1 Air

5.1.1 Occupational exposure

Exposure levels for different types of asbestos and other mineral fibres vary considerably within and between industries.

This discussion will be limited to data obtained by the Membrane Filter Method and expressed as fibre/ml. On the basis of a review of historical data, ranges of levels in various industries without or with poor dust suppression measures are illustrated in Fig. 4. In recent years, concentrations in many countries have been much lower than those illustrated because of the introduction of engineering controls. For example, results of more recent personal exposure measurements made during various operations involving the manufacture of asbestos-containing products in the United Kingdom between 1972 and 1978 indicate that, in most cases (54 - 86.5%), levels were below 0.5 fibres/ml (Table 8). Data from various branches of the asbestos industry in France (Table 9), indicate levels that are achievable by current dust control methods.

The reduction in levels over time is even greater than is reflected by the data, because of the increased sensitivity (3x) of the currently-used Membrane Filter Method, compared with the sensitivity of previously-used methods for the determination of airborne asbestos.



Average asbestos fibre concentrations (between crossbeams) and short-term peak concentrations (darts) at work places in the various branches of the international asbestos industry, without or with few or poor dust suppression measures, as well as maximum concentrations in the general environment. Adapted from: Robock (1981).

However, it should be noted that there are countries in which effective dust control measures have not been introduced; current levels in these countries may approach those illustrated in Fig. 4 (Oleru, 1980).

Table 8. Asbestos levels in different manufacturing industries in the United Kingdom, 1972-78[a]

Industry	Number of results	Percentage of results[b]		
		< 0.5	< 1.0	< 2.0
		(fibres/ml)		
Asbestos cement	845	86.5	95.0	98.5
Millboard/paper	135	87.0	98.2	99.6
Friction materials	900	71.0	85.5	95.0
Textiles	1304	58.5	80.7	95.0
Insulation board	545	54.0	72.5	88.6

[a] From: Health and Safety Commission (1979).
[b] 4-h samples.

Table 9. Asbestos fibre concentrations in 1984 in various branches of the asbestos industry in France[a]

Branch	Fibre concentrations (fibre/ml)				Total number of points
	< 0.5	0.5 - 1	1 - 2	> 2	
Asbestos cement					
Numbers[b]	261	11	6	1	279
Percentage	93.5	3.9	2.1	0.3	
Friction materials					
Numbers	249	84	55	8	396
Percentage	62.8	21.2	13.8	2.0	
Textile					
Numbers	81	25	17	1	124
Percentage	65.3	20.1	13.7	0.8	
Others					
Numbers	41	14	0	1	56
Percentage	73.2	25.0	0	1.7	
Total					
Numbers	632	134	78	11	855
Percentage	73.9	15.6	9.1	1.2	

[a] From: AFA (1985).
[b] Numbers of points in work-place areas.

5.1.2 Para-occupational exposure

Members of the families of asbestos workers handling contaminated work clothes (a practice which should be discouraged), and, in some cases, members of the the general population may be exposed to elevated concentrations of airborne asbestos fibres. Asbestos has been used widely in building materials for domestic application (e.g., asbestos-cement products and floor tiles), and elevated airborne levels have been measured during the manipulation of these materials (e.g., home construction and renovation by the homeowner).

In this and the following section, only data obtained by electron microscopy will be considered, because of the necessity of identifying asbestos and distinguishing it from other inorganic

fibres that may also be present in ambient air. In addition, only data obtained using direct preparation methods without alteration of the fibrous material and reported as fibre number concentrations will be included.

Asbestos levels in the air of mining towns in Quebec have been determined recently by transmission electron microscopy using direct transfer sample preparation techniques. Samples were collected in June 1983 at 11 sites in 5 mining communities located downwind from asbestos mines. Sampling was also conducted at a control site in Sherbrooke, Quebec. The overall mean asbestos concentrations in the samples from the mining towns were 47.2 fibres/litre (total) and 7.8 fibres/litre (> 5 µm). Mean values for each of the sites sampled ranged up to 97.5 fibres/litre (total) and 20.6 fibres/litre (> 5 µm). For the control community, the mean values were lower - 14.7 fibres/litre (total) and 0.7 fibres/litre (> 5 µm) (Lebel, 1984).

Measurements were carried out in 1983 and 1984 in various mining areas in Canada and South Africa (Robock et al., 1984; Selles et al., 1984) using scanning electron microscopy with energy dispersive X-ray analysis (Asbestos International Association, 1984). Total inorganic fibre and asbestos fibre concentrations, using the counting criteria used in the Membrane Filter Method (> 5 µm in length; < 3 µm in diameter; aspect ratio > 3:1) and evaluated in the same laboratory, are shown in Table 10.

Levels of asbestos in the vicinity of industrial sources in Austria have also been reported (Felbermayer & Ussar, 1980). Applying the counting criteria described above, levels in samples taken in the vicinity of an asbestos deposit in Rechnitz averaged 0.2 fibres/litre (range 0 - 0.5 fibres/litre). In the vicinity of an asbestos-cement plant (Vöcklabruck), the mean concentration was 0.5 fibres/litre (range 0 - 2.2 fibres/litre).

Table 10. Fibre concentrations in mining areas of Canada and South Africa[a,b]

Area	Locations	Concentration (fibres/litre, longer than 5 µm)	
		Total inorganic	Asbestos
Canada (Quebec area)			
Residential	(1)	3.2	1.8
areas near	(2)	3.1	0.9
asbestos mines	(3)	0.9	0.2
South Africa			
Downwind mill	(1)	600.0	600.0[c]
	(2)	81.6	80.3
	(3)	8.6	8.6
	(4)	300.0	300.0[d]
	(5)	10.6	9.3
	(6)	4.9	2.4
Residences of	(1)	6.3	6.0
asbestos mine	(2)	7.4	7.1
workers	(3)	2.7	2.0
	(4)	11.0	11.0
	(5)	3.2	3.2
	(6)	8.1	7.3

Table 10 (contd.)

Area	Locations	Concentration (fibres/litre, longer than 5 µm)	
		Total inorganic	Asbestos
Residential areas near asbestos mines	(1)	1.0	0.8
	(2)	0.6	0.3
	(3)	1.1	0.7
	(4)	0.4	0.2
	(5)	0.8	0.2
	(6)	0.8	0.5
Near a magnesium mine		1.5	0.1
Near an iron ore mine		1.5	0.3

[a] From: Robock et al. (1984) and Selles et al. (1984).

[b] Practical limits of error, 95% (Poisson's distribution), for the calculated concentrations of fibres/litre depend on the number of fibres found in 1 mm^2 of the total filter surface; for 0.1 fibre/litre, the range is 0.002 - 0.6 fibres/litre; for 1 fibre/litre, the range is 0.5 - 1.8 fibres/litre).

[c] Unprotected tailing dump.

[d] Truck loaded with soil.

In general, the data indicate that levels of airborne asbestos fibres (> 5 µm in length) in residential areas in the vicinity of industrial sources are within the range of those in urban locations (up to 10 fibres/litre) or, in some cases, slightly higher.

5.1.3 Ambient air

Available data on asbestos levels in ambient air, determined by a variety of sampling, instrumental, and counting techniques, were reviewed by Lanting & den Boeft (1979). Levels were significantly lower than those in the occupational environment.

More recent data on levels of asbestos in outdoor air, determined by currently-accepted techniques, are presented in Table 11. Only levels measured as fibre count concentrations are presented as these are relevant to health effects. On the basis of these data, it can be concluded that levels of asbestos fibres (length > 5 µm) at remote locations are generally less than 1 fibre/litre. Levels in urban air generally range from < 1 up to 10 fibres/litre (occasionally, levels exceed this value). Mean concentrations of other inorganic fibres of the same dimensions are generally up to an order of magnitude higher, or occasionally more.

Recently, there has been concern about potential exposure to asbestos in the air of public buildings with friable surfaces of sprayed asbestos-containing insulation. Sprayed asbestos was used extensively between the 1940s and 1970s on structural surfaces (to retard collapse during fire) and on ceilings (for purposes of acoustic and thermal insulation and decoration). The results of available studies on asbestos levels in indoor air are presented in Table 12. These values are usually within the range of those found in ambient air (i.e., generally do not exceed 1 fibre/litre, but may be higher, up to 10 fibres/litre).

5.2 Levels in Other Media

Asbestos is introduced into water by the dissolution of asbestos-containing minerals and ores, from industrial effluents, atmospheric pollution, and asbestos-cement piping. The presence of asbestos fibres in drinking-water was first reported in Canada in 1971 (Cunningham & Pontefract, 1971) since when surveys of asbestos concentrations in various public water supplies have been conducted in Canada (Canada, Environmental Health Directorate, 1979), the Federal Republic of Germany (Meyer, 1984), the United Kingdom (Commins, 1979), and the USA (Millette et al., 1980).

On the basis of a compendium of published and unpublished surveys in which 1500 water samples from 406 cities in the USA were analysed (using various sample-preparation techniques), it was concluded that the majority of the population consumes drinking-water containing asbestos fibre levels of less than 1 x 10^6/litre[a] (Millette et al., 1980). In some areas, however, levels of between 1 and 100 x 10^6 fibres/litre were recorded and levels as high as 600 x 10^6 fibres/litre were reported for one water supply contaminated with amphibole fibres from the processing of iron ore.

A nation-wide survey of asbestos levels in drinking-water from 71 locations across Canada (serving 55% of the population) was the basis for an estimation that 5% of the population receives water containing levels higher than 10 x 10^6 fibres/litre, about 0.6% receives water having more than 100 x 10^6 fibres/litre (Canada, Environmental Health Directorate, 1979). Levels as high as 100 x 10^6 fibres/litre in some areas were attributable to erosion from natural sources. Levels in drinking-water supplies in the United Kingdom have been reported to range up to 2.2 x 10^6 fibres/litre (Commins, 1979).

The size distribution of asbestos fibres in water supplies differs from that of airborne asbestos. In general, fibre lengths are much shorter; median values of 0.5 - 0.8 µm have been reported (Canada, Environmental Health Directorate, 1979). Available data also indicate that the release of fibres from asbestos-cement piping is related to the aggresivity of the water (Canada, Environmental Health Directorate, 1979; Meyer, 1984), and that conventional treatment processes involving chemical coagulation followed by filtration effectively reduce levels in drinking-water supplies.

Table 11. Fibre concentrations in outdoor air

Area	Concentration (fibres/litre)[a]			Counting criteria
	Total inorganic	Asbestos		
		Total	> 5 µm	
AUSTRIA				
Leoben (heavy traffic)	7.0		4.6	length: > 5 µm diameter: 0.2 - 3 (SEM)
Schalchham (low traffic)	1.7		0.1	length: > 5 µm diameter: 0.2 - 3 (SEM)
Village with asbestos-cement	4.6		< 0.1	length: > 5 µm diameter: 0.2 - 3

roofing				(SEM)
Village without asbestos-cement roofing	4.3		< 0.1	length: > 5 µm diameter: 0.2 - 3 (SEM)
Remote rural areas	1.4		< 0.1	length: > 5 µm diameter: 0.2 - 3 (SEM)

Table 11. (contd.)

Area	Concentration (fibres/litre)[a]			Counting criteria
	Total inorganic	Asbestos		
		Total	> 5 µm	
CANADA				
Ontario				
Metropolitan Toronto			< 2 - 9	length: > 5 µm diameter: all (TEM)
Southern Ontario			< 2 - 4	length: > 5 µm diameter: all (TEM)
Toronto (busy intersection)			0 - 13[b]	length: > 5 µm diameter: all (TEM)
Mississauga			0 - 11[b]	length: > 5 µm diameter: all (TEM)
Oakville			0 - 8[b]	length: > 5 µm diameter: all (TEM)
Bracebridge (remote rural location)			0 - 2[b]	length: > 5 µm diameter: all (TEM)
Peterborough			0 - 4[b]	length: > 5 µm diameter: all (TEM)
Quebec				
Sherbrooke			0.7	length: > 5 µm diameter: all (TEM)

Table 11. (contd.)

Area	Concentration (fibres/litre)[a]			Counting criteria
	Total inorganic	Asbestos		
		Total	> 5 µm	
GERMANY, FEDERAL REPUBLIC OF				
Wanne-Eickel	----	----		
300 m downwind	90.0 |	| 10	2.0	length: > 5 µm

from asbestos-cement plant				diameter: 0.2 - 3 (SEM)
700 m downwind from asbestos-cement plant	70.0		4	0.8	length: > 5 µm diameter: 0.2 - 3 (SEM)
1000 m downwind from asbestos-cement plant	60.0		4	0.6	length: > 5 µm diameter: 0.2 - 3 (SEM)
Dortmund		all			
dwelling area	30.0	lengths > all diameters	3 <	0.2	length: > 5 µm diameter: 0.2 - 3 (SEM)
crossing with heavy traffic	60.0		8	0.9	length: > 5 µm diameter: 0.2 - 3 (SEM)
Gelsenkirchen	50.0		10	5.0	calculated length: > 5 µm diameter: 0.2 - 3 (SEM)
Düsseldorf	20.0		6	1.0	calculated length: > 5 µm diameter: 0.2 - 3 (SEM)

Table 11. (contd.)

Area	Concentration (fibres/litre)[a]			Counting criteria
	Total inorganic	Asbestos		
		Total	> 5 µm	
SOUTH AFRICA				
Johannesburg (centre/traffic)	3.2		0.2	length: > 5 µm diameter: 0.2 - 3 (SEM)
Langa (asbestos-cement application)	1.7		0.2	length: > 5 µm diameter: 0.2 - 3 (SEM)
Soweto (asbestos-cement application)	1.4		0.2	length: > 5 µm diameter: 0.2 - 3 (SEM)
Frankfort (rural)	0.2		< 0.1	length: > 5 µm diameter: 0.2 - 3 (SEM)
at Cape Point (reference)	< 0.1		< 0.1	length: > 5 µm diameter: 0.2 - 3 (SEM)
USA				
California				

Upwind of an asbestos plant		< 0.2 - 11	length: all diameter: all

[a] Practical limits of error, 95% (Poisson's distribution), for the calculated c
fibres/litre depend on the number of fibres found in 1 mm^2 of the total filte
fibre/litre, the range is 0.002 - 0.6 fibres/litre; for 1 fibre/litre, the r
fibres/litre.

[b] 95% confidence limits.

Table 12. Levels of asbestos fibre concentrations in indoor air

Area	Number of samples	Concentration[a] (fibres/litre)	Counting criteria	Refe
Canada				
In 3 public buildings with amosite-containing insulation	not applicable	< 2[b]	length: > 5 µm diameter: all	Chat
In 7 public buildings with chrysotile-containing insulation	not applicable	< 4 to < 9[b]	length: > 5 µm diameter: all	Chatf
In 19 public buildings with asbestos-containing insulation	14	0 to 0.3	length: > 5 µm diameter: all	Pin
Germany, Federal Republic of				
Sporting halls (sprayed crocidolite	45	0.1 to 1.1	length: > 5 µm diameter: 0.2 - 3 µm	Ins Fib (19
Schools (sprayed crocidolite)	5	0.1 to 11.0	length: > 5 µm diameter: 0.2 - 3 µm	Ins Fib (19
Public buildings (asbestos-cement air ducts)	5	0.1 to 0.2	length: > 5 µm diameter: 0.2 - 3 µm	Ins Fib (19
Public buildings (asbestos-cement sheets)	3	0.1 to 0.2	length: > 5 µm diameter: 0.2 - 3 µm	Ins Fib (19
Public buildings (sprayed asbestos)		1.0 to 10.0	length: > 5 µm diameter: 0.2 - 3 µm	Loh
Homes (electrical storage heaters)		0.1 to 6.0	length: > 5 µm diameter: 0.2 - 3 µm	Loh

[a] Practical limits of error, 95% (Poisson's distribution), for the calculated c
fibres/litre depend on the number of fibres found in 1 mm^2 of the total filte
fibre/litre (range 0.002 - 0.6 fibres/litre) and for 1 fibre/litre (range 0.

[b] 95% confidence limits.

The extent of asbestos contamination of solid foodstuffs has not been well studied because a simple, reliable analytical method is lacking. Foods that contain soil particles, dust, or dirt almost certainly contain asbestos fibres. Foodstuffs may also contain asbestos from water or from impure talc, which is used in coated rice, and as an antisticking agent for moulded foods (Eisenberg, 1974). Asbestos may also be introduced into foods from

impure mineral silicates, such as talc, soapstone, or pyrophyllite, used as carriers for spray pesticides (Kay, 1974).

Asbestos fibres have been detected in beverages. Concentrations of 0.151 x 10^6 fibres/litre have been found in some English beers (Biles & Emerson, 1968), and concentrations of 4.3 - 6.6 x 10^6 fibres/litre have been recorded in Canadian beers (Cunningham & Pontefract, 1971); levels between 1.7 and 12.2 x 10^6 fibres/litre have been found in soft drinks. It has been suggested that asbestos filters used for the clarification of beverages and other liquids may have contributed to the asbestos content. However, the presence of asbestos in the water used to constitute these beverages has complicated interpretation of the data.

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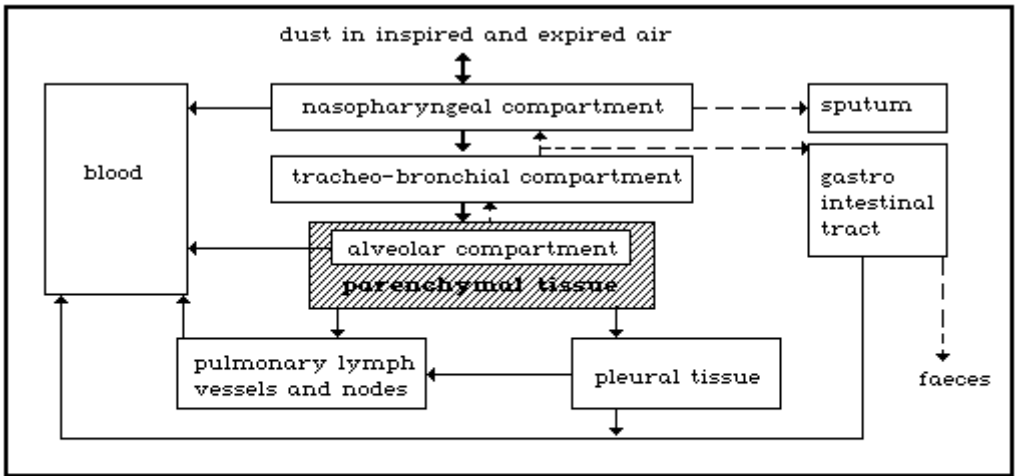
[a] Unless otherwise specified, levels in drinking-water are all fibres visible by TEM.

6. DEPOSITION, TRANSLOCATION, AND CLEARANCE

Although most of the data concerning the deposition, translocation, and clearance of fibres have been obtained in studies with asbestos, it is likely that other natural mineral fibres behave in a similar manner.

6.1 Inhalation

In 1966, the ICRP Task Group on Lung Dynamics (1966) published a lung model that subdivided the respiratory tract into three compartments: the nasopharynx, the tracheobronchial, and the pulmonary or alveolar region. The deposition, clearance, and translocation of particles in each of these three compartments was described. This scheme of pathways was modified for fibres by Bignon et al. (1978) as shown in Fig. 5.



General scheme for the deposition, clearance, translocation, and retention of fibres. (Heavy arrows: deposition; light dotted arrows: clearance pathway; light arrows: translocation pathways). Diagram of Bignon et al. (1978) derived from ICRP lung model by the Task Group on Lung Dynamics (1966).

6.1.1 Asbestos

6.1.1.1 Fibre deposition

(a) *Models*

There are five mechanisms of deposition of particles in the

respiratory tract (i.e., inertial impaction, sedimentation, interception, diffusion, and electrostatic precipitation).

Sedimentation is determined principally by the aerodynamic diameter of particles.

The geometric diameter and density of a fibre largely determine the aerodynamic diameter with fibre length being of secondary importance. It has been estimated that an asbestos fibre of 3 μm diameter would have approximately the same settling velocity as a 10 μm sphere with a density = 1.0 g/m^3 (Timbrell, 1982) and thus,

it is generally agreed that all asbestos fibres with a diameter greater than 3 μm are not respirable. However, it should be noted that this cut-off value is relevant only for asbestos and other fibres of similar densities. For more information concerning the deposition of airborne particles in the respiratory tract, see Stöber et al. (1970) and Doull et al., ed. (1980).

Interception is most important for longer fibres (Timbrell, 1972). Fibres are more subject to interception at bifurcations in the lower respiratory tract than isometric particles because of the probability of nonaxial alignment and entrainment in secondary flow patterns. The branching of the lower respiratory tract in animals is generally less symmetrical than that in human beings. Therefore, there may be interspecies differences in airborne fibre deposition.

(b) *Experimental data*

Studies of deposition patterns and efficiencies in hollow airway casts of the human bronchial tree using monodisperse spherical particles have shown that:

(a) the deposition efficiency per airway generation increases distally, reaching a peak in the second to fifth generation, and decreases subsequently with generation number down to at least the eighth generation; particle size and flow rate determine in which generation the peak deposition occurs; and

(b) the deposition of inhaled particles per unit surface area is generally much greater in the vicinity of the bifurcations than at other surfaces (Schlesinger et al., 1977, 1982; Chan & Lippmann, 1980).

Detailed quantitative data on deposition patterns and efficiencies for fibres at specific airway sites are not available. In the absence of such data, it is reasonable to assume that the deposition will be similar, though probably higher, for fibres, than for particles of more compact shapes, and that the additional deposition of fibres through interception will increase the amount without radically changing the pattern of deposition. Harris & Fraser (1976) give a quantitative comparison for selected fibre lengths.

Experimental evidence indicates that penetration into the alveolar part of the rat lung decreases sharply for glass or asbestos fibres with aerodynamic diameters exceeding 2 μm and that deposition in the tracheobronchial airways increases with increasing fibre length (Morgan et al., 1980).

Timbrell (1972) studied the deposition of asbestos fibres in hollow airway casts of pig lungs extending to the respiratory

bronchioles. The author found that, for comparable mass concentrations of UICC asbestos[a], there was about 5 times more bronchial airway deposition for the "curly" chrysotile fibres than for the straighter amphibole forms. This was attributed to the

effective increase in chrysotile diameter due to the diameters of the "curl" and to the greater probability of amphiboles to be aligned parallel to the airway axes by the shear flow. These results were consistent with those of additional studies described in the same paper, in which retention in the rat lung was measured one day after a 10-week inhalation exposure. The retention of 3 types of UICC amphiboles was about 6 times greater than that of 2 types of UICC chrysotiles.

The deposition of chrysotile asbestos in the peripheral lung airways of rats exposed for 1 h to 4.3 mg respirable chrysotile/m^3 was studied by Brody et al. (1981). In rats killed immediately after exposure, asbestos fibres were rarely seen by scanning electron microscopy in alveolar spaces or on alveolar duct surfaces, except at alveolar duct bifurcations. Concentrations were relatively high at bifurcations nearest the terminal bronchioles, and lower at the bifurcations of more distal ducts. In rats killed after 5 h, the patterns were similar, but the concentrations were reduced.

6.1.1.2 Fibre clearance, retention, and translocation

The fate of fibres deposited on surfaces within the lungs depends on both the site of deposition and the characteristics of the fibres. Within the first day, fibres deposited in the tracheobronchial airways can be carried proximally on the mucous surface to the larynx, and can be swallowed (Fig. 5). It has been suggested, though not proved, that a small fraction of the fibres might penetrate the epithelium of the tracheobronchial tree.

In the non-ciliated airspaces below the terminal bronchioles, fibres are cleared much more slowly from their deposition sites by various less effective mechanisms and pathways, which can be classified into 2 broad categories, i.e., translocation and disintegration.

Translocation refers to a change in the location of the intact fibre primarily along the epithelial surface: (a) to dust foci at the respiratory bronchioles; (b) on to the ciliated epithelium at the terminal bronchioles; or (c) into and through the epithelium, with subsequent migration to interstitial storage sites or along lymphatic drainage pathways. Short fibres (generally < 5 µm), ingested by alveolar macrophages as well as unincorporated fibres, may be translocated.

Disintegration refers to a number of processes, including subdivision of the fibres along parting planes (either in length or diameter), partial dissolution of components of the matrix, which creates a more porous fibre of relatively unchanged external size, or surface etching of the fibres, thus changing external

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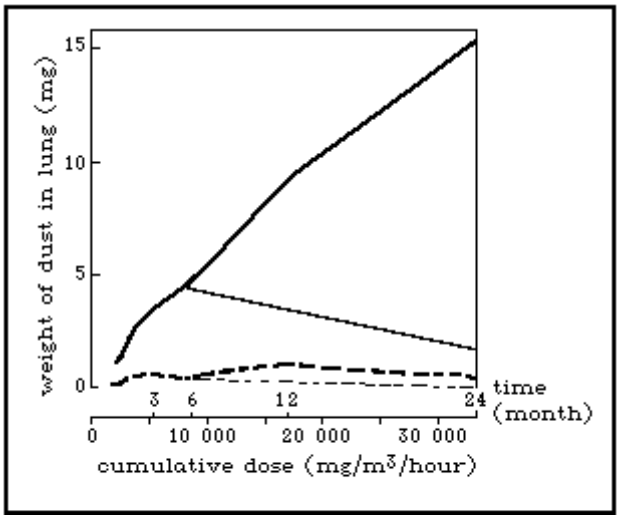
[a] Standard reference samples of asbestos collected in 1966 for experimental use under the auspices of the Union Internationale Contre le Cancer.

dimensions. Unlike amphibole fibres which are less soluble in lung fluids, chrysotile fibres undergo partial dissolution within the lungs after fibrillation (i.e., fibre splitting along the fibre

length). Predominant changes in the fibre, with time, include a decrease in magnesium, and an increase in iron content (Langer et al., 1970, 1972). Mg^{2+} contributes to both the structural integrity and the positive charge of the fibre. The process of leaching can cause fragmentation and more rapid disappearance of chrysotile from the lung compared with that of amphibole types of asbestos (Morris et al., 1967).

The results of studies of the short-term retention and clearance of asbestos in rats, reported by Wagner & Skidmore (1965), indicated that over a period of 2 months following a 6-week period of exposure to about 30 mg/m^3 of respirable dust, the clearance patterns for chrysotile, amosite, and crocidolite could each be described by single exponential functions. However, the rate of clearance for chrysotile was higher by a factor of 3 than that for amosite and crocidolite. In addition, the retention of chrysotile, as measured a few days after the end of the 6-week exposure period, was only about one third that of the amphiboles. Later work by Wagner et al. (1974) indicated that, after prolonged exposure (6 - 12 months), the lung burden of chrysotile reached a plateau, whereas a continued increase was observed for the amphiboles. This difference was attributed to the enhanced clearance rate of chrysotile (Fig. 6).

In a study on rats conducted by Middleton et al. (1979), the retention of chrysotile was approximately one quarter that of the amphiboles and appeared to be related to the airborne asbestos level during dusting; at higher airborne levels (1.3 - 9.4 ng/m^3), the retention of chrysotile was lower than of the amphiboles.



Mean weight of dust in lungs of rats in relation to dose and time. Modified from: Wagner et al. (1974).

Muhle et al. (1983) investigated the effects of cigarette smoke on the retention of UICC chrysotile (type A) and UICC crocidolite in rats. Results showed a doubling of crocidolite fibres in the lungs of the cigarette smoke-exposed group compared with animals not exposed to cigarette smoke. A plateau was found for chrysotile as in the study of Wagner et al. (1974). This plateau was not influenced by cigarette smoke. This difference between the two fibre types can be explained by a higher deposition rate of chrysotile in the upper airways compared with crocidolite and a decrease in deep lung clearance induced by cigarette smoke. There is some evidence that tracheobronchial clearance is not influenced by cigarette smoke (Lippmann et al., 1980). In man, smoking reduces long-term deep lung clearance (Cohen et al., 1979).

On the other hand, the results of studies reported by Morgan et al. (1975, 1977a), who performed single exposures administered through a head mask, neither confirmed the fast clearance nor the lower retention of chrysotile. Middleton et al. (1979) concluded that clearance could be described in terms of an exponential model, though somewhat modified compared with that used by Morgan et al. (1977a).

The clearance model used to describe the results of these short-term studies was not applicable to long-term (1-year) inhalation studies (Davis et al., 1978). It was suggested, therefore, that the observations in long-term studies should be explained by an impairment of the clearance mechanism in lungs with high fibre burdens.

Available data indicate that fibre length is an important determinant of clearance. While results of studies with asbestos are not available, Morgan & Holmes (1980) studied the effect of fibre length on the retention of glass fibres in rat lungs by means of serial sacrifices. The 1.5 µm diameter glass fibres were administered by intratracheal instillation. The macrophage-mediated mechanical clearance was less effective for fibres 10 µm in length than for 5 µm fibres. It was ineffective for fibres of 30 µm or more. As supporting evidence, Morgan et al. (1980) cited the work of Timbrell & Skidmore (1971) on the dimensions of anthophyllite fibres in the lungs of Finnish workers. The results of their study suggested that the maximum fibre length for mechanical clearance was 17 µm.

Results of studies by Pooley & Clark (1980) indicated that the size distribution of amosite and crocidolite fibres in airborne samples was similar to that found in organs. Later it was noted that the proportion of longer fibres of both minerals found in the lung was increased, probably because of the more efficient clearance of the shorter fibres. It was difficult to compare the size distribution of airborne chrysotile with that in the lung because of the breakdown of chrysotile fibre aggregates and fibre bundles.

The effects of intermittent exposure to high doses of asbestos (defined by the author as peak) on fibre retention in the lungs of rats were studied by Davis et al. (1980b). Four groups of rats inhaled UICC preparations of amosite or chrysotile. Two of the groups were exposed respectively to the 2 asbestos types for 5 days/week, 7 h/day, for 1 year. The 2 other groups were treated with amosite and chrysotile, respectively, at 5 times the previous dose, but for only 1 day per week for 1 year. The results showed that after the 12-month inhalation period, the levels of both chrysotile and amosite in lungs were similar regardless of whether "peak" (1-day/week exposure) or "even" (5 days/week exposure) dosing had been used. During the following 6 months, asbestos was cleared from the lungs of the "peak" chrysotile group more slowly than that from the lungs of the "even" chrysotile group, but clearance from the "peak" amosite group was faster than that from the "even" group.

The movement of inhaled fibres from the epithelial surfaces into the lymphatic and circulatory systems was described by Lee et al. (1981). Groups of rats, hamsters, and guinea-pigs inhaled potassium octatitanate (Fybex), potassium titanate (PKT), and UICC amosite. The mean diameters (0.2 - 0.4 µm) and lengths (4.2 - 6.7 µm) were nominally similar for all three types of fibre. Numerous

dust cells were transported to the tracheobronchial and mediastinal lymph nodes, where some dust cells penetrated into the blood or lymphatic circulation. The dust cells migrated directly from the lymph nodes into adjacent mediastinal adipose tissue. Dust-laden giant cells were occasionally found in the liver, and there was widespread migration of the fibres into other organs, without any significant tissue response. On the basis of these results, it was proposed that lymphatic vessels were a main route of dust cell migration. However, it is most unlikely that the pathways that were demonstrated to be important in this study represent the predominant routes for clearance at exposure levels normally encountered in the ambient and occupational environment. It is more likely that they may be important following exposures to massive concentrations of dust (3100 fibres/ml). More experimental work with lower concentrations of fibres is necessary.

In the inhalation study of Brody et al. (1981) (section 6.1.1.1), the examination of tissues by transmission electron microscopy revealed that chrysotile fibres deposited on the bifurcations of the alveolar ducts were taken up, at least partially, by type I epithelial cells during the 1-h inhalation exposure. In the 5-h period after exposure, significant amounts were cleared from the surface, and taken up by both type I epithelial cells and alveolar macrophages. In the 24-h follow-up exposure, there was an influx of macrophages into the alveolar duct bifurcations. These observations suggest that there may be direct fibre penetration of the surface epithelium.

Thus, in summary, available data indicate that chrysotile is more likely than the amphiboles to be deposited in the upper airways of the respiratory tract. In addition, chrysotile is cleared more efficiently from the lungs; thus, there is greater retention of the amphiboles. Fibre length is an important determinant of clearance, with shorter fibres being cleared more readily, and cigarette smoking affects deep-lung but not

tracheobronchial clearance. There were no consistent effects on clearance and retention of fibres with intermittent exposure to high doses compared with continuous exposure to lower levels.

6.1.2 Ferruginous bodies

Mineral fibres inhaled and retained in the lungs may become coated with a segmented deposit of iron containing protein, forming club-shaped ferruginous bodies (Davis, 1964; Milne, 1971). Those for which the core is asbestos are commonly called asbestos bodies. Using light microscopy, they have been found in large numbers in individuals occupationally exposed to asbestos (Ashcroft & Heppleston, 1973) and, using optical and electron microscopy, in the lungs of most adults who have lived in urban areas (Thomson & Graves, 1966; Bignon et al., 1970; Selikoff et al., 1972; Davis & Gross, 1973; Oldham, 1973). Probably fewer than 1% of the fibres in the lung become coated (Gaensler & Addington, 1969). No etiological significance has been attributed to the formation of asbestos bodies; their occurrence alone merely indicates exposure to asbestos and not necessarily the presence of disease (Longley, 1969; Milne, 1971; Churg & Warnock, 1980).

6.1.3 Content of fibres in the respiratory tract

The mineral fibre content of organs of deceased persons who had been occupationally exposed to asbestos has been investigated. Such determinations require tissue digestion procedures that do not change the fibre structure, and sophisticated analysis to identify

single submicroscopic fibres. The reported mineral content in the lungs of workers exposed to fibres ranged from 1 to 10 g/kg (dry weight); levels in the general population are about 0.3 g/kg (dry weight) (Beattie & Knox, 1961).

No conclusions concerning the regional distribution of fibres in the lung can be drawn on the basis of available data (Le Bouffant, 1980; Sebastien et al., 1980b).

6.2 Ingestion

An important question in the evaluation of the possible risks associated with the ingestion of asbestos is whether fibres can migrate from the lumen into and through the walls of the gastrointestinal tract to be distributed within the body and subsequently cleared. There is considerable disagreement concerning this subject, largely because of the difficulty of controlling external contamination of tissue samples in available studies and because of limitations in existing analytical techniques.

Detailed reviews of the available data have been published (Cook, 1983; Toft et al., 1984). It is not possible to conclude with certainty that asbestos fibres do not cross the gastrointestinal wall. However, available evidence indicates that, if penetration does occur, it is extremely limited. Cook (1983) has suggested that 10^{-3} to 10^{-7} of ingested fibres penetrate the gut wall.

There is no available information on the bioaccumulation/ retention of ingested asbestos fibres. Simulated gastric juice has been shown to alter the physical and chemical properties of chrysotile fibres and, to a lesser extent, crocidolite fibres (Seshan, 1983). Available data concerning the possible elimination of asbestos in the urine of human beings are contradictory and inconclusive (Cook & Olson, 1979; Boatman, 1982).

7. EFFECTS ON ANIMALS AND CELLS

7.1 Asbestos

For a pollutant, such as asbestos, where there is a great deal of information on the human health effects associated with exposure, the results of toxicological studies are important, not only to assist in assessing the causality of associations observed in epidemiological studies, but also to elucidate the mechanisms of toxicity, to define biologically important physical and chemical properties, and to develop hypotheses for further epidemiological study. The results of toxicological studies on asbestos have also imparted information on dose-response relationships and the role of fibre type, size, and shape in the pathogenesis of asbestos-related diseases. However, conclusions concerning the importance of these variables are necessarily limited, because of the inability to adequately characterize fibre size in the administered material. In the following section, the results of recent studies are emphasized, since experimental methods have improved considerably in the past few years.

7.1.1 Fibrogenicity

7.1.1.1 Inhalation

Data concerning the fibrogenicity of inhaled asbestos in animal species are presented in Table 13.

Fibrosis has been observed in many animal species (e.g., guinea-pigs, rats, hamsters, monkeys), following inhalation of both chrysotile and the amphiboles. In several of the studies, the incidence and severity were approximately linearly dose-related (Wagner et al., 1974, 1980; Wehner et al., 1979) and, as has been observed in human studies, there was progression of the disease following cessation of exposure (Wagner et al., 1974, 1980). In general, it has been observed that shorter fibres are less fibrogenic (Davis et al., 1980a).

The results of the early studies regarding the relative fibrogenicity of various fibre types are confusing and contradictory mainly because, usually, only the airborne mass concentrations were measured; the numbers or size distribution of the fibres were not considered. In addition, there may have been surface artifacts in the mineral, produced during sample preparation, which blunted activity.

Table 13. Inhalation studies - fibrogenicity

Species	Number	Protocol[a]	Results
Guinea-pig, rabbit, and Vervet monkey	16-24 guinea-pigs, 2-4 rabbits, and 3-4 Vervet monkeys in exposed groups	exposure to ~ 30 000 p/ml of chrysotile (7-10% fibres > 10 µm), amosite, or crocidolite from South African mills for various periods of time (e.g., up to 24 months for guinea-pigs exposed to chrysotile; lifetime for rabbits and Vervet monkeys exposed to chrysotile, but only 14 months for these species when exposed to amosite)	asbestos bodies pr 3 species exposed types; chrysotile caused fibrosis in and monkeys but no amosite caused asb all 3 species; it to draw conclusion the relative patho the different fibr because of the var of exposure and la characterization o
SPF Wistar rat	total of 1013 rats; group sizes of 19-58	groups exposed to 9.7 - 14.7 mg/m^3 of UICC amosite, anthophyllite, crocidolite, chrysotile (Canadian), or chrysotile (Rhodesian) for periods of 1 day, 3, 6, 12, or 24 months	less asbestosis fo than for the other progression of asb following cessatio exposure for all d
SPF white Wistar rat of the Han strain	groups of 48 animals	study designed so that both mass and fibre number could be examined; 5 groups exposed to 10 mg/m^3 UICC chrysotile, crocidolite, or amosite (550 fibres/ml amosite > 5 µm; 390 fibres/ml chrysotile > 5 µm or 430 fibres/ml crocidolite > 5 µm) for 12 months	chysotile caused f fibrosis than eith even when the fibr were similar

Table 13. (contd.)

Species	Number	Protocol[a]	Results
Male Syrian	total of 96 exposed and 96	two groups exposed for 3 h/day, 5 days/week to	slight pulmonary f only in the 15-mon

golden hamster	control animals	either 1 µg/litre (5-13 fibres/ml, > 5 µm) or 10 µg/litre (30-118 fibres/ml, > 5 µm) A/C aerosol (chrysotile content 10.5%) for up to 15 months	group; higher inci severity with incr after 5-month expo µg/litre dose; inc incidence of sligh after exposure to 10 µg/litre dose f after 15 months, n between exposed an groups; authors su the minimal respon due to changes dur of the fibres that the toxicity
Rat (strain not specified)	groups sizes of of 48 animals	designed to compare the pathological effects of exposure to UICC samples with those of factory samples; 4 groups exposed to UICC amosite, UICC chrysotile, factory amosite, or factory chrysotile at 10 mg/m^3 for 12 months; animals permitted to complete life span	factory amosite mo than UICC sample

Table 13. (contd.)

Species	Number	Protocol[a]	Results
SPF Wistar rat of the AF/HAN strain	group sizes of 48 animals	study designed to compare the pathological effects of peak dosing to those of even dosing; 2 groups exposed to either UICC amosite at 10 mg/m^3 or UICC chrysotile at 2 mg/m^3, 7 h per day, 5 days per day, 5 days per week for 1 year and 2 groups exposed to either amosite at 50 mg/m^3 or chrysotile at 10 mg/m^3, 1 day each week, for 1 year	levels of peribron fibrosis generally "peak" dosing grou "even" dosing grou of interstitial fi slightly higher fo "peak" dosing
Caesarian-derived Wistar rat	group sizes of 24 (6 and 12 months exposure) and 48 (3 months exposure)	exposure for periods of 3, 6, or 12 months to SFA chrysotile (430 fibres/ml > 5 µm), Grade 7 chrysotile (1020 fibres/ml > 5 µm) or UICC chrysotile (3150 fibres/ml > 5 µm) at 10.8 mg/m^3	progression of fib end of exposure fo inhaling all types 12 months; UICC pr least as much fibr 2 samples in all 6

[a] Unless otherwise specified, exposures were for 6 - 8 h/day, 5 days/week.

However, in an inhalation study by Davis et al. (1978), chrysotile caused more lung fibrosis in rats than either crocidolite or amosite, even when the fibre numbers (length > 5 µm) in the dust clouds were similar. The authors suggested that the greater fibrogenicity of chrysotile might be related to the fact that chrysotile clouds contained many more fibres over 20 µm long. The observation that shorter fibres are less fibrogenic was confirmed in a study by the same group, in which rats were exposed for 12 months to 10 mg/m^3 of either short-fibred (1% > 5 µm) or

long-fibred (30% > 5 µm) amosite (Bolton et al., 1983a).

7.1.1.2 Intrapleural and intraperitoneal injection

Fibrosis has also been observed following intrapleural (Smith et al., 1965; Burger & Engelbrecht, 1970; Davis, 1970, 1971, 1972) and intraperitoneal injection (Jagatic et al., 1967; Shin & Firminger, 1973; Engelbrecht & Burger, 1975) of asbestos. The results of these studies have confirmed that short fibres are less fibrogenic (Burger & Engelbrecht, 1970; Davis, 1972).

7.1.1.3 Ingestion

Several studies of the effects of ingested asbestos on proliferation and other biochemical variables in the epithelial cells of the gastrointestinal tract have been conducted (Amacher et al., 1974; Epstein & Varnes, 1976; Jacobs et al., 1977). Although some changes (e.g., an increase in incorporation of tritiated thymidine) have been noted in some studies at various times following administration, no consistent pattern has emerged.

The histopathological effects of ingested asbestos on the gastrointestinal wall have been examined, but the results of these studies have also been contradictory. Though Jacobs et al. (1978) observed light and electron microscopic evidence of cellular damage in the intestinal mucosa of rats fed 0.5 or 50 mg of chrysotile per day, for 1 week or 14 months, no pathological changes were found on light and electron microscopic histological examination of tissue sections of the gastrointestinal tract of rats that had consumed approximately 250 mg of UICC amosite, chrysotile, or crocidolite, per week, for periods of up to 25 months (Bolton et al., 1982a). Similarly, tissue examination by light microscopy did not reveal any pathological changes in the wall of the small intestine of Wistar rats that had consumed 100 mg UICC amosite, daily, for 5 days (Meek & Grasso, 1983).

7.1.2 Carcinogenicity

7.1.2.1 Inhalation

Exposure conditions in inhalation studies approach more closely the circumstances of human exposure to asbestos and are of most relevance for the assessment of human health risks. The results of the most significant inhalation carcinogenicity studies in various animal species are presented in Table 14. Although fibrosis has been observed in several animal species following inhalation of

different types of asbestos (section 7.1.1), a consistently increased incidence of bronchial carcinomas and pleural mesotheliomas has been observed only in the rat.

In an extensive and well conducted and controlled series of studies, Wagner et al. (1974) exposed groups of Wistar SPF rats (n = 19 - 58) to the 5 UICC asbestos samples at concentrations ranging from 10 to 15 mg/m^3, for periods ranging from 1 day to 24 months (35 h/week). Exposure had very little effect on average survival. Average survival times varied from 669 to 857 days for exposed animals and from 754 to 803 days for controls. In the exposed animals, there were 50 adenocarcinomas, 40 squamous cell carcinomas, and 11 mesotheliomas. None of these tumours appeared prior to 300 days from the first exposure, and the incidence of lung cancer was greatest in animals surviving 600 days. On the basis of analyses of the severity of asbestosis in animals with tumours, taking survival into account, it was concluded that the

animals with lung tumours had significantly ($P < 0.001$) more asbestosis than those without. Seven malignancies of the ovary and eight of male genito-urinary organs were observed in the exposed groups of approximately 700 rats. No malignancies were observed at these sites in controls. These differences were not statistically significant and the incidence of malignancy at other sites was little different from that in the controls. No data on the relationship between tumour incidence at extra-pulmonary sites and asbestos dose were provided.

In a study conducted by Davis et al. (1978), rats were exposed to chrysotile, crocidolite, or amosite at 2.0 or 10.0 mg/m^3 for 12 months. All malignant pulmonary tumours occurred in chrysotile-exposed animals. The authors suggested that the greater carcinogenicity of chrysotile might be related to the fact that chrysotile contained many more fibres over 20 µm in length. In addition to the lung tumours, extrapulmonary neoplasms included a relatively large number of peritoneal connective tissue malignancies, including a leiomyofibroma on the wall of the small intestine. The relationship between these tumours and exposure to asbestos is uncertain, however.

In a recent study, inhalation of short-fibred amosite (1% > 5 µm) at 10 mg/m^3 did not produce fibrosis or pulmonary tumours in Wistar rats (n = 48). In contrast, there was extensive fibrosis and over 30% incidence of tumours in a group similarly exposed to long-fibred amosite (30% > 5 µm; 11% > 10 µm) (Davis et al., in press).

Table 14. Inhalation studies - carcinogenicity

Species	Number	Protocol[a]	Results
rat, rabbit, guinea-pig, gerbil, mouse	12 (controls); 20-69 (exposed)	exposure to chrysotile, crocidolite, or amosite for 4 h/day, 4 days/week, for 2 years; mean concentration = 50 mg/m^3; light microscopic fibre count of chrysotile: 54 fibres/ml; amosite: 864 fibres/ml, crocidolite: 1105 fibres/ml	increased lung tumou incidence in rats (7 those with adequate record)
SPF Wistar rat	total of 1013 rats; group sizes of 19-58	groups exposed to UICC amosite, anthophyllite, crocidolite, chrysotile (Canadian), or chrysotile (Rhodesian), at 9.7 - 14.7 mg/m^3, for periods of 1 day, 3, 5, 6, 12, or 24 months, for 35 h/week	higher incidence of with 12 months expos with 6 months, but l difference following months exposure; of which metastasized, 1 chrysotile-exposed g crocidolite-exposed 1 in anthophyllite-e groups; of 11 mesoth occurred following e crocidolite and 4 fo exposure to Canadian 2 mesotheliomas occu following 1-day expo positive association the incidence of asb lung cancer; no asso between exposure and gastrointestinal can

			incidence

Table 14 (contd.)

Species	Number	Protocol[a]	Results
Syrian golden hamster	102 animals per group	animals exposed to UICC Canadian chrysotile at 23 µg/litre for 7 h/day, 5 days/week, for 11 months; half of animals also exposed for 10 min 3 times a day to cigarette smoke for duration of their life span; one control group exposed to smoke + sham dust, one exposed to sham smoke + sham dust	10 out of 12 lung ad found in 510 hamster occurred among the 1 in the asbestos-expo groups, indicating a neoplastic response; of laryngeal lesions malignant tumours si lower in asbestos + exposed group than i exposed control grou due to significantly life span in asbesto animals
SPF white Wistar rat of the Han strain	group size = 48	experiment designed so that both mass and fibre number could be examined; 5 groups exposed to UICC chrysotile, crocidolite, or amosite at 2 or 10 mg/m^3 (550 amosite fibres/ml > 5 µm; 390 chrysotile fibres/ml > 5 µm or 430 crocidolite fibres/ml > 5 µm)	all malignant pulmon neoplasms occurred i chrysotile-exposed a the authors suggeste the greater pathogen chrysotile might be greater number of fi > 20 µm in length

Table 14. (contd.)

Species	Number	Protocol[a]	Results
rat (strain not specified)	group size = 48	designed to compare the pathological effects of exposure to UICC samples with those of factory samples; 4 groups exposed to UICC amosite, UICC chrysotile, factory amosite, or factory chyrsotile at 10 mg/m^3 for 12 months; animals permitted to complete life span	factory chrysotile p similar levels of lu pathology to those p UICC sample except t slightly smaller num bronchial carcinoma produced by the fact little carcinogenicit both amosite samples the analysis of fibr each of the samples, concluded that "whil genicity and carcino both depend upon the of relatively long f dust clouds, differe are involved in each and tumour productio the largest fibres"
SPF Wistar rat, AF/HAN strain	group size = 48	study designed to compare the pathological effects of "peak" dosing with those of "even" dosing; 2 groups exposed to UICC amosite at 10 mg/m^3 or	no differences in th incidence of pulmona neoplasms between "p groups and "even" do the authors concluded

		UICC chrysotile at 2 mg/m^3, 7 h/day, 5 days/week for 1 year and 2 groups exposed to amosite at 50 mg/m^3 or chrysotile at 10 mg/m^3 1 day/week for 1 year	indication that short of high-dust exposur asbestos factory wou in significantly grea than would be indicat raised overall dust the day in question however, 2 bronchial in the "peak" dosing group and none in th dosing group)

Table 14. (contd.)

Species	Number	Protocol[a]	Results
Barrier-protected Caesarian-derived Wistar rat	group sizes = 24 (6 and 12 months exposure) and 48 (3 months exposure)	exposure for periods of either 3, 6, or 12 months to SFA chrysotile (430 fibres/ml > 5 µm) or UICC chrysotile (3150 fibres/ml > 5 µm) at 10.8 mg/m^3	tumour yield signifi greater with UICC ch than with Grade 7

[a] Unless otherwise specified, exposures were for 6 - 8 h/day, 5 days/week.

The results of inhalation studies impart some useful information concerning dose-response relationships and the carcinogenic potential of asbestos of various types and fibre sizes. An approximately linear relationship between the incidence of lung cancer and dose has been found in several studies (Wagner et al., 1974, 1980; Davis et al., 1978) and, although insufficient numbers of mesotheliomas have been produced in inhalation studies to draw definitive conclusions, it has been noted that most have been found in animals that received a high total dose of asbestos (Davis, 1979). However, the incidence following a short period of exposure (i.e., 1 day) has been greater than would be expected on the basis of a linear hypothesis for the dose-response relationship (Wagner et al., 1974). It is also of interest to note that in two studies (Davis et al., 1978; Wagner et al., 1980), all of the mesotheliomas observed (3) occurred in the groups exposed for the shortest period.

7.1.2.2 Intratracheal instillation

Factors that affect the deposition of fibres in the respiratory tract are not taken into consideration in studies involving intratracheal injection and therefore it is difficult to extrapolate the results directly to man. In addition, the greater incidence of infection following exposure by this route often complicates the interpretation of the results. However, the results of such investigations have confirmed the observations in inhalation studies. Furthermore, significantly-increased incidences of both mesothelioma and lung cancer have been observed in dogs concomitantly exposed to cigarette smoke (inhalation) and asbestos (intratracheally) (Humphrey et al., 1981).

7.1.2.3 Direct administration into body cavities

Wagner (1962) first reported that "it is possible to produce tumours which appear to be arising from the mesothelial cells of the pleura by inoculating certain dusts into the pleural cavities

of rats". Since then, numerous studies involving the injection or implantation of asbestos into the pleural or peritoneal cavities of various species have been conducted; the results of the most important of these studies are summarized in chronological order in Table 15.

Table 15. Intrapleural and intraperitoneal administration studies

Species	Number	Protocol	Results
Wistar rat	11 groups; 10 animals/group	intrapleural injection of 50 mg of 3 samples of crocidolite from South African mines, 3 samples from mills in the same region, 2 samples of chrysotile from mines, 1 sample of amosite, 99.9% pure silica dust or pure carbon black	30 months after expo pleural mesothelioma crocidolite-treated chrysotile-treated r 1 rat receiving pure authors concluded "i possible to produce which appear to be a from the mesothelial the pleura by inocul certain dusts into t pleural cavities of
Syrian Golden hamster	15 animals/ exposed group; 15 untreated controls	intrapleural injection of 25 mg of soft chrysotile (average fibre length 67 µm), harsh chrysotile (36 µm) and amosite (18 µm); also soft chrysotile in diet (10 g/kg) (10 g/kg) of chrysotile-treated animals; amosite (10 g/kg) in diet of amosite-treated animals	granulomatous inflam and fibrosis in hams receiving all 3 type tumours, possibly mesotheliomas; 2 in chrysotile-treated h and 3 in amosite-tre hamsters
SPF Wistar rat and "standard" rat	48 males, 48 females/exposed group	intrapleural injection of 20 mg of Transvaal amosite (91% < 5 µm in length) superfine grade of Canadian chrysotile (92% < 5 µm), North West Cape crocidolite (70% < 5 µm); extracted crocidolite (86% < 5 µm), silica or saline	appreciable proporti animals treated with of asbestos develope mesothelioma; large tumours found in ani receiving crocidolit 55/94, standard: 62/ tumours in amosite-t group (SPF: 38/96, s 26/84) and period be inoculation and deve

Table 15. (contd.)

Species	Number	Protocol	Results
SPF Wistar rat and "standard" rat (contd.)			of mesothelioma much than with the other authors note "the hi incidence of these n following the inocul chrysotile was unexp (SPF: 61/96, standar
Female pathogen-free Osborne-	1200	40 mg of 17 materials applied on a fibrous glass vehicle to the pleura including 3 types of asbestos in 7	amosite,chrysotile, different types of c produced equally hig (58-75%) of mesothel

Mendel rat		forms, 6 types of fibrous glass, 2 types of silica, etc; 2-year observation period	hand-milled crocidol exposed to extraneou metallic mining yiel related tumour respo comparable with thos standard reference m crocidolite; standar caused fewer tumours when reduced to subm fibrils; pulverized of mill and nickel m fibrous glass vehicl not induce tumours; of fine fibre-glass approach length of a produced moderately incidence (12-18%); concluded "the simpl incriminating featur carcinogenicity and seems to be a durabl perhaps in a narrow

Table 15. (contd.)

Species	Number	Protocol	Results
SPF Wistar rat	12 - 36	intrapleural injections of 0.5, 1, 2, 4, or 8 mg of SFA chrysotile and crocidolite (from Northeast Cape mine); intrapleural injection of 20 mg of Canadian chrysotile samples, SFA chrysotile, or saline (control); intrapleural injection of 20 mg of the 5 UICC samples, brucite or barium sulfate; intrapleural injections of ceramic fibre, fibre glass, glass powder, aluminium oxide, and 2 samples of SFA chrysotile	the risk of developi mesothelioma at a gi after injection was proportional to dose SFA chrysotile and c of the UICC standard samples, crocidolite most carcinogenic an of oils by benzene e did not alter the carcinogenicity of t samples; results wer consistent with the that finer fibres ar carcinogenic
Rat (strain not specified)		3 intrapleural injections of 20 mg of chrysotile from filters at 2 USSR mines (99% fibres < 5 µm in length)	mesotheliomas in 46% exposed rats
Osborne-Mendel rat	30 in each exposed group	pleural implantation on a fibrous glass vehicle of 40 mg of 17 samples of fibrous materials of diverse types or dimensional distribution	fibres < 1.5 µm in d and > 8 µm in length highest probability mesotheliomas

Table 15. (contd.)

Species	Number	Protocol	Results
Osborne-Mendel	30 - 50 in each exposed group	pleural implantation on a fibrous glass vehicle of	percentage probabili pleural mesothelioma

rat		40 mg of 37 samples, which were variations of 7 fibrous materials; fibre-size distributions similar to asbestos	from 0 to 100%, lesi groups with low prob tumours were highly and fibres were comp contained within mac lesions in high tumo probability groups w relatively acellular abundance of collage long fibres in inter tissue
Wistar rat	total of 1086	intraperitoneal injection of 9 fibrous dusts (chrysotile, milled chrysotile, crocidolite, palygorskite, nemalite, gypsum, 3 types of glass fibres) and 8 granular dusts; injected doses between 2 and 100 mg; observation period 30 months	fibrous dusts (excep gypsum fibres) induc malignant tumours of peritoneum (6 mg chr 2 mg crocidolite-39% fibres JM 104-27%); response relationshi chrysotile and 2 typ fibres; reduction in carcinogenicity of c after milling to ver fibres; carcinogenic greatest for fibres length > 3 µm and di < 1 µm; durability o also important

Table 15. (contd.)

Species	Number	Protocol	Results
Rat	8	inhalation of 3000 WLM radon 222 over one month and intrapleural injection of 2 mg chrysotile after 71 days	all animals develope tumours including 7 mesotheliomas, autho concluded "synergist effect obvious"
	10	whole body irradiation - 230 rads for 1 day and intrapleural injection of 2 mg chrysotile after 125 days or 150 rads and 1% chrysotile in diet for 6 months after 35 days	extrapulmonary tumou irradiated controls receiving asbestos o by intrapleural inje specific localizatio asbestos exposed ani
Barrier-protected Caeserian-derived Wistar rat	48/exposed group; 48 in control group	intrapleural injection of 20 mg of SFA, UICC Canadian or Grade 7 chrysotile	allowing for differe survival times, SFA twice as carcinogeni Grade 7, which was 3 carcinogenic as UICC results not well cor with results of an i study with these mat
SPF male Sprague Dawley rat	16 in HCl-treated chrysotile-exposed group; > 32 in all other exposed groups; 32	intrapleural injection of 20 mg untreated UICC chrysotile A or 4 samples leached to various extents (10 - 90% Mg removed) by oxalic acid or HCl; also crocidolite or glass fibre	in life-time observa period, a total of 6 pleural mesothelioma cancer, and 9 perito mesotheliomas in the of 304 animals; prop cancer lower than ex

	control animals		because of early dea infection; carcinoge of chrysotile with 4 removed; authors con "size is not the onl involved in the indu pleural cancers by m fibres"

Table 15. (contd.)

Species	Number	Protocol	Results
NEDH rat	--	intrapleural, intraperitoneal, and intratracheal administration of 2 mg of UICC Canadian or Rhodesian chrysotile, with or without ancillary radiation treatment (1000 rads-whole body) or injection of 1 mg 3-MC	a significant incide (3.8%) of mesotheliom 159 rats treated wit alone; this incidenc increased to 11.8% i also receiving radia treatment (borderlin statistical signific 25.5% in animals als administered 3-MC (s increase); early tis responses were simil asbestos reactions w specific pathologica attributable to radi 3-MC
Female Wistar rat	3 groups, 20 animals/group	intraperitoneal injection of 50 mg milled UICC crocidolite (fibre lengths 3 - 5 µm), amorphous UICC crocidolite, or saline	life-time observatio mesotheliomas (40%) amorphous crocidolit group; 3 mesotheliom in fibrous crocidoli group and none in sa group; statistically significant differen questioned the fibro structure of asbesto predominant cause of mesothelioma and sug submicroscopic parti be important in indu tumours

Table 15. (contd.)

Species	Number	Protocol	Results
AF/HAN Wistar rat	7 groups, 32 animals/group	intraperitoneal injection of 25 mg of 5 samples of UICC chrysotile and factory amosite collected from airborne asbestos clouds of inhalation study	production of mesoth tumours in 94 - 100% animals in 6 groups; more carcinogenic th heated chrysotile (8 carcinogenic; some c between carcinogenic fibre length; good c between carcinogenic *in vitro* cytotoxici
AF/HAN	17 groups;	intraperitoneal injection of	mesothelial tumours

SPF Wistar	19-48 animals per group	0.01 - 25 mg elutriated UICC chrysotile and crocidolite	of animals; graded d response for both ch and crocidolite; for dose, more tumours i chrysotile than in crocidolite-exposed

The introduction of massive doses into body cavities does not simulate the route of exposure of man to fibrous dusts such as asbestos. However, such studies have made it possible to clarify a number of questions that could not feasibly be investigated using the inhalation model, since insufficient numbers of mesotheliomas occur following exposure by this route. The most important contribution of such studies has been to focus attention on the importance of fibre size and shape in the pathogenesis of asbestos-associated diseases. In 1972, on the basis of their study involving intrapleural implantation of 17 fibrous materials in rats, Stanton & Wrench first hypothesized that "the simplest incriminating feature for both carcinogenicity and fibrogenicity seems to be a durable fibrous shape, perhaps in a narrow range of size". On the basis of the results of further studies, Stanton & Layard (1978) prepared a model in which carcinogenicity was expressed as a function of fibre length and width; in general, fibres with maximum potency were longer than 8 µm and less than 1.5 µm in diameter (Wagner et al., 1973; Stanton et al., 1977).

In an extensive study, Stanton et al. (1981) implanted 72 dusts containing fibres of various sizes in the pleura of Osborne-Mendel rats. The correlation coefficients for the logit of tumour probability with the common logarithm of number of particles per microgram in different dimensional ranges are presented in Table 16. The probability of the development of pleural mesotheliomas was highest for fibres with a diameter of less than 0.25 µm and lengths greater than 8 µm. However, probabilities were also "relatively" high for fibres in other size categories (i.e., with diameters of up to 1.5 µm and lengths greater than 4 µm). The authors also noted that there might be a low level of tumour response for fibres outside these size ranges.

Table 16. Correlation coefficients of logit of tumour probability with common logarithm of number of particles per microgram in different dimensional ranges[a]

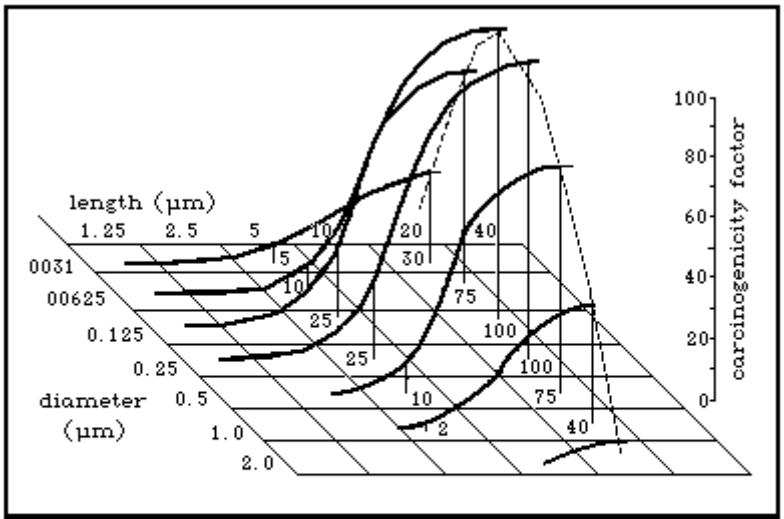
Fibre diameter (µm)	Fibre length (µm)		
	(≤ 4)	(> 4 - 8)	(> 8)
> 4	-	-0.28	-0.30
> 1.5 - 4	-0.45	-0.24	0.13
> 0.25 - 1.5	0.01	0.45	0.68
≤ 0.25	0.20	0.63	0.80

[a] From: Stanton et al. (1981).

In an extensive series of studies involving intraperitoneal administration, Pott & Friedrichs (1972) and Pott et al. (1976a) induced peritoneal mesotheliomas in Wistar rats injected with different varieties of asbestos, fine glass fibres, and nemalite (magnesium hydroxide). Few or no tumours developed following

administration of several amorphous dusts that were chemically

similar to one of the forms of asbestos. Very few tumours developed following administration of 100 mg of UICC chrysotile fibres shortened by ball-milling for 4 h, compared with 6.25 mg of the original sample. The results of further studies confirmed that tumour incidence for relatively low doses (0.5 - 2 mg) of dust samples with a sufficient number of durable long and thin fibres was high. Tumour incidence for unstable, long, thin fibres (e.g., leached fibres and slag wool) was much lower (Pott et al., 1984). On the basis of some of these studies, a working hypothesis on the carcinogenic potency of fibres as a function of length and diameter was developed and is presented in Fig. 7. For example, this model predicts that 100 fibres, 2 µm in length, have the same carcinogenic potency as 4 fibres, 5 µm in length, or 1 fibre, 20 µm in length (hypothetically). Again, it should be noted that there may be a low level of tumour response for fibres outside the size range indicated on the diagram. In addition, on the basis of the results of these studies, it has been concluded that the physical and chemical constitution of fibres influences the carcinogenic potential insofar as it determines the stability in the body.



Hypothesis on the carcinogenic potency of a fibre as a function of its size with some data on "carcinogenicity factors" that suggest a yardstick for the carcinogenic potential of fibres. From: Pott (1978).

These observations concerning the importance of fibre size and shape in tumour induction have given rise to speculation that mesotheliomas may be caused by physical irritation caused by fibres that are carried to the pleural surface by both lymphatic transport within macrophages or by direct penetration of free fibres (Davis, 1981; Craighead & Mossman, 1982). A great deal of attention has been focused on this "carcinogenic subset" of fibres. However, there are still several unanswered questions concerning the relative importance of fibres with dimensions in the critical range for mesothelioma induction (Harington, 1981).

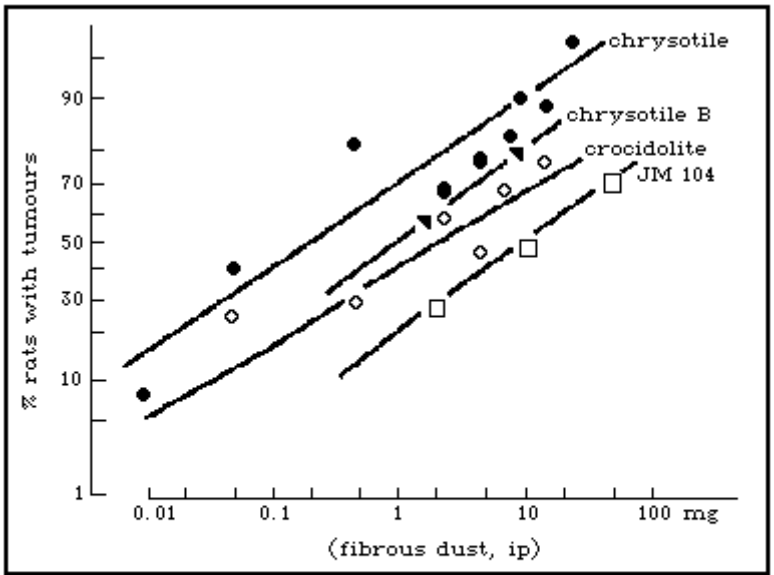
Acid leaching of chrysotile significantly decreased the carcinogenic potency after intrapleural injection in rats (Morgan et al., 1977b; Lafuma et al., 1980; Monchaux et al., 1981); it is uncertain whether these effects are a function of change in fibre size or number, chemical modification, or other factors. In several other studies on mice and rats (Roe et al., 1967; Wagner et al., 1973), variation in the trace metal content did not have any effect on carcinogenic potency (Gross & Harley, 1973).

Results of studies involving intrapleural or intraperitoneal

injection, or implantation have also imparted some information on dose-response relationships, the relative potency of various fibre types, and the time course of the development of asbestos-related disease. There was evidence of a dose-response relationship for malignant tumour incidence following exposure to both chrysotile and crocidolite, in several of the studies (Wagner et al., 1973; Smith & Hubert, 1974; Bolton et al., 1983b). Fig. 8 shows the regression line for dose-response relationships after intraperitoneal injection of chrysotile, crocidolite, and glass fibres (Johns-Manville 104), derived from the results of Pott et al. (1976a), Bolton et al. (1983b), and Pott et al. (1984), showing a somewhat higher potency of chrysotile.

In several studies, crocidolite was more potent in the induction of malignant neoplasms than an equal mass of chrysotile (Gross & Harley, 1973; Wagner et al., 1973; Engelbrecht & Burger, 1975; Monchaux et al., 1981). However, other studies did not confirm the higher potency of crocidolite (Wagner & Berry, 1969; Stanton & Wrench, 1972), while in two more recent studies, chrysotile was found more potent in inducing mesotheliomas than an equal mass of crocidolite (Bolton et al., 1983b) or amosite (Bolton et al., 1982b). The distribution of fibre sizes was not well characterized in these studies, and the need for caution in the interpretation of such results cannot be overemphasized. For example, the similar incidence of mesotheliomas in groups of rats exposed to UICC crocidolite (2.83%) and Canadian chrysotile (2.9%) in the inhalation studies of Wagner et al. (1974) contrasted with the authors' observation in an earlier study that 3 times as many malignant neoplasms resulted in the crocidolite-exposed group following intrapleural injection of equal masses of the 2 samples.

Data available from studies involving intrapleural injection also indicate that the lifetime risk of mesothelioma is greater in animals exposed at a younger age. Berry & Wagner (1976) injected doses of equal masses of crocidolite into the pleura of two groups of rats, one at the age of 2 months and the other at the age of 10 months. In the group exposed at the earlier age, 40% developed mesotheliomas; in the second group, the incidence was only 19%. The former group also experienced a longer latency period.



Regression lines for dose-response relationships after intraperitoneal injection of chrysotile, crocidolite, and glass fibres Johns-Manville 104. From: Pott et al. (1976a, 1984) and Bolton et al. (1983b).

There is still some controversy concerning the histological nature of malignant tumours induced by the intrapleural and intraperitoneal inoculation of animals (Harington, 1981). In addition, aerodynamic factors that affect fibre deposition, defence mechanisms that determine the differential retention of fibres within the lung, and factors that determine penetration of fibres from the alveolar space to the pleura were not taken into consideration in this experimental model. However, the results of implantation studies can be integrated with the observations from other investigations that finer fibres are more likely to penetrate to the periphery of the lung, and that short fibres (< 5 µm) are more effectively cleared from the lungs by macrophages than long fibres, which cannot be phagocytosed by single cells (Harington, 1981). However, the need for caution in the extrapolation of the results of intrapleural injection studies to predict the potency of various fibre samples with respect to the induction of mesotheliomas and other types of cancer, such as lung cancer, must be emphasized. In a recent study, described in Table 15, tumour incidences following intrapleural injection and inhalation of the same samples of chrysotile were not well correlated (Wagner et al., 1980). The authors suggested that problems of aggregation of fibres, in the suspension prepared for intrapleural injection, might have resulted in different size distributions.

7.1.2.4 Ingestion

Studies on the effects of ingested asbestos on animal species have been reviewed (Toft et al., 1984), and the results of the most recent and extensive of these studies are presented in Table 17.

On the basis of their review, Toft et al. (1984) concluded that there was no conclusive evidence from the toxicological studies conducted to date, that ingested asbestos is carcinogenic. The results of early studies were inconclusive because of shortcomings in study design; many of the investigations were conducted for relatively short periods of time with insufficient numbers of test and control animals, and the studies were not designed to allow measurement of dose-response relationships. In addition, the administered asbestos was often not well characterized. In later, more extensive studies, increases in gastrointestinal tumour incidence were observed in some of the test groups in some of the studies; however, these increases were not observed consistently. Moreover, there was no evidence of a dose-response relationship in any of the studies.

The Task Group noted that, in a recent well-conducted study, the incidence of benign epithelial neoplasms was significantly higher in comparison with pooled controls from contemporary lifetime asbestos feeding studies in the same laboratory (US NTP, 1985). However, the increase was not statistically-significant in comparison with concurrent controls and was limited to one sex. In addition, the study was not designed to investigate exposure-response relationships. It is of interest to note that no increase in tumour incidence was observed following administration of short-range chrysotile, which was composed of size ranges more similar to those found in drinking-water.

Some of the toxicological studies on ingested asbestos that have been conducted recently by various investigators have been very extensive (Donham et al., 1980; McConnell, 1982a,b). However, there have been several criticisms concerning the suitability with respect to extrapolation to man of the vehicles in which asbestos has been administered, the fibre size of the administered asbestos, and the fat content of the animal diets.

7.1.3 *In vitro studies*

The effects of mineral dusts and especially of asbestos fibres on cell cultures have been investigated intensively over the last decades.

According to Allison (1973), 4 cell types are potential targets for asbestos *in vivo:* (a) macrophages, (b) mesothelial cells, which undergo malignant transformation, (c) fibroblasts, which participate in the fibrogenic reaction, and (d) pulmonary epithelial cells, which can also undergo malignant transformation. These cells, proliferating cell lines, and erythrocytes have been used *in vitro* studies.

The present position is that, with the combined use of several test systems, the findings can be used to predict, with some certainty, the fibrogenicity of dusts and fibres *in vivo.* Prediction of carcinogenicity is less reliable, but the findings may be of some use in predicting mesothelioma. As the tests can be completed within a few weeks, they may be usefully employed in the selection of materials to be tested *in vivo.* The tests are also of use in the study of mechanisms.

Table 17. Toxicological studies - ingested asbestos

Species	Number of test animals	Protocol	Results
Syrian Golden hamster	60	0.5 mg amosite/litre drinking-water over the lifetime	no tumours
	60	5 mg amosite/litre drinking-water	3 malignant tumours inclu a peritoneal mesothelioma early squamous cell carci of the forestomach
	60	50 mg amosite/litre in drinking-water over the lifetime	1 malignant tumour; autho concluded "tumours not tr related"
Male Wistar rat	25	250 mg amosite per week in dietary margarine supplement, for periods up to 25 months	1 malignant tumour in gas muscle layer
	25	250 mg chrysotile per week in dietary margarine supplement, for periods up to 25 months	1 pleural histiocytic tum significant increase in incidence of benign tumou tissues other than the ga intestinal tract; authors unlikely that these benig tumours were treatment-re because of lack of eviden widespread penetration or dissemination of fibres
	25	250 mg crocidolite per week in dietary margarine supplement, for periods up to 25 months	no primary malignant lesi the gastrointestinal muco

Table 17. (contd.)

Species	Number of test animals	Protocol	Results
F 344 rat	500	10% chrysotile in the diet over the lifetime	5 tumours including 1 mes incidence not statistical significantly greater tha control group
Syrian golden hamster	250 males 250 females	1% amosite in the diet fed to nursing mothers and over the lifetime of the pups	no adverse effects on bod gain and survival; no statistically-significant in tumour incidence
	250 males 250 females	1% short-range chrysotile (98% < 10 µm in length) in the diet fed to nursing mothers and over the lifetime of the pups	significant increase in a cortical adenomas in male considered to be treatmen related
	250 males 250 females	1% intermediate range chrysotile (65% > 10 µm in length) in the diet fed to nursing mothers and over the lifetime of the pups	significant increase in a cortical adenomas in male females; not considered t treatment-related
F 344 rat	250 males 250 females	1% tremolite in the diet fed to the dams and over the lifetime of the pups	no overt toxicity and no effects on survival rate; statistically-significant in tumour incidence

Table 17. (contd.)

Species	Number of test animals	Protocol	Results
F 344 rat	250 females 250 males	1% amosite in the diet fed to the dams and over the lifetime of the pups	no overt toxicity and no effects on survival rate; statistically-significant in tumour incidence in th intestinal tract; the bio significance of increases the rates of C-cell carci the thyroid and monocytic in male rats is questiona
F 344 rat	250 males 250 females	1% short-range chrysotile (98% < 10 µm in length in the diet fed to nursing mothers and over the lifetime of the pups	no overt toxicity and no effects on survival rate; significant increase in t incidence
	250 females 250 males	1% intermediate range chrysotile (65% > 10 µm in length) in the diet fed to nursing mothers and over the lifetime of the pups	no overt toxicity and no effects on survival rate; increase in benign epithe neoplasms in large intest of males; insignificant w compared with concurrent (88), but significant whe

compared with pooled cont

Reviews have been made by Harington et al. (1975), Beck (1980), and Gormley et al. (1980), and, more recently, these assays have received particular attention (Schluchsee Meeting, 1985).

7.1.3.1 Haemolysis

Although haemolysis alone is not a good predictor of *in vivo* pathogenesis (Richards et al., 1980), it is a useful model for the interaction of mineral dust with cell membranes. The haemolytic activity of fibres is related to size (Schnitzer & Pundsack, 1970), and surface charge ("zeta potential") (Harington et al., 1975; Light & Wei, 1980). Chrysotile induces haemolysis more rapidly than the amphiboles (Schnitzer & Pundsack, 1970; Harington et al., 1975). Haemolysis by chrysotile fibres may be related to the adsorption of the red blood cell membranes on the fibres and not to an interaction between magnesium from the fibres and sialic acid from the red blood cells (Jaurand et al., 1983).

7.1.3.2 Macrophages

Because of their important role in fibrogenesis, macrophages have been intensively investigated in cell cultures. The cultured macrophages are usually derived by bronchioalveolar lavage or from the peritoneum after appropriate stimulation.

Two types of cytotoxic effects in macrophages have been observed: (a) a rapid form that can occur within minutes of contact between fibres and macrophages and reflecting interaction with the membrane, and (b) a delayed effect that occurs within days (Allison, 1973). The effects are more marked with chrysotile than with amphibole fibres (Harington et al., 1975).

Allison (1973) investigated the limits of the size of fibres that can be ingested by phagocytosis. Irrespective of the type of asbestos, short fibres (< 5 µm) were readily and completely taken up by phagocytosis, whereas long fibres (> 25 µm) were not. The cells attached to, or enveloped the ends of, the latter, but portions remained outside the cells. The long fibres caused localized damage to the cell membrane while they were being phagocytosed; in addition, energy metabolism was increased (Beck et al., 1971). Obviously, fibres with a length that exceeds the cell diameter remain partially extracellular.

In macrophages and in macrophage-like cells (P 388 D_1), long asbestos fibres caused increased permeability to two lysosomal enzymes (beta-glucuronidase, beta-galactosidase) and to the cytoplasmic enzyme lactic acid dehydrogenase (Beck et al., 1972; Davies, 1980). This enzyme release is coupled with an increase in permeability to extracellular dyes, and often occurs in the absence of cell death. Asbestos fibres interfere with the normal digestion of secondary lysosomes, resulting, in some cases, in accumulation of acid hydrolases. After membrane damage by asbestos fibres, the lysosomal enzymes can also leak into the cytoplasm. Partly-damaged alveolar macrophages may lead to cellular malfunction in the lungs. Asbestos fibres also stimulate the secretion of proteolytic enzymes such as elastase (White & Kuhn, 1980). If these enzymes are not counterbalanced by antiproteases, lung tissue damage can occur.

7.1.3.3 Fibroblasts

Beck et al. (1971) reported that long fibres of chrysotile were not completely phagocytosed by proliferating mouse fibroblasts,

type L 929.

In lung fibroblast cultures, chrysotile has been shown to be highly cytotoxic when first added and to induce biochemical and morphological alterations (Richards & Jacoby, 1976). It has also been shown that, if lung fibroblast-like cells are continuously exposed to small quantities of chrysotile, their ability to synthesize collagen is increased (Hext et al., 1977). Fibroblasts undergo a maturation process leading to rapid cellular aging.

7.1.3.4 Cell-lines and interaction with DNA

The UICC reference samples of asbestos have not shown mutagenic activity in bacterial assays (Chamberlain & Tarmy, 1977; Light & Wei, 1980), possibly because of the lack of uptake of fibres by this type of cell.

Asbestos-induced sister chromatid exchanges in cultured Chinese hamster ovarian fibroblast cells have been reported by Livingston et al. (1980) and in Chinese hamster cells by Sincock & Seabright (1975) and Huang (1979). In Huang's study, it was reported that amosite, crocidolite, and chrysotile were weakly mutagenic. At 10 and 100 µg fibre/ml, chrysotile completely inhibited cell growth (Livingston et al., 1980); cells exposed to amosite and crocidolite proliferated only at the lower concentration. Crocidolite significantly elevated the sister chromatid exchange rate and larger (> 5 µm) chromosomes were most sensitive. The chromosomal aberrations found in Chinese hamster cells by Sincock et al. (1982) could not be detected in primary human fibroblast or in human lymphoblastoid cell lines.

In tracheal epithelial cells, chrysotile and crocidolite did not cause breakage of DNA (Mossman et al., 1983). Hahon & Eckert (1976) found that exposure to asbestos fibres resulted in an almost 90% depression in viral interferon induction in cell monolayers.

For a review of the effects of asbestos on epithelial cells, pleural mesothelial cells, and other cell-lines see Beck (1980).

7.1.3.5 Mechanisms of the fibrogenic and carcinogenic action of asbestos

An overview of possible mechanisms of the fibrogenic and carcinogenic action of asbestos is presented in Table 18.

Fibrogenic potential

When macrophages interact with silica, they produce a fibroblast-stimulating factor (Heppleston & Styles, 1967). The incomplete phagocytosis of asbestos fibres may induce the same process (Beck et al., 1972). There is some evidence that the immune system is stimulated by the effects of mineral dusts on the macrophages (Pernis & Vigliani, 1982); the authors supposed that this process was mediated by the production of interleukin-1, which also stimulates fibroblasts. However, Miller et al. (1978) concluded from their studies that quartz and crocidolite had quite different biological effects on the macrophages and that the development of pulmonary fibrosis might, to some extent, be caused by different mechanisms in each instance.

Table 18. Some possible mechanisms of action of asbestiform fibres in the development of fibrosis (F), mesothelioma

(M), and lung cancer (C)

Mechanism or possible important effects	Disease
Incomplete phagocytosis, release of enzymes, and free radicals	F, C, M
Effects on the immune system	F, C, M
Effects on cell differentiation	F, C, M
Alteration in cell proliferation processes[a]	F, C, M
Interaction with DNA	C, M
Adsorption and transfer of polycyclic aromatic hydrocarbons	C

[a] Increase not only in cell proliferation but effects on intracellular processes, such as DNA or protein synthesis.

The release of oxygen-free radicals after incomplete phagocytosis of fibres may cause peroxidation of membranes and damage to macromolecules (Mossman & Landesman, 1983). This could be a possible mechanism of the induction of asbestos-related diseases.

Carcinogenic potential

The mechanisms of carcinogenesis of asbestos are not well understood. However, several hypotheses have been proposed, and these will be discussed briefly in the light of the experimental findings just reviewed. For a more detailed discussion, see US NRC/NAS (1984).

There is no convincing evidence from cellular tests that asbestos initiates tumours through direct interaction with DNA (genotoxicity). Fewer data are available concerning the genotoxicity of the other asbestiform mineral fibres; however,

erionite has been reported to induce unscheduled DNA repair in some mammalian cell lines (Poole et al., 1983). Another hypothesis is that asbestos does not induce tumours through direct interaction with DNA, but may act as a promotor[a]. For the purposes of this discussion, mesothelioma and lung cancer will be considered separately.

(a) *Mesothelioma*

It has been hypothesized that asbestos initiates mesotheliomas, since there is no evidence from experimental studies that asbestos or any other natural mineral fibres promote mesotheliomas initiated by other agents. Furthermore, there is no association between smoking and mesothelioma incidence in asbestos workers (US NRC/NAS, 1984). This hypothesis is strengthened by the observation of chronic preneoplastic reactions of mesothelial cells following the intrapleural or intraperitoneal injection of long fibres in animal species (US NRC/NAS, 1984).

Available data also indicate that it is fibres of a specific

size that act as initiators of mesothelioma. Durable, longer (> 5 µm), and thinner (< 1 µm) fibres of various minerals induce high mesothelioma rates after intrapleural and intraperitoneal administration, while, under the same circumstances, granular dusts or thick or short fibres of the same materials are considerably less potent. Indeed, there is a clear quantitative relationship between fibre size distribution and carcinogenic potential. In addition to the fibre concentration and size, durability (splitting, solubility, disintegration), and migration activity account for the variations observed in mesothelioma incidence in animals.

(b) *Lung cancer*

In the case of bronchogenic cancer, there is evidence that factors other than fibre size, such as adsorbed environmental pollutants (polycyclic aromatic hydrocarbons, etc), and tobacco smoke, can contribute to the total carcinogenic potential of mineral fibres.

Therefore, the extent to which results regarding the quantitative relationships obtained in the intrapleural and intraperitoneal injection studies on animals may be extrapolated to bronchial cancer is not clear. Some important reservations are necessary. Wagner et al. (1980) did not find the same order of rank for the carcinogenicity of three chrysotile varieties after inhalation and intrapleural injection in rats. However, there is some evidence from inhalation studies that longer fibres are more carcinogenic. Some authors see similarities between asbestos and promotors such as phorbol ester (Topping & Nettesheim, 1980; Craighead & Mossman, 1982).

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[a] For the purposes of this document, a promotor is defined as an agent that increases the tumourigenic response to a genotoxic carcinogen, when applied after the carcinogen, without being carcinogenic itself.

7.1.3.6 Factors modifying carcinogenicity

One of the mechanisms proposed for the induction of lung tumours by asbestos fibres is the adsorption and transfer of polycyclic aromatic hydrocarbons into cells ("carrier hypothesis").

Equal milligram amounts of crocidolite asbestos, carbon, hematite, and kaolin have been compared for their ability to bind and release the radiolabelled polycyclic aromatic hydrocarbon and 3-methylcholanthrene (3MC), into culture medium (Mossman & Craighead, 1982). Asbestos did not adsorb more 3MC or release greater amounts of the hydrocarbon than the other materials.

The results of Bogovski et al. (1982) showed low lung-tumour rates in rats after intratracheal instillations of either benzo(*a*)pyrene or chrysotile, alone (6.1% after 5 x 5 mg benzo(*a*)pyrene, 3.7% after 5 x 1 mg chrysotile, 2.6% in the control group). The instillation of a mixture of the 2 substances yielded 40% lung tumours, and the addition of phenol (1% in polyglycin), 78.9% lung tumours. However, the tumour yield following exposure to a mixture of chrysotile and benzo(*a*)pyrene was lower in the studies of Smith et al. (1970) on hamsters and of Pylev (1972) on rats. After intraperitoneal or intrapleural injections, the chrysotile-induced tumour rate was not augmented by benzo(*a*)pyrene (Pott et al., 1972; Pylev, 1980).

A syncarcinogenicity in man of polycyclic aromatic hydrocarbons

and chrysotile was proposed when organic substances containing benzo(*a*)pyrene were found in chrysotile (Harington, 1962; Pylev & Shabad, 1973). However, the amounts were very low (2 - 240 µg benzo(*a*)pyrene per kg chrysotile). The doses of benzo(*a*)pyrene given in the studies of Bogovski et al. (1982) were 10^7 to 10^9 times higher than would be received if administering equal amounts of natural chrysotile. Thus, it appears very dubious that contamination with polycyclic aromatic hydrocarbons enhances the carcinogenicity of asbestos significantly. Lakowicz & Bevan (1980) reported that the adsorption of benzo(*a*)pyrene on chrysotile and anthophyllite greatly enhanced their rates of uptake in the liver microsomes, compared with a microcrystalline dispersion of benzo(*a*)pyrene. Crocidolite, from which the natural organic substances had been removed by extraction, produced a tumour incidence after intrapleural administration in rats similar to that produced by untreated samples (Wagner & Berry, 1969; Stanton & Wrench, 1972). Therefore, available data do not provide conclusive support for the "carrier hypothesis".

7.2 Other Natural Mineral Fibres

There is a paucity of toxicological data concerning natural mineral fibres other than asbestos. The results of some available studies are presented in Tables 19 (*in vivo* studies) and 20 (*in vitro* studies).

Only preliminary *in vitro* studies have been conducted with some of the natural mineral fibres. The results of such assays vary considerably depending on the test system employed and factors that influence the pathogenicity of mineral dusts *in vivo* (e.g., deposition, clearance, and immunological reactivity) are absent *in vitro*. Thus, such studies should be considered as only the first stage of a multi-tier toxicological test protocol for the assessment of potential hazards for human health.

The results of preliminary *in vivo* studies involving intrapleural or intraperitoneal administration to animals are available for some natural mineral fibres. However, introduction into body cavities is an unnatural route of exposure that does not take into account deposition and clearance in the respiratory tract, but such studies do provide important information on the characteristics of particles that influence pathogenicity and the relative potency of various fibre types.

Exposure conditions in inhalation studies approach most closely the circumstances of human exposure to natural mineral fibres and are most relevant for the assessment of health risks to man. However, only two such studies involving exposure to natural mineral fibres other than asbestos (erionite, attapulgite, and sepiolite) have been conducted to date.

Interpretation of the small amount of toxicological data on natural mineral fibres other than asbestos is also complicated by the fact that, in some studies, only the mass of the administered material has been determined, while the origin of samples and fibre count or size distribution has often not been reported.

In this section, the available data are discussed according to mineral type under the following headings: attapulgite, sepiolite, wollastonite, and erionite.

Table 19. *In vivo* studies - natural mineral fibres other than asbestos

Fibre type	Source and fibre	Protocol	Number	Species	Results

	size distribution				
Palygorskite (Attapulgite)	Spanish; fibre size distribution not reported	inhalation of 10 mg/m^3 for 12 months; 4 animals sacrificed at 3, 6, and 12 months	40	F 344 rat	fibrosis g months: 3.3 1.1), 6 mo (control: 12 months: control: 1
Attapulgite	Spanish; fibre size distribution not reported (without ultrasonication)	intrapleural inoculation of unspecified dose; animals observed for life span	40	F 344 rat	10 mesothe survivors time perio administra
Attapulgite	Spanish; fibre size distribution not reported (with ultrasonification)	intrapleural inoculation of unspecified dose; animals observed for life span	40	F 344 rats	5 mesothel (chrysotil mesotheliо survivors 19 survivo unspecifie following
Attapulgite	two samples from Attapulgus, Georgia; purity > 90% "composed entirely of short fibres of consistently small diameter"	intrapleural implantation of 40 mg; animals observed for 2 years	30-50	Osborne-Mendel rat	tumour inc (7%) for b
Attapulgite	source not reported; fibre length < 5 µm 70%	intraperitoneal injection - 3 x 25 mg; animals observed for life span	33-34	Wistar rat	76.5% of a developed chrysotile mesotheliо (chrysotil mesotheliо first tumo (chrysotil days) afte

Table 19. (contd.)

Fibre type	Source and fibre size distribution	Protocol	Number	Species	Results
Sepiolite	Spanish; fibre size distribution not reported	inhalation of 10 mg/m^3 for 12 months; 4 animals sacrificed at 3, 6, and 12 months	40	F 344 rat	fibrosis g months: 3.1 1.1), 6 mo (control: 12 months: (control:
Sepiolite	Spanish; fibre size distribution not reported (without ultrasonification)	intrapleural inoculation of unspecified dose; animals observed for life span	40	F 344 rats	0 mesothel survivors time perio administra
Wollastonite	4 samples from Canadian mine; only one sample completely fibrous;	intrapleural implantation of 40 mg; animals observed for 2	30-50	Osborne-Mendel rats	tumour inc (25%), 3/2 2/25 (8%),

	fibres "relatively large"	years			
Erionite	New Zealand - frequency of fibres < 0.5 µm in diameter and > 4 µm in length = 1.9%	inhalation of 10 mg/m^3 for 1 year; 4 animals sacrificed at 3, 6, and 12 months	40	F 344 rat	no mesothe the animals sacrificed after expo
Erionite	Oregon - frequency of fibres < 0.4 µm in diameter and > 5 µm in length = 13.3%	inhalation of 10 mg/m^3 7 h/day, 5 days per week, for 1 year; 4 animals sacrificed at 3, 6, and 12 months	40	F 344 rat	mesotheliol (96.4%) of animals no 12 months exposure; time 580 d

Table 19. (contd.)

Fibre type	Source and fibre size distribution	Protocol	Number	Species	Results
Erionite	New Zealand - frequency of fibres <0.5 µm in diameter and > 4 µm in length = 1.9%	intrapleural inoculation of 20 mg; animals observed for life span	40	F 344 rat	6 mesothel survivors time perio administra
Erionite	Oregon - frequency of fibres < 0.5 µm in diameter and > 4 µm in length = 9.5%	intrapleural inoculation of 20 mg; animals observed for life span	40	F 344 rat	40 mesothe mean survi 390 days
Erionite	Karain - frequency of fibres < 0.5 µm in diameter and > 4 µm in length = 2.9%	intrapleural inoculation of 20 mg; animals observed for life span	40	F 344 rat	38 mesothe mean survi 435 days
Erionite	"sedimentary erionite" source and fibre size distribution not reported	intrapleural injection of 25 mg; animals observed for life span	40	Sprague-Dawley rat	incidence iomas afte 52.5% (UIC chrysotile mesotheliol
Erionite	source not reported; average length 1 µm (95% < 8 µm); average width 0.1 µm (94.4% < 1 µm)	intraperitoneal injection of 10 or 30 mg; animals observed for life span	10	Swiss albino male mouse	malignant tumours in (60%) 8 - after admi malignant tumours in (50%) chry treated co between 9

Table 19. (contd.)

Fibre type	Source and fibre size distribution	Protocol	Number	Species	Results
Erionite	"sedimentary	intraperitoneal	40	Sprague	incidence

	erionite"; source and fibre size distribution not reported	injection of 25 mg; animals observed for life span		Dawley rat	iomas afte 2.5% (UICC chrysotile mesothelio
Erionite	naturally-occurring from Colorado, USA	intraperitoneal injection of 10 mg; animals observed for life span	50	BALB/c mouse	peritoneal in 21/42 d animals (5 and 23 mon exposure
Erionite	naturally-occurring from Nevada, USA	intraperitoneal injection of 0.5, 2, or 10 mg; animals observed for life span	50	BALB/c mouse	peritoneal in 6/18 (3 group), 24 (2-mg grou (38%) (10-m

Table 20. *In vitro* studies - natural mineral fibres other than asbestos

Fibre type	Source and fibre size distribution	Results	R
Attapulgite	Spanish; thinnest fibres 0.02 - 0.03 µm wide; mean length > 0.8 µm and aspect ratio > 17	more haemolytic in human red blood cells than UICC chrysotile A	B
Attapulgite	"short-fibre"; source and distribution of sizes not reported	cytotoxic in mouse peritoneal macrophages but not in A 549 and V79-4 cells	C
	"long-fibre"; source and distribution of sizes not reported	cytotoxic in all 3 cell types (see above)	
Attapulgite	relatively pure sample from mine in Attapulgus, Georgia; "fibres of small or smaller diameter range than diameter range for chrysotile"	minimal inhibition of colony-forming efficiency of I-407 cells (16% vs 54% for equal dose of amosite)	R
Attapulgite	source and fibre size distribution not reported	alteration in thymidine incorporation by lung fibroblasts at 48 h; 63% of that observed for chrysotile B	L

Table 20. (contd.)

Fibre type	Source and fibre size distribution	Results	R
Sepiolite	source not reported; "short-fibre" (90% < 0.5 µm)	not cytotoxic in mouse peritoneal macrophages; A549 or V79-4 cells	C
	source not reported; "long-fibre" (90% < 3.5 µm)	cytotoxic in all 3 cell types (see above)	
Wollastonite	source and fibre size distribution not reported	no release of lysosomal enzymes nor damage to membrane in rabbit alveolar macrophages exposed to	P

		250 µg/ml; far less cytotoxic than chrysotile	
Erionite	Oregon; 6.2 x 10^3 fibres/µg of dust; median length 1.7 µm, 4.3% > 6 µm	increase in morphological transformation and unscheduled DNA repair synthesis in C3H10T1/2 cells and unscheduled DNA repair synthesis in A549 cells; more active than UICC chrysotile and crocidolite	Pc

7.2.1 Fibrous clays

7.2.1.1 Palygorskite (Attapulgite)

The preliminary results of an inhalation study indicate that the degree of fibrosis for animals sacrificed following exposure to Spanish attapulgite for 3, 6, or 12 months was similar to that for animals exposed to crocidolite (Wagner, 1982). The fibre size distribution of the attapulgite and the administered dose were not reported in the early published account of the preliminary results of this study.

In a study involving intrapleural administration in rats (Wagner, 1982), Spanish attapulgite was less potent in inducing mesothelial tumours than equal masses of UICC chrysotile B, while, in another study involving intraperitoneal injection of attapulgite of unreported origin (Pott et al., 1976a), it was more potent than chrysotile A. The fibre size distribution of the attapulgite samples was not specified in the first of the above two studies, while, in the second, 30% of fibres were more than 5 µm in length. In a further study, the incidence of tumours following intrapleural implantation of attapulgite in rats was low (7% versus 48.3% for UICC crocidolite); this low value was well correlated with the low proportion of fibres in the critical size range (< 0.25 µm in diameter; > 8 µm in length) in the administered material (samples from the mine in Attapulgus, Georgia) (Stanton et al., 1981).

The results of *in vitro* assays of the toxicity of attapulgite have been somewhat contradictory. However, the fibre size distributions of the administered samples have not been reported in the published accounts of most of the studies. Attapulgite has been more haemolytic in red blood cells than UICC chrysotile A (Bignon et al., 1980) and UICC B (Nolan & Langer, personal communication, 1985); it should be noted, however, that this is not considered to be a particularly good predictive assay for the *in vivo* pathogenesis of mineral dusts. In another assay, the alteration in thymidine incorporation by lung fibroblasts exposed to attapulgite was 63% of that observed for chrysotile B (Lemaire et al., 1982) and "minimal inhibition" of the colony-forming efficiency of I-407 cells by attapulgite (16% versus 54% for an equal dose of amosite) has been reported (Reiss et al., 1980).

It has also been reported that "short-fibre" attapulgite is cytotoxic for mouse peritoneal macrophages but not for A549 and V79-4 cells, whereas "long-fibre" attapulgite is cytotoxic in all 3 cell types (Chamberlain et al., 1982). On the basis of the correlation of the results observed in previous *in vitro* studies in these cell lines and *in vivo* investigations, it has been inferred by Chamberlain et al. (1982) that "short-fibre" attapulgite may be "fibrogenic" in *in vivo* studies, whereas "long-fibre" attapulgite may be "fibrogenic and carcinogenic". Using P388D1 cells, Lipkin (1985) did not find any cytotoxic effects with

short-fibred American or French attapulgite. Attapulgite fibres have also been shown to bind environmental carcinogenic hydrocarbons such as benzo(*a*)pyrene and nitrosonornicotine (Harvey et al., 1984).

7.2.1.2 Sepiolite

The preliminary results of an inhalation study indicate that the degree of fibrosis for animals sacrificed after exposure to sepiolite for 3, 6, or 12 months was similar to that for animals exposed to crocidolite (Wagner, 1982). Additional details on the fibre size distribution of the sepiolite and on the study protocol were not reported in the early published account of the preliminary results of this study.

No mesothelial tumours were reported in 40 F 344 rats, at an unspecified period prior to study completion, following intrapleural administration of sepiolite (Wagner, 1982). "Short-fibre" sepiolite was not cytotoxic in mouse peritoneal macrophages, A549, or V79-4 cells, whereas "long-fibre" sepiolite was cytotoxic in all three systems (Chamberlain et al., 1982).

7.2.2 Wollastonite

In studies involving the intrapleural implantation in rats of 4 samples of wollastonite from a Canadian mine, the mesothelial tumour incidence varied from 0 to 25% (versus 48.3% for UICC crocidolite) (Stanton et al., 1981).

In *in vitro* studies, wollastonite has been relatively non-toxic in the cell systems studied to date. There was no release of lysosomal enzymes nor damage to the membrane in rabbit alveolar macrophages exposed to wollastonite, at doses much greater than the concentrations of chrysotile known to be cytotoxic in this system (Pailes et al., 1984). In addition, wollastonite was found to be far less haemolytic in red blood cells than asbestos (Hefner & Gehring, 1975; Vallyathan et al., 1984), and, whereas asbestos inhibits virus-induced interferon production from mammalian cells in culture (Hahon & Eckert, 1976) wollastonite enhances this natural defence mechanism (Hahon et al., 1980).

Recent evidence for the *in vitro* biological activity of wollastonite shows that these natural mineral fibres induce effects on pulmonary macrophages that may simulate events occurring in the lung following dust exposure, such as impaired phagocytic capacity of the exposed macrophages, and serum complement activation, as measured by dose-related increases in pulmonary macrophage chemotaxis (Warheit et al., 1984).

7.2.3 Fibrous zeolites - erionite

In an inhalation study (Wagner et al., 1985) in which animals were exposed for one year to erionite from several sources, at 10 mg/m^3 7 h/day, 5 days per week, a remarkably high incidence of mesotheliomas (96.4%) occurred in the animals that remained 12 months after exposure (sample from Oregon) (frequency of fibres < 0.4 µm in diameter and > 5 µm in length = 13.3%). For comparison, mesotheliomas were present in only 15 (1.4%) of 1056 rats exposed in earlier studies to similar concentrations of various forms of asbestos for periods varying from 1 day to 2 years

(Reeves et al., 1974; Wagner et al., 1974; Davis et al., 1978). The time to development of the tumours in the Oregon erionite-exposed animals was approximately half of that observed in

crocidolite-exposed animals (Wagner, 1982). No mesotheliomas occurred in rats exposed by inhalation to New Zealand erionite (frequency of fibres < 4 µm in diameter and > 4 µm in length = 1.9%) for one year (Wagner, 1982).

In studies involving injection into the body cavities of animals, erionite has been extremely potent in the induction of mesothelial tumours; indeed one author reported that it is the "most potent known experimental carcinogenic agent for the pleural mesothelium" (Maltoni et al., 1982b). For example, in a study involving the intrapleural administration in rats of 20 mg of erionite from Oregon, the mesothelial tumour incidence was 100%; for samples originating from Karain this value was 95% (Wagner et al., 1985). The incidence of tumours after 67 weeks, in rats receiving an intrapleural injection of 25 mg of "sedimentary erionite" of unreported origin, was 52.5% (UICC Canadian chrysotile 0%) (Maltoni et al., 1982a,b). In the same study, the incidence of tumours following intraperitoneal injection of a similar amount of the same material was considerably less (2.5%) (UICC Canadian chrysotile 2.5%). On the basis of these results, the authors concluded that there was a different degree of "responsiveness of the pleura and peritoneum to erionite and crocidolite" (crocidolite was more potent in inducing tumours following intraperitoneal administration). However, a high incidence (6/10, 60%) of malignant tumours has been noted in another study in which 10 mg of erionite (average length 1 µm; average width 0.1 µm) was administered intraperitoneally to mice (incidence in chrysotile-exposed animals, 2/4, 50%) (Suzuki, 1982). No peritoneal tumours were observed in male BALB/c mice that had been administered erionite by a single intraperitoneal injection and had died less than 7 months after exposure. Between 7 and 23 months after administration, there were mesotheliomas in all the erionite-treated groups: 10 mg Colorado erionite, 21/42 (50%), 10 mg Nevada erionite, 3/8 (38%), 2 mg Nevada erionite, 24/44 (55%), and 0.5 mg Nevada erionite, 6/18 (33%).

Available data also indicate that some forms of erionite are more toxic in *in vitro* systems than crocidolite and chrysotile. A sample of erionite from Oregon increased morphological transformation in mammalian C3H1OT1/2 cells and unscheduled DNA repair synthesis in A549 cells to a greater extent than UICC chrysotile and crocidolite (Poole et al., 1983). The authors noted that fewer fibres in the sample of erionite administered were in the "pathogenic" size range (4.3% > 6 µm long, median length 1.7 µm), compared with the UICC crocidolite, and suggested that there might be some property of erionite that makes it quantitatively more active.

7.2.4 Assessment

Although, in general, the toxicological information is not adequate to assess the potential risks associated with exposure to most of these fibrous minerals, it can be concluded, with some certainty, that some forms of erionite may be particularly hazardous. This conclusion is based on the observed potency of the mineral in the induction of mesothelial tumours following both intrapleural implantation and inhalation. It has been suggested by one author that erionite may be "the most dangerous of the natural fibres" (Wagner, 1982) and by another that it is the most potent known experimental carcinogenic agent for the pleural mesothelium (Maltoni et al., 1982).

8. EFFECTS ON MAN

8.1 Asbestos

The epidemiological studies discussed below are categorized according to whether the asbestos exposure was occupational (mining and milling, manufacturing, or product application), para-occupational (neighbourhood of an asbestos industrial plant, or home of an asbestos worker), or exposure of the general population (air or water).

8.1.1 Occupational exposure

Inhalation of asbestos dust can cause fibrosis of the lung (asbestosis), changes in one or both surfaces of the pleura, bronchial carcinoma, mesothelioma of the pleura and peritoneum, and possibly cancers of other sites.

8.1.1.1 Asbestosis

This is clinically diagnosed on the basis of a history of exposure to asbestos, clinical signs and symptoms, chest radiograph appearances, and tests of lung function. These indices show the usual range of severity typical of biological processes, making diagnosis easy and certain in advanced cases, but difficult and uncertain in the earliest stages of the disease.

Under recent exposure conditions, asbestosis will rarely be detectable, even in its early stages, in less than 20 years from first exposure. In the majority of cases, asbestosis will advance after cessation of exposure (Berry, 1981; Jones, R.N., et al., 1980; Navratil, 1982), though early cases do not show any appreciable radiographic change over many years, provided that there is no further exposure (Gregor et al., 1979; Rubino et al., 1979a; Liddell & McDonald, 1980).

The 1968 British Occupational Hygiene Society standard of 2 fibres/ml for chrysotile was based on a retrospective study of a factory population, which did not include those who had left the factory and were still alive (Peto, 1978). Further follow-up of a larger population, including ex-employees, showed that the annual incidence of crepitations in men with cumulative doses below 100 fibre/ml years was of the order of 2% (Acheson & Gardner, 1979), and a recent analysis suggests that the lifelong risk of developing early signs of asbestosis may be even higher (Berry et al., 1979).

There is no substantial evidence that asbestos fibre type influences the frequency or severity of pulmonary fibrosis. However, the risk may be higher in the textile industry than in mining and milling, or in the manufacture of friction products (McDonald, 1984).

As deaths due to asbestosis may appear on death certificates under another guise and are most frequently included in deaths due to non-malignant respiratory disease, information on mortality due specifically to asbestosis is usually incomplete.

For workers who in the past suffered very heavy exposure, such as English textile workers first exposed before 1933 (Knox et al., 1968) or North American insulation workers (Selikoff et al., 1979), this distinction was not important, as the excess risk was so large that the estimated excess was more or less the same by either criterion; but for less heavily-exposed workers, whose mortality experience is more relevant for the purpose of estimating risks at lower exposure levels, neither estimate is satisfactory, as mortality due to respiratory disease varies substantially over time

and between countries and social classes, and expected numbers are therefore unreliable. Asbestosis mortality in heavily-exposed workers is related to time since first exposure and intensity of exposure, but not to age (Knox et al., 1968), and is increased by cigarette smoking (Hammond et al., 1979). If the risk were linearly related to intensity of exposure at lower levels, these relationships would provide a basis for estimating low-level risks (Peto, 1978), but this seems implausible for such a generalized progressive condition.

8.1.1.2 Pleural thickening, visceral, and parietal

Exposure to asbestos may produce acute or chronic visceral pleurisy, which tends to run parallel to the severity of the accompanying asbestosis, and thus, is a feature of those with heavy occupational exposure to asbestos. In contrast, parietal pleural thickening (plaques) is often not associated with asbestosis and tends to occur also in those with only light occupational exposure; it may also be a marker for those exposed environmentally. A high prevalence of pleural plaques in a number of countries across Europe has been attributed to environmental exposure to various mineral fibres. Pleural changes are related to the time from first exposure rather than to accumulated exposure (Rossiter et al., 1972). Pleural calcification is occasionally seen as a very late consequence of occupational exposure.

8.1.1.3 Bronchial cancer

The first reports (Gloyne, 1935; Lynch & Smith, 1935), suggesting that asbestos might be related to lung cancer occurrence were followed by approximately 60 case reports over the next 20 years. The first epidemiological confirmation of this association was published by Doll (1955). Since then, over 30 cohort studies have been carried out in industrial populations in several countries. The majority have shown an excess lung cancer risk (McDonald, 1984), but several studies have shown no significant excess mortality from bronchial tumours, even though some mesotheliomas occurred (Rossiter & Coles, 1980; Thomas et al., 1982; Berry & Newhouse, 1983; Ohlson & Hogstedt, 1985).

(a) *Type of asbestos*

It is not clear whether chrysotile, crocidolite, and amosite differ in their potential to cause lung cancer. Occupational exposures to these fibres usually occur under different industrial circumstances and with the exception of mining and milling,

mixtures of asbestos fibre types are often present. With regard to mining, Australian crocidolite miners experienced approximately 5 times the lung cancer risk of Canadian chrysotile miners (Hobbs et al., 1980); however, it is not known whether the exposure levels or other risk factors such as smoking were comparable in these 2 populations. In manufacturing, both Enterline & Henderson (1973) and Hughes & Weill (1980) presented evidence suggesting a lower lung cancer risk from pure chrysotile exposure than from a mixture of chrysotile and amphiboles, but these results were not definitive. Recent studies of 2 textile plants, one using chrysotile only (McDonald et al., 1983a), the other using a mixture of chrysotile and amphiboles (McDonald et al., 1983b), showed no difference in lung cancer risk between the two. However, as with the mining studies, it is difficult to make such cross-study comparisons, because of possible differences in the actual exposure levels and other risk factors. In gas-mask manufacture, in the 1940s, those exposed to crocidolite had a greater excess of lung

cancer than those using only chrysotile (McDonald & McDonald, 1978).

(b) *Industrial processes*

Cumulative asbestos exposure was estimated for each individual in 10 studies on 9 industrial populations, using both duration and intensity information. In two of these studies, both on asbestos cement workers (Albin et al., 1983; Finkelstein, 1983), the reported results are difficult to interpret. Both had relatively small numbers of lung cancer deaths but substantial mortality from mesothelioma, and both failed to reveal any consistent relationship between the observed excess lung cancer and exposure. The 8 remaining studies (Table 22) revealed approximately linear exposure-response relationships, but the estimated slopes of these lines varied considerably. Much uncertainty is associated with each estimated slope, because of many factors, including the limited exposure measurements made during the relevant time periods. The estimated slopes, however, exhibit a pattern according to industrial process, with the lowest values reported for miners and friction product workers; the highest for textile workers, and intermediate values in other manufacturing plants.

The variations in these results may be related to the state and physical treatment of the asbestos in different situations, the dust clouds thus containing asbestos fibres of different physical dimensions. A detailed review of other exposure-response estimates for lung cancer in different cohorts has recently been published by the US NRC/NAS (1984).

Table 21. Standardized mortality ratios for cancers of the lung, gastrointestin and other sites in asbestos workers (number of deaths in parentheses)[a]

Sex	Type of exposure	Period of observation	Standardized mortality ratio for: Lung cancer	Gastro-intestinal cancer	Other cancer	Number of mesothel-iomas	
Male	Mining, chrysotile	1946-75[b]	1.03 (9)	1.03 (15)	0.94 (13)	1	F
		1951-75[b]	1.22 (224)	1.03 (209)	1.05 (317)	10	M
Male	Manufacture, chrysotile	1936-77[c]	0.85 (28)	0.91 (18)	0.93 (26)	2	T
		1958-77[b]	2.00 (59)	1.46 (25)	1.28 (35)	1	M
		1958-77[b,c]	1.49 (84)	1.14 (59)	1.16 (70)	0	M
		1953-83[b,c]	1.61 (113)	1.10 (47)	0.84 (48)	17	P
Male	Manufacture, mixed	1941-79[d]	1.03 (143)	0.96 (103)	0.88 (77)	8	B
		1947-80	1.96 (57)	1.11 (19)	1.00 (28)	5	A
		1944-76	1.72 (44)	1.04 (31)	0.95 (89)	3	C
Male	Manufacture, amosite	1941-73	6.29 (84)	2.07 (26)	1.62 (42)	11	S
Male	Insulation, mixed	1943-62[b]	7.00 (42)	2.99 (29)	1.04 (17)	7	S
		1967-76	4.24 (397)	1.67 (89)	1.98 (258)	102	S
		1933-75[d]	2.38 (103)	1.18 (40)	1.39 (38)	46	M
Male	Shipyards	1947-78	0.84 (84)	0.83 (68)	1.11 (87)	31	I
Male	Various	-	3.07 (55)	1.05 (16)	1.29 (36)	23	I V

Female	Manufacture, mixed	1936-75 1941-79[d]	8.44 (27) 0.53 (6)	1.96 (20) 1.06 (29)	1.62 (33) 0.85 (51)	21 2	
Female	Various	-	2.06 (27)	1.28 (15)	0.99 (90)	7	

[a] From: Doll & Peto (1985).
[b] Twenty or more years after first employment.
[c] Some little exposure to amphiboles.
[d] Ten or more years after first employment.
[e] Cases of cancer and incidence ratios, not deaths.

Table 22. Exposure-response relationships for bronchial cancer[a]

Location	Process	Fibre type	Slope for increased lung cancer risk[b] (fibres/ml years)	Slope for increased lung cancer risk[b] (mppcf years)	Conversion factor (mppcf to fibre/ml) authors	Conversion factor (mppcf to fibre/ml) other
Canada						
Quebec	mining/ milling	chrysotile	-	0.0014	1 5	- -
USA						
Connecticut	friction products	chrysotile	-	0.000	-	any
Louisiana	cement products	mixed	-	0.0044	-	1
Pennsylvania	textile	mixed	-	0.051	-	1 3 5
South Carolina[c]	textile	chrysotile	0.023	-	NA	NA
			-	0.082	- -	3 5
				0.051 -	- -	3 5
area not stated	mixed	mixed	-	0.00658	- - -	1 3 5
United Kingdom						
area not stated	friction products	chrysotile	0.00058	-	NA	NA

[a] Modified from: Canada, National Health and Welfare (1984); report of Committee
[b] Adjusted to relative risk or SMR = 1 at zero dose.
[c] Studies in same factory.
NA = not applicable.

(c) *Co-carcinogens*

Because of a lack of information on smoking in most cohorts, it

has been possible to compare the lung cancer risk associated with asbestos exposure at different levels of smoking exposure in only a few studies. Although there is evidence of an effect of asbestos in the absence of smoking, it is not clear whether the effects of the 2 carcinogens are multiplicative or additive (if multiplicative, then asbestos exposure at a given level would multiply the risk among various smoking groups by the same constant; if additive, then the risk due to asbestos exposure would be added arithmetically to the smoking risk).

A review of the available studies (Saracci, 1981) and a recent report based on the Canadian mining population (Liddell et al., 1983) suggest that the joint effect of these two exposures is probably more than additive but not always multiplicative.

If asbestos acts, at least in part, as a promoter rather than an initiator of lung cancer, then exposures other than personal smoking may also be important. In particular, passive smoking, air pollution, or ionizing radiation may play a role, but no human data are available, as yet, concerning the combined effects of these factors with asbestos.

8.1.1.4 Mesothelioma

The majority of known cases of mesothelioma arise as a result of occupational or para-occupational exposure to asbestos or other fibrous minerals, but all series have shown some cases where no such fibre exposure has seemed probable. It has been suggested that it is likely that there are other causes of mesothelioma (Peterson et al., 1984). No association with smoking has been observed (McDonald, 1984).

(a) *Fibre type*

No reliable exposure-response information is available for mesothelioma. The 8 studies with adequate measurements of exposure intensity and duration showed only a small number of cases of mesothelioma, and, in at least 4 of the 7 populations studied, exposure was to mixed fibre types. Semi-quantitative data (Newhouse & Berry, 1979; Seidman et al., 1979; Hobbs et al., 1980) have suggested that increased risk of mesothelioma may be related to the duration and intensity of asbestos exposure. Other factors, particularly the time from first exposure, may also be important (Rossiter & Coles, 1980; Peto et al., 1982; Browne, 1983a,b).

Definitive conclusions cannot be drawn in the absence of exposure-response information for individual fibre types. However, available evidence suggests a substantial difference between chrysotile and the amphiboles (especially crocidolite) in their capacity to cause mesothelioma. The evidence is summarized below.

1. Substantial numbers of cases have occurred in naval dockyard cities where amphibole exposure, especially during World War II, was probably heavy (Harries, 1968; McDonald & McDonald, 1978). Of special interest is the study of Rossiter & Coles (1980) at Devonport dockyard in which 31 cases of mesothelioma were observed among a total of 1043 deaths ($P << 0.001$), but no excess of lung cancer.

2. Case-referent surveys in North America have shown very high risks associated with insulation work that usually entailed exposure to amphibole/chrysotile mixtures (McDonald & McDonald, 1980; Langer (on the basis of tissue analysis), personal communication, 1985).

3. Short-term exposure to pure crocidolite of workers engaged in the manufacture of military gas masks in Canada (McDonald & McDonald, 1978) and the United Kingdom (Jones, J.S.P. Et al., 1980) resulted in an extraordinarily high incidence of cases of mesothelioma. The same was true, but to a lesser extent, in workers in Australian (Hobbs et al., 1980), and South African crocidolite mines (Tolent et al., 1980), and in an American insulation products plant in which only amosite was used (Seidman et al., 1979). In contrast, very few cases have been reported among chrysotile production workers in Canada, Italy, South Africa, and the USSR.

4. Cohort studies on workers in 2 textile plants in the USA showed a 50-fold greater lung cancer excess than in chrysotile miners. In one of these plants, only chrysotile was used, and there was one case of mesothelioma; in the other, small quantities of amphibole were used, and there were 20 cases of mesothelioma. In a third plant, manufacturing friction products from chrysotile only, there was little or no excess of lung cancer and no mesotheliomas (McDonald & Fry, 1982; McDonald, 1984).

5. Cases of mesothelioma in 4 asbestos factories in the Province of Quebec were all associated with the use of amphibole (McDonald, 1980).

6. Electron microscopy case-referent surveys in North America (McDonald et al., 1982) and in the United Kingdom (Jones, J.S.P. Et al., 1980), have shown a substantial excess of amphibole fibres in the lung in mesothelioma cases compared with controls but no difference in chrysotile fibres. However, variations in the persistence of different fibre types in the lung complicate the interpretation of the results of tissue burden studies.

7. In a friction products plant studied by Berry & Newhouse (1983) in which only chrysotile was used (except in a well-defined area of one workshop, where crocidolite was processed for 9 years), the only excess mortality comprised 10 deaths from pleural mesothelioma, 8 or perhaps 9 in men who had worked with the crocidolite.

8. Five cases of mesothelioma were reported by Acheson et al. (1982) among 219 deaths in women who had manufactured military gas masks (containing crocidolite) compared with 1 case among 177 deaths in women manufacturing civilian masks (containing chrysotile); this woman had also worked with crocidolite in another factory where other cases of mesothelioma occurred.

9. There were 5 cases of mesothelioma among 136 deaths, 20 or more years after first employment, in a London insulation products factory in which only amosite was used (Acheson et al., 1981).

An indication of the different risks for both pleural and peritoneal mesothelioma is shown in Table 21, in which studies with the relevant information are listed. In terms of absolute numbers of mesotheliomas, greater risks were associated with crocidolite and possibly amosite exposures than with chrysotile exposure alone. Exposure to mixed fibres generally resulted in an intermediate risk. Results of studies not reporting the mesothelioma site are consistent with these findings.

The reasons for the different mesothelioma risks associated with different fibre types could include differences in the

physical dimensions of the fibres and the possibilities of higher effective doses, increased peripheral deposition, and/or longer tissue persistence for amphibole exposure than for chrysotile.

(b) *Industrial process*

Current information does not suggest an important differential in risk according to the industrial process.

8.1.1.5 Other cancers

Many cohort studies on different populations have suggested that cancer at sites other than the lung, pleura, and peritoneum has resulted from occupational exposure to asbestos. In contrast, other studies have shown no excesses of cancer at other sites.

(a) *Gastrointestinal cancers*

In 18 out of 30 cohort studies on asbestos workers, the number of deaths from gastrointestinal cancer exceeded the number expected; in the 12 remaining studies, there was no excess (McDonald, 1984). SMRs for gastrointestinal cancer in various cohorts are presented in Table 21. However, these excesses are difficult to assess because of confounding factors such as social class and geographical variations, and because of possible misdiagnosis. Moreover, there is no evidence of dose-related effects. Thus, a causal relationship with asbestos has not been established. This subject has been reviewed recently by Acheson & Gardner (1983), the Ontario Royal Commission on Asbestos (1984), and Doll & Peto (1985).

(b) *Kidney cancer*

The excess of kidney cancer observed by Selikoff et al. (1979) has not been supported by any other study so far. A causal relationship has not been established.

(c) *Laryngeal cancer*

Evidence concerning this cancer is conflicting. In addition to the small excess noted by Selikoff et al. (1979), 2 case-control studies, one in Liverpool by Stell & McGill (1973), and the other in Toronto by Shettigara & Morgan (1975), produced evidence of increased risk. On the other hand, there was no excess in Quebec miners and millers (McDonald et al., 1980), and the results of a case-control study in London by Newhouse et al. (1980) were also negative. However, Doll & Peto (1985) concluded that "on the present evidence, we conclude that asbestos should be regarded as one of the causes of laryngeal cancer". Again, the relationship, though plausible, has not been firmly established. The excess, if any, would be small in comparison with bronchial cancer.

(d) *Other sites*

Among insulation workers, 252 deaths were certified as due to "other cancer", but 54 of these were reclassified on review as mesothelioma and 28 as lung cancer (Selikoff, 1982). Reanalysis of the data has suggested that a substantial part, and perhaps all, of the apparent excess due to other cancers can be attributed to misdiagnosis. Two sites particularly liable to be certified incorrectly are the pancreas and liver; 16 of the 49 deaths certified as due to pancreatic cancer were, in fact, due to peritoneal mesothelioma (Selikoff & Seidmann, 1981). There is, therefore, little evidence of a causal relationship between

asbestos and cancers of these other sites.

There have been three studies in which there was an excess mortality from ovarian tumours in workers exposed to mixed fibres (Acheson et al., 1982; Wignall & Fox, 1982; Newhouse et al., 1980), but, in two other studies, no increase was found (Acheson et al., 1982; Berry & Newhouse, 1983).

8.1.1.6 Effects on the immune system

Changes in immunological variables have been observed in patients with asbestosis and in experimental animals exposed to asbestos; however the significance of these changes in the etiology of asbestosis is not clear. It is also important to note that, though few data are available, it is possible that exposure to other particles may effect similar changes.

Pernis et al. (1965) reported a significant increase in rheumatic factors in asbestos workers with diagnosed asbestosis. Increases in non-organ-specific anti-nuclear antibodies and rheumatoid factors have also been reported by Turner-Warwick & Parkes (1970), Lange et al. (1974), Kagan et al. (1977b), and

Navratil & Jezkova (1982). In addition, changes characteristic of idiopathic interstitial pulmonary fibrosis, such as increased levels of the immunoglobulins IgA, IgG, IgM, IgE, and complement components 3 and 4 (Lange et al., 1974; Kagan et al., 1977a; Lange, 1982) have been observed in patients with asbestosis. On the basis of these observations, it has been concluded that asbestos can trigger immunological mechanisms that are involved in lung fibrosis (Huuskonen et al., 1978; Lange, 1980). A decrease in the number of T cells (Kang et al., 1974; Kagan et al., 1977a), defects in cell-mediated immunity, and a deficiency of the generation of the migration inhibition factor (MIF) have also been shown in persons with asbestosis (Lange et al., 1978). It has been suggested that changes in T-cell subpopulations affect immunoregulatory phenomena with a resulting decrease in T-cell-mediated immunity and increase in B-cell activity. This could explain the known increased production of autoantibodies, hypergammaglobulinaemia, and increase in immune complexes noted in patients with asbestosis (Salvaggio, 1982).

A detailed review of immunological changes associated with asbestosis and a discussion of the important role of alveolar macrophages in the etiology of this disease has been published by Kagan (1980).

The immunological status of individuals with asbestos-related cancers has been described in only a limited number of reports (Ramachander et al., 1975; Haslam et al., 1978). These studies indicate that the mitogenic lymphocyte response is impaired in such patients.

8.1.2 Para-occupational exposure

8.1.2.1 Neighbourhood exposure

Pleural calcification has been associated with exposure to asbestos in the environment. An increased prevalence of pleural calcification was observed in a Finnish population residing in the vicinity of an anthophyllite mine (Kiviluoto, 1960), and similar observations were made in populations living in the vicinity of an anthophyllite mine in Bulgaria (Zolov et al., 1967), an actinolite mine in Austria (Neuberger et al., 1982), and an asbestos factory

in Czechoslovakia (Navratil & Trippe, 1972).

There is some evidence, mainly from case series and retrospective case-control studies, that the risk of mesothelioma may be increased for individuals who live near asbestos mines or factories; however, the proportion of mesothelioma patients with neighbourhood exposure to asbestos varies markedly in different series. In an early review, of 33 cases of mesothelioma in the Northeast Cape province of South Africa (Wagner et al., 1960), approximately 50% were individuals with no occupational exposure who had lived in a crocidolite-mining area. In 1977, Webster further reported that, of 100 cases of mesothelioma in South Africa with no identified occupational exposure, 95 had been exposed to crocidolite and only 1 to amosite (Webster, 1977). Newhouse &

Thompson (1965) observed 11 otherwise unexposed cases (30.6% of patients in the series) who had lived within 0.5 mile of an "asbestos factory" using mixed amphiboles in London. Data on cases of mesothelioma observed in the neighbourhood of shipyards were reviewed by Bohlig & Hain (1973), who reported 38 cases of "non-occupational" mesothelioma, which occurred during a 10-year period in residents in the vicinity of a Hamburg asbestos plant. However, in a study conducted in Canada, excluding individuals with occupational or household exposure to asbestos, only 2 out of the 254 (0.75%) cases of mesothelioma recorded in Quebec between 1960 and 1978 lived within 33 km of the chrysotile mines and mills (McDonald, 1980). In addition, in a systematic investigation of all 201 cases of mesothelioma and 19 other pleural tumours reported to the Connecticut Tumour Registry, between 1955 and 1977, and 604 randomly-selected decedent controls, there was no association between incidence and neighbourhood exposure (Teta et al., 1983).

Few data are available on the length of residence of the patients in the vicinity of the plants in these studies. Out of 413 notified cases of mesothelioma in the United Kingdom in 1966-67, 11 individuals (2.7%), who were not asbestos workers and who did not have household exposure, had lived within one mile of an asbestos factory for periods of 3 - 40 years. In a review of cases of mesothelioma in 52 female residents of New York state, diagnosed between 1967 and 1968, three otherwise "unexposed" patients (5.8%) lived within 3.6 km of asbestos factories for 18 - 27 years (Vianna & Polan, 1978). In most of the studies, there were few data concerning the type of asbestos to which neighbourhood residents were exposed.

Four ecological[a] epidemiological studies have been conducted to investigate the relationship between exposure to asbestos in the environment and disease (Fears, 1976; Graham et al., 1977; Pampalon et al., 1982; Siemiatycki, 1983). On the basis of the analysis of cancer incidence data from the Quebec Tumour Registry, the risk for residents of asbestos-mining communities was from 1.5 to 8 times greater than that for those in rural Quebec counties, for 10 different cancer sites among males, and for 7 sites among females. The higher risks in males were attributed, in part, to occupational exposure. There was increased risk of cancer of the pleura in both sexes, which decreased with increasing distance of residence from the asbestos mines. The authors emphasized the limitations of their study and recommended that information concerning other exposures and lifestyle factors should be considered in more powerful case-control studies.

An additional ecological study has been completed (Pampalon et al., 1982; Siemiatycki, 1983). Mortality between 1966 and 1977 in agglomerations (several municipalities) around the asbestos-mining

communities of Asbestos and Thetford Mines was compared with that of the Quebec population. A statistically-significant excess of

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[a] For the purposes of this document, an ecological epidemiological study is one in which exposure is assessed for populations rather than individuals.

cancer among males in these agglomerations was attributed to occupational exposure. A telephone survey indicated that 75% of the men in these communities had worked in the mines (Siemiatycki, 1983). For women, whose exposure had been confined to the environment or, in some cases, to environmental exposure and family contact, there were no statistically-significant excesses of mortality due to all causes (standard mortality rate[a], SMR = 0.89), all cancers (SMR = 0.91), digestive cancers (SMR = 1.06), respiratory cancers (SMR = 1.07), or other respiratory disease (SMR = 0.58). Similarly, there were no significant excesses when the mortality rate at age less than 45 was considered or when the reference population was confined to towns of similar size. Unfortunately, very few causes of mortality were examined in this study, and the classes were fairly broad. The authors concluded that the results were consistent with the hypothesis of no excess risk, though an SMR of 1.1 - 1.4 for lung cancer could not be ruled out in such a study.

In a recently-completed study, no significant differences in the incidence of cancer of the lung or stomach were found in two Austrian towns, one near natural asbestos deposits and one with an asbestos-cement production plant, in comparison with local and national population statistics (community size and agricultural index were taken into consideration) (Neuberger et al., 1984).

In another ecological study conducted in the USA, in which there was some attempt to control for the urban effect, geographical gradient and socioeconomic class, there was no correlation between general cancer mortality rates and the location of asbestos deposits (Fears, 1976).

Ecological studies such as those described above are considered to be insensitive, because of the large number of confounding variables, which are difficult to eliminate. In addition, true excess cancer risk is probably underestimated in such studies, because of population mobility over a latent period of several decades (Polissar, 1980). Case-control and cohort studies are generally more powerful than ecological epidemiological studies, because exposure and outcome are assessed for individuals rather than for populations. One relevant cohort study has been conducted. Mortality data for men who lived within 0.5 miles of an amosite factory in Paterson, New Jersey in 1942 were compared with data in 5206 male residents of a similar Paterson neighbourhood with no asbestos plant (Hammond et al., 1979). All men who worked in the factory were excluded. Approximately 780 (44% of the "exposed" population) and 1735 (46% of the "unexposed" population) died during the 15-year period 1962-76. With respect to total deaths, deaths from cancer (all sites combined), and lung cancer, mortality experience was slightly worse in the "unexposed" population during this period. Therefore, there was no evidence of increased risk attributable to neighbourhood exposure.

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[a] Ratio of the number of deaths observed to the number of deaths expected, if the study population had the same structure as the standard population.

In summary, available data indicate that the risk of pleural plaques and mesothelioma may be increased in populations residing in the vicinity of asbestos mines or factories. However, there is no evidence that the risk of lung cancer is increased in similarly-exposed populations. However, it should be noted that, in the past, airborne fibre levels near asbestos facilities were generally much higher than they are today. For example, Bohlig & Hain (1973) mentioned that before the second World War, there was "visible snowfall-like air pollution" from an asbestos factory in Germany. It is also claimed that, 20 years ago in Quebec mining communities,"snow-like films of asbestos" accumulated regularly (Siemiatycki, 1983).

8.1.2.2 Household exposure

Measurements made by Nicholson et al. (1980) in the homes of miners and non-miners in a chrysotile-mining community in Newfoundland, showed that fibre concentrations were several times higher in the former than the latter. Studies of both Newhouse & Thompson (1965) in the United Kingdom and of McDonald & McDonald (1980) in North America showed more cases of household exposure in mesothelioma patients than in controls, after exclusion of occupation. Two further epidemiological surveys have specifically addressed the question. Vianna & Polan (1978) studied the asbestos-exposure history of all 52 histologically confirmed fatal cases of mesothelioma in females in New York State (excluding New York City), in 1967-77, with matched controls. Excluding 6 cases exposed at work, 8 others had a husband and/or father who worked with asbestos; none of their matched controls had a history of domestic exposure whereas the reverse was true in only one pair. Information on latency was not given, but 2 of the 8 whose husbands were asbestos workers were aged only 30 and 31 years, respectively.

In a study by Anderson et al. (1979), over 3100 household contacts of 1664 surviving employees of the Paterson amosite asbestos plant, were identified in the period 1973-78. From over 2300 still living, 679 subjects who themselves had never been exposed to asbestos occupationally, and 325 controls of similar age distribution, were selected for radiographic and other tests. Small opacities and/or pleural abnormalities were observed in 35% of the household contacts and 5% of the controls. Pleural changes were more frequent than parenchymal changes. The readings were made by 5 experienced readers and though the interpretation was by consensus, it was made without knowledge of exposure category. The mortality experience of this population of household contacts is also under study; the method has not yet been adequately described but at least 5 cases of mesothelioma and excess mortality from lung cancer have been reported.

8.1.3 General population exposure

(a) *Inhalation*

Pleural calcification has been associated with exposure to mineral fibres in the environment. Increased prevalence has been observed in populations living in the vicinity of deposits of

anthophyllite, tremolite, and sepiolite in Bulgaria (Burilkov & Michailova, 1970), and tremolite deposits in Greece (Bazas et al., 1981; Constantopoulos et al., 1985). However, increased prevalence of pleural calcification has also been observed in populations without any identifiable asbestos exposure (Rous & Studeny, 1970).

There is very little direct epidemiological evidence on the effects of urban asbestos air pollution. The question was addressed to some extent in analyses of the extensive surveys of malignant mesothelial tumours undertaken by McDonald & McDonald (1980) in Canada during the period 1960-75, and in the USA in 1972. Systematic ascertainment through 7400 pathologists yielded 668 cases which, with controls, were investigated primarily for occupational factors. After exclusion of those with occupational, domestic, or mining neighbourhood exposure, the places of residence of women were examined for the 20 to 40-year period before death. Of 146 case-control pairs, 24 cases and 31 controls had lived in rural areas only, and 82 cases and 79 controls had lived in urban areas only. These very small differences could easily be due to chance, quite apart from the greater likelihood of case recognition in urban than rural areas and the contribution of exposure in the immediate neighbourhood of plants, such as that in Paterson, New Jersey.

Some indication of the possible impact of general atmospheric air pollution can be obtained from the study of sex differences in the trends of mesothelioma mortality. This approach was explored in a recent analytical review by Archer & Rom (1983) and McDonald (1985). The industrial exploitation of asbestos began early in the present century and accelerated sharply during the period before and during the first world war. Given the usual latency for mesothelioma of 20 - 40 years, it might be expected that the effects of asbestos exposure would be seen in the 1950s, especially in men. There are several sets of data from Canada, Finland, the United Kingdom, and the USA, which show that mortality in males was indeed rising steeply (up to 10% per annum), whereas in women, it is doubtful whether there was any increase. Since there was evidence that both occupational and domestic exposure accounted for some cases in women, there is little room left for any material effect attributable to general environment exposure.

(b) *Ingestion*

It has been postulated that asbestos fibres in drinking-water, and perhaps also in food, could conceivably increase the incidence of alimentary cancers in populations exposed over many years. This is a complex question, as the exposures are intermittent and the concentrations vary. However, even in industrial cohorts, the association of asbestos exposure with alimentary cancer is irregular (McDonald, 1984) and not wholly convincing (Acheson & Gardner, 1983).

Ecological epidemiological studies have been conducted in several areas with relatively high concentrations of asbestos and similar mineral fibres in the drinking-water supplies in Duluth,

Canadian cities, Connecticut, Florida, the San Francisco Bay area, and Utah. Only one relevant analytical epidemiological study has been conducted, the locale of which was Puget Sound, Washington. The results of these studies have been reviewed (Marsh, 1983; Toft et al., 1984) and are presented in Table 23.

In 5 of the areas (Connecticut, Florida, Quebec, the San Francisco Bay area, and Utah), the contaminating fibres were predominantly chrysotile in concentrations ranging from below detection to 200 x 10^6 fibres/litre. In the sixth population (Duluth), exposure was to an amphibole mineral in a similar range of concentrations, though it is not clear to what extent the particles were truly asbestos.

There has been no consistent evidence of an association between cancer incidence or mortality and ingestion of asbestos in drinking-water in the studies conducted in Canada (Wigle, 1977; Toft et al., 1981), Connecticut (Harrington et al., 1978; Meigs et al., 1980), Duluth (Mason et al., 1974; Levy et al., 1976; Sigurdson et al., 1981), Florida (Millette et al., 1983), and Utah (Sadler et al., 1981). However, all of these studies had limitations (Toft et al., 1984). The Duluth and Connecticut studies both had the disadvantage of relatively recent onset of exposure (1955 in Duluth, mostly since 1955 in Connecticut) and in Connecticut and Florida, asbestos fibre concentrations in most water supplies were very low (< 10^6 fibres/litre). The Canadian studies included localities with longstanding exposures to high concentrations of asbestos (> 100 x 10^6 fibres/litre), but the populations at risk were relatively small and cancer incidence data were not available.

In the ecological epidemiological study conducted in San Francisco, there was evidence of an association between exposure to asbestos in drinking-water and the incidence of gastrointestinal cancer (Kanarek et al., 1980; Conforti et al., 1981). This study had several advantages including long-standing, relatively high but variable concentrations of asbestos in water supplies, a large population at risk, i.e., the power of the study was good, and population-based cancer incidence data (Toft et al., 1984). However, there were several confounding factors that complicate interpretation of the results of the San Francisco Bay area study. Reanalysis, taking population density into account, reduced the significance of the relationship observed between ingested asbestos and cancer in males and increased the significance of the association for females (Conforti, 1982). Graphical reanalysis of the data also indicated that there were differences in cancer incidence within San Francisco compared with the surrounding census tracts; this "San Francisco effect" may undermine the significance of the association that was observed in the California study (Tarter, 1982).

Table 23. Epidemiological studies: asbestos in drinking-water

Study area	Fibre type	Population and exposure	Study design	Results
Duluth, Minnesota	amphibole (mine tailings)	~100 000 exposed to 1 - 65 x 10^6 fibres/ litre for 15 - 20 years	ecological: comparison of age-adjusted cancer incidence rates (1969-74) in Duluth with those in Minneapolis and St. Paul	no evide increas gastroir cancers presen asbesto
	amphibole (mine tailings)	~100 000 ex- exposed to 1 - 65 x 10^6 fibres/ litre for 15 - 20 years	ecological: determination of SMRs (1950-69) for Duluth with comparison population (Minnesota)	no evide increas gastroir cancers presenc asbesto
Connecticut	chrysotile (asbestos-cement pipe)	~580 000 exposed to 1 x 10^6 fibres/ litre for ~20 years	ecological: determination of standardized cancer incidence ratios (1935-73) from Connecticut Tumor Registry data;	authors largely results concent asbestos

			towns grouped by exposure to asbestos in drinking-water and population density; multiple regression analysis with a series of independent variables concerning population density, socioeconomic status, and drinking-water quality	drinkin

Table 23. (contd.)

Study area	Fibre type	Population and exposure	Study design	Results
Florida (Escambia county)	chrysotile (asbestos-cement pipe)	~200 000 exposed to < 10 x 10^6 fibres/litre; long-standing contamination (~40 years)	ecological: comparison of SMRs for 7 cancer sites among 3 exposure groups	no evide associa use of A deaths gastroi and rel limited and ana
Quebec	chrysotile (mining activities)	~30 000 ex-exposed to ~200 x 10^6 fibres/litre; long-standing contamination (~80 years)	ecological: comparison of observed to expected cancer mortality (1964-73), calculated on the basis of Quebec mortality rates specific for sex, site, period, and age	no consi convinci evidence increas risks a to inge drinking contami asbesto

Table 23. (contd.)

Study area	Fibre type	Population and exposure	Study design	Results
Quebec (contd.)	chrysotile (mining activities and natural erosion)	~25 000 in Thetford Mines and 100 000 in Sherbrooke exposed to ~100 x 10^6 fibres/litre; long-standing contamination (~80 years)	ecological: comparison of ASMRs (1966-76) for 71 municipalities across Canada stratified by asbestos concent-rations in drinking-water, use of chlorination; ASMRS for Sherbrooke compared with those for 7 municipalites with low concentrations of asbestos in drinking-water matched for water source (surface), use of chlorination, and population size; stepwise multiple regression analysis with 13 independent variables	no consi convinc of incr cancer attribut ingestio drinkin contami asbesto

			concerning socioeconomic status, drinking-water quality, and mobility	
California (Bay Area)	chrysotile	~3 000 000 exposed to ~36 x 10^6 fibres/ litre; longstanding contamination (~60 years)	ecological: determination of standardized cancer incidence ratios for 722 census tracts (1969-74) from Third National Cancer Survey data; census tracts aggregated by asbestos concentration and income or education; log linear regression analysis with 6 independent variables	evidence positive associat exposur relatio between concentr drinkin cancer

Table 23. (contd.)

Study area	Fibre type	Population and exposure	Study design	Results
Utah	chrysotile (asbestos-cement pipe)	24 000 exposed to unknown concentrations for 20 - 30 years	ecological: comparison of cancer incidence data from Third National Cancer Survey data for several Utah communities	positiv associa gall bl in fema kidney leukaem but stu control socioec populat and mig
Washington (Puget Sound)	chrysotile	population of Seattle, Everett, and Tacoma metropolitan areas exposed to ~200 x 10^6 fibres/litre; longstanding contamination (~60 years)	case-control: determination of odds ratios for cancer incidence (1974-77) and mortality (1955-75) in two groups of census tracts aggregated according to asbestos estimates of length of exposure for cases in high-exposure area; 2 control groups	authors that st not pro evidenc cancer the inge asbesto drinkin

Studies, such as those described above, are considered to be insensitive because of the large number of confounding variables, which are difficult to eliminate, and the potential to underestimate cancer risk due to population mobility over a latent period of several decades. In the more powerful case-control study conducted in the Puget Sound area, which included data on individual exposures based on length of residence and water source, there was no consistent evidence of a cancer risk due to the ingestion of asbestos in drinking-water.

Thus, the studies conducted to date provide little convincing evidence of an association between asbestos in public water supplies and cancer induction.

8.2 Other Natural Mineral Fibres

The present review of minerals that may occur in fibrous form will be confined to the fibrous clays, fibrous zeolites, and wollastonite. Although the effects of human exposure to these fibres should be described in the same sequence as those for asbestos, it is not possible with the very scanty epidemiological data available. Instead, such information, as exists, will be examined under 4 main mineralogical headings.

8.2.1 Fibrous clays

8.2.1.1 Palygorskite (attapulgite)

The biological effects of these mineral fibres were reviewed by Bignon et al. (1980). They mention only a 41-year-old man with pulmonary fibrosis who had been exposed for 3 years in attapulgite mining in France, and a 60-year-old woman treated for 6 months with a drug containing attapulgite, who was excreting fibres in the urine. They state that there have not been any epidemiological studies of attapulgite workers. However, surveys are in progress in the USA.

8.2.1.2 Sepiolite

There appears to have been only one epidemiological survey of workers exposed to sepiolite, i.e., a radiographic study of 63 men engaged in trimming sepiolite stones in Eskisehir, Turkey, in the manufacture of souvenirs. They had been employed from 1 to 30 years (mean 11.9 years), and 10 showed radiographic evidence of pulmonary fibrosis. However, more than half of those with fibrosis came from dusty rural regions that were rich in tremolite asbestos and zeolite deposits; silica and deatom particles were also present (Baris et al., 1980).

8.2.2 Wollastonite

Surveys have been made of wollastonite-mine and -mill workers in New York State and of workers exposed to this mineral in a Finnish limestone quarry. In the American studies (Shasby et al., 1979; Hanke et al., 1984), 57 workers were examined in 1976 and

1982. Three cases of category 1 simple pneumoconiosis were found and statistical analysis suggested that the more heavily exposed had a significantly greater decline in peak expiratory flow. In the Finnish surveys (Huuskonen et al., 1983a,b), slight pulmonary fibrosis was detected radiologically in 14 men, and bilateral pleural changes in 13 men out of 46 exposed for 10 years or more. Preliminary results from a cohort study on 238 of the quarry workers showed no excess mortality, but the authors noted that one woman with 20 years exposure died from a malignant retroperitoneal mesenchymal tumour, 30 years after first employment.

8.2.3 Fibrous zeolites - erionite

The remarkable incidence of mesothelial tumours in some remote Anatolian villages was first reported by Baris (1975). The results of intensive environmental and epidemiological studies have since been described (Baris et al., 1978, 1979; Lilis, 1981; Saracci et al., 1982; Sébastien et al., 1983). In Karain, with a population of less than 600 in 1977, 42 cases of malignant mesothelioma occurred during the previous 8 years. In Tuzkoy, a larger village of 2729 inhabitants 5 km away, at least 27 cases occurred in the period 1978-80 (Artvinli & Barris, 1979). Both sexes were equally affected and at an appreciably younger age than is usual in occupational cases. Although many questions remain unanswered,

there appears to be little doubt that this disastrous situation was largely attributable to environmental exposure, from infancy, to fine zeolite fibres of volcanic origin, which occur in local dust and which have been identified in the lung tissue of patients. The elemental composition of most of these fibres was consistent with erionite. Little asbestos outcropping is used in this area of Turkey (Rohl et al., 1982).

9. EVALUATION OF HEALTH RISKS FOR MAN FROM EXPOSURE TO ASBESTOS AND OTHER NATURAL MINERAL FIBRES

9.1 Asbestos

9.1.1 General considerations

The results of extensive epidemiological and toxicological studies have confirmed that health risks due to asbestos exposure are mainly associated with inhalation. The risks from ingestion seem to be negligible, by comparison.

Estimation of the risks from asbestos is more complex than for most other substances because of the nature of the material. Asbestos is a crystalline, relatively insoluble material of several different types, the biological effect of which is influenced by several factors including the diameter and length of the fibres and the length of their retention in the lung. The sources of the fibre and the way they are manipulated in the various processes from mining to final demolition markedly influence the hazards. Therefore, it is not possible to make a simple risk assessment or derivation of dose-response curve for asbestos.

The principle asbestos-related hazards for man are two types of respiratory cancer: bronchial carcinoma and mesothelioma; the latter affects the pleural surfaces and may also occur in the peritoneum. Both types of cancer progress rapidly and have low survival rates, and the detection of these health effects would be relatively easy, if it were not for the fact that many cases of bronchial cancer can, in general, be attributed to cigarette smoking. At present, it is not possible to separate cases specifically due to smoking or to asbestos exposure. There is epidemiological evidence of a more than additive effect on lung cancer risk with concurrent exposure to asbestos and cigarette smoke. Thus, overall, smoking is a major contributory factor to the bronchial cancer risk attributed to asbestos exposure.

Until about 30 years ago, mesotheliomas were so rare that they were not recorded separately in national cancer statistics. It is now known that the majority of these tumours are related to asbestos exposure but not to smoking. However, studies of several groups of mesothelioma cases have consistently shown a small proportion in which a link with exposure to asbestos could not be identified historically, or, in some cases, could not be associated with excess asbestos fibres in the lungs.

In addition to the respiratory cancers, asbestos inhalation causes fibrosis of the lungs (asbestosis). In the early part of the century, this was the principle asbestos-related health risk, because lung cancer was rare (presumably because there was little smoking). With very heavy exposures to asbestos, the disease became manifest within as short a period as 5 years. At lower dust levels, the disease may not appear for 20 years from first exposure. In some countries, conditions have greatly improved and it is likely that asbestosis will no longer be the cause of

significant asbestos-related mortality. The incidence of asbestosis among asbestos-exposed workers appears to be declining. Jacobson et al. (1984) have reported a low prevalence of detectable X-ray changes in asbestos workers initially employed in 1971 or later to fibre levels meeting current standards in the United Kingdom. There is no epidemiological evidence suggesting that asbestosis has resulted from exposure in the general environment.

From this it will be seen that the risk of cancer has recently become the health risk of main concern in relation to asbestos. This concern has been increased by the belief that there may be no threshold for many carcinogens below which there is no risk, but this "no threshold" hypothesis has not been proved in the case of asbestos. It may be that the risk is epidemiologically undetectably low at the concentrations of airborne asbestos that can be measured only at the high sensitivity of electron microscopy.

The need to consider the full implications of the "no threshold" hypothesis for the induction of cancers by asbestos has led to much effort to use past experience with high-level occupational exposures to predict the possible hazards at much lower levels where no excess risks have actually been observed. This applies both to the occupational setting (to set occupational exposure limits) and to possible risks in the general environment.

There are two broad approaches to assessing health risks:

1. The qualitative approach, making use of a variety of empirical observations related to particular past situations.

2. The quantitative approach, using mathematical models based on the numerical data on the environmental levels of asbestos in the past and the incidence of asbestos-related cancers.

9.1.2 Qualitative approach

9.1.2.1 Occupational

There are several studies concerning occupationally exposed groups (section 8) in which the conditions in the past have not caused a detectable increase in bronchial cancer and in which the numbers of those involved, the time since first exposure, and the completeness of follow-up were such that even a moderate increase in bronchial cancer risk should have been detected. The experience in these factories suggests that it may be possible to use asbestos under particular circumstances with no detectable excess of bronchial cancer.

Mesotheliomas are not necessarily related to bronchial cancers. Detection occurs many years after first exposure, the latency period often being longer than that for bronchial cancer. Mesotheliomas have appeared more frequently in subjects with exposure to amphiboles than in those exposed to chrysotile.

9.1.2.2 Para-occupational exposure

Mesothelioma mortality has been found to be elevated in populations exposed in an indirect or para-occupational manner. These fibre exposures originated from mining and milling operations, from factories releasing fibres into neighbourhoods, or from asbestos carried home on the clothing of workers. However, levels associated with such exposures appear to be extremely variable, and it is not possible to derive quantitative estimates

of risk from these data.

In several studies, excess risk of lung cancer from para-occupational exposure has not been reported. For many years, in the past, environmental pollution in the chrysotile asbestos mining areas was very high with reports of "snow-like" conditions persisting for long periods. However, studies on such populations have not shown any significant asbestos-related excess of cancers (section 8). Conditions in recent years have been improved by the introduction of adequate control measures. Marked differences in mesothelioma incidence have been observed in southern Africa. The incidence was very high in the crocidolite mining areas, very low around the amosite mines, and apparently undetectable in the chrysotile areas of Zimbabwe and Swaziland (Wagner, 1963b; Webster, 1977).

9.1.2.3 General population exposure

For the general environment, the Task Group concluded that:

(a) the major fibre type observed in the general environment is chrysotile; the average fibre concentration ranges over three orders of magnitude from remote rural to large urban areas;

(b) chrysotile fibres in the general environment are virtually all less than 5 µm in length and possess diameters that require electron microscopy for visualization; these fibres have not been characterized in work-place environments, nor have they been considered in computing dose-response estimates for human disease; and

(c) the risk of mesothelioma and bronchial cancer, attributable to asbestos exposure in the general population, is undetectably low; the risk of asbestosis is practically nil.

9.1.3 Quantitative approach

Assessment of health risks from exposure to asbestos fibres must take into account all the previously discussed factors regarding the physical and chemical properties of the fibre types, measurements of exposure, and biological response in both human beings and animals. On this basis, the Task Group emphasized specific principles and then commented on the most frequently cited assessment models.

(a) *Fibre type*

The Task Group believed that any risk model for mesothelioma must distinguish among the fibre types.

The human data reviewed by the Task Group indicate that the asbestos-related diseases observed in the work-place are a function of fibre type. The amphiboles have been associated with asbestosis, mesothelioma, and lung cancer. The association of chrysotile with the first two diseases has also been established, but its association with mesothelioma is less clear. Of the total of 320 mesotheliomas reported for all cohort studies on asbestos-exposed workers, only 12 occurred in workers exposed to chrysotile alone, though the majority of workers studied were exposed to chrysotile. The mesothelioma incidence in chrysotile-exposed workers appeared to be less than that in workers exposed to crocidolite or amosite. However, animal studies have not shown

conclusive evidence of a lower carcinogenic potency of chrysotile.

(b) *Fibre size and amount*

The importance of fibre size in the etiology of disease has been well demonstrated by asbestos implantation and inhalation studies on animals. Occupational exposure in different industries involves exposure to a range of fibre dimensions, and these differences in fibre size, both length and diameter, may be responsible for variations in lung cancer rates observed in different industries. Short fibres ($\leq$ 5.0 µm) appear to be less active biologically than long fibres ($\geq$ 5.0 µm) of the same type. However, there are limited data for human populations on the contribution to health effects associated with exposure to fibres much shorter than 5 µm. The Task Group believed that extrapolating disease experience in the work-place, derived on the basis of measurements of long fibres, to the ambient air, which contains mainly short fibres, introduced a major variable of unknown consequence.

Historically, work-place exposures to asbestos have been measured using a variety of non-specific methods. Currently, such measurements are made, in most cases, by using membrane filter collection and subsequent analysis by phase contrast light microscopy. With phase contrast light microscopy, the number of fibres per volume of air are determined. However, by convention, only fibres > 5 µm in length, with diameters smaller than 3 µm, and having an aspect ratio of $\geq$ 3:1 are counted. These fibres were chosen because they were believed to represent the biologically-relevant part of the respirable fraction. In addition, there is no comparability between the results obtained by the Membrane Filter Method and those obtained by any other currently available methods (especially those expressed in mass units). As a consequence, pooling of data obtained using different methods is inappropriate. Thus, the size of the data base that can be used to construct reliable dose-response relationships is severely reduced. The Task Group believed that, even in the occupational setting, dose-response relationships are ill-defined

in terms of fibre size, fraction of biologically-relevant dust, and fibre dose. For this last parameter, the use of cumulative dose may not be appropriate in calculating dose-response relationships.

(c) *Mechanism of action*

Once inhaled, chrysotile tends to split longitudinally and degrade chemically. As a result, its residence time in the lung is shorter than that of other asbestos types. Residence time in tissue is considered to be an integral part of dose. In addition, asbestos may act as a promotor (section 7.1.3.5). These factors have not been taken into account in models for quantitative risk assessment.

9.1.3.1 Bronchial cancer

At low levels of asbestos exposure, such as those that occur in the general environment, the excess cancer incidence is too low to be detected directly. Efforts to provide an estimate of what they might be, using the incidence observed at high occupational levels and then extrapolating downwards to the effects at low or very low levels, has been carried out using a linear model relating incidence and dose (concentration x time). The validity of such linear extrapolation cannot be proved for such low levels, but

fits reasonably well with the response observed at higher levels. It is likely that it overestimates rather than underestimates the risk at low levels.

The most widely-used model for the effects of asbestos exposure on lung cancer incidence assumes that the relative risk is increased in approximate proportion to both the intensity (fibre/ml) and duration of exposure, irrespective of age, smoking habit, or time since exposure. This can be summarized by the formula:

$$I_A(d,f,a,s) = I_U(a,s) \times (1 + K_L \times d \times f) \quad (1)$$

where $I_A(d,f,a,s)$ denotes lung cancer incidence among asbestos workers aged "a" who smoke "s" cigarettes per day and have been exposed for a total duration of "d" years at an average level of "f" fibre/ml. I_U denotes lung cancer incidence at the same age "a" in an unexposed population with similar smoking habits, and K_L is a constant, characteristic of the mineral type and distribution of fibre dimensions of the asbestos. The relative risk, which equals $1 + K_L \times d \times f$, is thus increased in proportion to d x f, the cumulative dose (fibre/ml years).

There are many uncertainties in using this formula. For example, there are no surveys in which there have been reliable and comparable fibre counts going back to the time when the observed occupational groups were first exposed. In the small number of surveys with dust estimations extending 20 or more years into the past, the indices of dust levels are not comparable, for example, particles per cubic foot in the chrysotile mining and milling

industry and fibres/ml in the textile industry, obtained using entirely different dust samplers. Confident conversion from one to the other measurement is not possible as different dust parameters were measured, and the conversion factor, when obtained, varied for different processes within the industry (section 5). Different authors have used different conversion factors.

In Equation 1, K_L, the "constant", represents a number of biologically important variables such as fibre type, size distribution of the airborne fibre, and the rate of lung clearance of the fibres, etc. These may well differ between different surveys.

Cigarette smoking is such an important factor that it is included in the model, but for many of the surveys, information about the number of cigarettes smoked was not available. Smoking habits, which may be rising in some developing countries and falling in industrialized countries, will render the predicted figures even less reliable. If smoking levels are rising, a higher absolute excess risk can be expected in the future, unless the asbestos dust levels are reduced.

The reservations concerning the reliability of the model indicate that it can be used to obtain only a very broad approximation of the lung cancer relative risk. The different values of the extrapolated risk estimates (generated predicting excess cancers per million people in the general population) varied over many orders of magnitude (US NRC/NAS, 1984).

9.1.3.2 Mesothelioma

For both pleural and peritoneal mesothelioma, the incidence has been reported to be approximately proportional to between the 2.6th

and 5th power of time since first exposure to asbestos, and to be independent of age or cigarette smoking habit. Such a model predicts that the effect of each day of exposure adds to overall incidence and is proportional to the intensity of exposure on that day. More formally, the predicted incidence rate (I), t years after first exposure, is proportional to $t^4-(t-d)^4$, where d is duration of exposure (Peto et al., 1982). These predicted incidence rates are roughly proportional to the duration of exposure for a period of up to 5 or 6 years, but the effect of further exposure falls progressively. According to the model, there is little increase in risk after exposure lasting beyond about 20 years (Peto, 1983).

The suggested model for the prediction of mesothelioma incidence (I) is thus:

$$I(t,f,d) = K_M \times f \times (t^4-(t-d)^4) \qquad (2)$$

where t denotes years since first exposure, f is the level of exposure in fibre/ml, and d is duration of exposure in years. The constant K_M depends on the type of fibre and the distribution of fibre dimensions of the asbestos.

As with the lung cancer model, there are reservations with the mesothelioma model. Some of the uncertainties raised for lung cancer also apply for mesothelioma. Additionally, the dose-response relationship indicated by the formula (Equation 2) is not supported by all of the data available, and fibre types are not distinguished. This last feature led the Task Group to the conclusion that the K_M value, which has been generated from amphibole and mixed fibre data, cannot be used for chrysotile.

The Task Group concluded that any number generated (number of cases per million people) will carry a variation over many orders of magnitude (For more information, see US NRC/NAS, 1984).

9.1.3.3 Risk assessment based on incidence of mesotheliomas in women

Because of the many sources of uncertainty and consequent error in risk estimation based on extrapolation, it is necessary to reconsider the possibility of some more direct approach. The incidence of malignant mesothelioma is a relatively specific indicator of mineral fibre exposure. If observed in a standardized manner for a sufficient length of time and in a large enough population, this index could have considerable sensitivity. In particular, the incidence of mesothelioma in women, if combined with case-referent field studies to estimate the contribution of direct and indirect occupational factors, could be used to assess the risk of asbestos exposure in the general environment (section 8). This approach was explored in recent analytical reviews by Archer & Rom (1983) and McDonald (1985). The industrial exploitation of asbestos began early in the present century and accelerated sharply during the period before and during the first world war. Given the usual latency for mesothelioma of 20 - 40 years, it might be expected to see the effects of asbestos exposure in the 1950s, especially in men. There are several sets of data from Canada, Finland, the United Kingdom, and the USA, which show that mortality in males is rising steeply (up to 10% per annum), whereas in women, it is doubtful whether there is any increase. Since there is evidence that both occupational and domestic exposure account for some cases in women, there is little room left for any material effect attributable to general environmental exposure. However, the sensitivity of this approach needs to be evaluated.

9.1.4 Estimating the risk of gastrointestinal tract cancer

Because of the inconsistent findings on gastrointestinal tract cancers and lack of data on exposure-response, the risk for this disease cannot be estimated.

9.2 Other Natural Mineral Fibres

Despite the scanty epidemiological information on populations exposed to many natural mineral fibres, the results of laboratory research suggest that all mineral fibres of similar size, shape, and persistence, may well carry the same or greater risks for man.

Until there is information to the contrary, it may be prudent to make this assumption. However, on the basis of available data, it can be concluded that some forms of fibrous zeolites (e.g., erionite) are particularly hazardous, causing mesothelioma in exposed populations.

9.3 Conclusions

9.3.1 Asbestos

9.3.1.1 Occupational risks

Among occupational groups, exposure to asbestos poses a health hazard that may result in asbestosis, lung cancer, and mesothelioma. The incidence of these diseases is related to fibre type, fibre size, fibre dose, and industrial processing. Adequate control measures should significantly reduce these risks.

9.3.1.2 Para-occupational risks

In para-occupational groups, which include persons with household contact and neighbourhood exposure, the risk of mesothelioma and lung cancer is generally much lower than for occupational groups. Risk estimation is not possible because of the lack of exposure data required for dose-response characterization. The risk of asbestosis is very low. These risks are being further reduced as a result of improved control practices.

9.3.1.3 General population risks

In the general population, the risks of mesothelioma and lung cancer attributable to asbestos cannot be quantified reliably and are probably undetectably low. Cigarette smoking is the major etiological factor in the production of lung cancer in the general population. The risk of asbestosis is virtually zero.

9.3.2 Other mineral fibres

On the basis of available data, it is not possible to assess the risks associated with exposure to the majority of other mineral fibres in the occupational or general environment. The only exception is erionite, for which a high incidence of mesothelioma in a local population has been associated with exposure.

10. PREVIOUS EVALUATIONS BY INTERNATIONAL BODIES

10.1. IARC

The carcinogenic risk of asbestos was evaluated in detail in

December 1976 by an International Agency for Research on Cancer Working Group (IARC, 1977), and this evaluation was reconsidered in 1982 by another Working Group (IARC, 1982). The summary evaluation from the later monograph is reproduced here.

1. "There was sufficient evidence for carcinogenicity to humans. Occupational exposure to chrysotile, amosite, anthophyllite, and mixtures containing crocidolite has resulted in a high incidence of lung cancer. A predominantly tremolitic material mixed with anthophyllite and small amounts of chrysotile also caused an increased incidence of lung cancer. Pleural and peritoneal mesotheliomas have been observed after occupational exposure to crocidolite, amosite, and chrysotile asbestos. Gastrointestinal cancers occurred in increased incidence in groups exposed occupationally to amosite, chrysotile, or mixed fibres containing crocidolite. An excess of cancer of the larynx was also observed in exposed workers. Mesotheliomas have occurred in individuals living in the neighbourhood of asbestos factories and crocidolite mines, and in people living with asbestos workers. Cigarette smoking and occupational exposure to asbestos fibres increase lung cancer incidence independently; when they occur together, they act multiplicatively" (IARC, 1977).

2. "There was sufficient evidence for carcinogenicity to animals. All types of commercial asbestos fibre that have been tested are carcinogenic to mice, rats, hamsters, and rabbits, producing mesotheliomas and lung carcinomas after inhalation exposure and after administration intrapleurally, intratracheally, or intraperitoneally" (IARC, 1977).

3. "There was inadequate evidence for activity in short-term tests. Asbestos was not mutagenic in *Salmonella typhimurium* or *Escherichia coli* (Chamberlain & Tarmy, 1977). It has been claimed to be weakly mugtagenic in Chinese hamster cells (Huang, 1979), but negative results in rat epithelial cells were published recently (Reiss et al., 1980). It has been reported that asbestos produces chromosomal anomalies in mammalian cells in culture (Sincock & Seabright, 1975; Huang et al., 1978), but this may be secondary to toxic damage. No increase in chromosomal anomalies was seen in cultured human cells treated with asbestos (Sincock et al., 1982). Sister chromatid exchanges were not increased in treated Chinese hamster cells (Price-Jones et al., 1980). No data on humans were available."

10.2. CEC

In 1977, a group of experts evaluated, for the Commission of European Communities, the public health risks of exposure to asbestos (CEC, 1977). The main conclusions of the report may be summarized as follows:

- bronchial carcinomas occur in asbestos-exposed workers, more or less independent of the type of asbestos; smoking increases the risk considerably;

- larynx carcinoma may be associated with past asbestos exposure; evidence of a causal relationship is not proven;

- gastrointestinal carcinomas have a slightly higher incidence in occupationally exposed workers, also in those with severe but short periods of exposure; the geographical distribution in the general population is not consistent

with that of para-occupational and neighbourhood exposure to asbestos;

- the incidence of mesothelioma is probably related to the type of asbestos; an effect of smoking is not evident; there exist indications that intermittent even short-term exposure may suffice to induce a mesothelioma after a long latent period;

- the prevalence of mesothelioma shows a typical geographical distribution: increased in regions with shipyards, heavy industry, asbestos industry, and some asbestos mines (especially crocidolite);

- occurrence of mesothelioma is much more specific (although not absolute) for previous asbestos exposure than occurrence of the other malignant tumours mentioned above;

- there is general agreement that the risk of mesothelioma is fibre related in the order crocidolite > amosite > chrysotile > anthophyllite, but the magnitude of the difference in risk is not well established;

- there exists a qualitative dose-response relationship, insofar that, in the occupational setting, the risk decreases with decreasing exposure;

- the intensity and/or duration of asbestos exposure necessary to induce a malignant tumour probably is the lowest/smallest in the case of mesothelioma;

- at present, there is no established evidence of general "true" environmental exposures of the public causing an increased incidence of asbestos-related tumours by inhalation or ingestion, but such a risk cannot be conclusively excluded on present evidence;

- there is no theoretical evidence for an exposure threshold below which cancers will not occur;

- there is no consensus yet whether only fibres longer than 5 µm carry a biological risk, whereas the general public is exposed relatively much more to short fibres (< 5 µm); the relationship between short and long fibres varies widely with the source of the fibrous dust; and

- it is not known whether some groups or members of the general public have a high susceptibility.

From this, it can be concluded that it is impossible to come to a reliable quantitative assessment of the risk of malignancies for the general public: present evidence does not point to there being a threshold level of dust exposure below which tumours will never occur. It is very likely that there is a practical level of exposure below which it will be impossible to detect any excess mortality or morbidity due to asbestos, despite the presence of this mineral in the tissues, especially the lung. Thus, it is possible that there is a level of exposure (perhaps already achieved in the general public) where the risk is negligibly small.

REFERENCES

ACGIH (1979) *Asbestos identification and measurement. Proceedings of a Topical Symposium,* Cincinatti, Ohio, American

Conference of Governmental Industrial Hygienists.

ACGIH (1983) *Air sampling instruments for evaluation of atmospheric contaminants,* 6th ed., Cincinatti, Ohio, American Conference of Governmental Industrial Hygienists.

ACHESON, E.D. & GARDNER, M.J. (1979) The ill-effects of asbestos on health. In: *Final Report of the Advisory Committe on Asbestos,* London, Health and Safety Commission, Vol. 2, pp. 7-83.

ACHESON, A.D. & GARDNER, M.J. (1983) *Asbestos: the control limit for asbestos,* London, Health and Safety Commission.

ACHESON, E.D., BENNETT, C., GARDNER, M.J., & WINTER, P.D. (1981) Mesothelioma in a factory using amosite and chrysotile asbestos. *Lancet,* **2**: 1403-1405.

ACHESON, E.D., GARDNER, M.J., PIPPARD, E.C., & GRIME, L.P. (1982) Mortality of two groups of women who manufactured gas masks from chrysotile and crocidolite asbestos: A 40-year follow-up. *Br. J. Ind. Med.,* **39**: 344-348.

ACHESON, E.D.,, GARDNER,, M.J., WINTER, P.D., & BENNETT, C. (1984) Cancer in a factory using amosite asbestos. *Int. J. Epidemiol.,* **13**: 3-10.

AFA (1985) *Report on dust measurement records to Asbestos International Association, London,* Association française de l'Amiante.

ALBIN, M. JAKOBSSON, K., ENGLAENDER, V., RANSTAM, J., WELINDER, H., WESTRUP, C., & MOLLER, T. (1983) Mortality and cancer morbidity in a cohort of asbestos-cement workers. In: *Proceedings of the 6th International Pneumoconiosis Conference, Bochum, 20-23 September, 1983.*

ALLISON, A.C. (1973) Experimental methods of cell and tissue culture: effects of asbestos particles on macrophages, mesothelial cells, and fibroblasts. In: Bogovski, P., Gilson, J.C., Timbrell, V., & Wagner, J.C., ed. *Biological effects of asbestos. Proceedings of a Working Conference, Lyons, 2-6 October, 1972,* Lyons, International Agency for Research on Cancer, pp. 89-93 (IARC Scientific Publications No. 8).

ALLISON, A.C., HARINGTON, J.S., & BADAMI, D.V. (1975) Mineral fibres: chemical, physiochemical and biological properties. *Adv. Pharmacol. Chemother.,* **12**: 291-402.

AMACHER, D.E., ALARIF, A., & EPSTEIN, S.S. (1974) Effects of ingested chrysotile on DNA synthesis in the gastrointestinal tract and liver of the rat. *Environ. Health Perspect.,* **9**: 319-324.

AMACHER, D.E., ALARIF, A., & EPSTEIN, S.S. (1975) The dose-dependent effects of ingested chrysotile on DNA synthesis in the gastrointestinal tract, liver, and pancreas of the rat. *Environ. Res.,* **10**: 208-216.

ANDERSON, H.A. (1983) Family contact exposure. In: *Proceedings of the World Symposium on Asbestos, Montreal, Canada, 25-27 May, 1982,* Montreal, Canadian Asbestos Information Centre, pp. 349-362.

ANDERSON, H.A., LILIS, R., DAUM, S.M., & SELIKOFF, I.J. (1979) Asbestosis among household contacts of asbestos factory workers. *Ann. NY Acad. Sci.,* **330**: 387-399.

ARCHER, J.E. & ROM, W.N. (1983) Trends in mortality of diffuse malignant mesothelioma of pleura. *Lancet,* **2**: 112-113.

ARTVINLI, M. & BARRIS, Y.I. (1979) Malignant mesotheliomas in a small villagge in the Anatolian region of Turkey. *J. Natl Cancer Inst.,* **63**: 17-27.

ASBESTOS INSTITUTE (1979) *Annual report,* Neuss, Federal Republic of Germany, 25 p.

ASBESTOS INTERNATIONAL ASSOCIATION (1982) *Reference method for the determination of airborne asbestos fibre concentrations at workplaces by light microscopy (Membrane Filter Method),* London, Asbestos International Association, 14 pp (AIA Health and Safety Publication RTM No. 1).

ASBESTOS INTERNATIONAL ASSOCIATION (1984) *Method for the determination of airborne asbestos fibres and other inorganic fibres by scanning electron microscopy,* London, Asbestos International Association, (AIA Health and Safety Publication RTM No. 2).

ASBESTOS RESEARCH COUNCIL (1971) *The measurement of airborne asbestos dust by the Membrane Filter Method,* Rochdale, United Kingdom, Asbestosis Research Council (Technical Note No. 1).

ASHCROFT, T. & HEPPLESTON, A.G. (1973) The optical and electron microscopic determination of pulmonary asbestos fibre concentration and its relation to the human pathological reaction. *J. Clin. Pathol.,* **26**: 224-234.

AUERBACH, O., HAMMOND, E.C., SELIKOFF, I.J., PARKS, V.R., KOSLOW, H.O., & GARFINKEL, L. (1977) Asbestos bodies in lung parenchyma in relation to ingestion and inhalation of mineral fibers. *Environ. Res.,* **14**: 286-304.

BARIS, Y.I. (1975) Pleural mesotheliomas and asbestos pleurosis due to environmental asbestos exposure in Turkey. Hacettepe *Bull. Med. Surg.,* **8**: 165-168.

BARIS, Y.I. (1980) The clinical and radiological aspects of 185 cases of malignant pleural mesothelioma. In: Wagner, J.C., ed. *Biological effects of mineral fibres. Proceedings of a Symposium held at Lyons, 25-27 September, 1979,* Lyons, International Agency for Research on Cancer, Vol. 2, pp. 937-945 (IARC Scientific Publications No. 30).

BARIS, Y.I., SAHIN, A.A., OEZESMI, M., KERSE, E., OEZEN, E., KOLACAN, B., ALTINOERS, M., & GOEKTEPELI, A. (1978) An outbreak of pleural mesothelioma and chronic fibrosing pleurisy in the village of Karain/Uerguep in Anatolia. *Thorax,* **33**: 181-192.

BARIS, Y.I., ARTVINLI, M., & SAHIN, A.A. (1979) Environmental mesothelioma in Turkey. *Ann. NY Acad. Sci.,* **330**: 423-432.

BARIS, Y.I., SAHIN, A.A., & ERKAN, M.L. (1980) Clinical and radiological study of sepiolite workers. *Arch. Environ. Health,* **35**: 343-346.

BARIS, Y.I., SIMONATO, L., SARACCI, R., SKIDMORE, J.W. & ART-VINLI, M. (1981) Malignant mesothelioma and radiological chest abnormalities in two villages in central Turkey. *Lancet,* **1**: 984-987.

BARRER, R.M. (1978) *Zeolites and clay minerals as sorbents and molecular sieves,* London, New York, San Francisco, Academic Press, 497 pp.

BAZAS, T., BAZAS, B., KITAS, D., GILSON, J.C., & MCDONALD, J.C. (1981) Pleural calcification in North-West Greece. *Lancet,* **2**: 254.

BEAMAN, D.R. & WALKER, H.J. (1978) Mineral fibre identification using the analytical transmission electron microscope. In: Gravatt, C.C., et al., ed. *Proceedings of a Workshop on Asbestos: Definitions and Measurement Methods,* Washington DC, National Bureau of Standards, pp. 249-269 (NBS Special Publication No. 506).

BEATTIE, J. & KNOX, J.F. (1961) Studies of mineral content and particle size distribution in the lungs of asbestos textile workers. In: Davis, C.N., ed. *Inhaled particles and vapours,* New York, Pergamon Press, pp. 419-433.

BECK, E.G. (1980) Experimental pathology *in vitro* studies related to asbestos and other mineral fibres. In: Wagner, J.C., ed. *Biological effects of mineral fibres. Proceedings of a Symposium held at Lyons, 25-27 September, 1979,* Lyons, International Agency for Research on Cancer, Vol. 1, pp. 385-400 (IARC Scientific Publications No. 30).

BECK, E.G., BRUCH, J., FRIEDRICHS, K.-H., HILSCHER, W., & POTT, F. (1971) Fibrous silicates in animal experiments and cell-culture morphological cell and tissue reactions according to different physical chemical influences. In: Walton, W.H., ed. *Inhaled particles. III. Proceedings of an International Symposium, London, 14-23 September, 1970,* Old Woking, Surrey, Unwin, Vol. 1, pp. 477-487.

BECK, E.G., HOLT, P.F., & MANOJLOVIC, N. (1972) Comparison of the effects on macrophage culture of glass fibre, glass powder, and chrysotile asbestos. *Br. J. Ind. Med.,* **29**: 280-286.

BEGER, P.J. (1933) [On asbestos bodies and pseudoasbestos bodies.] *Virchows Arch.,* **290**: 280-353 (in German).

BERRY, G. (1973) Hygiene standards theory and application. In: Bogovski, P., Gilson, J.C., Timbrell, V., & Wagner, J.C., ed. *Biological effects of asbestos. Proceedings of a Working Conference, Lyons, 2-6 October, 1972,* Lyons, International Agency for Research on Cancer, pp. 145-149 (IARC Scientific Publications No. 8).

BERRY, G. (1981) Mortality of workers certified by pneumoconiosis medical panels as having asbestosis. *Br. J. Ind. Med.,* **38**: 130-137.

BERRY, G. & LEWINSOHN, H.C. (1979) Dose-response relationships for asbestos-related disease: implications for hygiene standards. Part 1. Morbidity. *Ann. NY Acad. Sci.,* **330**: 185-194.

BERRY, G. & NEWHOUSE, M.L. (1983) Mortality of workers manufacturing friction materials using asbestos. *Br. J. Ind.*

Med., **40**: 1-7.

BERRY, G. & WAGNER, J.C. (1976) Effects of age at inoculation on occurrence of mesothelioma in rats. *Int. J. Cancer,* **17**: 477.

BERRY, G., GILSON, J.C., HOLMES, S., LEWINSOHN, H.C., & ROACH, S.A. (1979) Asbestosis: a study of dose-response relationships in an asbestos textile factory. *Br. J. Ind. Med.,* **36**: 98-112.

BERUFSGENOSSENSCHAFTEN INSTITUTE FUR ARBEITSSICHEREIT (1985) [Safety rules for dust generating handtools in contact with asbestos cement.] *Hauptverb. Gewerbl. Berufsgenoss. Zh.,* **1**(April): 616 (in German).

BGS (1983) *British Geological Survey world mineral statistics 1979-83: 70th anniversary issue.*

BIGNON, J., GONI, J., BONNAUD, G., JAURAND, M.C., DUFOUR, G., & INCHON, M.C. (1970) Incidence of pulmonary ferruginous bodies in France. *Environ. Res.,* **3**: 430-442.

BIGNON, J., SEBASTIEN, P., & GAUDICHET, A. (1978) Measurement of asbestos retention in the human respiratory system related to health effects. In: *Proceedings of the Workshop on Asbestos: Definition and Measurement Methods, July 1977,* Gaithersburg, Maryland, National Bureau of Standards, pp. 95-119 (National Bureau of Standards Special Publication 506).

BIGNON, J., SEBASTIEN, P., GAUDICHET, A., & JAURAND, M.C. (1980) Biological effects of attapulgite. In: Wagner, J.C., ed. *Biological effects of mineral fibres. Proceedings of a Symposium held at Lyons, 25-27 September, 1979,* Lyons, International Agency for Research on Cancer, Vol. 1, pp. 163-181 (IARC Scientific Publications No. 30).

BILES, B. & EMERSON, T. (1968) Examination of fibres in beer. *Nature (Lond.),* **219**: 93-94.

BLEJER, J.P. & ARLON, P.F. (1973) Talc: a possible occupational and environmental carcinogen. *J. Occup. Med.,* **15**: 92-97.

BOATMAN, E. (1982) Analysis of urines from residents drinking water containing asbestos in the Pacific Northwest. Paper presented at the *US EPA Summary Workshop on Ingested Asbestos, Cincinnati, Ohio, 13-14 October.*

BOATMAN, E.S., MERRILL, T., O'NEILL, A., POLISSAR, L., & MILLETTE, J.R. (1983) Use of quantitative analysis of urine to assess exposure to asbestos fibres in drinking-water in the Puget Sound region. *Environ. Health Perspect.,* **53**: 131-139.

BOBYLEVA, A.T., BUKHANTSEVA, R.M., LOVTSOVA, S.E., & SADILOVA, M.S. (1961) The amount of dust in residential districts of the city of Asbest and its effect on children's health. *Arch. environ. Health,* **2**: 727.

BOGOVSKI, P., KUENG, A., & WINKMANN, F. (1982) [Phenols, other components of oil shale tars and asbestos as factors modifying the action of benzo(*a*)pyrene.] *Arch. Geschwulstforsch.,* **52**: 49-55 (in German).

BOHLIG, H. & HAIN, E. (1973) Cancer in relation to environmental exposure, type of fibre, dose, occupation, and duration of exposure. In: Bogovski, P., Gilson, J.C., & Wagner, J.C., ed. *Biological effects of asbestos. Proceedings of a Working Conference, Lyons, 2-6 October, 1972,* Lyons, International Agency for Research on Cancer, pp. 217-221 (IARC Scientific Publications No. 8).

BOLTON, R.E. & DAVIS, J.M.G. (1976) The short-term effect of prolonged asbestos ingestion in rats. *Ann. Occup. Hyg.,* **19**: 121-128.

BOLTON, R.E., DAVIS, J.M., & LAMB, D. (1982a) The pathological effects of prolonged asbestos ingestion in rats. *Environ. Res.,* **29**: 134-150.

BOLTON, R.E., DAVIS, J.M.G., DONALDSON, K., & WRIGHT, A. (1982b) Variations in the carcinogenicity of mineral fibres. V. Inhaled particles. *Ann. Occup. Hyg.,* **26**: 569-582.

BOLTON, R.E., VINCENT, J.H., JONES, A.D., ADDISON, J., & BECKETT, S.T. (1983a) An overload hypothesis for pulmonary clearance of UICC amosite fibres inhaled by rats. *Br. J. Ind. Med.,* **40**: 264-272.

BOLTON, R.E., DAVIS, J.M.G., MILLER, B., DONALDSON, K., & WRIGHT (1983b) The effects of dose of asbestos on mesothelioma production in the laboratory rat. In: *Proceedings of the 6th International Pneumoconiosis Conference, Bochum, Federal Republic of Germany, 20-23 September, 1983,* Bergban-Berufsgenossenschaft, International Labour Office, pp. 1029-1035.

BONSER, G.M. & CLAYSON, D.B. (1967) Feeding of blue asbestos to rats. *Br. Emp. Cancer Campaign, Res. Rep.,* **45**: 242.

BOWES, D.R., LANGER, A.M., & ROHL, A.N. (1977) Nature and range of mineral dusts in the environment. *Phil. Trans. R. Soc. London A,* **286**: 593-610.

BREELING, J.L. (1974) Potential hazard from eating rice coated with glucose and talc. *J. Am. Med. Assoc.,* **228**: 101.

BRITISH OCCUPATIONAL HYGIENE SOCIETY (BOHS) (1968) Hygiene standard for chrysotile asbestos dust. *Ann. Occup. Hyg.,* **11**: 47-69.

BRODY, A.R., HILL, L.H., ADKINS, B., & O'CONNOR, R.W. (1981) Chrysotile asbestos inhalation in rats: deposition pattern and reaction of alveolar epithelium and pulmonary macrophages. *Am. Rev. Respir. Dis.,* **123**: 670-679.

BROWNE, K. (1983a) Asbestos-related mesothelioma: epidemiological evidence for asbestos as a promoter. *Arch. environ. Health,* **38**: 261-266.

BROWNE, K. (1983b) The epidemiology of mesothelioma. *J. Soc. Occup. Med.,* **33**: 189-194.

BRUCKMANN, J. & RUBINO, R.A. (1975) Asbestos, rationale behind a proposed air quality standard. *J. Air Pollut. Control Assoc.,* **25**: 1207-1215.

BURGER, B.F. & ENGELBRECHT, F.M. (1970) The biological effects of long and short fibres of crocidolite and chrysotile A after intrapleural injection into rats. *S. Afr. Med. J.,* **44**: 1268.

BURILKOV, T. & MICHAILOVA, L. (1970) Asbestos content in the soil and endemic pleural asbestosis. *Environ. Res.,* **3**: 443-451.

BYROM, J.C., HODGSON, A.A., & HOLMES, S. (1969) A dust survey carried out in buildings incorporating asbestos-based materials in their construction. *Ann. Occup. Hyg.,* **12**: 141-145.

CANADA, ENVIRONMENTAL HEALTH DIRECTORATE (1979) *A national survey for asbestos fibres in Canadian drinking-water,* Ottawa, Environmental Health Directorate, Canada.

CANADA, NATIONAL HEALTH AND WELFARE (1984) *Rapport du comité d'experts chargé d'informer le ministère de la santé nationale et du bien-être social sur le fondement scientifique des normes relatives a l'amiante dans les milieux de travail,* Ottawa, National Health and Welfare.

CARTER, L.J. (1977) Asbestos: trouble in the air from Maryland Rock Quarry. *Science,* **197**: 237-240.

CARTER, R.E. & TAYLOR, W.G. (1980) Identification of a particular amphibole asbestos fibre in tissues of persons exposed to a high oral intake of the mineral. *Environ. Res.,* **21**: 85-93.

CEC (1977) *Public health risks of exposure to asbestos,* Oxford, Pergamon Press Ltd (Report of the Working Group of Experts to the Commission of the European Communities) (EUR 5653e).

CHAMBERLAIN, M. & TARMY, E.M. (1977) Asbestos and glass fibres in bacterial mutation tests. *Mutat. Res.,* **43**: 159-164.

CHAMBERLAIN, M., DAVIES, R., BROWN, R.C., & GRIFFITHS, D.M. (1982) *In vitro* test for the pathogenicity of mineral dusts. *Ann. Occup. Hyg.,* **26**: 583-592.

CHAN, T.L. & LIPPMANN, M. (1980) Experimental measurements and empirical modelling of the regional deposition of inhaled particles in humans. *Am. Ind. Hyg. Assoc. J.,* **41**: 399-409.

CHATFIELD, E.J. (1982) Prospects for new methods of analysis and measurement of fibres in environmental samples. In: *Proceedings of the World Symposium on Asbestos, Montreal, Canada, 25-27 May, 1982,* Montreal, Canadian Asbestos Information Centre, pp. 401-418.

CHATFIELD, E.J. (1983) *Measurement of asbestos fibre concentrations in ambient atmospheres* (Report prepared for the Royal Commission on Matters of Health and Safety Arising from the Use of Asbestos in Ontario, Toronto, Ontario).

CHATFIELD, E.J., GLASS, R.W., & DILLON, M.J. (1978) *Preparation of water samples for asbestos fibre counting by electron microscopy,* Athens, Georgia, US Environmental Protection Agency, 132 pp (EPA Report No. 600/4-78-001, PB 280183).

CHERRY, J. (1983) An investigation of the reproducibility of

counting and sizing of asbestos fibres by SEM. In: *Proceedings of the 4th International Colloquium on Dust-Measuring Techniques and Strategy,* Edinburgh, Scotland, 1982.

CHURG, A. & WARNOCK, M.L. (1980) Asbestos fibers in the general population. *Am. Rev. Respir. Dis.,* **122**: 669-687.

CLARK, R.L. (1982) *MSHA Standard method for fibre identification by electron microscopy,* Washington DC, National Bureau of Standards, pp. 207-210 (NBS Special Publication No. 619).

CLEMMENSEN, J. & HJALGRIM-JENSEN, S. (1981) Cancer incidence among 5686 asbestos cement workers followed from 1943 through 1976. *J. Ecotoxicol. Environ. Saf.*, **5**: 15-23.

CLIFTON, R.A. (1975) Asbestos. In: *Minerals yearbook 1973,* Washington DC, US Department of the Interior, Bureau of Mines, pp. 171-179.

CLIFTON, R.A. (1980) Asbestos. In: *Minerals yearbook 1978-1979. I. Metals and minerals,* Washington DC, US Department of the Interior, Bureau of Mines, pp. 91-101.

CLIFTON, R.A. (1985) Asbestos. In: *Mineral facts and problems,* Washington DC, US Department of the Interior (Bureau of Mines Bulletin No. 675).

COFFIN, D.L., PALEKAR, L.D., & COOK, P.M. (1982) Tumorigenesis by a ferroactinolite mineral. *Toxicol. Lett.,* **13**: 143-150.

COLE, D.A., STEVENS, R.H., & WILL, L.A. (1982) Identification of carcinogens by measurement of cell-mediated immunity. III. Immunity to asbestos-induced rat peritoneal mesothelioma. *Environ. Res.,* **28**: 77-83.

COHEN, D., ARAI, S., & BRAIN, J.D. (1979) Smoking impairs long-term dust clearance from the lung. *Science,* **204**: 514-517.

COMMINS, B.T. (1979) *Asbestos in drinking-water: A review,* Medmenham, United Kingdom, Water Research Centre, 36 pp (Water Research Technical Report TR 100).

CONFORTI, P. (1982) Effects of population density on the California Bay area study. Presented at the *US EPA Summary Workshop on Ingested Asbestos, Cincinnati, Ohio, 13-14 October, 1982.*

CONFORTI, P.M., KANAREK, M.S., JACKSON, L.A., COOPER, R.C., & MURCHIO, J.C. (1981) Asbestos in drinking-water and cancer in the San Francisco Bay Area: 1969-1974 incidence. *J. Chron. Dis.,* **34**: 211-224.

CONSTANTOPOULOS, S.H., GOUDEVENOS, J.A., SARATZIS, N., LANGER, A.M., SELIKOFF, I.J., & MOUTSOPOULOS, H.M. (1985) Metsovo lung: pleural calcification and restrictive lung function in Northwestern Greece and environmental exposure to mineral fibre as etiology. *Environ. Res.,* **38**: 319-331.

COOK, P.M. (1983) Review of published studies on gut penetration by ingested asbestos fibres. *Environ. Health Perspect.,* **53**: 121-130.

COOK, P.M. & OLSON, G.F. (1979) Ingested mineral fibres: elimination in human urine. *Science,* **204**: 195-198.

COOK, P.M., GLASS, G.E., & TUCKER, J.H. (1974) Asbestiform amphibole minerals: detection and measurement of high concentrations in municipal water supplies. *Science,* **185**: 853-855.

COOPER, R.C. & MURCHIO, J.C. (1974) Preliminary studies of asbestiform fibres in drinking-water. In: *Proceedings of the Fifth Annual Conference on Environmental Toxicology,* Dayton, Ohio, Wright-Patterson Air Force Base, Aerospace Medical Research Laboratory, pp. 61-73 (AMRL-TR-74-125).

CRAIGHEAD, J.E. & MOSSMAN, B.T. (1982) The pathogenesis of asbestos-associated diseases. *New Engl. J. Med.,* **306**(24): 1446-1455.

CRALLEY, L.J. (1971) Electromotive phenomenon in metal and mineral particulate exposures: relevance to exposure to asbestos and occurrence of cancer. *Am. Ind. Hyg. Assoc. J.,* **32**: 653-661.

CRAPO, J.D., BARRY, B.E., BRODY, A.R., & O'NEILL, J.J. (1980) Morphological, morphometric and microanalytical studies on lung tissue of rats exposed to chrysotile asbestos in inhalation chambers. In: Wagner, J.C., ed. *Biological effects of mineral fibres. Proceedings of a Symposium held at Lyons, 25-27 September, 1979,* Lyons, International Agency for Research on Cancer, Vol. 1, pp. 273-283 (IARC Scientific Publications No. 30).

CRAWFORD, N.P. & COWIE, A.J. (1984) Quality control of airborne asbestos fibre counts in the United Kingdom: the present position. *Ann. Occup. Hyg.,* **28**: 391-398.

CUNNINGHAM, H.M. & PONTEFRACT, R.D. (1971) Asbestos fibres in beverages and drinking-water. *Nature (Lond.),* **232**: 332.

CUNNINGHAM, H.M., MOODIE, C.A., LAWRENCE, G.A., & PONTEFRACT, R.D. (1977) Chronic effects of ingested asbestos in rats. *Arch. Environ. Contam. Toxicol.,* **6**: 507-513.

DAVIES, R. (1980) The effect of mineral fibres on macrophages. In: Wagner, J.C., ed. *Biological effects of mineral fibres. Proceedings of a Symposium held at Lyons, 25-27 September, 1979, Lyons,* International Agency for Research on Cancer, Vol. 1, pp. 419-424 (IARC Scientific Publications No. 30).

DAVIS, J.M.G. (1963) An electron microscopy study of the effect of asbestos dust on the lung. *Br. J. Exp. Pathol.,* **44**: 454.

DAVIS, J.M.G. (1964) The ultrastructure of asbestos bodies from human lung. *Br. J. Exp. Pathol.,* **45**: 642-646.

DAVIS, J.M.G. (1970) The long-term fibrogenic effects of chrysotile and crocidolite asbestos dust injected into the pleural cavity of experimental animals. *Br. J. Exp. Pathol.,* **51**: 617.

DAVIS, J.M.G. (1971) Epithelial outgrowths from lung tissue following intrapleural injection of asbestos dust in

experimental animals. *Int. J. Cancer,* **7**: 238-248.

DAVIS, J.M.G. (1972) The fibrogenic effects of mineral dust injected into the pleural cavity of mice. *Br. J. Exp. Pathol.,* **53**: 190.

DAVIS, J.M.G. (1979) Current concepts in asbestos fiber pathogenicity. In: Lemen, R. & Dement, J.M, ed. *Dusts and disease,* Park Forest South, Pathotox Publishers Inc.

DAVIS, J.M.G. (1981) The biological effects of mineral fibres. *Ann. Occup. Hyg.,* **24**: 227.

DAVIS, J.M.G. & GROSS, P. (1973) Are ferruginous bodies an indication of atmospheric pollution by asbestos? In: Bogovski, P., Gilson, J.C., Timbrell, V., & Wagner, J.C., ed. *Biological effects of asbestos. Proceedings of a Working Conference, Lyons, 2-6 October, 1972,* Lyons, International Agency for Research on Cancer, pp. 328-242 (IARC Scientific Publications No. 8).

DAVIS, J.M.G., BECKETT, S.T., BOLTON, R.E., COLLINGS, P., & MIDDLETON, A.P. (1978) Mass and number of fibres in the pathogenesis of asbestos-related lung disease in rats. *Br. J. Cancer,* **37**: 673-688.

DAVIS, J.M.G., BECKETT, S.T., BOLTON, R.E., & DONALDSON, K. (1980a) A comparison of the pathological effects in rats of the UICC reference samples of amosite and chrysotile collected from the factory environment. In: Wagner, J.C., ed. *Biological effects of mineral fibres,* Lyons, International Agency for Research on Cancer, 285 pp (IARC Scientific Publication No. 30).

DAVIS, J.M.G., BECKETT, S.T., BOLTON, R.E., & DONALDSON, K. (1980b) The effects of intermittent high asbestos exposure (peak dose levels) on the lungs of rats. *Br. J. Exp. Pathol.,* **61**: 272-280.

DAVIS, J.M.G., ADDISON, J., BOLTON, R.E., DONALDSON, K., JONES, A.D., & SMITH, T. (in press) The pathogenicity of long versus short fibre samples of amosite asbestos administered to rats by inhalation and intraperitoneal injection. *Br. J. Exp. Pathol.*

DEMENT, J.M., HARRIS, R.L., SYMONS, M.J., & SHY, C. (1982) Estimates of dose-response for respiratory cancer among chrysotile asbestos textile workers. In: Walton, W.H., ed. *Inhaled particles. V. Proceedings of an International Symposium, Cardiff, 8-12 September, 1980,* Oxford, Pergamon Press, pp. 869-883 (*Ann. Occup. Hyg.,* **26**: 869-887).

DIXON, R.N. & TAYLOR, C.J. (1979) In: Johari, O., ed. *Asbestos fibre counting by automatic image analysis. Scanning electron microscopy,* SEM Inc., AMF O'Hare, pp. 361-366 (JL 60666).

DOLL, R. (1955) Mortality from lung cancer in asbestos workers. *Br. J. Ind. Med.,* **12**: 81-86.

DOLL, R. & PETO, J. (1985) *Effects on health of exposure to asbestos,* London, United Kingdom Health and Safety Commission, Her Majesty's Stationery Office.

DONHAM, K.J., BERG, J.W., WILL, L.A., & LEININGER, J.R. (1980) The effects of long-term ingestion of asbestos on the colon of F 344 rats. *Cancer,* **45**: 1073.

DOULL, J., KLAASSEN, C.D., & AMDUR, M.O., ed. (1980) *Casarett and Doull's toxicology. The basic science of poisons,* 2nd ed., New York, MacMillan Publishing Co., pp. 1-778.

DUNNIGAN, J. (1982) Modification of asbestos fibres: biological considerations. In: *Proceedings of the World Symposium on Asbestos, Montreal, Canada, 25-27 May, 1982,* Montreal, Canadian Asbestos Information Centre, pp. 390-394.

EISENBERG, W.V. (1974) Inorganic particle content of foods and drugs. *Environ. Health Perspect.,* **9**: 183-191.

ELMES, P.C. & SIMPSON, M.J.C. (1977) Insulation workers in Belfast. A further study of mortality due to asbestos exposure (1940-75). *Br. J. Ind. Med.,* **34**: 174-180.

ENGELBRECHT, F.M. & BURGER, B.F. (1975) Mesothelial reaction to asbestos and other irritants after intraperitoneal injection. *S. Afr. Med. J.,* **49**: 87-90.

ENTERLINE, P.E. & HENDERSON, V. (1973) Type of asbestos and respiratory cancer in the asbestos industry. *Arch. Environ. Health,* **27**: 312-317.

EPSTEIN, S.S. & VARNES, M. (1976) The short-term effects of ingested chrysotile asbestos on DNA synthesis in the pancreas and other organs of a primate. *Experientia (Basel),* **32**: 602-604.

ERDREICH, L.S. (1983) Comparing epidemiologic studies of ingested asbestos for use in risk assessment. *Environ. Health Perspect.,* **53**: 99-104.

EUROPEAN ECONOMIC COMMUNITIES (1983) *Council directive on the protection of workers from the risks related to exposure to asbestos at work,* Brussels, EEC.

FEARS, T.R. (1976) Cancer mortality and asbestos deposits. *Am. J. Epidemiol.,* **104**(5): 523-526.

FELBERMEYER, W. (1983) [VDI Conference on fibrous dusts: measurement, effect, correction, Strassbourg, 1982.] *VDI-Berichte,* **475**: 143-146 (in German).

FELBERMAYER, W. & USSAR, M. (1980) *[Environmental damage caused by disintegration of asbestos cement sheeting under the influence of the weather,]* Leoben, Austria, Institute for Umweltschutz and Emissions fragen (in German).

FINKELSTEIN, M.M. (1983) Mortality among long-term employees of an Ontario asbestos-cement factory. *Br. J. Ind. Med.,* **40**: 138-144.

FINN, M.B. & HALLENBECK, W.H. (1985) Detection of chrysotile asbestos in workers' urine. *Am. Ind. Hyg. Assoc. J.,* **46**: 162-169.

FISCHBEIN, A., ROHL, A.N., LANGER, A.M., & SELIKOFF, I.J. (1979) Dry wall construction and asbestos exposure. *Am. Ind. Hyg. Assoc. J.,* **40**: 402.

FOERSTER, H. (1983) [Natural fibre emissions in the Federal Republic of Germany.] *VDI-Ber.,* **475**: 373-376 (in German).

FOWLER, D.P. (1977) *Disposal and emission of asbestos in the USA,* Menlo Park, California, Stanford Research Institute.

FRIEDRICHS, K.H. (1983) [VDI Conference on fibrous dusts: measurement, effect, correction, Strassbourg, 1982.] *VDI-Berichte,* **475**: 113-116 (in German).

GAENSLER, E.A. & ADDINGTON, W.W. (1969) Asbestos in ferruginous bodies. *New Engl. J. Med.,* **280**: 488-492.

GALE, R.W. & TIMBRELL, V. (1980) Practical application of magnetic alignment of mineral fibres for hazard evaluation. In: Wagner, J.C., ed. *Biological effects of mineral fibres. Proceedings of a Symposium held at Lyons, 25-27 September, 1979,* Lyons, International Agency for Research on Cancer, Vol. 1, pp. 53-60 (IARC Scientific Publications No. 30).

GARDNER, M.J. (1983) Tumour incidence after asbestos exposure in Great Britain with special reference to the cancer risk of the non-occupational population. *VDI-Ber.,* **475**: 185-190.

GAUDICHET, A., SEBASTIEN, P., CLARK, N.J., & POOLEY, F.D. (1980) Identification and quantification of asbestos fibres in human tissues. In: Wagner, J.C., ed. *Biological effects of mineral fibres. Proceedings of a Symposium held at Lyons, 25-27 September, 1979,* Lyons, International Agency for Research on Cancer, Vol. 1, pp. 61-68 (IARC Scientific Publication No. 30).

GAZE, R. (1965) The physical and molecular structure of asbestos. *Ann. NY Acad. Sci.,* **132**: 23-30.

GIBBS, G.W. (1979) Etiology of pleural calcification: a study of Quebec chrysotile asbestos miners and millers. *Arch. environ. Health,* **34**: 76-83.

GIBBS, G.W. & HWANG, C.Y. (1980) Dimensions of airborne asbestos fibres. In: Wagner, J.C., ed. *Biological effects of mineral fibres. Proceedings of a Symposium held at Lyons, 25-27 September, 1979,* Lyons, International Agency for Research on Cancer, Vol. 1, pp. 69-78 (IARC Scientific Publications No. 30).

GIBEL, W., LOHS, K., HORN, K.-H., WILDNER, G.P., & HOFFMANN, F. (1976) [Experimental studies on the carcinogenic activity of asbestos fibres.] *Arch. Geschwulstforsch.,* **46**: 437-442 (in German).

GLOYNE, S.R. (1935) Two cases of squamous carcinoma of the lung occuring in asbestosis. *Tuberculosis,* **17**: 5.

GORMLEY, I.P., BROWN, R.C., CHAMBERLAIN, M., & DAVIES, R. (1980) The *in vitro* effects of mineral dusts. *Ann. Occup. Hyg.,* **23**: 225-228.

GRAHAM, S. (1981) Methodological problems in ecologic studies of the asbestos-cancer relationship. *Environ. Res.,* **25**: 35-49.

Gottardi G, Galli E (1985) *Natural Zeolites*, Berlin, Springer Verlag.

GRAHAM, S., BLANCHET, M., & ROHRER, T. (1977) Cancer in asbestos-mining and other areas of Quebec. *J. Natl Cancer Inst.,* **59**(4): 1139-1145.

GREGOR, A., PARKES, R.W., AU BOIS, R., & TURNER-WARWICK, M. (1979) Radiographic progression of asbestosis: preliminary report. *Ann. NY Acad. Sci.,* **330**: 147-156.

GROSS, P. & HARLEY, R.A. (1973) Asbestos-induced intrathoracic tissue reactions. *Arch. Pathol.,* **96**: 245-250.

GROSS, P., TREVILLE, R.T.P. De, TOLKER, E.B., KASCHAK, M., & BABYAK, M.A. (1967) Experimental asbestosis. The development of lung cancer in rats with pulmonary deposits of chrysotile asbestos dust. *Arch. Environ. Health,* **15**: 343-355.

GROSS, P., RUSSEL, A., HARLEY, R.A., SWINBURNE, L.M., DAVIS, J.M., & GREENE, W.B. (1974) Ingested mineral fibers. Do they penetrate tissue or cause cancer? *Arch. Environ. Health,* **29**: 341-347.

GROTH, D.H., KOMMINENI, C., & MACKEY, G.R. (1980) Carcinogenicity of beryllium hydroxide and alloys. *Environ. Res.,* **21**: 63-84.

GYLSETH, B., BAUNAN, R., & BRUUN, R. (1981) Analysis of inorganic fiber concentrations in biological samples by scanning electron microscopy. *Scand. J. Work environ. Health,* **7**: 101-108.

HAHON, N. & ECKERT, H.L. (1976) Depression of viral interferon induction in cell monolayers by asbestos fibres. *Environ. Res.,* **11**: 52-65.

HAHON, N., BOOTH, J.A., BOEHLECKE, B.A., & MERCHANT, J.A. (1980) Enhanced viral interferon induction by the mineral wollastonite. *J. Interferon Res.,* **1**: 49.

HAIN, E., DALQUEN, P., BOHLIG, H., DAHBERT, A., & HING, I. (1974) Restrospective study of 150 cases of mesothelioma in Hamburg area. *Int. Arch. Arbeitsmed.,* **33**: 15-37.

HALLENBECK, W.H. & PATEL-MANDLIK, K.J. (1979) Presence of fibres in the urine of a baboon gavaged with chrysotile asbestos. *Environ. Res.,* **20**: 335-340.

HALLENBECK, W.H., CHEN, E.H., HESSE, C.S., PATEL-MANDLIK, K., & WOLFF, A.H. (1978) Is chrysotile asbestos released from asbestos-cement pipe into drinking-water? *J. Am. Water Works Assoc.,* **70**: 97-102.

HAMMOND, E.C., SELIKOFF, I.J., & SEIDMAN, H. (1979) Asbestos exposure, cigarette smoking, and death rates. *Ann. NY Acad. Sci.,* **330**: 473-490.

HANKE, W., SEPULVEDA, M.J., WATSON, A., & JANKOVIC, J. (1984) Respiratory morbidity in wollastonite workers. *Br. J. ind. Med.,* **41**: 474-479.

HARINGTON, J.S. (1962) Natural occurrence of oils containing 3,4-benzpyrene and related substances in asbestos. *Nature*

(Lond.), **193**: 43-45.

HARINGTON, J.S. (1981) Fiber carcinogenesis: epidemiological observation and the Stanton hypothesis. *J. Natl Cancer Inst.,* **67**: 977-989.

HARINGTON, J.S., ALLISON, A.C., & BADAMI, D.V. (1975) Mineral fibres: chemical, physico-chemical, and biological properties. *Adv. Pharmacol. Chemother.,* **12**: 291-402.

HARRIES, P.G. (1968) Experience with asbestos disease and its control in Great Britain's naval dockyards. *Environ. Res.,* **11: 261-267.**

HARRINGTON, J.M, CRAUN, G.F., MEIGS, J.M., LANDRIGAN, P.J., FLANNERY, J.T., & WOODHULL, P.S. (1978) An investigation of the use of asbestos cement pipe for public water supply and the incidence of gastrointestinal cancer in Connecticut 1935-73. *Am. J. Epidemiol.,* **107**: 96.

HARLOW, G.E., KIMBALL, M.R., DOWTY, E., & LANGER, A.M. (1985) Observations on amosite/grunerite dusts. In: *Proceedings of the 2nd International Congress on Applied Mineralogy in the Minerals Industry, Los Angeles, California, 22-25 February, 1984,* California, The Metallurgical Society of AIME.

HARRIES, P.G. (1968) Asbestos hazards in naval dockyards. *Ann. Occup. Hyg.,* **11**: 135-145.

HARRIS, R.L. & FRASER, D.A. (1976) A model for deposition of fibers in the human respiratory system. *Am. Ind. Hyg. Assoc. J.,* **37**: 73-89.

HARVEY, G., PAGE, M., & DUMAS, L. (1984) Binding of environmental carcinogens to asbestos and mineral fibres. *Br. J. Ind. Med.,* **41**: 396-400.

HARWOOD, C. & BLASZAK, T. (1974) *Characterization and control of asbestos emissions from open sources,* Research Triangle Park, North Carolina, US Environmental Protection Agency, 195 pp (EPA Report No. 650/2-74-090, PB 238925).

HASLAM, P.L., LUKOSZEK, A., MERCHANT, J.A., & TURNER-WARWICK, M. (1978) Lymphocyte responses to phytohaemagglutin in patients with asbestosis and pleural mesothelioma. *Clin. Exp. Immunol.,* **31**: 178-188.

HEALTH AND SAFETY COMMISSION (1979) *Asbestos volume 1: final report of the advisory committee,* London, Her Majesty's Stationary Office.

HEFFELFINGER, R., MELTON, C., & KIEFER, D. (1972) *Development of a rapid survey method of sampling and analysis for asbestos in ambient air,* Research Triangle Park, North Carolina, US Environmental Protection Agency, 4 pp (Report No. APTD 0965).

HEFNER, R.E. & GEHRING, P.J. (1975) A comparison of the relative rates of hemolysis induced by various fibrogenic and non-fibrogenic particles with washed rat erythrocytes *in vitro. Am. Ind. Hyg. Assoc. J.,* **36**: 734.

HEIDERMANNS, G. (1969) [Hazard of silicosis by the technical

usage of finely grained materials.] *Staub-Reinhalt. Luft,* **29**(2): 45-48 (in German).

HEIDERMANNS, G. (1973) [Determination of asbestos content through optical and chemical analysis procedures, radiography and infra-red spectrography.] *Staub-reinhalt. Luft,* **2**: 66-70 (in German).

HENDERSON, V.I. & ENTERLINE, P.E. (1979) Asbestos exposure: factors associated with excess cancer and respiratory disease mortality. *Ann. NY Acad. Sci.,* **330**: 117-126.

HEPPLESTON, A.G. & STYLES, J.A. (1967) Activity of a macrophage factor in collagen formation by silica. *Nature (Lond.),* **214**: 521-522.

HEXT, P.M., HUNT, J., DODGSON, K.S., & RICHARDS, R.J. (1977) The effects of long-term exposure of lung fibroblasts strains to chrysotile asbestos. *Br. J. Exp. Path.,* **58**: 160-167.

HILDING, A.C., HILDING, D.A., LARSON, D.M., & AUFDENHEIDE, A.C. (1981) Biological effects of ingested amosite asbestos, taconite tailings, diatomaceous earth, and Lake Superior water in rats. *Arch. Environ. Health,* **36**: 298.

HILL, J.W., ROSSITER, C.E., & FODEN, D.W. (1984) A pilot respiratory study of workers in a MMMF plant in the United Kingdom. In: *Biological effects of man-made mineral fibers, Proceedings of a WHO/IARC Conference, 20-22 April, 1982,* Copenhagen, World Health Organization, Vol. 2, pp. 413-419.

HOBBS, M.S.T., WOODWARD, S.D., MURPHY, B., MUSK, A.W., & ELDER, J.E. (1980) The incidence of pneumoconiosis, mesothelioma, and other respiratory cancer in men engaged in mining and milling crocidolite in Western Australia. In: Wagner, J.C., ed. *Biological effects of mineral fibres. Proceedings of a Symposium held at Lyons, 25-27 September, 1979,* Lyons, International Agency for Research on Cancer, Vol. 2, pp. 615-625 (IARC Scientific Publications No. 30).

HOLT, P.F. (1982) Translocation of asbestos dust through the bronchiolar wall. *Environ. Res.,* **27**(2): 255-260.

HOLT, P.F., MILLS, J., & YOUNG, D.K. (1964) The early effects of chrysotile asbestos dust on the rat lung. *J. Pathol. Bacteriol.,* **87**: 15-23.

HOLT, P.F., MILLS, J., & YOUNG, D.K. (1965) Experimental asbestosis with four types of fibre: importance of small particles. *Ann. NY Acad. Sci.*, **132s**: 87.

HOLT, P.F., MILLS, J., & YOUNG, D.K. (1966) Experimental asbestosis in the guinea-pig. *J. Pathol. Bacteriol.,* **92**: 185.

HROMEK, J. (1962) The mass incidence of characteristic pleural changes in citizens of the western part of the former Juhlava region. *Rozhl. Tuberk.,* **22**: 405-415.

HUANG, S.L. (1979) Amosite, chrysotile, and crocidolite asbestos are mutagenic in Chinese hamster lung cells. *Mutat. Res.,* **68**: 265-274.

HUANG, S.L., SAGGIORO, D., MICHELMANN, H., & MALLING, H.V. (1978) Genetic effects of crocidolite asbestos in Chinese

hamster lung cells. *Mutat. Res.,* **57**: 225-232.

HUGGINS, C.W., DENNY, M.V., & SHELL, H.R. (1962) *Properties of palygorskite, an asbestiform mineral,* Washington DC, Department of the Interior, US Bureau of Mines (Report of Investigation 6071).

HUGHES, J. & WEILL, H. (1980) Lung cancer risk associated with manufacture of asbestos-cement products. In: Wagner, J.C., ed. *Biological effects of mineral fibres. Proceedings of a Symposium held at Lyons, 25-27 September, 1979,* Lyons, International Agency for Research on Cancer, Vol. 2, pp. 627-635 (IARC Scientific Publications No. 30).

HUMPHREY, E.W., EWING, S.L., WRIGLEY, J.V., NORTHRUP, W.F., KERSTEN, T.E., MAYER, J.E., & VARGO, R.L. (1981) The production of malignant tumors of the lung and pleura in dogs from intratracheal asbestos instillation and cigarette smoking. *Cancer,* **47**(8): 1994-1999.

HURLBLUT, C.S. (1971) *Dana's manual of mineralogy,* 18th ed., New York, John Wiley and Sons, 579 pp.

HUUSKONEN, M.S., RAESAENEN, J.A., HAERKOENEN, H., & ASP, S. (1978) Asbestos exposure as a cause of immunological stimulation. *Scand. J. Respir. Dis.,* **59**: 326-332.

HUUSKONEN, M.S., TOSSAVAINEN, A., KOSKINEN, H., ZITTING, A., KORHONEN, O., NICKELS, J., KORHONEN, K., & VAARANEN, V. (1983a) Wollastonite exposure and lung fibrosis. *Environ. Res.,* **30**: 291-304.

HUUSKONEN, M.S., JAERVISALO, J., KOSKINEN, H., NICKELS, J., RAESAENEN, J., & ASP, S. (1983b) Preliminary results from a cohort of workers exposed to wollastonite in a Finish limestone quarry. *Scand. J. Work environ. Health,* **9**: 169-175.

IARC (1977) *Asbestos,* Lyons, International Agency for Research on Cancer, 106 pp (IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Man, Vol. 14).

IARC (1982) *Chemicals, industrial processes and industries associated with cancer in humans,* Lyons, International Agency for Research on Cancer, Suppl. 4, p. 52 (IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Man, Vol. 1-29).

ILO (1984) *Safety in the use of asbestos,* Geneva, International Labour Office, ca. 120 pp (ILO Code of Practice).

INDUSTRIAL MINERALS (1978) *Mineral fibres: a review,* London, Vol. 133, pp. 19-31.

INSTITUTE FOR APPLIED FIBROUS DUST RESEARCH (1984) *Test reports,* Neuss, Federal Republic of Germany.

ISO (1981) Size definitions for particle sampling: recommendations of ad hoc working group appointed by Committee TC 146 of the International Standards Organization. *Am. Ind. Hyg. Assoc. J.,* **42**: A/64-A/68.

ISO (1984) *Proposed analytical method for determination of asbestos fibres in air,* Geneva, International Standards Organization.

JACOBS, R., DODGSON, K.S., & RICHARDS, R.J. (1977) A preliminary study of biochemical changes in the rat small intestine following long-term ingestion of chrysotile asbestos. *Br. J. Exp. Pathol.,* **58**: 541-548.

JACOBS, R., HUMPHRYS, S., DOGSON, K.S., & RICHARDS, R.J. (1978) Light and electron microscope studies of the rat digestive tract following prolonged and short-term ingestion of chrysotile asbestos. *Br. J. Exp. Pathol.,* **59**: 443-453.

JACOBSON, M., MILLER, B.G., & MURDOCK, R.M. (1984) Experience with the ILO (1980) classification in an epidemiological study of asbestos workers' chest radiographs. In: *Proceedings of the VIth International Pneumoconiosis Conference, Bochum, Federal Republic of Germany, 1983,* Bergbau-Berufsgenossenschaft, pp. 868-881.

JAGATIC, J., RUBNITZ, E., GODWIN, C., & WEISKOPF, W. (1967) Tissue response to intraperitoneal asbestos with preliminary report of acetate toxicity of heat-treated asbestos in mice. *Environ. Res.,* **1**: 271-230.

JAURAND, M.-C., MAGNE, L., & BIGNON, J. (1983) Mechanism of haemolysis by chrysotile fibres. *Toxicol. Lett.,* **15**: 205-211.

JOHN, W., BERNER, A., SMITH, G., & WESOLOWKI, J.J. (1976) *Experimental determination of the number and size of asbestos fibres in ambient air,* Springfield, Virginia, US National Technical Information Service.

JONES, J.S.P., ROBERTS, G.H., POOLEY, F.D., CLARK, N.J., SMITH, P.G., OWEN, W.G., WAGNER, J.C., BERRY, G., & POLLOCK, D.J. (1980) The pathology and mineral content of lungs in cases of mesothelioma in the United Kingdom in 1976. In: Wagner, J.C., ed. *Biological effects of mineral fibres. Proceedings of a Symposium held at Lyons, 25-27 September, 1979,* Lyons, International Agency for Research on Cancer, Vol. 1, pp. 187-199 (IARC Scientific Publications No. 30).

JONES, R.N., DIEM, J.E., GLINDMEYER, H., & WEILL, H. (1980) Progression of asbestos radiographic abnormalities: relationships to estimates of dust exposure and annual decline in lung function. In: Wagner, J.C., ed. *Biological effects of mineral fibres. Proceedings of a Symposium held at Lyons, 25-27 September, 1979,* Lyons, International Agency for Research on Cancer, Vol. 2, pp. 537-43 (IARC Scientific Publications No. 30).

KAGAN, E. (1980) The alveolar macrophage: immune derangement and asbestos-related malignancy. *Sem. Oncol.,* **8**(3): 258-267.

KAGAN, E., SOLOMON, A., COCHRANE, J.C., BEICHSNER, E.I., GLUCKMANN, J., ROCKS, P.H., & WEBSTER, I. (1977a) Immunological studies of patients with asbestosis. I. Studies of cell mediated immunity. *Clin. Exp. Immunol.,* **28**: 261-267.

KAGAN, E., SOLOMON, A., COCHRANE, J.C., KUBA, P., ROCKS, P.H., & WEBSTER, J. (1977b) Immunological studies of patients with asbestosis. II. Studies of circulating lymphoid cell number and humoral immunity. *Clin. Exp. Immunol.,* **28**: 268-275.

KANAREK, M.S., CONFORTI, P.M., JACKSON, L.A., COOPER, R.C., & MURCHIO, J.C. (1980) Asbestos in drinking-water and cancer

incidence in the San Francisco Bay Area. *Am. J. Epidemiol.,* **112**: 54-72.

KANAREK, M.S., CONFORTI, P.M., & JACKSON, L.A. (1981) Chrysotile asbestos fibers in drinking-water from asbestos-cement pipe. *Environ. Sci. Technol.,* **15**: 923-925.

KANG, K.-Y., SERA, Y., OKOCHI, T., & YAMAMURA, Y. (1974) T lymphocytes in asbestosis. *New. Engl. J. Med.,* **291**: 735-736.

KAUFMANN, R., HILLENKAMP, F., & WECHSUNG, R. (1979) The laser microprobe mass analyser (LAMMA). *Med. Progr. Technol.,* **6**: 109-121.

KAY, G.H. (1974) Asbestos in drinking-water. *J. Am. Water Works Assoc.,* **66**: 513-514.

KEENAN, R.G. & LYNCH, J.R. (1970) Techniques for the detection, identification, and analysis of fibres. *Am. Ind. Hyg. Assoc. J.,* **31**: 587-597.

KIM, W.S., CARTER, J.W., & KUPEL, R.E. (1981) Quick screening test for asbestos. *Am. Ind. Hyg. Assoc. J.,* **42**: 198-201.

KIVILUOTO, R. (1960) Pleural calcification as a roentgenologic sign of non-occupational endemic anthophyllite-asbestosis. *Acta radiol.,* **194**(Suppl.): 1-67.

KIVILUOTO, R., MEURMAN, L.O., & HAKAMA, M. (1979) Pleural plaques and neoplasia in Finland. *Ann. NY Acad. Med.,* **330**: 31-33.

KNOX, J.F., HOLMES, S., DOLL, R., & HILL, I.D. (1968) Mortality from lung cancer and other causes among workers in an asbestos textile factory. *Br. J. Ind. Med.,* **25**: 293-303.

KOLEV, K. (1982) Experimentally-induced mesothelioma in white rats in response to intraperitoneal administration of amorphous crocidolite asbestos: preliminary report. *Environ. Res.,* **29**: 123-133.

KORHONEN, K. & TOSSAVAINEN, A. (1981) [Wollastonite - a fibrous industrial mineral.] *Vuoriteollisuus,* **39**: 38-45 (in Finnish).

KOSKINEN, H., JAERVISALO, J., HUUSKONEN, M.S., KOIVULA, T., MUTANEN, P., & PITKAENEN, E. (1983) Serum lysosomal enzyme activities in silicosis and asbestosis. *Eur. J. Resp. Dis.,* **64**: 182-188.

KRAMER, J., MUDROCH, O., & TIHOR, S. (1974) *Asbestos in the environment,* Burlington, Ontario, Research Advisory Board, International Joint Commission and Environment Canada, 50 pp.

KUSCHNER, M., LEE, R., ROBECK, G.G., ROSSUM, J.R., SCHNEIDERMANN, M.A., & TAYLOR, E.W. (1974) A study of the problem of asbestos in water. *J. Am. Water Works Assoc.,* **66**: 1-3.

LAAMANEN, A.N., NORO, L., & RAUNIO, V. (1965) Observations on atmospheric air pollution caused by asbestos. *Ann. NY. Acad. Sci.,* **132**: 240-251.

LAFUMA, J., MORIN, M., PONCY, J.L., MASSE, R., HIRSCH, A., BIGNON, J., & MONCHAUX, G. (1980) Mesothelioma induced by intrapleural injection of different types of fibres in rats; synergistic effect of other carcinogens. In: Wagner, J.C., ed. *Biological effects of mineral fibres. Proceedings of a Symposium held at Lyons, 25-27 September, 1979,* Lyons, International Agency for Research on Cancer, Vol. 1, pp. 311-320 (IARC Scientific Publications No. 30).

LAKOWICZ, J.R. & BEVAN, D.R. (1980) Benzo(*a*)pyrene uptake into rat liver microsomes: effects of adsorption of benzo(*a*)pyrene to asbestos and non-fibrous particulates. *Chem.-biol. Interact.,* **29**: 129-138.

LANGE, A. (1980) An epidemiological survey of immunological abnormalities in asbestos workers. I. Nonorgan and organ-specific autoantibodies. *Environ. Res.,* **22**: 162-175.

LANGE, A. (1982) Anergy and autoimmunity in asbestos-exposed people. *Arch. Immunol. Ther. Exp.,* **30**: 211-218.

LANGE, B.A. & HAARTZ, J.C. (1979) Determination of microgram quantities of asbestos by X-ray diffraction: chrysotile in thin dust layers of matix material. *Anal. Chem.,* **15**: 520-525.

LANGE, A., SMOLIK, R., & ZATONSKI, W. (1974) Autoantibodies and serum immunoglobulin levels in asbestos workers. *Int. Arch. Arbeitsmed.,* **32**: 313-325.

LANGE, A., CHMIELARCZYK, R.S.W., GARNCAREK, D., & GIELGIER, Z. (1978) Cellular immunity in asbestosis. *Arch. Immunol. Ther. Exp.,* **26**: 899-903.

LANGER, A.M. & NOLAN, R.P. (1985) Physicochemical properties of minerals relevant to biological activities: state of the art. In: Beck, T. & Bignon, J., ed. *Proceedings of the 3rd International Workshop on In vitro Testing of Mineral Dusts, October, 1984,* Berlin, Heidelberg, New York, Springer-Verlag.

LANGER, A.M., RUBIN, I., & SELIKOFF, I.J. (1970) Electron microprobe analysis of asbestos bodies. In: Shapiro, H.A., ed. *Pneumoconiosis. Proceedings of the International Conference, Johannesburg, 1969,* Capetown, London, Oxford University Press, pp. 57-69.

LANGER, A.M., RUBIN, I.B., SELIKOFF, I.J., & POOLEY, F.D. (1972) Chemical characterization of uncooked asbestos fibres from the lungs of asbestos workers by electron microprobe analysis. *J. Histochem. Cytochem.,* **20**: 735-740.

LANGER, A.M., ASHLEY, R., BADEN, V., BERKLEY, C., HAMMOND, E.C., MACKLER, A.D., MAGGIORE, C.J., NICHOLSON, W.J., ROHL, A.N., RUBIN, I.B., SASTRE, A., & SELIKOFF, I.J. (1973) Identification of asbestos in human tissues. *J. Occup. Med.,* **15**: 287-295.

LANTING, R.W. & DEN BOEFT, J. (1979) *Atmospheric pollution by asbestos fibres,* Luxembourg, Commission of the European Communities, 180 pp (CEC Report EUR 6768 EN, Report G 908, November 1979).

LEBEL, J. (1984) *Review of fibre concentrations in Quebec asbestos mining towns,* Quebec, Quebec Asbestos Mining Association.

LE BOUFFANT, L. (1980) Physics and chemistry of asbestos dust. In: Wagner, J.C., ed. *Biological effects of mineral fibres. Proceedings of a Symposium held at Lyons, 25-27 September, 1979,* Lyons, International Agency for Research on Cancer, Vol. 1, pp. 15-33 (IARC Scientific Publications No. 30).

LEE, K.P., BARRAS, C.E., GRIFFITH, F.D., WARITZ, R.S., & LAPIN, C.A. (1981) Comparative pulmonary responses to inhaled inorganic fibres with asbestos and fiberglass. *Environ. Res.,* **24**: 167-191.

LEE, R.J., KELLEY, J.F., & WALKER, J.S. (1982) *Considerations in the analysis and definition of asbestos using electron microscopy,* Cincinnati, Ohio, American Conference of Governmental Industrial Hygienists, pp. 132-137 (NBS Special Publication No. 619).

LEINEWEBER, J.P. (1980) Dust chemistry and physics: mineral wool and vitreous fibers. In. Wagner, J.C., ed. *Biological effects of mineral fibres. Proceedings of a Symposium held at Lyons, 25-27 September, 1979,* Lyons, International Agency for Research on Cancer, Vol. 2, pp. 881-900 (IARC Scientific Publications No. 30).

LEMAIRE, I., GINGRAS, D., & LEMAIRE, S. (1982) Thymidine incorporation by lung fibroblasts as a sensitive assay for biological activity of asbestos. *Environ. Res.,* **28**: 399.

LEVY, B.S., SIGURDSON, E., MANDEL, J., LAUDON, E., & PEARSON, J. (1976) Investigating possible effects of asbestos on city water: surveillance of gastorintestinal cancer in Duluth, Minnesota. *Am. J. Epidemiol.,* **103**:362.

LIDDELL, F.D.K. (1983) Tumour incidence after asbestos exposure in the general population of Canada. *VDI-Ber.,* **475**: 179-183.

LIDDELL, F.D.K. & MCDONALD, J.C. (1980) Radiological findings as predictors of mortality in Quebec asbestos workers. *Br. J. Ind. Med.,* **37**: 257-267.

LIDDELL, F.D.K., THOMAS, D.C., GIBBS, G.W., & MCDONALD, J.C. (1983) Fibre exposure and mortality from pneumoconiosis, respiratory and abdominal malignancies in chrysotile production in Quebec, 1926-75. Presented at the *Third International Symposium on Epidemiology in Occupational Health, Singapore, September 1983.*

LIEBEN, J. & PISTAWKA, H. (1967) Mesothelioma and asbestos exposure. *Arch. Environ. Health.,* **14**: 559-568.

LIGHT, W.G. & WEI, H.T. (1980) Surface charge and a molecular basis for asbestos toxicity. In: Brown, R.C. Et al., ed. *The in vitro effect of mineral dusts,* London, Academic Press, pp. 139-145.

LILIS, R. (1981) Fibrous zeolites and endemic mesothelioma in Cappadocia, Turkey. *J. Occup. Med.,* **23**: 548-550.

LIPKIN, L.E. (1985) Failure of attapulgite to produce tumours: prediction of this result by *in vitro* cytotoxicity test. In: Beck, E.G. & Bignon, J., ed. *In vitro effects of*

mineral dusts, Berlin, Springer-Verlag.

LIPPMANN, M., YEATES, D.B., & ALBERT, R.E. (1980) Deposition, retention, and clearance of inhaled particles. *Br. J. Ind. Med.,* **37**: 337-362.

LIVINGSTON, G.K., ROM, W.N., & MORRIS, M.V. (1980) Asbestos-induced sister-chromatid exchanges in cultured Chinese hamster ovarian fibroblast cells. *J. Environ. Pathol. Toxicol.,* **4**(2/3): 373-382.

LOHRER, W. (1983) [Asbestos-exposed interiors: analysis and evaluation of risk potentials.] *Staub-Reinhalt. Luft,* **43**: 434-438 (in German).

LONGLEY, E.O. (1969). The many faces of asbestos disease. *Med. J. Aust.,* **56**: 1063-1066.

LYNCH, K.M. & SMITH, W.A. (1935) Pulmonary asbestosis. III. Carcinoma of lung in asbestos-silicosis. *Am. J. Cancer,* **24**: 56.

LYNCH, K.M., MCIVER, F.A., & CAIN, J.R. (1957) Pulmonary tumours in mice exposed to asbestos dust. *Arch. Ind. Health,* **15**: 207.

MCCONNEL, E.E. (1982a) NIEHS carcinogenesis bioassay of amosite asbestos in Syrian golden hamsters. Presented at *Summary Workshop on Ingested Asbestos, Cincinnati, Ohio, 13-14 October, 1982,* Cincinnati, Ohio, US Environmental Protection Agency, Health Effects Research Laboratory.

MCCONNEL, E.E. (1982b) NIEHS carcinogenesis bioassay of chrysotile asbestos in Syrian golden hamsters. Presented at *Summary Workshop on Ingested Asbestos, Cincinnati, Ohio, 13-14 October, 1982,* Cincinnati, Ohio, US Environmental Protection Agency, Health Effects Research Laboratory.

MCCONNELL, E.E., RUTLER, H.A., ULLAND, B.M., & MOORE, J.A. (1983) Chronic effects of dietary exposure to amosite asbestos and tremolite in F344 rats. *Environ. Health Perspect.,* **53**: 27-44.

MCCONNELL, E.E., WAGNER, J.C., SKIDMORE, J.W., & MOORE, J.A. (1984) A comparable study of the fibrogenic and carcinogenic effects of UICC Canadian chrysotile B asbestos and microfibres (JM 100). In: *Biological effects of man-made mineral fibres, Proceedings of a WHO/IARC Conference, 20-22 April,* Copenhagen, World Health Organization, Vol. 2, pp. 234-250.

MCDONALD, A.D. & FRY, J.S. (1982) Mesothelioma and fiber type in three American asbestos factories preliminary report. *Scand. J. Work environ. Health,* **8**(Suppl. 1): 53-58.

MCDONALD, A.D. & MCDONALD, J.C. (1978) Mesothelioma after crocidolite exposure during gasmask manufacture. *Environ. Res.,* **17**: 340-346.

MCDONALD, A.D. & MCDONALD, J.C. (1980) Malignant mesothelioma in North America. *Cancer,* **46**: 1650-1656.

MCDONALD, A.D., MCDONALD, J.C., & POOLEY, F.D. (1982) Mineral fibre content of lung in mesothelial tumours in North America. In: Walton, W.H., ed. *Inhaled particles. V. Proceedings of an International Symposium, Cardiff, 8-12*

September, 1980, Oxford, Pergamon Press, pp. 417-422 (*Ann. occup. Hyg.,* **26**: 417-422).

MCDONALD, A.D., FRY, J.S., WOOLLEY, A.J., & MCDONALD, J.C. (1983a) Dust exposure in an American chrysotile textile plant. *Br. J. Ind. Med.,* **40**: 361-367.

MCDONALD, A.D, FRY, J.S., WOOLLEY, A.J., & MCDONALD, J.C. (1983b) Dust exposure and mortality in an American factory using chrysotile, amosite, and crocidolite in mainly textile manufacture. *Br. J. Ind. Med.,* **40**: 368-374.

MCDONALD, A.D., FRY, J.S., WOOLLEY, A.J., & MCDONALD, J.C. (1984) Dust exposure and mortality in an American chrysotile asbestos friction products plant. *Br. J. Ind. Med.,* **41**: 151-157.

MCDONALD, J.C. (1980) Asbestos-related disease: an epidemiological review. In: Wagner, J.C., ed. *Biological effects of mineral fibres. Proceedings of a Symposium held at Lyons, 25-27 September, 1979,* Lyons, International Agency for Research on Cancer, Vol. 2, pp. 587-601 (IARC Scientific Publications No. 30).

MCDONALD, J.C. (1984) Mineral fibres and cancer. *Ann. Acad. Med. Singapore,* **13**: 345-352.

MCDONALD, J.C. (1985) Health implications of environmental exposure to asbestos. *Environ. Health Perspect.,* **62**: 319-328.

MCDONALD, J.C. & MCDONALD, A.D. (1977) Epidemiology of mesothelioma from estimated incidence. *Prev. Med.,* **6**: 426-446.

MCDONALD, J.C. & MCDONALD, A.D. (1981) Mesothelioma as an index of asbestos impact. In: Peto, R. & Schneiderman, M., ed. *Quantification of occupational cancer,* Cold Spring Harbor, Cold Spring Harbor Laboratory, pp. 73-82 (Banbury Report 9).

MCDONALD, J.C., LIDDELL, F.D.K., GIBBS, G.W., EYSSEN, G.E., & MCDONALD, A.D. (1980) Dust exposure and mortality in chrysotile mining, 1910-1975. *Br. J. Ind. Med.,* **37**: 11-24.

MALTONI, C., MINARDI, F., & MORISI, L. (1982a) The relevance of the experimental approach in the assessment of the oncogenic risks from fibrous and non-fibrous particles. The ongoing project of the Bologna Institute of Oncology. *Med. Lav.,* **73**(4): 394-407.

MALTONI, C., MINARDI, F., & MORISI, L. (1982b) Pleural mesotheliomas in Sprague-Dawley rats by erionite: first experimental evidence. *Environ. Res.,* **29**: 238-244.

MANCUSO, T.F. & COULTER, E.J. (1963) Methodology in industrial health studies. The cohort approach, with special reference to an asbestos company. *Arch. Environ. Health,* **6**: 210-226.

MARFELS, H., SPURNY, K., BOOSE, C., SCHOERMANN, J., OPIELA, H., ALTHAUS, W., & WEISS, G. (1984a) [Measurements of fibrous dusts in ambient air of the Federal Republic of Germany. I. Measurements in the vicinity of an industrial source.] *Staub-Reinhalt. Luft,* **44**: 259-263 (in German).

MARFELS, H., SPURNY, K., BOOSE, C., SCHOERMANN, J., OPIELA, H., ALTHAUS, W., & WEISS, G. (1984b) [Measurements of

fibrous dusts in ambient air of Federal Republic of Germany. II. Measurements on a busy crossing of a large town.] *Staub-Reinhalt. Luft,* **44**: 410-414 (in German).

MARSH, G.M. (1983) Review of epidemiologic studies related to ingested asbestos. *Environ. Health Perspect.,* **53**: 49-56.

MASON, T.J., MCKAY, E.W., & MILLER, R.W. (1974) Asbetos-like fibres in Duluth water supply: relation to cancer mortality. *J. Am. Med. Assoc.,* **228**: 1019.

MEEK, M.E. & GRASSO, P. (1983) An investigation of the penetration of ingested asbestos into the normal and abnormal intestinal mucosa of the rat. *Food Chem. Toxicol.,* **21**: 193-200.

MEEK, M.E., SHANNON, H.S., & TOFT, P. (1985) Case study: Asbestos in toxicological risk assessment. In: Clayson, D.B., Krewski, D., & Munro, I., ed. *Toxicological risk assessment,* Boca Raton, Florida, CRC Press, Vol. 2, pp. 121-165.

MEIGS, J.W., WALTER, S.D., HESTON, J.F., MILLETTE, J.R., CRAUN, G.E., WOODHULL, R.S., & FLANNERY, J.T. (1980) Asbestos cement pipe and cancer in Connecticut 1955-74. *J. environ. Health,* **42**: 187.

MEYER, E. (1984) [Presence of asbestos fibres in drinking water.] In: Fischer, M. & Meyer, E., ed. *[Assessment of the cancer risk from asbestos,],* Munich, Medizin Verlag, pp. 62-78 (in German).

MEYLAN, W.M., HOWARD, P.H., LANDE, S.S., & HANCHET, A. (1978) *Chemical market input/output analysis of selected chemical substances to assess source of environmental contamination: asbestos,* Washington DC, US Environmental Protection Agency (EPA Report No. 560/6-78-005).

MICHAELS, L. & CHISSICK, S.S., ed. (1979) *Asbestos: properties, applications, and hazards,* New York, John Wiley and Sons, 553 pp.

MIDDLETON, A.P., BECKETT, S.T., & DAVIS, J.M.G. (1979) Further observations on the short-term retention and clearance of asbestos by rats, using UICC reference samples. *Ann. Occup. Hyg.,* **22**: 141-152.

MILLER, A., LANGER, A., TIERSTEIN, A., & SELIKOFF, I. (1975) "Non-specific" interstitial pulmonary fibrosis. *New Engl. J. Med.,* **292**: 91-93.

MILLER, A.B. (1978) Asbestos fibre dust and gastrointestinal malignancies. Review of literature with regard to a cause/effect relationship. *J. Chron. Dis.,* **31**: 22-33.

MILLER, K. (1978) The effects of asbestos on macrophages. *CRC Crit. Rev. Toxicol.,* **5**: 319-354.

MILLER, K., WEBSTER, I., HANDFIELD, R.I.M., & SKINE, M.I. (1978) Ultrastructure of the lung in the rat following exposure to crocidolite asbestos and quartz. *J. Pathol.,* **124**: 39-44.

MILLETTE, J.R., CLARK, P.J., & PANSING, M.F.(1979a) *Exposure to asbestos from drinking-water in the United States,* Cincinnati, Ohio, US Environmental Protection Agency, Health

Effects Research Laboratory, Office of Research and Development, 86 pp (EPA Report No. 600/1-79-028).

MILLETTE, J.R., TWYMAN, J.D., HANSEN, E.C., CLARK, P.J., & PANSING, M.F. (1979b) Chysotile, palygorskite, and halloy site in drinking-water. *Scanning Electron. Microsc.,* **1**: 579-586.

MILLETTE, J.R., CLARK, P.J., PANSING, F.M., & TWYMAN, J.D. (1980) Concentration and size of asbestos in water supplies. *Environ. Health Perspect.,* **34**: 13-25.

MILLETTE, J.R., CRAUN, G.F., STOBER, J.A., KRAEMER, D.F., TOUSIGNANT, H.G., HILDAGO, E., DUBOISE, R.L., & BENEDICT, J. (1983) Epidemiology study of the use of asbestos-cement pipe for the distribution of drinking-water in Escambia County, Florida. *Environ. Health Perspect.,* **53**: 91-98.

MILNE, J.E.H. (1971) Developmental changes in asbestos bodies and their significance. *Trans. Soc. Occup. Med.,* **214**: 118-121.

MOATAMED, F., ROM, W.N., & CASEY, K.R. (1981) Early response to injected fibrous erionite in the mouse peritoneum and rat lung. *Am. Rev. Respir. Dis.,* **123**(Annual Meeting Supplement): 144 (abstract).

MONCHAUX, G., BIGNON, J., JAURAND, M.C., LAFUMA, J., SEBASTIEN, P., MASSE, R., HIRSCH, A., & GONI, J. (1981) Mesotheliomas in rats following inoculation with acid-leached chrysotile asbestos and other mineral fibers. *Carcinogenesis,* **2**: 229-236.

MORGAN, A. (1979) Fibre dimensions: their significance in the deposition and clearance of inhaled fibrous dust. In: Lemen, R. & Dement, J.M., ed. *Dusts and disease,* Park Forest South, Illinois, Pathotox Publishers Inc., pp. 87-96.

MORGAN, A. & CRALLEY, L.J. (1973) Chemical characteristics of asbestos and associated trace elements. In: Bogovski, P., et al., ed. *Biological effects of asbestos. Proceedings of a Working Conference, Lyons, 2-6 October, 1972,* Lyons, International Agency for Research on Cancer, pp. 113-118 (IARC Scientific Publications No. 8).

MORGAN, A. & HOLMES, A. (1980) Concentrations and dimensions of coated and uncoated asbestos fibres in the human lung. *Br. J. Ind. Med.,* **37**: 25-32.

MORGAN, A., EVANS, J.C., EVANS, R.J., HOUNAM, R.J., HOLMES, A., & DOYLE, S.G. (1975) Studies on the deposition of inhaled fibrous material in the respiratory tract of the rat and its subsequent clearance using radioactive tracer techniques. II. Deposition of the UICC Standard Reference Samples of Asbestos. *Environ. Res.,* **10**: 196-207.

MORGAN, A., EVANS, J.C., & HOLMES, A. (1977a) Deposition and clearance of inhaled fibrous minerals in the rat. Studies using radioactive tracer technique. In: Walton, W.H., ed. *Inhaled particles. IV. Part 1. Proceedings of an International Symposium, Edinburgh, 22-26 September, 1975,* Oxford, Pergamon Press, pp. 259-272.

MORGAN, A., DAVIS, P., WAGNER, J.C., BERRY, G., & HOLMES, A. (1977b) The biological effects of magnesium-leached chrysotile asbestos. *Br. J. Exp. Pathol.,* **58**: 465-473

MORGAN, A., BLACK, A., EVANS, N., HOLMES, A., & PRITCHARD, J.N. (1980) Deposition of sized glass fibres in the respiratory tract of the rat. *Ann. Occup. Hyg.,* **23**: 353-366.

MORRIS, T.G., ROBERTS, W.H., SILVERTON, R.E., SKIDMORE, J.W., WAGNER, J.C., & COOK, G.W. (1967) Comparison of dust retention in specific pathogen free and standard rats. In: Davies, C.N., ed. *Inhaled particles and vapours,* London, Pergamon Press, Vol. 2, pp. 205-213.

MOSSMAN, B.T. & CRAIGHEAD, J.E. (1982) Comparative cocarcinogenic effects of crocidolite asbestos, hematite, kaolin, and carbon in implanted tracheal organ cultures. *Ann. occup. Hyg.,* **26**(1-4): 553-567.

MOSSMAN, B.T. & LANDESMAN, J.M. (1983) Importance of oxygen-free radicals in asbestos-induced injury to airway epithelial cells. *Chest,* **83**: 50-51.

MOSSMAN, B.T., EASTMAN, A., LANDESMAN, J.M., & BRESNICK, E. (1983) Effects of crocidolite and chrysotile asbestos on cellular uptake, metabolism, and DNA after exposure of hamster tracheal epithelial cells to benzo(*a*)pyrene. *Environ. Health Perspect.,* **51**: 331-336.

MUHLE, H., SPURNY, K., & POTT, F. (1983) [Inhalation experiments on retention, lung clearance, and migration of asbestos and glass fibres in dependence of cigarette smoking.] *VDI-Ber.,* **475**: 247-251 (in German).

MUMPTON, F.A. (1979) *Reconnaissance study of the association of zeolites with mesothelioma cancer occurrences in central Turkey,* Brockport, New York, State University College, 49 pp.

NAVRATIL, M. (1982) *[Asbestos of the lung and its complications,]* Prague, Avicenum (in Czech).

NAVRATIL, M. & JEZKOVA, Z. (1982) Antibodies against pulmonary tissue in individuals with long-term exposure to asbestos dust. *Cas. Lek. Ces.,* **121**: 1608-1611.

NAVRATIL, M. & TRIPPE, F. (1972) Prevalence of pleural calcification in persons exposed to asbestos dust, and in the general population in the same district. *Environ. Res.,* **5**: 210-216.

NEUBERGER, M., RABER, A., & FRIEDL, H.P. (1982) *[Epidemiology of asbestos-linked lung diseases in Austria. XVIth Congress of the Austrian Society for Lung Diseases,]* Vienna, Hoffmann, pp. 127-130 (in German).

NEUBERGER, M., KUNDI, M., & FRIEDL, H.P. (1984) Environmental asbestos exposure and cancer mortality. *Arch. environ. Health,* **39**: 261-265.

NEWHOUSE, M.L. & BERRY, G. (1976) Predictions of mortality from mesothelial tumours in asbestos factory workers. *Br. J. ind. Med., **33**: 147-151.*

NEWHOUSE, M.L. & BERRY, G. (1979) Patterns of mortality in asbestos factory workers in London. *Ann. NY Acad. Sci.,* **330**: 53-60.

NEWHOUSE, M.L. & THOMPSON, H. (1965) Mesothelioma of pleura and peritoneum following exposure to asbestos in the London area. *Br. J. Ind. Med.,* **22**: 261-269.

NEWHOUSE, M.L., GREGORY, M.M., & SHANNON, H. (1980) Etiology of carcinoma of the larynx. In: Wagner, J.C., ed. *Biological effects of mineral fibres. Proceedings of a Symposium held at Lyons, 25-27 September, 1979,* Lyons, International Agency for Research on Cancer, Vol. 2, pp. 687-695 (IARC Scientific Publications No. 30).

NEWHOUSE, M.L., OAKES, D., & WOOLLEY, A.J. (1985) Mortality of welders and other craftsmen at a shipyard in northeast England. *Br. J. Ind. Med.,* **42**: 406-410.

NICHOLSON, W.J. (1974) Analysis of amphibole asbestiform fibres in municipal water supplies. *Environ. Health Perspect.,* **9**: 165-173.

NICHOLSON, W.J. (1976) Case study 1: asbestos - the TLV approach. *Ann. NY Acad. Sci.,* **227**: 152-169.

NICHOLSON, W.J. & PUNDSACK, F.L. (1973) Asbestos in the environment. In: Bogovski, P., Gilson, J.C., Timbrell, V., & Wagner, J.C., ed. *Biological effects of asbestos. Proceedings of a Working Conference, Lyons, 2-6 October, 1972,* Lyons, International Agency for Research on Cancer, pp. 126-130 (IARC Scientific Publications No. 8).

NICHOLSON, W.J., MAGGIORE, C.J., & SELIKOFF, I.J. (1972) Asbestos contamination of parenteral drugs. *Science,* **177**: 171-173.

NICHOLSON, W.J., SELIKOFF, I.J., SEIDMAN, H., LILIS, R., & FORMBY, P. (1979) Long-term mortality experience of chrysotile miners and millers in Thetford Mines, Quebec. *Ann. NY Acad. Sci.,* **330**: 11-21.

NICHOLSON, W.J., ROHL, A.N., WEISMAN, I., & SELIKOFF, I.J. (1980) Environmental asbestos concentrations in the United States. In: Wagner, J.C., ed. *Biological effects of mineral fibres. Proceedings of a Symposium held at Lyons, 25-27 September, 1979,* Lyons, International Agency for Research on Cancer, Vol. 2, pp. 823-827 (IARC Scientific Publications No. 30).

OECD (1984) *Control of toxic substances in the atmosphere: asbestos,* Paris, Organisation for Economic Cooperation and Development (Environment Committee: Air Management Policy Group ENV/AIR/81.18, 2nd Revision).

OHLSON, C.-G. & HOGSTEDT, C. (1985) Lung cancer among asbestos cement workers. A Swedish cohort study and a review. *Br. J. Ind. Med.,* **42**: 397-402.

OLDHAM, P.D. (1973) A trial of techniques for counting asbestos bodies in tissue. In: Bogovski, P. Et al., ed. *Biological effects of asbestos. Proceedings of a Working Conference, Lyons, 2-6 October, 1972,* Lyons, International Agency for Research on Cancer, pp. 45-49 (IARC Scientific Publications No. 8).

OLERU, H.G. (1980) Pulmonary function of control and industrially-exposed Nigerians in asbestos, textile, and

toluene isocyanate foam factories. *Environ. Res.,* **23**: 137-148.

ONTARIO ROYAL COMMISSION ON ASBESTOS (1984) *Report of the Royal Commission on Matters of Health and Safety arising from the use of Asbestos in Ontario, Vol. One, two, and three,* Ontario, Toronto, Ontario Ministry of the Attorney General.

PAILES, W.H., JUDY, D.J., RESNICK, H., & CASTRANOVA, V. (1984) Relative effects of asbestos and wollastonite on alveolar macrophages, *J. Toxicol. Environ. Health,* **14**: 497.

PAMPALON, R., SIEMIATYCKI, J., & BLANCHET, M. (1982) Environmental asbestos pollution and public health in Quebec. *L'Union Médicale du Canada,* **111**: 475-489.

PERNIS, B. & VIGLIANI, E.C. (1982) The role of macrophages and immunocytes in the pathogenesis of pulmonary disease due to mineral dusts. *Am. J. Ind. Med.,* **3**(2): 133-137.

PERNIS, B., VIGLIANI, E.C., & SELIKOFF, I.J. (1965) Rheumatoid factors in the serum of individuals exposed to asbestos. *Ann. NY Acad. Sci.,* **132**: 112-120.

PETERSON, J.T., GREENBERG, S.D., & BUFFLER, P.A. (1984) Non-asbestos related malignant mesothelioma. *Cancer,* **54**: 951-960.

PETO, J. (1978) The hygiene standard for chrysotile asbestos. *Lancet,* **1**: 484-489.

PETO, J. (1980) Lung cancer mortality in relation to measured dust levels in an asbestos textile factory. In: Wagner, J.C., ed. *Biological effects of mineral fibres. Proceedings of a Symposium held at Lyons, 25-27 September, 1979,* Lyons, International Agency for Research on Cancer, Vol. 2, pp. 829-836 (IARC Scientific Publications No. 30).

PETO, J. (1983) Dose and time relationships for lung cancer and mesothelioma in relation to smoking and asbestos exposure. In: *Proceedings of a Symposium on Asbestos, Bundesgesundheitsamt, West Berlin, 17-19 February, 1982,* Berlin, Dietrich Reimer Verlag, pp. 126-132.

PETO, J., SEIDMAN, H., & SELIKOFF, I.J. (1982) Mesothelioma mortality in asbestos workers: implications for models of carcinogenesis and risk assessment. *Br. J. Cancer,* **45**: 124-135.

PETO, J., DOLL, R., GOFFE, T., & CLAYTON, R. (in press) Mortality of workers in a Rochdale asbestos textile factory. *Ann. Occup. Hyg.*

PHYSICIANS' DESK REFERENCE (1983) *Physicians' desk reference for nonprescription drugs,* 4th ed., Oradell, New Jersey, Medical Economics Co., Inc, 804 pp.

POLISSAR, L. (1980) The effect of migration on comparison of disease rates in geographic studies in the United States. *Am. J. Epidemiol.,* **111**: 1975.

POLISSAR, L., SEVERSON, R.K., BOATMAN, E.S., & THOMAS, D.B. (1982) Cancer incidence in relation to asbestos in drinking-water in the Puget Sound region. *Am. J. Epidemiol.,* **116**: 314.

POOLEY, F.D. (1972) Electron microscope characteristics of inhaled chrysotile asbestos fibre. *Br. J. Ind. Med.,* **29**: 146-153.

POOLEY, F.D. & CLARK, N.J. (1979) Quantitative assessment of inorganic fibrous particulates in dust samples with an analytical transmission electron microscope. *Ann. Occup. Hyg.,* **22**: 253-271.

POOLEY, F.D. & CLARK, N.J. (1980) A comparison of fibre dimension in chrysotile, crocidolite, and amosite particles from samples of airborne dust and from post-mortem lung tissue specimens. In: Wagner, J.C., ed. *Biological effects of mineral fibres. Proceedings of a Symposium held at Lyons, 25-27 September, 1979,* Lyons, International Agency for Research on Cancer, Vol. 1, pp. 79-86 (IARC Scientific Publications No. 30).

POOLE, A., BROWN, R.C., TURVER, C.J., SKIDMORE, J.W., & GRIFFITHS, D.M. (1983) *In vitro* genotoxic activities of fibrous erionite. *Br. J. Cancer,* **47**: 697.

POTT, F. (1978) Some aspects on the dosimetry of the carcinogenic potency of asbestos and other fibrous dusts. *Staub - Reinh. Luft,* **38**: 486-490.

POTT, F. (1980) [Animal experiments.] In: Umweltbundesamt, ed. *[Air quality criteria - environmental burden by asbestos and other fine fibrous dusts,]* Berlin, E. Schmidt, pp. 333-360 (Umweltbundesamt. Berichte 7/80) (in German).

POTT, F. & FRIEDRICHS, K.-H. (1972) [Tumours of the rat after intraperitonal injection of fibrous dusts.] *Naturwiss.,* **59**: 318 (in German).

POTT, F., HUTH, F., & FRIEDRICHS, K.-H. (1972) [Tumours of the rat after intraperitoneal injection of milled chrysotile and benzo(*a*)pyrene.] *Zbl. Bakt. Hyg., I. Abt. Orig. B.,* **155**: 463-469 (in German).

POTT, F., FRIEDRICHS, K.-H., & HUTH, F. (1976a) [Results of animal experiments concerning the carcinogenic effect of fibrous dusts and their interpretation with regard to the carcinogenesis in humans.] *Zbl. Bakt. Hyg., I. Abt. Orig. B.,* **162**: 467-505 (in German).

POTT, F., DOLGNER, R., FRIEDRICHS, K.H., & HUTH, F. (1976b) Effet oncologique des poussières fibreuses. Expériences sur les animaux et leurs relations avec la carcinogénèse humaine. *Ann. Anat. Pathol.,* **21**: 237.

POTT, F., HUTH, F., & SPURNEY, K. (1980) Tumor induction after intraperitoneal injection of fibrous dusts. In: Wagner, J.C., ed. *Biological effects of mineral fibres. Proceedings of a Symposium held at Lyons, 25-27 September, 1979,* Lyons, International Agency for Research on Cancer, Vol. 1, pp. 337-342 (IARC Scientific Publications No. 30).

POTT, F., SCHLIPKOETER, H.W., ZIEM, U., SPURNY, K., & HUTH, F. (1984) New results from implantation experiments with mineral fibres. In: *Biological effects of man-made mineral fibres. Proceedings of a WHO/IARC Conference, Copenhagen, 20-22 April, 1982,* Copenhagen, World Health Organization, Vol.

2, pp. 286-302.

POTTS, W.J., LEDERER, T.S., & GEHRING, P.I. (1978) Hemolysis of washed rat erythrocytes *in vitro* by dust particles. *Am. Ind. Hyg. Assoc. J.,* **39**: 497.

PRICE-JONES, M.J., GUBBINGS, G., & CHAMBERLAIN, M. (1980) The genetic effects of crocidolite asbestos: comparison of chromosome abnormalities and sister-chromatid exchanges. *Mutat. Res.,* **79**: 331-336.

PYLEV, L.N. (1972) [Morphological lesions in rats lungs, induced by intratracheal injection of chrysotile asbestos alone and with benzo(*a*)pyrene.] *Vopr. Oncol.,* **18**: 40-45 (in Russian).

PYLEV, L.N. (1980) Pretumorous lesions, lung and pleural tumors induced by asbestos in rats, Syrian golden hamsters, and monkey *Macaca rhesus.* In: Wagner, J.C., ed. *Biological effects of mineral fibres. Proceedings of a Symposium held at Lyons, 25-27 September, 1979,* Lyons, International Agency for Research on Cancer, Vol. 1, pp. 343-355 (IARC Scientific Publications No. 30).

PYLEV, L.N. & SHABAD, L.M. (1973) Some results of experimental studies in asbestos carcinogenesis. In: Bogovski, P., Gilson, J.C., Timbrell, V., & Wagner, J.C., ed. *Biological effects of asbestos. Proceedings of a Working Conference, Lyons, 2-6 October, 1972,* Lyons, International Agency for Research on Cancer, pp. 99-105 (IARC Scientific Publications No. 8).

RAHMAN, Q., VISWANATHAN, P.N., & ZAIDI, S.H. (1977) Some new perspectives on the biological effects of asbestos. *Environ. Res.,* **14**: 487-498.

RAJHANS, G.S. & BRAGG, G.M. (1978) *Engineering aspects of asbestos dust control,* Ann Arbor, Michigan, Ann Arbor Scientific Publishers, 191 pp.

RAJHANS, G.S. & SULLIVAN, J.L. (1981). *Asbestos sampling and analysis,* Ann Arbor, Michigan, Ann Arbor Scientific Publishers, 260 pp.

RAMACHANDER, K., SCHLECHTER, R., PHELPS, B., & CHAHINIAN, P. (1975) Immunocompetence in patients with pleural mesothelioma. *Proc. Am. Assoc. Cancer Res.,* **16**: 142.

RAUNIO, V. (1966) Occurrence of unusual pleural calcification in Finland. *Ann. Med. Int. Fenn.,* **55**(suppl. 47): 1-61.

REEVES, A.L., PURO, H.E., & SMITH, R.G. (1974) Inhalation carcinogenesis from various forms of asbestos. *Environ. Res.,* **8**: 178-202.

REISS, B., MILLETTE, J.R., & WILLIAMS, G.M. (1980) The activity of environmental samples in a cell culture test for asbestos toxicity. *Environ. Res.,* **22**: 315.

RICHARDS, R.J. & JACOBY, F. (1976) Light microscope studies on the effect of chrysotile asbestos and fibre glass on the morphology and reticulin formation of cultured lung fibroblasts. *Environ. Res.,* **11**: 112-121.

RICHARDS, R.J., GEORGE, G., HUNT, J., & TETLEY, T.D. (1980) The relationship between the haemolytic potential of certain particulates and their reactivity at the lung surface in view. In: Brown, R.C. Et al., ed. *The in vitro effects of mineral dusts,* London, Academic Press, pp. 323-332.

ROBOCK, K. (1979) Based on available data, can we project an acceptable standard for industrial use of asbestos? Absolutely. *Ann. NY Acad. Sci.,* **330**: 205-210.

ROBOCK, K. (1981) [The environmental hazard caused by the processing of asbestos cement products.] *Staub-reinhalt. Luft,* **8**: 309-310 (in German).

ROBOCK, K. (1982) Monitoring the workplace: problems and progress. State-of-the-art (automatic counting methods) and international efforts for standardizing of methods. In: *Proceedings of the World Symposium on Asbestos, Montreal, Canada, 25-27 May, 1982,* Montreal, Canadian Asbestos Information Centre, pp. 104-116.

ROBOCK, K. (1984) [Comparison of different measuring procedures in relation to conditions at the workplace.] In: Fischer, M. & Meyer, E., ed. *[Assessment of the cancer risk from asbestos,]* (BBA Schriften 2/84) (in German).

ROBOCK, K. & TEICHERT, U. (1978) Techniques, strategies, and results of dust measurement in the asbestos industries. In: *Proceedings of the 5th International Conference on Pneumoconiosis, Caracas, 29 October - 3 November, 1978,* Geneva, International Labor Office.

ROBOCK, K., ISSEROW, L.W., & SELLES, D.J.A. (1984) Research on the concentration and identification of dust particles in ambient air by electron microscopy. General description of the method. In: *Proceedings of the 6th International Conference on Air Pollution, Pretoria, South Africa.*

ROE, F.J.C., CARTER, R.L., WALTERS, M.A., & HARINGTON, J.S. (1967) The pathological effects of subcutaneous injections of asbestos fibres in mice: migration of fibers to submesothelial tissues and induction of mesotheliomata. *Int. J. Cancer,* **2**: 628-638.

ROHL, A.N., LANGER, A.M., & SELIKOFF, I.J. (1977) Environmental asbestos pollution related to use of quarried serpentine rock. *Science,* **196**: 1319-1322.

ROHL, A.N., LANGER, A.M., MONCURE, G., SELIKOFF, I.J., & FISHBEIN, P. (1982) Endemic pleural disease associated with exposure to mixed fibrous dust in Turkey. *Science,* **216**: 518-520.

ROOKER, S.J., VAUGHAN, N.P., & LE GUEN, J.M. (1982) On the visibility of fibres by phase contrast microscopy. *Am. Ind. Hyg. Assoc. J.,* **43**: 505-515.

ROSKILL REPORT ON ASBESTOS (1983) *Asbestos. IV. The economics of asbestos,* 4th ed., London, Roskill Information Services, Ltd.

ROSSITER, C.E. & COLES, R.M. (1980) H.M. Dockyard, Devonport: 1947 mortality study. In: Wagner, J.C., ed. *Biological effects of mineral fibres. Proceedings of a*

Symposium held at Lyons, 25-27 September, 1979, Lyons, International Agency for Research on Cancer, Vol. 2, pp. 713-721 (IARC Scientific Publications No. 30).

ROSSITER, C.E., BRISTOL, L.J., CASTIER, P.H., GILSON, J.C., GRAINGER, T.R., SLUIS-CREMER, G.K., & MCDONALD, J.C. (1972) Radiographic changes in chrysotile asbestos mine and mill workers of Quebec. *Arch. Environ. Health,* **24**: 388-400.

ROUS, V. & STUDENY, J. (1970) Aetiology of pleural plaques. *Thorax,* **25**: 270-284.

RUBINO, G.F., SCABSETTI, G., DONNA, A., & PALESTRO, G. (1972) Epidemiology of pleural mesothelioma in North-Western Italy (Piedmont). *Br. J. Ind. Med.,* **29**: 436-442.

RUBINO, G.F., NEWHOUSE, M.L., MURRAY, R., SCANSETTI, G., PIOLATTO, G., & ARESINI, G. (1979a) Radiologic changes after cessation of exposure among chrysotile asbestos miners in Italy. *Ann. NY Acad. Sci.,* **330**: 157-161.

RUBINO, G.F., PIOLATTO, G., NEWHOUSE, M.L., SCANSETTI, G., ARESINI, G.A., & MURRAY, R. (1979b) Mortality of chrysotile asbestos workers at the Balangero mine, Northern Italy. *Br. J. ind. Med.,* **36**: 187-194.

SADLER, T.D., ROM, W.N., LYON, J.L., & MASON, J.O. (1981) *The use of asbestos-cement pipe for public water supply and the incidence of cancer in selected communities in Utah, 1967-76,* Salt Lake City, Utah, University of Utah (Graduate thesis cited in Marsh, 1983).

SALVAGGIO, J.E. (1982) Overview of occupational immunologic lung disease. *J. Allergy clin. Immunol.,* **70**: 5-10.

SAMUDRA, A.V., HARWOOD, C.F., & STOCKHAM, J.D. (1978) *Electron microscope measurement of airborne asbestos concentrations,* Research Triangle Park, North Carolina, US Environmental Protection Agency, Environmental Sciences Research Laboratory, 49 pp (EPA Report No. 600/2-77-178-Rev., PB 285945).

SARACCI, R. (1981) Personal-environmental interactions in occupational epidemiology. In: McDonald, J.C., ed. *Recent advances in occupational health,* London, Churchill Livingstone, pp. 119-128.

SARACCI, R., SIMONATO, L., BARIS, Y., ARTVINLI, M., & SKIDMORE, J. (1982) The age mortality curve of endemic pleural mesothelioma in Karain, central Turkey. *Br. J. Cancer,* **45**: 147-149.

SAWYER, R.N. & SPOONER, C.M. (1979) *Asbestos-containing materials in public buildings: a guidance document,* Washington DC, US Environmental Protection Agency.

SCHLESINGER, R.B. & LIPPMANN, M. (1978) Selective particle deposition and bronchogenic carcinoma. *Environ. Res.,* **15**: 424-431.

SCHLESINGER, R.B., BOHNING, D.E., CHAN, T.L., & LIPPMANN, M. (1977) Particle deposition in a hollow cast of the human tracheobronchial tree. *J. Aerosol Sci.,* **8**: 429-445.

SCHLESINGER, R.B., CONCATO, J., & LIPPMANN, M. (1982) Particle deposition during exhalation: a study in replicate casts of the human upper tracheobronchial tree. In: *Proceedings of the International Symposium on Aerosols in the Mining and Industrial Work Environment, Minneapolis, Minnesota.*

SCHLUCHSEE MEETING (1985) *In vitro* effects of mineral dusts. In: Beck, E.G. & Bignon, J., ed. *Ecological sciences,* Berlin, Springer Verlag, Vol. III, pp. 1-548 (NATO ASI Series No. G).

SCHNITZER, R.J. & PUNDSACK, F.L. (1970) Asbestos haemolysis. *Environ. Res.,* **3**: 1-13.

SEBASTIEN, P., FONDIMARE, A., BIGNON, J., MONCHAUX, G., DESBORDES, J., & BONNAUD, G. (1977) Topographic distribution of asbestos fibres in human lung in relation to occupational and non-occupational exposure. In: Walton, W.H., ed. *Inhaled particles. IV. Part 2. Proceedings of an International Symposium, Edinburgh, 22-26 September, 1975,* Oxford, Pergamon Press Ltd, pp. 435-446.

SEBASTIEN, P., BILLON, M.A., JANSON, X., BONNAUD, G., & BIGNON, J. (1978) Utilisation du microscope électronique à transmission (MET) pour la mesure des contaminations par l'amiante. *Arch. Mal. Prof. Méd. Trav. Sécur. Soc. (Paris),* **39**: 229-248.

SEBASTIEN, P., MASSE, R., & BIGNON, J. (1980a) Recovery of ingested asbestos fibres from the gastrointestinal lymph in rats. *Environ. Res.,* **22**: 201-216.

SEBASTIEN, P., JANSON, X., GAUDICHET, A., HIRSCH, A., & BIGNON, J. (1980b) Asbestos retention in human respiratory tissues: comparative measurements in lung parenchyma and in parietal pleura. In: Wagner, J.C., ed. *Biological effects of mineral fibres. Proceedings of a Symposium held at Lyons, 25-27 September, 1979,* Lyons, International Agency for Research on Cancer, Vol. 1, pp. 237-246 (IARC Scientific Publications No. 30).

SEBASTIEN, P., MCDONALD, J.C., CORNEA, G., & GACHEM, A. (1983) Electron microscopical characterization of respirable airborne particles in a Tunisian phosphate mine. In: *Proceedings of the 6th International Pneumoconiosis Conference, Bochum, Federal Republic of Germany, 20-23 September, 1983,* Bergban-Berufsgenossenschaft, International Labour Office, Vol. 3, pp. 1650-1665.

SEIDMAN, H., SELIKOFF, I.J., & HAMMOND, E.C. (1979) Short-term asbestos work exposure and long-term observation. *Ann. NY Acad. Sci.,* **330**: 61-89.

SEIDMAN, H., SELIKOFF, I.J., & HAMMOND, E.C. (1982) Mortality of brain tumors among asbestos insulation in the United States and Canada. *Ann. NY Acad. Sci.,* **381**: 160.

SELIKOFF, I.J. (1979) Mortality experience of insulation workers in the United States and Canada, 1943-1976. *Ann. NY Acad. Sci.,* **330**: 91-116.

SELIKOFF, I.J. (1982) *Disability compensation for asbestos-associated disease in the United States,* New York, Mount Sinai School of Medicine, City University of New York, 691 pp (Report to the US Department of Labor, Environmental

Sciences Laboratory).

SELIKOFF, I.J. & HAMMOND, E.C. (1975) Multiple risk factors in environmental cancer. In: Fraumeni, J.F., ed. *Persons at high risk of cancer,* New York, Academic Press, pp. 467-483.

SELIKOFF, I.J. & LEE, D.H.K. (1978) *Asbestos and disease,* London, Academic Press, 549 pp.

SELIKOFF, I.J. & SEIDMAN, H. (1981) Cancer of the pancreas among asbestos insulation workers. *Cancer,* **47**: 1469-1473.

SELIKOFF, I.J., CHURG, J., & HAMMOND, E.C. (1964) Asbestos exposure and neoplasia. *J. Am. Med. Assoc.,* **188**: 22-26.

SELIKOFF, I.J., NICHOLSON, W.J., & LANGER, A.M. (1972) Asbestos air pollution. *Arch. Environ. Health,* **25**: 1-13.

SELIKOFF, I.J., HAMMOND, E.C., & SEIDMAN, H. (1979) Mortality experience of insulation workers in the United States and Canada, 1943-1976. *Ann. NY Acad. Sci.,* **330**: 91-116.

SELLES, D.J.A., ISSEROW, L.W., & ROBOCK, K. (1984) Results of sampling in mining and non-mining areas. In: *Proceedings of the 6th International Conference on Air Pollution,* Pretoria, South Africa.

SESHAN, K. (1983) How are the physical and chemical properties of chrysotile asbestos altered by a 10-year residence in water and up to 5 days in simulated stomach acid? *Environ. Health Perspect.,* **53**: 143-148.

SHABAD, L.M., PYLEV, L.N., KRIVOSHEEVA, L.V., KULAGINA, T.F., & NEMENKO, B.A. (1974) Experimental studies on asbestos carcinogenicity. *J. Natl Cancer Inst.,* **52**: 1175-1187.

SHASBY, D.M., PETERSEN, M., HODOUS, T., BOEHLECKE, B., & MERCHANT, J. (1979) Respiratory morbidity of workers exposed to wollastonite through mining and milling. In: Lemen, R. & Dement, J.M., ed. *Dust and disease,* Park Forest South, Illinois, Pathotox Publishers Inc., pp. 251-256.

SHETTIGARA, P.T. & MORGAN, R.W. (1975) Asbestos, smoking, and laryngeal carcinoma. *Arch. Environ. Health,* **30**: 517-519.

SHIN, M.L. & FIRMINGER, H.I. (1973) Acute and chronic effects of intraperitoneal injection of two types of asbestos in rats with a study of the histopathogenesis and ultrastructure of resulting mesotheliomas. *Am. J. Pathol.,* **70**: 291.

SHRIDE, A.F. (1973) Asbestos. In: Brobst, D. & Pratt, W., ed. *US mineral resources,* Washington DC, US Department of the Interior, pp. 63-72 (Geological Survey Professional Paper 820).

SIEMIATYCKI, J. (1983) Health effects on the general population (mortality in the general population in asbestos mining areas). In: *Proceedings of the World Symposium on Asbestos, Montreal, Canada, 25-27 May, 1982,* Montreal, Canadian Asbestos Information Centre.

SIGURDSON, E.E. (1983) Observations of cancer incidence surveillance in Duluth, Minnesota. *Environ. Health Perspect.,* **53**: 61-67.

SIGURDSON, E.E., LEVY, B.S., MANDEL, J., MCHUGH, R., MICHIENZI, L.J., JAGGER, H., & PEARSON, J. (1981) Cancer morbidity investigations: lessons for the Duluth study of possible effects of asbestos in drinking-water. *Environ. Res.,* **25**: 50.

SINCOCK, A.M. & SEABRIGHT, M. (1975) Induction of chromosome changes in Chinese hamster cells by exposure to asbestos fibers. *Nature (Lond.),* **257**: 56-58.

SINCOCK, A.M., DELHANTY, J.D.A., & CASEY, G. (1982) A comparison of the cytogenetic response to asbestos and glass fibre in Chinese hamster and human cell lines. Demonstration of growth inhibition in primary human fibroblasts. *Mutat. Res.,* **101**: 257-268.

SMITH, W.E. & HUBERT, D.D. (1974) The intrapleural root as a means for estimating carcinogenicity. In: Karbe, E. & Park, J. F., ed. *Experimental lung cancer, carcinogenesis, and bioassay,* New York, Springer, pp. 92-101.

SMITH, W.E., MILLER, L., CHURG, J., & SELIKOFF, I.J. (1965) Mesotheliomas in hamsters following intrapleural injection of asbestos. *J. Mt. Sinai Hosp.,* **32**: 1-8.

SMITH, W.E., MILLER, L., & CHURG, J. (1970) An experimental model for study of carcinogenesis in the respiratory tract. In: *Morphology of experimental respiratory carcinogenesis,* Oak Ridge, Tennessee, US Atomic Energy Commission, pp. 299-316 (US AEC Symposium Series 21).

SMITH, W.E., HUBERT, D.D., SOBEL, H.J., PETERS, E.T., & DOERFLER, T.E. (1980) Health of experimental animals drinking water with and without amosite asbestos and other mineral particles. *J. Environ. Pathol. Toxicol.,* **3**: 277-300.

SPEIL, S. & LEINEWEBER, J.P. (1969) Asbestos minerals in modern technology. *Environ. Res.,* **2**: 166-208.

SPURNY, K.R. (1983) Natural fibrous zeolites and their carcinogenicity: a review. *Sci. Total Environ.,* **30**: 147-166.

SPURNY, K.R. & GENTRY, J.W. (1982) Filtration efficiency studies for fibrous particles. In: *World Filtration Congress III, 13-17 September, 1982,* Philadelphia, Pennsylvania, The Filtration Society.

SPURNY, K.R., STOEBER, W., OPIELA, H., & WEISS, G. (1979a) On the evaluation of fibrous aerosols in remote ambient air. *Sci. Total Environ.,* **11**: 1-40.

SPURNY, K., POTT, F., HUTH, F., WEISS, G., & OPIELA, H. (1979b) [Identification and carcinogenic effect of fibrous actinolite of a quarry.] *Staub - Reinhalt. Luft,* **39**: 386-389 (in German).

SPURNY, K.R., SCHOERMANN, J., & KAUFMANN, R. (1981) Identification and microanalysis of mineral fibres by LAMMA. *Fresenius' Z. Anal. Chem.,* **308**: 274-279.

STANTON, M.F. & LAYARD, M. (1978) The carcinogenicity of fibrous minerals. In: Gravatt, C.C. Et al., ed. *Proceedings of the Workshop on Asbestos: Definitions and Measurement Methods,*

Washington DC, July 18-20, 1977, Gaithersburg, Maryland, National Bureau of Standards, pp. 143-151 (National Bureau of Standards. Special Publication 506).

STANTON, M.F. & WRENCH, C. (1972) Mechanisms of mesothelioma induction with asbestos and fibrous glass. *J. Natl Cancer Inst.,* **48**: 797-821.

STANTON, M.F., LAYARD, M., TEGERIN, A., MILLER, E., MAY, M., & KENT, E. (1977) Carcinogenicity of fibrous glass: pleural response in the rat in relation to fibre dimension. *J. Natl Cancer Inst.,* **58**: 587-603.

STANTON, M.F., LAYARD, M., TEGERIN, A., MILLER, E., MAY, M., MORGAN, E., & SMITH, A. (1981) Relation of particle dimension to carcinogenicity in amphibole asbestoses and other fibrous minerals. *J. Natl Cancer Inst.,* **67**(5): 965-975.

STEEL, E.B. & SMALL, J.A. (1985) Accuracy of transmission electron microscopy for analysis of asbestos in ambient environment. *Anal. Chem.,* **57**: 209-213.

STEEL, E.B., SMALL, J.A., & SHERIDAN, P. (1982) *Analytical errors in asbestos analysis by analytical electron microscopy,* Washington DC, National Bureau of Standards, pp. 162-168 (NBS Special Publication No. 619).

STELL, P.M. & MCGILL, T. (1973) Asbestos and laryngeal cancer. *Lancet,* **11**: 416-417.

STOBER, W., FLACHSBART, H., & HOCHRAINER, D. (1970) [The aerodynamic diameter of latex aggregates and asbestos fibres.] *Staub-Reinhalt. Luft,* **30**: 277-285 (in German).

STOREYGARD, A.R. & BROWN, A.L. (1977) Penetration of the small intestinal mucosa by asbestos fibres. *Mayo Clin. Proc.,* **52**: 809-812.

SULLIVAN, R. & ATHANASSIADIS, Y. (1969) *Preliminary air pollution survey of asbestos,* Raleigh, North Carolina, US Department of Health, Education and Welfare, 94 pp.

SUNDIUS, N. & BYGDEN, A. (1938) [Dust content in asbestosis and properties of asbestos bodies.] *Arch. Gewebepathol.,* **8**: 26-70 (in German).

SUZUKI, J. (1982) Carcinogenic and fibrogenic effects of zeolites: preliminary observations. *Environ. Res.,* **27**: 433-445.

SUZUKI, J. & KOHYAMA, N. (1984) Malignant mesotheliomas induced by asbestos and zeolite in the mouse peritoneal cavity. *Environ. Res.,* **35**: 277-292.

TARTAR, M.E. (1981) Pattern recognition in the context of an asbestos cancer threshold study. In: *Proceedings of the 13th Annual Symposium Interface: Computer Science Statistic.*

TARTER, M. (1982) Graphical reanalysis of the California Bay area study. Presented at the *US EPA Summary Workshop on Ingested Asbestos, Cincinnati, Ohio, 13-14 October, 1982.*

TASK GROUP ON LUNG DYNAMICS (1966) Deposition and retention models for internal dosimetry of the human respiratory tract. *Health Phys.,* **12**: 173-208 (Comm. II, ICRP).

TAYLOR, D.G., BARON, P.A., SHULMAN, S.A., & CARTER, J.W. (1984) Identification and counting of asbestos fibres. *Am. Ind. Hyg. Assoc. J.,* **45**: 84-88.

TAYLOR, M. (1978) Methods for the quantitative determination of asbestos and quartz in bulk samples using X-ray diffraction. *Analyst,* **103**: 1009-1020.

TETA, M.J., LEWINSOHN, H.C., MEIGS, J.W., VIDONE, R.A., MOWAD, L.Z., & FLANNERY, J.T. (1983) Occupational and geographic associations. *J. Occup. Med.,* **25**: 749-755.

THERIAULT, G. & GRAND-BOIS, L. (1978) Mesothelioma and asbestos in the province of Quebec 1969-1972. *Arch. Environ. Health,* **33**: 15-19.

THOMAS, H.F., BENJAMIN, I.T., ELWOOD, P.C., & SWEETNAM, P.M. (1982) Further follow-up study of workers from an asbestos cement factory. *Br. J. Ind. Med.,* **39**: 273-276.

THOMSON, J.G. & GRAVES, W.M. (1966) Asbestos as an urban air contaminant. *Arch. Pathol.,* **81**: 458-464.

TIMBRELL, V. (1965) The inhalation of fibrous dusts. *Ann. NY* Acad. Sci., **132**: 255-273.

TIMBRELL, V. (1972) Inhalation and biological effects of asbestos. In: Mercer, T.T. Et al., ed. *Assesssment of airborne particles,* Springfield, Illinois, C.C. Thomas, pp. 429-445.

TIMBRELL, V. (1975) Alignment of respirable asbestos fibres by magnetic fields. *Ann. Occup. Health,* **18**: 229-311.

TIMBRELL, V. (1980) Measurement of fibres in human lung tissue. In: Wagner, J.C., ed. *Biological effects of mineral fibres. Proceedings of a Symposium held at Lyons, 25-27 September, 1979,* Lyons, International Agency for Research on Cancer, Vol. 1, pp. 113-126 (IARC Scientifific Publications No. 30).

TIMBRELL, V. (1982) Retention of fibers in human lungs. In: Walton, W.H., ed. *Inhaled particles. V. Proceedings of an International Symposium, Cardiff, 8-12 September, 1980,* Oxford, Pergamon Press, pp. 347-369.

TIMBRELL, V. & SKIDMORE, J.W. (1971) The effect of shape on particle penetration and retention in animal lungs. In: Walton, W.H., ed. *Inhaled particles. III. Proceedings of an International Symposium, London, 14-23 September, 1970,* Old Woking, Surrey, Unwin, Vol. 1, pp. 49-56.

TOFT, P., WIGLE, D., MERANGER, J.C., & MAO, Y. (1981) Asbestos and drinking-water in Canada. *Sci. Total Environ.,* **18**: 77-89.

TOFT, P., MEEK, M.E., WIGLE, D.T., & MERANGER, J.C. (1984) *Asbestos in drinking-water,* Ottawa, Ontario, Canada, Department of National Health & Welfare, Health Protection Branch (CRC Critical Reviews in Environmental Control).

TOLENT, J.M., HARRISON, W.O., SOLOMAN, A., & WEBSTER, J. (1980) A survey of black mineworkers of the Cape crocidolite mines. In: Wagner, J.C., ed. *Biological effects of mineral fibres. Proceedings of a Symposium held at Lyons, 25-27*

September, 1979, Lyons, International Agency for Research on Cancer, Vol. 2, pp. 723-729 (IARC Scientific Publications No. 30).

TOPPING, D.C. & NETTESHEIM, P. (1980) Two-stage carcinogenesis studies with asbestos in Fischer 344 rats. *J. Natl Cancer Inst.,* **65**(3): 627-630.

TOPPING, D.C., NETTESHEIM, P., & MARTIN, D.H. (1980) Toxic and tumorigenic effects of asbestos on tracheal mucosa. *J. environ. Pathol. Toxicol.,* **3**: 261-275.

TURNER-WARWICK, M. & PARKES, W.R. (1970) Circulating rheumatoid and antinuclear factors in asbestos workers. *Br. med. J.,* **2**: 492-495.

ULLMANN'S ENCYCLOPAEDIA OF TECHNICAL CHEMISTRY (1982) Weinheim, Deerfield Beach, Basel, Vol. 21, p. 406 (in German).

UMWELTBUNDESAMT (UBA) (1980) *[Environmental pollution by asbestos and other fibrous dusts,]* Berlin, Erich Schmidt Verlag, 411 pp (Umweltbundesamt, Berichte 7/80) (in German).

US BUREAU OF MINES (1982) *Minerals yearbook 1981,* Washington DC, US Department of the Interior, Vol. 1.

US EPA (1974) *A preliminary report on asbestos in the Duluth, Minnesota area,* Washington DC, US Environmental Protection Agency, Office of Technological Analysis.

US EPA (1978) *Electron microscope measurement of airborne asbestos concentrations. A provisional methodology manual,* Research Triangle Park, North Carolina, US Environmental Protection Agency (EPA Report 600/2-77-178).

US EPA (1980) *Ambient water quality criteria for asbestos,* Washington DC, US Environmental Protection Agency (EPA Report No. 440/5-80-022, PB 81-117-335).

US EPA (1983) *Asbestos fibre determination in water samples: preparation techniques - improved analytical method and rapid screening,* US Environmental Protection Agency (Project Summary EP 1.89/2:600/S4-83-044).

US NIOSH (1972) *Criteria for a recommended standard: occupational Exposure to Asbestos,* Washington DC, US Department of Health, Education and Welfare, Public Health Services and Mental Health Administration, National Institute for Occupational Safety and Health (DHEW Publication No. 72-10267).

US NIOSH (1973) *The industrial environment: its evaluation and control,* Cincinnati, Ohio, US National Institute of Occupational Safety and Health.

US NIOSH (1977) *Asbestos fibers in air. NIOSH manual of analytical methods,* 2nd ed., Cincinnati, Ohio, National Institute for Occupational Safety and Health, Vol. 1.

US NIOSH (1984) *Revised NIOSH asbestos counting method. NIOSH manual of analytical methods,* Cincinnati, Ohio, US National Institute of Occupational Safety and Health.

US NRC/NAS (1977) *Drinking-water and health,* Washington DC, National Research Council, Safe Drinking-Water Committee, National Academy of Sciences, pp. 150-151.

US NRC/NAS (1984) *Asbestiform fibers: non-occupational health risks,* Washington DC, US National Research Council, Committee on Nonoccupational Health Risks of Asbestiform Fibers, pp. 177-180.

US NTP (1983) *Lifetime carcinogenesis studies of amosite asbestos in Syrian golden hamsters,* Research Triangle Park, North Carolina, US National Toxicology Program (NIH Publication No. 84-2505).

US NTP (1985) *Toxicology and carcinogenesis studies of chrysotile asbestos in F344/N rats (feed study),* Research Triangle Park, North Carolina, US National Toxicology Program, 390 pp (Technical Report Series No. 295; NIH Publication No. 86-2551).

VALIC, F. (1983) *ILO encyclopaedia of occupational health and safety, Vol. 1,* Geneva, International Labour Office, p. 601.

VALLYATHAN, V., ROBINSON, V., REASOR, M.J., & STETTLER, F. (1984) Wollastonite and asbestos cytotoxicity. *Am. Rev. respir. Dis.,* **129**: A178.

VEREIN DEUTSCHER INGENIEURE (1984) *[Measuring of inorganic fibrous particles in ambient air - scanning electron microscopical method]* (in German).

VIANNA, N.J. & POLAN, A.K. (1978) Non-occupational exposure to asbestos and malignant mesothelioma in females. *Lancet,* **2**: 1061-1063.

VORWALD, A.J., DUNKAN, T.M., & PRATT, P.C. (1951) Experimental studies of asbestosis. *Arch. Ind. Hyg. Occup. Med.,* **3**: 1-83.

WAGNER, J.C. (1962) Experimental production of mesothelial tumours by implantation of dust in laboratory animals. *Nature (Lond.),* **196**: 180.

WAGNER, J.C. (1963a) Asbestosis in experimental animals. *Br. J. Ind. Med.,* **20**: 1.

WAGNER, J.C. (1963b) Asbestos dust and malignancy. In: *Proceedings of the XIV International Congress of Occupational Health, Madrid, 1963,* pp. 3, 1066-1067.

WAGNER, J.C. (1982) Health hazards of substitutes. In: *Proceedings of the World Symposium on Asbestos, Montreal, Canada, 25-27 May, 1982,* Montreal, Canadian Asbestos Information Centre, pp. 244-266.

WAGNER, J.C. & BERRY, G. (1969) Mesotheliomas in rats following inoculation with asbestos. *Br. J. Cancer,* **23**: 567-581.

WAGNER, J.C. & SKIDMORE, J.W. (1965) Asbestos dust deposition and retention in rats. *Ann. NY Acad. Sci.,* **132**: 77-86.

WAGNER, J.C., SLEGGS, C.A., & MARCHAND, P. (1960) Diffuse pleural mesothelioma and asbestos exposure in the Northwestern Cape Province. *Br. J. Ind. Med.,* **17**: 260-271.

WAGNER, J.C., BERRY, G., & TIMBRELL, V. (1973) Mesotheliomata in rats after inoculation with asbestos and other minerals. *Br. J. Cancer,* **28**: 175-185.

WAGNER, J.C., BERRY, G., SKIDMORE, J.W., & TIMBRELL, V. (1974) The effects of the inhalation of asbestos in rats. *Br. J. Cancer,* **29**: 252-269.

WAGNER, J.C., BERRY, G., COOKE, T.L., HILL, R.J., POOLEY, F.D., & SKIDMORE, J.W. (1977) Animal experiments with talc. In: Walton, W.H., ed. *Inhaled particles. IV. Part 2. Proceedings of an International Symposium, Edinburgh, 22-26 September, 1975,* Oxford, Pergamon Press, pp. 647-654.

WAGNER, J.C., BERRY, G., SKIDMORE, J.W., & POOLEY, F.D. (1980) The comparative effects of three chrysotiles by injection and inhalation in rats. In: Wagner, J.C., ed. *Biological effects of mineral fibres. Proceedings of a Symposium held at Lyons, 25-27 September, 1979,* Lyons, International Agency for Research on Cancer, Vol. 1, pp. 363-372 (IARC Scientific Publications No. 30)

WAGNER, J.C., SKIDMORE, J.W., HILL, R.J., & GRIFFITHS, D.M. (1985) Erionite exposure and mestotheliomas in rats. *Br. J. Cancer,* **51**: 727-730.

WALTON, W.H. (1982) The nature, hazards and assessment of occupational exposure to airborne asbestos dust: a review. *Ann. Occup. Hyg.,* **25**: 117-247.

WARHEIT, D.B., HILL, L.H., & BRODY, A.R. (1984) *In vitro* effects of crocidolite asbestos and wollastonite on pulmonary macrophages and serum complement. *Scanning Elect. Microscop.,* **2**: 919-926.

WARREN, S., BROWN, C.E., CHUTE, R.N., & FEDERMAN, M. (1981) Mesothelioma relative to asbestos, radiation, and methylcholanthrene. *Arch. Pathol. Lab. Med.,* **105**: 305.

WEBSTER, I. (1974) The ingestion of asbestos fibres. *Environ. Health Perspect.,* **9**: 199-202.

WEBSTER, I. (1977) Methods by which mesothelioma may be diagnosed. In: Glen, H.W., ed. *Proceedings of Asbestos Symposium, Johannesburg, South Africa, 1977,* Randburg, National Institute for Metallurgy, pp. 3-8.

WEHMANN, H.J. & PLANTHOLT, B.A. (1974) Asbestos fibrils in beverages. I. Gin. *Bull. Environ. Contam. Toxicol.,* **11**: 267-272.

WEHNER, A.P. (1980) Effects of inhaled asbestos, asbestos plus cigarette smoke, asbestos-cement, and talc baby powder in hamsters. In: Wagner, J.C., ed. *Biological effects of mineral fibres. Proceedings of a Symposium held at Lyons, 25-27 September, 1979,* Lyons, International Agency for Research on Cancer, Vol. 1, pp. 373-376 (IARC Scientific Publications No. 30).

WEHNER, A.P., BUSCH, R.H., OLSON, R.J., & CRAIG, D.K. (1974) *Investigation of co-carcinogenicity of asbestos, cobalt oxide, nickel oxide, diethylnitrosamine, and cigarette smoke,* Bethesda, Maryland, Richland, Washington, Battelle-Northwest (Final report to National Cancer Institute).

WEHNER, A.P., BUSCH, R.H., OLSON, R.J., & CRAIG, D.K. (1975) Chronic inhalation of asbestos and cigarette smoke by hamsters. *Environ. Res.,* **10**: 368.

WEHNER, A.P., STUART, B.O., & SANDERS, C.L. (1979) Inhalation studies with Syrian golden hamsters. *Prog. Exp. Tumor Res.,* **24**: 177.

WEILL, H., HUGHES, J., & WAGGENSPACK, C. (1979) Influence of dose and fiber type on respiratory malignancy risk in asbestos cement manufactoring. *Am. Rev. Respir. Dis.,* **120**: 345-354.

WEISBURGER, J.H. & WILLIAMS, G.M. (1980) Chemical carcinogens. In: Doull, J. Et al., ed. *Casarett and Doull's toxicology,* New York, Macmillan Publishing Co., Inc, pp. 84-138.

WEISS, W. (1977) Mortality of a cohort exposed to chrysotile asbestos. *J. Occup. Med.,* **19**: 737-740.

WESTLAKE, G.E., SPJUT, H.J., & SMITH, M.N. (1965) Penetration of colonic mucosa by asbestos particles. An electron microscopic study in rats fed asbestos dust. *Lab. Invest.,* **14**: 2029-2033.

WHITE, R. & KUHN, C. (1980) Effects of phagocytosis of mineral dust on elastase secretion by alveolar and peritoneal exudative macrophage. *Arch. Environ. Health,* **35**: 106-109.

WHITWELL, F., SCOTT, J., & GRINSHOW, M. (1977) Relationship between occupations and asbestos-fibre content of the lungs in patients with pleural mesothelioma, lung cancer, and other diseases. *Thorax,* **32**: 377-386.

WHO (1984) *Evaluation of exposure to airborne particles in the work environment,* Geneva, World Health Organization (WHO Offset Publication No. 80).

WIGLE, D.T. (1977) Cancer mortality in relation to asbestos in municipal water supplies. *Arch. Environ. Health,* **32**: 185.

WIGLE, D.T., MAO, Y., TOFT, P., & MERANGER, J.C. (1981) Cancer mortality and drinking-water quality in selected Canadian municipalities. In: *Proceedings of the Workshop on the Compatibility of Great Lakes Basin Cancer Registries,* Windsor, International Joint Commission, pp. 41-57.

WIGNALL, B.K. & FOX, A.J. (1982) Mortality of female gas-mask assemblers. *Br. J. Ind. Med.,* **39**: 34-38.

WRIGHT, W.W., ROM, W.N., & MOATMED, F. (1983) Characterization of zeolite fiber sizes using scanning electron microscopy. *Arch. Environ. Health,* **38**: 99-103.

WYLLIE, D.M. (1973) Asbestos filter sheets. *Filtr. Sep.,* **10**: 175-178.

ZOLOV, C., BOURILKOV, T., & BABADJOV, L. (1967) Pleural asbestosis in agricultural workers. *Environ. Res.,* **1**: 287.

See Also:
Toxicological Abbreviations