PHILOSOPHICAL TRANSACTIONS OF THE ROYAL SOCIETY A MATHEMATICAL, PHYSICAL & ENGINEERING SCIENCES

Medicine and Mineralogy [and Discussion]

J. C. Gilson, Nancy Tait, J. Zussman and R. G. Burns

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ENVIRONMENTAL MINERALOGY

Medicine and mineralogy

By J. C. Gilson
M.R.C. Pneumoconiosis Unit, Llandough Hospital, Penarth, S. Glamorgan

[Plate 1]

The article deals with the health hazards caused by mineral dusts, and by asbestos fibres in the induction of cancers in particular. Mineral dusts cause damage by inhalation, rarely by ingestion or ingress into the skin. In the lung, bronchitis, fibrosis (pneumoconiosis), and cancers may result. Few mineral dusts cause cancers, and asbestos is unique in causing two separate types within the lung. Epidemiological and other studies of groups of asbestos workers have shown important differences in risk with the type of fibre and the type of job. All types of asbestos cause fibrosis and an excess of bronchial cancers which are, however, also closely cigarette related. Crocidolite is especially related to cancers of the surface of the lung (mesotheliomas). Mining and milling of chrysotile, the most used type of asbestos, have caused few mesotheliomas, despite heavy dust exposures in the past.

The diseases induced by asbestos are dose-related. Where it has been possible to divide the groups of asbestos workers into those with different levels of past exposure, the least exposed groups have shown small or no excess of asbestos-related diseases despite their exposures having been considerably higher than that likely to have been encountered by the general public. Present evidence indicates that the general public have not been at risk of asbestos-related diseases, but more evidence is required about the proportion of all mesotheliomas which are related to asbestos. The new techniques of mineralogy when applied at a micro level to the dust in tissues, and particularly in the lung, may be of great help in answering this important problem. Some comparisons of the mortality from occupationally related cancers, accidents, smoking habits, and general diseases are given. Current research into the biomedical effects of natural fibrous mineral dusts is likely to be of great value in ensuring that the new man made mineral fibres now being developed are manufactured and used under circumstances which will cause no ill effects to health.

It is perhaps a sign of the times and what has been called man's neurosis about his environment that this Session is concerned with health hazards of minerals rather than the part they play in man's adaptation to his environment or his enjoyment of the landscape! Perhaps nearer the 21st century when mineralogists have helped resolve this neurosis, a similar session will be opened by a landscape painter. The shape, colour, and composition of the minerals are the very source of the art and even the pigments used. Ample proof of this has been seen in the recent exhibitions in London of the work of Turner, Constable, and Millet.

I will briefly describe some of the ways mineral dusts affect health; how the risks are measured; and how mineralogists may help solve some of the current problems.

Table 1 lists the more important factors influencing the health hazards. Mineral dusts very rarely cause damage by penetration of the skin. It is of interest that neither coal nor asbestos dusts, both of which can cause severe damage to the lung, produces any important response in the skin. The coal scars of the miner are remarkably free from fibrosis and asbestos 'corns'

apparently never lead to cancers of the skin. Man has become well adapted to ingestion of mineral dusts; the gut is rarely the route of entry causing ill health; but a possible exception will be mentioned later. Inhalation is the principal route, and the lung the organ most frequently damaged.

TABLE 1. FACTORS AFFECTING HEALTH HAZARDS FROM MINERALS

Site of ingress to body:
skin; ingestion; inhalation
Type of response:
irritation (bronchitis)
fibrosis (scarring)
cancers
Dose
Particle size and shape
Composition
Solubility in tissues

The effects on the lung are irritation – with the production of bronchitis; scarring with the formation of fibrosis; and of special concern recently – the induction of cancers. Extensive research in recent years (Gilson 1970) has shown that those exposed to mineral dusts, especially in mining, usually have an increased prevalence of bronchitis, but the effect of the dust is rather small compared to that of cigarette smoking. Scarring of the lung by quartz dust – silicosis – is man's oldest occupational disease. It must date back to his first use of flint tools. A remarkable demonstration of this risk continued until after World War II at Brandon in Suffolk among the flint 'knappers'. The miner used a metal pick the shape of an antler to remove the flints from shallow pits. These were split into flakes with a hammer to the desired size and shape to make gunflints. Very high quartz content dust produced caused severe silicosis, complicated by tuberculosis (Hunter 1975). No power tools were used by the 'knappers' and the men's exposures must have been very similar to that of primitive man forming his flint tools. Another type of fibrosis on the surface of the lung has recently been shown to occur in small areas in Finland, Bulgaria, and Czechoslovakia (Dresden Conference 1968). It is thought to be due to dust raised during cultivation or perhaps in the general atmosphere. The mineral has not been firmly established, but is thought to be tremolite or other asbestiform minerals. Despite the bizarre appearance of chest radiographs, the condition does not seem to cause much illness.

The induction of cancers in the lung by mineral dusts is at present the source of most concern. Much publicity has been given to asbestos on this account. The association between fibrosis of the lung caused by asbestos dust – asbestosis – and bronchial cancers was first recognized in 1935. About 20 years later a second and previously very rare type of cancer on the surface of the lung – mesothelioma – was shown to have an unusually specific relation to asbestos and to the crocidolite form in particular (Wagner, Gilson, Berry & Timbrell 1971). Asbestos is very unusual in this respect. Silica and coal do not cause lung cancer. Indeed, the death rate from lung cancer is lower in coalminers than in the general public. If we exclude minerals which are radioactive or contain substances such as arsenic or chromium, we are left with a single group of minerals – those commercially known as asbestos – where an association between exposure to the dust and cancers has been proved. It is perhaps very surprising that this group of chain silicates with their low solubilities and inertness should be carcinogenic.

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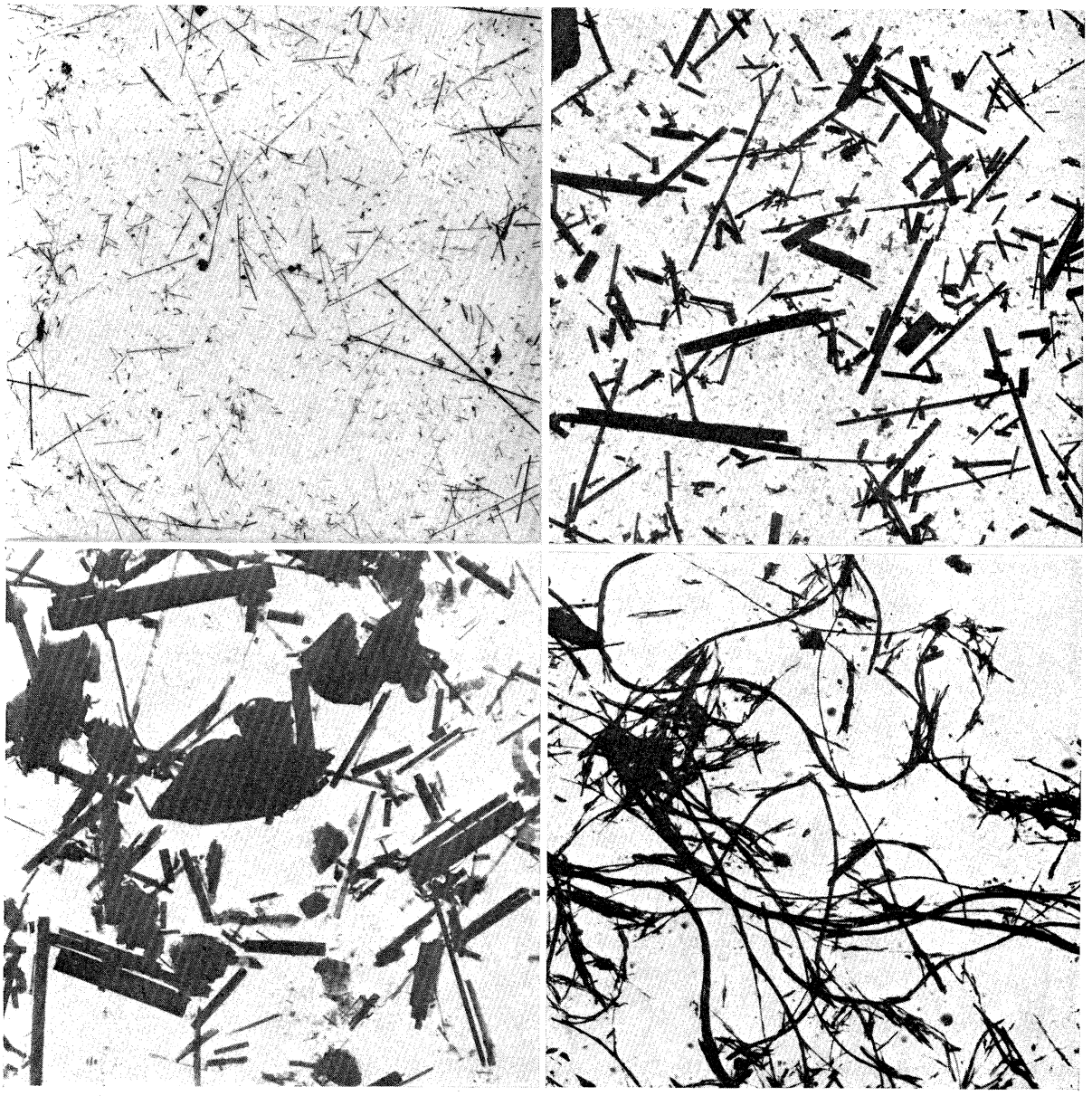
crocidolite amosite



anthophyllite chrysotile

FIGURE 1. The four types of asbestos (magn. × 1500).

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Importance of dose and particle size

The dose of dust inhaled and the duration of its retention are of the greatest importance. We all have a small amount of minerals in our lungs. Minerals, which in larger amounts cause well-recognized diseases, in small amounts produce no effect. Silicosis, for example, is never seen except following occupational exposures. Coalworkers' pneumoconiosis does not occur from filling the home scuttles – even when one could afford to do so daily! Coal merchants hardly ever develop the disease. The small amounts of asbestos present in the lungs of the urban population (Oldham 1973) have not produced detectable fibrosis, even when expert pathologists have made a special study of the lungs. However, current concepts of the mechanisms of carcinogenesis lead to the hypothesis that there may be no threshold level below which cancers will never occur. It is this theoretical consideration which is at the back of current concern about asbestos. This hypothesis does not contradict the view that the risk is dose-related and at very low levels of exposure may be too small to be detectable.

The damage to the lung is caused deep in its smallest airways and on its outer surface. The falling speed of a particle is the principal factor affecting its deep penetration into the lung. For rounded particles of unit density, this is less than about 5 μm diameter. For fibres, the diameter rather than the length controls the falling speed. Fibres 3 μm in diameter or less, but up to 100 μm in length, get deep into the lung (Timbrell 1970). Curved fibres like chrysotile, though very small in diameter, readily get across the airstream in the lung and so impact higher up the air ducts than the straight fibres of the amphiboles. The dose of fibrous dust to the lung is, therefore, importantly affected by the fibre diameter and shape. It appears likely that the much higher incidence of mesotheliomas in those mining and milling crocidolite than amosite may be due to the finer and shorter fibres of crocidolite (figure 1, plate 1; Timbrell 1973).

The solubility of the dust is also important. Carbonates such as limestone do not produce fibrosis even after massive exposures; they are readily dissolved in the tissue fluids. Silica and coal remain long in the lung. The lower incidence of disease caused by chrysotile than the amphiboles may in part be due to the greater solubility of chrysotile and in part the difference in shape of the fibres.

Detecting and measuring the health risk

I am concerned here primarily with the cancer risks. Table 2 shows the steps in detecting and measuring the risk. Clinical acumen has often been the starting point. A doctor spots an apparent association between the man's occupation and his disease. Proof that this association is real and not simply chance can come from comparing the occupations of a group of cases of this disease collected from hospital records with that of patients with other diseases. These first two steps, however, give no information about the magnitude of the risk – that is to say, what proportion of the exposed group develop the cancer and how the cancer risk compares with that in the general population. Few cancers have only one cause and a number – for example, bronchial – are known to have several. To measure the magnitude of the excess risk of a particular type of cancer, cohort studies are used. A defined group – say, all those employed in a factory or mine between 1935 and 1945 – are followed up to find out who are alive and dead; and in the dead the causes of death. These are then related to the national or regional figures to give an observed and expected figure, and hence the excess over expected. This is a laborious procedure and the results are only valid if the trace rates of the cohort exceed

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about 90 %. Such studies have to be repeated in several different situations and countries to sort out the effects of a particular occupation or a particular type of mineral. The results may not provide all the comparisons one would wish. For example, in asbestos the exposures to one type of fibre tend to occur only in those mining and milling. Industries often used a mixture of fibre in the past, so that it is difficult to separate the effects of the kind of job from the type of asbestos.

TABLE 2. STEPS IN DETECTION AND ESTIMATION OF RISKS

1. Clinical observation
2. Case/control studies
   proof of association
3. Cohort studies
   estimates of excess risk
4. Cohort and environmental studies
   dose response relation and prediction of future risks

In its simplest form this cohort approach does not help in predicting the risk in other groups, and particularly to the general public. The excess cancers in the whole group are the results of exposures many years before, often 20 or more (because of the long latent period between first exposure and the appearance of the cancer). An improvement on this approach is, therefore, to use past information about dustiness – either measured directly or estimated from those with long experience in the mine or factory. It may then be possible to divide a whole group into three or four sub-groups with varying intensities of past exposures. This can be very helpful, because if the excess cancer risk is found to be limited to those with the heaviest past exposure and not detectable in those with lesser exposure, tentative extrapolation of likely risk under improved factory conditions or to the general public may be possible. Those with the least exposure in industry may be known to have had much higher exposures than would ever have occurred in the general public – two to three orders greater.

TABLE 3. PROPORTION (%) OF ALL DEATHS DUE TO LUNG CANCER AND MESOTHELIOMAS IN COHORTS OF ASBESTOS WORKERS AND THE GENERAL POPULATION

	lung cancer	mesoth.	no. of surveys	total men
Asbestos				
insulation†	18–26	5–9	6	26500
factories†	8–21	1–7	5	10800
mining and milling‡	2–10	0–0.2	3	13700
gen. popl.				
England & Wales	9	*ca.* 0.007		
U.S.A.	5			
Canada	5			

† Mixed fibre exposures.
‡ Chrysotile (2); anthophyllite (1).
From McDonald 1975, 18th Int. Congress Occup. Hlth.

Table 3 summarizes the evidence about mortality from bronchial cancers and mesotheliomas from 14 recent cohort studies covering about 50000 workers in the asbestos industry in five countries. The insulation workers have the highest excess risk for both cancers. The mining and milling groups have the lowest excess risks; most of these men in this group were chrysotile-exposed, and in this type of exposure an excess risk of bronchial cancers only occurred in the

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most heavily exposed sub-groups. There were very few mesotheliomas in these mining groups; indeed, none in the anthophyllite miners.

The greatest excess of bronchial cancers and mesotheliomas are in those exposed to a mixture of fibres (and other dusts) in the insulation workers. Amphibole exposures were heavy in these insulation workers. Experience in the mines in South Africa suggests there is a much higher risk of mesothelioma from crocidolite than from amosite or chrysotile. In the course of these and other studies it has been shown that mesotheliomas, which are very rare in the general public (probably < 1 per million per year), have sometimes occurred in those exposed to relatively little dust – in what is called para-occupational exposures; by this is meant, in the home from asbestos-dusted clothing or where the houses were situated near dusty mines or factories. The dose of asbestos required to cause mesotheliomas is likely to be less than that needed to cause asbestosis or an excess of bronchial cancer, and more likely to be amphibole than chrysotile.

TABLE 4. ASBESTOS AND LUNG CANCER

1. Heavy exposures to all commercial types of asbestos may cause bronchial cancers; the risk is dose and type (?) related
2. Cigarette smoking and asbestos dust are multiplicative in effect; asbestos dust alone is a weak bronchial carcinogen
3. Mesotheliomas are dose and type of asbestos related: crocidolite > amosite > chrysotile > anthophyllite (risk not detected)
4. The lung burden of asbestos in those not occupationally or para-occupationally exposed has not produced a detectable excess risk of mesotheliomas or bronchial cancers

Table 4 summarizes current understanding of the relation between asbestos exposure and lung cancers. Research continues, and particularly in relation to the detection of a risk, if any, from the small amount of asbestos which is present in most of our lungs. A part of this inquiry is the need to establish the length and diameter of the fibres most likely to cause mesotheliomas.

The importance of this is great. We know that respirable fibres encountered in industry and near mines can cause mesotheliomas, but is this also true for the much shorter and smaller fibres which make up most of the very small mass of asbestos in the general atmosphere? It is in this field that mineralogists have, I think, an important contribution to make. There are no good estimates of past dust exposure to members of the general public. But by measuring the amount and type of asbestos and other minerals in thin lung sections of those dying of a variety of causes, it should be possible to show whether or not correlations exist between the dust burden and specific diseases. For example, there are perhaps 30 cases of mesothelioma per year in the United Kingdom, with no apparent past dust exposure to asbestos. Do the lungs of these individuals contain more, less, or the same amount of asbestos as those dying of diseases not related to exposure to asbestos – for example, accidents? This is the type of problem which Dr F. D. Pooley's approach of a complete mineral analysis of the dust at a micro level should be able to solve.

Mention must briefly be made of cancers of other organs than the lung as a result of asbestos dust. A few aspects of the problem are clear; many are uncertain and require further research. Mesotheliomas (peritoneal) occur on the surface of the gut, as well as on the lung. These abdominal cancers are certainly related to asbestos, but it is not known whether the asbestos reaches the abdomen by ingestion and then through the gut wall or direct via the lung and the lymph channels. It has not yet been possible to produce peritoneal mesotheliomas in rats by feeding asbestos.

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The cohort approach mentioned above has shown that in heavily exposed asbestos workers, especially insulation workers, there has been an excess risk of gastro-intestinal tumours – usually much smaller than the lung cancer excess. The problem is whether these are causally related to asbestos. The regional variations in incidence of gastric cancers are considerable, and there has been a general decline in many industrialized countries over the last 30 years. Present evidence suggests the gastro-intestinal cancer risk is small, even after heavy exposure to asbestos and is, therefore, likely to be very small, probably undetectable in the general population as a result of ingestion of minute amounts – on a mass basis – of asbestos or other fibrous minerals occurring naturally in water supplies or gaining access to them through filters, or from asbestos cement pipes (Committee of The American Water Works Association Research Foundation 1974).

TABLE 5. LUNG CANCERS IN PERSPECTIVE: DEATHS (MALE AND FEMALE) IN ENGLAND AND WALES, 1973, AND ESTIMATED PROPORTIONS BY CAUSE

site	no.	cause	estimated %
bronchial ICD 162	32176	cigarettes	90
		asbestos and cigarettes	< 1
		others	> 9
pleura ICD 163.0	163	asbestos	85
		others	15

TABLE 6. ESTIMATED OCCUPATIONAL MORTALITY (MILLIONS PER YEAR)

cancers			accidents	
wood workers	nasal	700	clothing mf.	3
asb. industry	lung	2000 M	bricks and cement	80
		4000 F	ship building	160
rubber workers	bladder	7000	coal face	600
nickel refining (up to 1925)	lung	15000	company directors	1800
β-naph. mf.	bladder	24000	deep-sea fishing	3000
			prof. divers	11000

Sources: U.K. statistics and Pochin (1975).

TABLE 7. ESTIMATED MORTALITY PER MILLION PER YEAR IN U.K.

(general accidents; personal habits; your age (male))

accidents		your age	
traffic	150	12	350
home	130	30	1000
suicide	80	42	3000
all	460	53	10000
cigarettes		63	30000
20/day	5000	77	100000

From Pochin (1974).

Perspectives

Man's understandable concern about the risks of death from cancer may distort his assessment of the absolute and relative risks. This is perhaps seen in the case of mesotheliomas. These tumours are so rare that until recently they were not separately listed on the International

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List of Diseases. Even now with the intensive search for such tumours following the demonstration of a close, but probably not unique, association with past exposure to asbestos, the deaths are about 1 per million of the general population per year, compared with about 1000 per million per year in men from bronchial cancers, mostly due to cigarette smoking. Table 5 shows the very large number of deaths from bronchial cancer in England and Wales compared to those from mesotheliomas, and also the very small contribution of asbestos to the bronchial cancer deaths.

The presentation of information on relative risks is not easy, but a step in this direction is seen in tables 6 and 7 from Pochin (1975). Table 6 shows that the mortality per million per year for a selection of occupationally related cancers varies greatly with the agent, from, for example, 700 for nasal cancers due to wood dust to 24000 for bladder cancers due to β naphthylamine, with asbestos at about 3000. It also shows the big differences of deaths by accidents in different groups, with over a 3000-fold difference between light industry and professional divers.

In general, the rates for occupational cancers in those exposed are greater than the occupational accidental deaths but, of course, the numbers of workers at risk from accidents are far greater. Table 7 compares accidents to which the general public are at risk; the effects of cigarette smoking; and all causes of deaths (related to age). It shows how important cigarette smoking is, the figure of about 5000 takes into account deaths from bronchial cancers, chronic bronchitis, and heart diseases. The table also shows how quickly age catches up upon us all. By middle age the death rate already exceeds that for most occupational cancers or occupationally linked accidents.

Speculations and conclusions

The theme of this meeting is forward looking towards the next century, and so speculation is permitted.

First, I expect mineralogists to be able to make an important contribution by identifying a small number of minerals with health hazards not yet recognized. Some of the hazards will be shown to be limited to quite small areas of the world. These discoveries may help to explain some of the rather large regional differences in cancer incidence in different organs.

Next, I expect the new techniques of mineralogy applied at a micro level to respirable dust, and particularly dust in the lung, to be of great value to elucidating the relation of the severity and type of disease with the type of mineral.

Next, I anticipate that in industrialized countries it will be shown that the cancer risks to the general public due to inhalation and ingestion of mineral dusts have been too small to be detectable, and will be accepted as negligible compared with other risks. This will go a long way to cure man's neurosis on this score.

Last, but I think important, is that the current research into the health hazards of dust from natural fibrous minerals will ensure that the exciting new range of man-made minerals are manufactured and used in complete safety.

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Discussion

Mrs Nancy Tait (38 *Drapers Road, The Ridgeway, Enfield, EN*2 8*LU*). Has it been demonstrated by experiments in the laboratory that the inhalation of asbestos dust combined with the smoke from cigarettes increases the risk of developing lung cancer, multiplicatively, or has all the evidence been provided by epidemiological studies?

J. Zussman (*Department of Geology, University of Manchester*). You did not mention among the methods of estimating the effects of exposure to asbestos dust, the rôle of animal experiments. Have you any comment on this subject?

R. G. Burns (*Department of Earth and Planetary Sciences, Massachusetts Institute of Technology, Cambridge, Massachusetts* 02139, *U.S.A.*). Fibre glass can be an irritant to the skin. Has there been any study made of fibre glass in the lungs? Does it cause extensive scarring, for example? Fibre glass would, of course, be difficult to identify by X-ray diffraction analysis.

J. C. Gilson. Animal experiments to test the interaction of asbestos and cigarette smoke on the incidence of bronchial cancer are in progress but not yet completed. The evidence is epidemiological and has been reported from both the U.S.A. and from the U.K.

The rat is particularly suitable for animal experiments because all the diseases of the lung seen in man are readily produced in the rat following inhalation of asbestos dust. However, it is not possible to extrapolate dose response results in the rat directly to man.

Several studies have been made of workers exposed to fibre glass during manufacture. Neither fibrosis of the lung nor an excess risk of lung cancer have been revealed. However, to add to the evidence further extensive epidemiological and animal experiments are now in progress in Europe and the U.S.A.

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crocidolite

amosite

anthophyllite

chrysotile

FIGURE 1. The four types of asbestos (magn. × 1500).