More Scientists Now See a Threshold in the Effect of Asbestos

Development of cancer proceeds in several steps, from the entering of a carcinogen into the body to development of clinical disease. At each of these steps the organism possesses defence mechanisms able to destroy the developing cancer cells. Only when all of these mechanisms are overwhelmed does the clinical cancer result.

Experience suggests that it takes large doses of a carcinogen to overwhelm these defences, and that there is a certain *threshold* under which the natural defences prevail. Low levels of exposures to carcinogen appear to be tolerated without harm. Low level exposure to the sun for example (Diagram 1).

A Controversial Hypothesis
In contrast to this experience, another school of thinking suggests that there is a linear relation between the dose of carcinogen and the development of cancer. This means that with decreasing dose, the effect (e.g. number of cases of cancer) gradually decreases along a straight line all the way to zero, so that even very small doses have some effect, and the only safe level is a zero dose. Thus, there is no threshold, and the notion that *"one molecule of a carcinogen"* or *"one fibre can kill"* results. (Diagram 2)

The latter concept is hypothetical, derived from wide extrapolations from results of epidemiological studies of consequences of the past exposures or from animal experiments, both done with exposures sometimes several orders of magnitude higher. Nevertheless this is the concept used by some authorities as the basis for proposals to ban asbestos.

Many scientists do not accept the *"one fibre can kill"* concept. J. Kleinerman, formerly pathologist with I. Selikoff, writes :

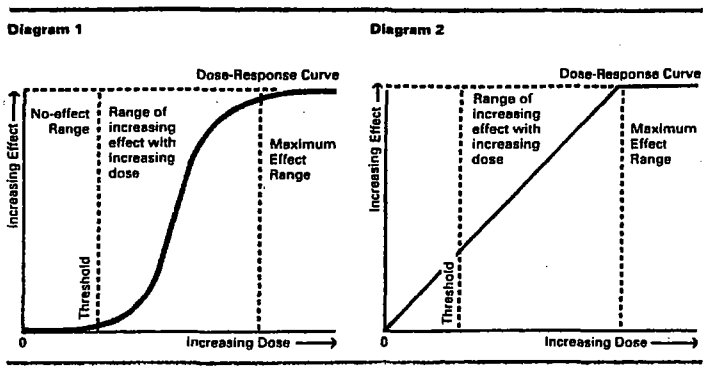
Recent studies suggest that a threshold of cumulative exposure exists below which the risk of lung cancer is not raised. Estimates of this threshold are in the range of 25 - 100 fibres/cc/years, an amount equivalent to the threshold lung burden of asbestosis. This has led to the concept that an increased risk for lung cancer as a result of asbestos exposure is present primarily where asbestosis is seen." (1988)

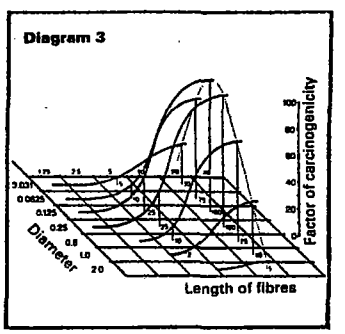
Fibrosis of the Lung vs Lung Cancer
Indeed, fibrosis of the lung tissue such as asbestosis, has been suggested to be a necessary precondition of asbestos-linked cancer of the lung by epidemiology, and the evidence is supported by animal experiments and pathology. "It is our opinion, that carcinoma of the lung associated with asbestos exposure is a result of scarring within the lung. ...There is little convincing evidence for significant genotoxicity of asbestos..." writes Dr. Kuschner (1987). In 356 cases of lung cancer in Suzuki's and Selikoff's asbestos insulation workers, all but a single case showed mild to severe lung fibrosis.

If pulmonary fibrosis (asbestosis) is a precondition without which a lung cancer is not attributable to asbestos, let us examine whether there is a threshold for asbestosis in epidemiological studies. At University of Boston, 1,632 asbestos workers exposed in shipyards and factories have been followed over a long period in a longitudinal investigation. Not one case of significant asbestosis was seen among those who started to work during the last 27 years (Gaensler, 1988). This is consistent with the everyday industrial experience that low exposures under modern control conditions have not led to any excess mortality from lung cancer and/or of mesothelioma (Browne, 1986).

It has been suggested that mesothelioma only develops on tissue changed by fibrosis of the pleura or peritoneum (Kuschner, 1987). This would suggest a threshold for mesothelioma.

Dr. Pott's Hypothesis
The effect of the dimensions of fibres on their carcinogenicity has been extensively studied. It has been established (Stanton) that the long and thin fibres are the biologically active ones while activity of very short fibres is questionable. Ten years ago, Dr. F. Pott proposed a hypothesis in which the activity of fibres only gradually decreased with decreasing length and with increasing diameter. No threshold of activity was considered. Along with



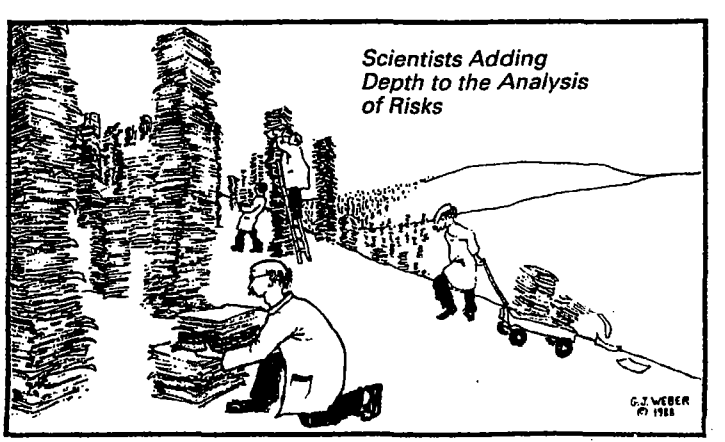


the view of *"one fibre can kill"* a new thesis *"very short fibres are also carcinogenic"* was developed and the Pott diagram was used for justification of this thesis. It is still occasionnally used by some authorities. (Diagram 3)

It is thus, of major interest that the author of this diagram, Dr. Friedrich Pott, a highly regarded experimental pathologist of Düsseldorf, surprised the scientific community by a recent article summarizing his recent research and proposing a new definition of a carcinogenic fibre (1987).

He proposed "to classify all natural and man-made mineral fibres with an aspect ratio of > 5:1 as carcinogenic when they are longer than 3 microns, thinner than 1 micron (or can split into such fine fibres) and when they can persist in the tissue for more than 3 years." For fibres which fail to persist in the tissue long enough, he introduced the term *durability threshold* value.

Pott's acceptance of critical dimensions for carcinogenicity of fibres, which negates the applicability of his earlier diagram, and the adding of a *durability threshold* concept, has important practical implications. According to the present Pott definition, there would be no cancer risk from asbestos in the environmental air, in buildings insulated with asbestos (if not disturbed), in the city air, in water, since practically all such fibres are under the threshold length of 3 microns. And chrysotile asbestos, in contrast with durable amphiboles, would probably come close to, or even under, the *threshold of durability.*



• Confirmation of the Different Potency of Fibres
• New Directions in Asbestos-Related Diseases

In August 1988, a world-wide conference on dust-related diseases, the seventh to be convened since 1930, was held in Pittsburgh, PA, USA. More than a thousand participants from more than 50 countries and all continents attended the conference, co-sponsored by the International Labour Office (Geneva) and a number of US government agencies, NIOSH, OSHA, MSHA and BOM.

Fibre Types and Pathogenic Potency

Four presentations added further weight to the evergrowing body of evidence for a difference in potency of asbestos fibre types. Dr. M. Neuberger of Vienna reported that the 5 mesothelioma cases found in his Austrian cohorts of A/C factory workers were all associated with pipe production; the only production sector in which crocidolite was used. Dr. Janet Hughes, of Tulane University in New Orleans, also reported that all 9 mesothelima cases found in A/C workers from two manufacturing plants were from the unit where pipes were produced, using crocidolite with chrysotile. Dr. E.A. Gaensler of Boston reported on asbestos-related diseases in 90 original employees of a filter paper plant using exclusively crocidolite (1951-1970), followed up to 1987. In this group, there were 34 with asbestosis and 8 deaths; 8 have died from lung cancer and 10 mesotheliomas were found. In a nearby plant using exclusively chrysotile (1962 up to the present), 90 workers employed for over 20 years were followed. Only two cases of minimal fibrosis were found, and no cases of mesothelioma or lung cancer have yet occured.

Finally, two presentations were made which concur with the widely held view that contrary to chrysotile, amphibole fibres are more durable, and accumulate in lung tissue. Dr. F.D. Pooley of the University of Wales in Cardiff, U.K., presented the results of assessments of fibrous mineral content of lung tissue samples from workers of a British asbestos textile plant, using predominantly chrysotile, and intermitently other asbestos fibre types. His data showed a predominance of amphibole fibres, which does not reflect the proportional use of the various asbestos types used in the plant. Dr. A. Tossavainen of the Institute of Occupational Health in Helsinki presented results of mineral lung contents of mesothelioma cases in Finland, 55% of which had possible, probable or definite asbestos exposure. The predominant fibrous minerals found were amosite, crocidolite and anthophyllite, while chrysotile and other inorganic fibres were only occasionnally found in some samples.

As more evidence is regularly brought forth of a greater risk from crocidolite than chrysotile, especially for mesothelioma, it will be interesting to see if some US regulatory agencies will modify their view that all asbestos fibre types are equally potent in their risk assessment models.

Fibrosis as a Precursor for Lung Cancer

Dr. M. Kuschner of the State University of New York, at Stoney Brook delivered a firm restatement of the hypothesis that the initial pathological response to inhaled long fibres was interstitial fibrosis, which then sets the stage for the eventual cancerous proliferation. In line with this concept, Dr. J. Hughes reported her observations on lung cancer mortality in relation to X-ray abnormalities in Louisiana asbestos-cement workers. No significant excess was found in workers with no abnormal- [illegible] with plaques, pleural thickening or calcifications. However, a significant excess was found in workers with opacities, the risk growing with increasing profusion of opacities.

Follow-Up Studies

Follow-up reports of cohorts previously studied were presented. Dr. Neuberger's study of asbestos-cement workers in Austria covered 540 deaths, where 52 from lung cancer were found. After adjustment for age and sex-specific smoking habits, there was no relationship between risk and cumulative exposure or length of exposures, indicating that the improved working environment of modern manufacturing plants effectively reduces disease and early deaths. Similar conditions were reported on by Dr. Albin of Sweden, who found that in her Swedish asbestos-cement workers cohort, neither morbidity nor mortality from lung cancer was significantly raised at median estimated intensity of exposure of 1.2 f/ml. A presentation by Drs. E.A. Gaensler and C. McLoud of Boston University, of New England workers showed that asbestosis is now developing much more slowly, if at all. Through X-ray readings of workers suffering from asbestosis, it was established that confined exposure to present day low exposure levels does not adversely affect progression of asbestosis. Improving the working environment also reduced disease and mortality in the West German asbestos-cement industry, as shown in E.G. Beck's study of the industry from 1981 to 1986. Overall, malignant respiratory diseases caused fewer deaths than other non-malignant and non-asbestos-related diseases.

Thus, the recently published findings in modern asbestos industry, showing the obvious benefits of adequate engineering controls and safe work practices, demonstrate that the safe use of asbestos, with no undue risk to workers, is a realistic goal. *

VIIth INTERNATIONAL PNEUMOCONIOSES CONFERENCE
Pittsburgh, Pennsylvania, United States, August 23-26, 1988

LE VIIe CONGRÈS INTERNATIONAL PNEUMOCONIOSES
À Pittsburgh en Pennsylvanie, États-Unis, Du 23 jusqu'au 26 août, 1988

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New Directions in Research

As asbestosis has declined in incidence and severity, with resulting decrease in asbestos-related lung cancer, more attention is now being given to changes of the pleura. Among the papers dealing with pleural changes, a strong distinction was made between a diffuse thickening of the pleura, which may cause some impairment of the lung function, and circumscribed pleural plaques.

Dr. E. Gaensler has followed 385 persons who have pleural plaques from 8 to 22 years. The circumscribed plaques by themselves had no perceptible effect on lung volumes and gas exchange. Neither their extent nor degree of calcification was related to lung function.

The increased interest in abnormalities of the pleura led to a special session devoted to revising the 1980 ILO classification of pneumoconiosis radiograms. An ICOH task force led by Dr. C. Rossiter presented a comprehensive proposal called "ILO Classification 1991." The practical application of the new proposed classification will now be studied.

Thus, in some major areas of asbestos-related diseases, presentations at the 1988 International Pneumoconiosis Conference reinforced conclusions, which had been reached at prior recent international meetings held in 1987, such as the WHO/IARC Symposium in Lyon and the XXIIth International Congress on Occupational Health in Sydney, namely that there is indeed a great difference in potency between the different asbestos fibre types. As was pointed out recently by Dr. J.C. Wagner and co-workers: "We believe therefore that chrysotile is the least harmful form of asbestos in every respect and that more emphasis should be laid on different biological effect of amphibole and serpentine asbestos fibre." (1) ■

(1) J.C. Wagner, M.L. Newhouse, B. Corrin, C.E.R. Rossiter and D.M. Griffiths, (1988). Correlation between fibre content of the lung and disease in East London asbestos factory workers. Brit. J. Ind. Med. 45:305-308.

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