

Chrysotile Biopersistence

The Misuse of Biased Studies

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Although it is widely accepted that exposure to any asbestos type can increase the likelihood of lung cancer, mesothelioma, and non-malignant lung and pleural disorders, manufacturers and some chrysotile miners' unions contend that chrysotile either does not cause disease or that there is insufficient evidence to reach a conclusion. At the same time, Dr. D.M. Bernstein has published several animal studies, financed by the Québec Chrysotile Institute, to determine chrysotile biopersistence in the lungs. Bernstein's study protocol induces a very short fiber half-life, from which he concludes weak chrysotile carcinogenicity. Bernstein's findings contradict results obtained by independent scientists. Bernstein's results can only be explained by an aggressive pre-treatment of fibers, inducing many faults and fragility in the fibers' structure, leading to rapid hydration and breaking of long fibers in the lungs. *Key words:* asbestos, Asbestos Institute, asbestos-related cancer, biopersistence, chrysotile, Chrysotile Institute.

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Asbestos minerals are divided into two large groups: serpentine and amphibole. Chrysotile is the only type of asbestos derived from serpentine minerals. There is general agreement among scientists and health agencies that exposure to any asbestos type, chrysotile or amphibole, may cause lung cancer, mesothelioma, and nonmalignant lung and pleural disorders.¹⁻¹⁰

However, chrysotile manufacturers, governments of asbestos-producing nations, and some asbestos miners' unions contend either that their products do not cause disease or that there is insufficient evidence to reach a reliable conclusion. They continue to oppose any measure that would ban the use of this material worldwide, and to promote the use of chrysotile around the world.¹¹ For example, Russia protested when health experts at the 2007 World Society Security Forum in Moscow called for a global asbestos ban because of the health risks associated with asbestos exposure. An asbestos industry head in Russia claimed that, "It's just a public relation campaign when they say that asbestos

can kill."¹² Scientists at the international forum, however, said that approximately 100,000 people die of asbestos disease each year. Russia is the top global asbestos producer, supplying approximately 40% of all asbestos. Russia opposes the ban because of the economic impact it would have. Russian experts claim that up to 500,000 Russian workers could lose their jobs if a global asbestos ban were passed.¹² Along with Russia, the largest asbestos producers are China, Canada, Kazakhstan, Brazil and Zimbabwe.

Canada dominates world trade with an annual export of about 300,000 tons of chrysotile asbestos. In that country, the Chrysotile Institute (CI), formerly known as the Asbestos Institute, is the lobbying arm of the asbestos industry. The CI touts a series of studies that concludes that chrysotile is safe to use.¹³ This paper serves as an example of how corporations have used science to achieve profit growth and escape liability at the expense of dead and injured workers.¹⁴

The CI helps fund and widely circulates a critical review of the World Health Organization's (WHO) document on the Elimination of Asbestos-related Diseases. The WHO states that, "Bearing in mind that there is no evidence for a threshold for the carcinogenic effect of asbestos and that increased cancer risks have been observed in populations exposed to very low levels, the most efficient way to eliminate asbestos-related diseases is to stop using all types of asbestos."¹⁵ In the CI-funded critique, Dr. Bernstein asserts that the scientific basis for the statements and the conclusions by WHO are challenged by numerous studies.¹⁶ This conclusion is largely based on data on the biopersistence of chrysotile in the lungs, and has led Quebec politicians to declare that one year after a period of inhaling chrysotile, "there is not a single fiber or after-effect in the human organism."¹⁷ Such declarations have very serious public health implications and are disputed by a significant body of scientific knowledge.

It is therefore essential to debate the experimental data on which such declarations are based. The data published by Bernstein and his colleagues are derived solely from inhalation studies with rats.¹⁸⁻²⁴ The early studies were funded by the Union Carbide Corporation, the former part owner of a chrysotile mill and mine which today holds millions of dollars of asbestos liability; while later studies were funded by asbestos producers through the CI.

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FACTORS DETERMINING THE CARCINOGENIC POTENCY OF MINERAL FIBERS

To what degree does fiber biopersistence (half-life) in the lungs determine the carcinogenic potency of those fibers? Experts assembled in 2005 by the International Agency for Research on Cancer (IARC) of the World Health Organization, concluded that:

The chemical composition of [asbestos] substitutes is a key factor influencing structure and physicochemical properties, such as surface area, surface reactivity, solubility, etc. Attention should be paid not only to the chemical composition of the fibers, their major and trace elements, but also to contaminants or accompanying elements, including their speciation. Fiber-derived free radical generation favors DNA damage and mutations. Surface properties are a determining factor in the inflammatory response.

In relation to fiber dimension and deposition, one can assume that there exists a continuous variation on the carcinogenic potency of respirable fibers, which increases with length.

Biopersistence of a fiber increases tissue burden, and therefore may increase any toxicity the fibers might possess. For synthetic vitreous fibers, there is evidence in animals that the potential for carcinogenicity increases with biopersistence. This has not been demonstrated, however, for other fibers.²⁵ Moreover Hughes et. al found that chrysotile and crocidolite were equipotent inducers of lung cancer in human beings.²⁶ Thus, in this example, it appears that biopersistence differences, if real, are unrelated to potency.

Several factors come into play in the existence and potency of a fiber's carcinogenicity. For all insoluble or relatively insoluble respirable particles, the main factor implicated in carcinogenicity is surface reactivity, which is linked to a fiber's chemical composition and structure.²⁷⁻²⁹ Dimensional characteristics and biopersistence are simply two additional, complementary parameters.

Divalent iron (also trivalent iron in some compounds) plays an important role in the interface that occurs between fibers (or particles) and a biological medium. Divalent iron, an electron donor, causes the formation of oxygen and nitrogen-activated radical species; these are extremely aggressive and play a key role in carcinogenesis.²⁷⁻³¹ Fe^{2+} ions are particularly common as a substitute for magnesium in Canadian chrysotile and in its primary fibrous contaminant, nemalite, a magnesium hydroxide which has been shown to induce mesothelioma in animal experiments.³¹

The WHO experts agree that fibers' carcinogenic properties vary as a function of their length. They emphasize that in the interest of cancer prevention we

need to take into account fibers shorter than 5 μm . The WHO report confirms the findings of studies conducted by the author and colleagues^{33,34} concluding that in the study of carcinogenesis there is no justification for limiting inquiry into asbestos carcinogenesis to fibers longer than 20 μm . These findings are in agreement with Tomatis and other researchers who conclude that "fibers of all lengths and diameters play a role in the induction of mesothelioma."³⁵⁻⁴¹ The WHO report puts the biopersistence factor in its proper place; i.e., one parameter among others in the causal chain leading to cancer, a factor itself linked to the chemical composition and structure of fibers and their contaminants.

For synthetic vitreous fibers, the relationship between chemical composition and biopersistence is obvious. In mineral wools (glass wool, rock wool, slag wool) there are alkaline and alkaline-earth ions (sodium, calcium, etc.) with a strong affinity for water. The higher their concentration in the given material, the faster water will cause that material to disintegrate in a biological medium and the weaker the biopersistence will be. In direct contrast, the extremely low concentration of these readily hydratable ions in refractory ceramic fibers, for example, sharply increases their persistence in a biological medium.

However, it would be wrong to conclude that the biopersistence of synthetic vitreous fibers is the only parameter of their carcinogenicity. French investigators, including the author, have demonstrated this in a study of six "historical" samples of mineral wools, all materials with low biopersistence.²⁹ Three glass wool samples containing less than 0.4% divalent iron appeared not to show any strongly oxidizing activity linked to oxygen radicals. The three samples were from companies where the exposed workers did not show an excess of lung cancer. Three older rock wool samples (dating from 1949 to 1974) actively produced highly aggressive radical oxygen species in an aqueous medium, and that activity was ranked in the same order as percentages of divalent iron (6.75–12% FeO). These samples came from companies where an excess of lung cancer in the exposed populations was detected. This excess appeared to be directly linked to the divalent iron content of the rock wool.

This study demonstrates that even at weak biopersistence levels, the carcinogenic activity of rock wool can be important. Nonetheless, Bernstein ignores these findings and concludes in a recent article that, "The amorphous structure of synthetic vitreous fibers facilitates designing fibers in use today with low biopersistence. Both the epidemiological data and the animal studies database provide strong assurance that there is little if any health risk associated with the use of synthetic vitreous fibers of low biopersistence."⁴²

THE BIOPERSISTENCE OF CHRYSOTILE AND BERNSTEIN STUDY RESULTS

It is known that chrysotile fibers vary in length by geological conditions present during and after their formation. They may also be affected by defects that break up the continuity of their crystalline structure, thus creating zones of fragility that are much more prone to hydration, together with breakage of long fibers into short ones and dispersion of fibers into elementary fibrils that appear either isolated or gathered in small numbers.

The Calidria mine in the United States offers an example of chrysotile whose structure was profoundly affected by geologic events—probably leaching. Not only is the chrysotile from this mine composed of an important proportion of short fibers, but its external surface area is three to four times that of other short-fiber commercial chrysotile. This means not only shorter diameters but also open porosity due to the many structural defects. This sample underwent rough treatment by lixiviation during its geological history, generating a great number of structural defects that make it extremely fragile in a biological medium.

These observations on differences in chrysotile fibers by geological history of the mine from which they are taken explain why Bernstein's animal experiments on rats¹⁸⁻²⁴ showed different biopersistence values from chrysotile taken from different mines (Canada, Calidria, Brazil). For example, in the Bernstein studies the half-life of chrysotile fibers varies from 16 days to 7 hours for Canadian and Calidria chrysotile, respectively. Those results are logical, have long been known, and the differences indicated could even appear on samples taken from different locations in the same mine.

The effects of structural modifications that occurred during the various geological periods can appear and even be strongly intensified in industrial settings, to say nothing of laboratories, when the fibers are ground, crushed, heated or otherwise treated mechanically or with water. All such operations may induce structural defects that result in zones on the fiber surface that are extremely fragile when attacked by water inside the lungs.^{43,44} The nature and intensity of preliminary treatments therefore affect the length of fiber half-life (biopersistence) in the lungs.

Bernstein says little, and in some cases nothing, about the treatment fibers were subjected to before their use as aerosols during his inhalation experiments. In a 1994 article, he refers to a pre-selection of long fibers by sedimentation in water; i.e., a treatment in an aqueous environment, which necessarily involves hydration and oxidation, the effect being to diminish fiber surface activity and damage fiber structure.¹⁸ In a 2003 article on Canadian chrysotile, Bernstein describes a grinding method involving high-speed rotation, particularly damaging to the mineral structure:

the sample is thrown against a "durable grinding surface."²⁰ In other articles,^{19,21-24} preliminary treatment of the fibers is described only with a reference to the two articles cited above. Given that lixiviation and intense grinding can seriously damage fiber structure and shorten half-life in the lungs, this preliminary treatment raises serious questions.

DIVERGENCES AMONG AUTHORS ON CHRYSOTILE FIBER BIOPERSISTENCE

Bernstein and colleagues' findings on the length of chrysotile half-life in the lungs diverge widely from those found by other research teams; Bernstein's time lengths are always shorter. Kimizuka et al.,⁴⁵ Roggli and Brody,⁴⁶ and Roggli et al.⁴⁷ observe that, contrary to Bernstein, the average length of fibers retained in the lungs increases with time.

The most interesting comparison is between Canadian chrysotile, studied both by Bernstein et al.^{20,23} and Coin et al.^{48,49} The two research groups did not study the same Canadian sample, and unfortunately, neither specified the nature of the treatment the material was subjected to before being used by aerosol to expose the rats. Bernstein²⁴ does give some indications about how Coin et al. treated their fibers—without including any precise references.

Bernstein and Coin obtained totally contradictory results one month after cessation of exposure (in Bernstein's experiment the rats were exposed 6 hours a day for 5 consecutive days; in Coin's there was a single 3-hour exposure). Bernstein found a short half-life for long fibers in the lungs (16 days for fibers measuring over 20 μm) whereas Coin found a minimum half-life of 114 days (for fibers measuring over 16 μm).

Coin et al. specify that, "Statistically, the clearance rate for fibers greater than 16 μm was not significantly different from zero (half-life infinity)."⁴⁸ This near-stability over time is explained by the fibers' decreasing average diameter combined with an increasing number of long fibers, a phenomenon due to longitudinal cleavage. In the same study, Coin et al. show that the fiber clearance rate is inversely correlated to fiber length: the half-life of fibers ranging from 0.5 to 4 μm is approximately 10 days, as opposed to 114 days for fibers over 16 μm .

In direct contrast, the studies by Bernstein et al. show fiber half-life increasing when fiber length decreases. In their chrysotile study, fibers over 20 μm have a half-life of 16 days as opposed to 107 days for fibers under 5 μm .²⁰ The increase in half-life length is explained in Bernstein's article by the fact that the long fibers get broken quickly, thus increasing the number of short fibers in the lungs and slowing clearance of them. In the Coin et al. experiment, the increased number of long fibers is due to longitudinal splitting due to breakage of the weak hydrogen bonds that

insure cohesion of fibrils within the fiber.⁴⁹ The number of short fibers is not significantly affected by a breakage of long fibers. In Coin's results, short fiber elimination is logically accelerated by phagocytosis, followed by conveyance and clearance by macrophages.

The fundamental difference between the results of the two research groups cannot be explained by lung overload, the term generally applied for a burden of over 1.5 mg. In the Coin et al. study the total load was only around 30 µg, while an overload in the Bernstein study would have resulted in longer fiber half-life. Moreover, contrary to what Bernstein claims,²⁴ the difference cannot be explained by an over-concentration of short fibers in Coin's protocol because in Coin's study 32% of the deposited fibers were shorter than 4 µm one day after exposure, while Bernstein et al. claim that 88% of the deposited fibers were shorter than 5 µm one day after cessation of exposure.

There would seem to be only one explanation for these contradictory results, and it concerns the density of structural defects in the fibers. Such defects break the structural continuity of long fibers, creating zones of fragility along the entire fiber length that in turn generate transverse breaks as soon as the fibers come in contact with an aqueous medium.

In general, the high incidence of transverse defects is the result of either ancient geological conditions or preliminary handling of the fibers.

Given the half-life results obtained by Bernstein—ranging from low to very low—it is likely that those results are strongly linked to the preliminary handling of the samples which generated multiple defects and breaks along the long fibers.

Bernstein et al. have only recently²⁴ shown an interest in the data that Coin et al. published in 1992—concerned first and foremost with a critique of Coin's study for overly severe preliminary grinding. If that had been the case, Coin's results would have been the opposite of what they are, since the first effect of such treatment is to increase the number of structural defects, thus weakening the long fibers and increasing the number of short ones. If there was any excessively severe grinding, it most likely occurred in Bernstein studies. Bernstein et al, thus appear incapable of justifying their results in relation to those obtained by Coin, Roggli and Brody.

CONCLUSION

The studies of chrysotile published by Bernstein and his colleagues lack scientific rigor and credibility. These studies in no way justify the authors' conclusion that chrysotile in vivo does not behave as a fiber but rather as a particle, or that exposure to chrysotile can only cause cancer if the lungs are subjected to extremely high or prolonged exposure.

Tomatis et al,³⁵ citing several other authors^{50–52} state that, "it has been repeatedly claimed that mesothe-

liomas can be caused by light and/or brief exposures." Despite Bernstein's assertions, in the case of chrysotile, even at half-lives shorter than several months or years, and especially in the case of renewed exposure day after day, oxidizing aggression against biological macromolecules, including DNA, will still manifest itself in several organs, and several researchers have shown chrysotile to be the predominant fiber found in the pleura.^{53–55}

There is also no justification for claiming that all biopersistent fibers maintain their original toxic effect for a long period in the lungs. Because of their composition and structure, certain fibers, in pulmonary medium, may cease to have surface activity and therefore lose their toxicity, whereas others may acquire newly surface-active sites following interactions with endogenous entities such as iron ions.

Bernstein's results do not constitute scientific progress. Quite to the contrary, they are being misused by the international asbestos producers' lobby to suggest that chrysotile is harmless. This dangerous assertion particularly compromises the health of workers in developing countries where living and working conditions, combined with inadequate health care, add to the morbidity and mortality resulting from exposure to chrysotile.

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