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Letter to the Editor re Bernstein et al: Health risk of chrysotile revisited. Crit Rev Toxicol, 2013; 43(2): 154–183

Murray M. Finkelstein

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Bernstein et al. (2013 Dunnigan J, Hesterberg T, et al. (2013). Health risk of chrysotile revisited. Crit Rev Toxicol, 43, 154–83 [Taylor & Francis Online], [Web of Science ®], [Google Scholar]) have presented their review of the health risks of chrysotile asbestos in your Journal. They state that “chrysotile, which is rapidly attacked by the acid environment of the macrophage, falls apart in the lung into short fibers and particles, while the amphibole asbestos persist creating a response to the fibrous structure of this mineral. Inhalation toxicity studies of chrysotile at non-lung overload conditions demonstrate that the long (>20 µm) fibers are rapidly cleared from the lung, are not translocated to the pleural cavity and do not initiate fibrogenic response”. The authors reviewed toxicology and epidemiology studies and concluded that, “The more recent toxicology studies demonstrate that chrysotile asbestos has a relatively short biopersistence and does not result in pathological response even through 90 d of exposure”. Surprisingly, Bernstein and colleagues completely ignored the human lung burden studies that refute their

conclusion about the short biopersistence of chrysotile.

In 1984, Churg and colleagues published a paper on the lung asbestos content in 6 long-term chrysotile miners and millers who had pleural mesothelioma (Churg et al., 1984Churg A, Wiggs B, Depaoli L, et al. (1984). Lung asbestos content in chrysotile workers with mesothelioma. Am Rev Respir Dis, 130, 1042–5 [PubMed], [Web of Science ®], [Google Scholar]). In five patients, only chrysotile ore components (chrysotile and tremolite/actinolite/anthophyllite types of amphibole asbestos) were found, while the sixth patient presented both chrysotile ore components and amosite. The mean number of fibers/g dry lung for the five patients with mesothelioma containing only chrysotile ore components was higher (chrysotile 64 million and tremolite group 540 million) than in a group of long-term chrysotile miner control subjects who had no asbestos-related disease (chrysotile 23 million, tremolite group 58 million). The concentration ratio of tremolite in the lungs of the mesothelioma cases compared to the control cases was 9.3, while the ratio of chrysotile was 2.8. They concluded that “our findings provide strong evidence that chrysotile mine dust (chrysotile and amphibole components) can produce mesotheliomas in humans; the greater relative amounts of tremolite group amphiboles present in the patients with mesothelioma raise the possibility that these fibers may be important in the pathogenesis of the tumors”. The authors found no need for explicit mention that the chrysotile fibers had not all been rapidly cleared from lung tissue, since they were found to be present in high concentrations.

Churg & Wiggs (1986Churg A, Wiggs B. (1986). Fiber size and number in workers exposed to processed chrysotile asbestos,

chrysotile miners, and the general population. Am J Ind Med, 9, 143–52 [Crossref], [PubMed], [Web of Science ®], [Google Scholar]) analyzed chrysotile and chrysotile-associated amphibole (largely tremolite) asbestos fibers in 21 workers exposed to various types of processed (milled) chrysotile ore, 20 long-term chrysotile miners, and 20 members of the general population (controls). Significantly greater amounts of both chrysotile and tremolite were found in processed-ore workers and miners than in controls. On average, the mean fiber lengths and aspect ratios for the mining and processed-ore-exposed workers were similar and were significantly greater than the values seen in the controls. In particular, only 5% of controls were found to have chrysotile fibers greater than 10 µm in length, whereas 40% of processed ore workers and 80% of miners retained these fibers in their lungs. No controls were observed to have chrysotile fibers greater than 20 µm in length in their lungs; these long chrysotile fibers were detected among 20–25% of the occupationally exposed.

Rogers et al. (1991Rogers AJ, Leigh J, Berry G, et al. (1991). Relationship between lung asbestos fiber type and concentration and relative risk of mesothelioma. A case-control study. Cancer, 67, 1912–20 [Google Scholar]) analysed lung tissue from 221 definite and probable cases of malignant mesothelioma reported to the Australian Mesothelioma Surveillance Program and compared the lung fiber burden to a control series of 359 postmortem cases. Univariate analyses showed statistically significant dose-response relationships between the odds ratio for mesothelioma and fiber concentration for all fiber concentration measures. Multiple logistic regression analysis showed that a model containing crocidolite greater than or equal to 10 µm, amosite less than 10 µm, and

chrysotile less than 10 µm as explanatory variables best described the data. The odds ratio for a 10-fold increase in fiber concentration (fibers/micrograms) of chrysotile, less than 10 µm in length, was 15.7 (95% CI, 6.1 to 40). In a subgroup of cases and controls with only chrysotile in the lungs, a significant trend in odds ratio with increasing fiber content was found. Once again, the authors found no need for explicit mention that the chrysotile fibers had not all been rapidly cleared from lung tissue, since they were found to be present in high concentrations, and a dose-response relation was found.

Dufresne et al. (1996Dufresne A, Begin R, Masse S, et al. (1996). Retention of asbestos fibres in lungs of workers with asbestosis, asbestosis and lung cancer, and mesothelioma in Asbestos township. Occup Environ Med, 53, 801–7 [Google Scholar]) published their analyses of the lung content of chrysotile and other fibers among Quebec asbestos miners and millers. In a comparison of the workers with controls, Dufresne et al. reported that geometric mean concentrations were higher in cases than in the controls for chrysotile fibres 5 to 10 µm long in patients with asbestosis with or without lung cancer; for tremolite fibres 5 to 10 µm long in all patients; for crocidolite, talc, or anthophyllite fibres 5 to 10 µm long in patients with mesothelioma; for chrysotile and tremolite fibres ≥10 µm long in patients with asbestosis. In a subsequent analysis of this material, Dufresne and I examined the time course of clearance of the chrysotile fibers (Finkelstein & Dufresne, 1999Finkelstein MM, Dufresne A. (1999). Inferences on the kinetics of asbestos deposition and clearance among chrysotile miners and millers. Am J Ind Med, 35, 401–12 [Crossref], [PubMed], [Web of Science ®], [Google

Scholar]). The mean time since leaving occupational exposure was 9.5 years (standard deviation: 8 years). Figure 5 of our paper showed that the lung burden of fibres 1–5 µm in length was greater than that of fibers 5–10 µm in length, which in turn was greater than that of fibers 10 or more microns in length. This pattern is consistent with the disruption of longer fibers, but it is also compatible with a greater concentration of shorter fibers in workplace air. The fiber burden of chrysotile fibers of all lengths was greater than that among controls even after 15 years from leaving exposure. We calculated the clearance half-times to be: 3.8 years for fibers <5 µm in length; to be 5.7 years for chrysotile fibers 5–10 µm in length; and to be 8 years for chrysotile fibers >10 µm in length. Recall that it takes 5 half-lives for 99% of the burden to be cleared in a first order exponential clearance process. Chrysotile fibers would thus be retained in the lung for decades after inhalation.

The human data concerning chrysotile retention in occupationally exposed populations are thus inconsistent with the statement of Bernstein and colleagues that chrysotile has a short biopersistence, yet Bernstein and colleagues completely failed to mention these data. The Instructions for Authors planning to submit to Critical Reviews in Toxicology state that “Critical Reviews in Toxicology provides up-to-date, *objective* analyses of topics related to the mechanisms of action, responses, and assessment of health risks due to toxicant exposure. The journal publishes *critical, comprehensive* reviews of research findings in toxicology and the application of toxicological information in assessing human health hazards and risks”. By failing to mention any of the data which contradict their conclusions, Bernstein and colleagues have

clearly not provided an objective analysis, and have created the impression that they have published a document to support the interests of the International Chrysotile Association, which, in cooperation with The Canadian Chrysotile Association, funded their work.

Declaration of interest

The author has appeared as an expert witness in litigation concerned with alleged health effects of exposure to chrysotile. The authors alone are responsible for the content and writing of this article.