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## TALC SHOULD NOT BE USED FOR PLEURODESIS IN PATIENTS WITH NONMALIGNANT PLEURAL EFFUSIONS

PLAINTIFFS' EXHIBIT 654

Andrew J. Ghio, Victor Roggli, and + Author Affiliations Sections:

To the Editor :

In the debate regarding the use of talc in pleurodesis, respiratory failure after intrapleural injection was cited as that complication potentially limiting employment of this agent  $(\underline{1}, \underline{2})$ . We agree with this appraisal in the treatment of patients with malignant recurrent effusions. However, there should continue to be concern regarding the use of talc for pleurodesis in individuals with nonmalignant pleural effusions and spontaneous pneumothorax. This dilemma results from a possible increased risk of malignant mesothelioma in those patients treated with talc. Consequently, an alternative agent should be employed in any individual without malignancy requiring pleurodesis.

Talc is not a uniform substance, and varies significantly in size and chemical composition, with the latter depending on geologic origin. This sheet silicate can be contaminated by asbestos. An association between carcinogenesis and exposure to asbestos included in talc appears credible. Certainly, noncarcinogenic effects of asbestos (pleural plaque formation) have been reported in patients instilled with talc for pleurodesis. The paucity of evidence of malignant mesothelioma occurring after the use of talc for pleurodesis may reflect either an inadequate latency period or an insufficient number in the investigations conducted. Assuming a risk of the same magnitude as that seen in the cohort of asbestos-exposed insulation workers ( $\underline{3}$ ), less than one case of mesothelioma would have been expected in the two investigations of patients exposure to talc suggest a potential association ( $\underline{6}$ ). Furthermore, epidemiologic studies demonstrate an excess mortality from lung and pleural carcinomas in talc miners and millers, while animal studies confirm an induction of mesothelioma after intrapleural injection of talc.

The assertion that contemporary purified preparations of talc do not contain asbestos, therefore eliminating a risk of mesothelioma, should be closely examined prior to its acceptance for clinical application. The methodology used to confirm the lack of asbestiform minerals in a finished product (i.e., X-ray diffraction, optical microscopy, and electron microscopy techniques) and its sensitivity must be provided. Even if the product is "asbestos-free," the mechanism of cancer induction by asbestos (i.e., metal-catalyzed radical generation) is similarly pertinent to talc and the occurrence of fibrous forms of the sheet silicate itself (Figures E1 and E2 in the online data supplement to this letter) raises issues about clearance and long-term safety. Simply stating that the talc is "asbestos-free" should not release us from a responsibility to the patient, especially when safe alternatives are available.

## References

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