

Fiber Types, Asbestos Potency, and Environmental Causation

A Peer Review of Published Work and Legal and Regulatory Scientific Testimony

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Scientific evidence and analysis offered in litigation and public policy testimony have an important role in occupational and environmental health, but are not subject to peer review. Critique and commentary, attempts at reproduction of results, and review of data offered in such testimony is essential. Peer review of such testimony should become part of the domain of medical and scientific journals. This paper is an effort to peer review the use of certain scientific methods in tort litigation and in testimony before regulatory agencies. In this issue of *IJOEH*, Azuma et al. show that background asbestos exposures can be considered to have caused mesothelioma. In contrast, epidemiologic studies and testimony by Teta et al. and Price and Ware, and pathologic studies and testimony by Roggli and others, claim that background exposures are benign. These are fatally flawed because of methodological and analytic errors. *Key words:* asbestos; litigation; peer review; chrysotile; public policy; mesothelioma

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Several recent episodes of the publication of works based on partial or fabricated data have again revealed the weakness of the peer review process. Dr. Scott Rubin fabricated data that appeared in at least 21 published peer-reviewed papers.^{1,2} Jonathan Leo exposed the fact that in an article published in *JAMA*, authors misrepresented their consulting arrangements with Forest laboratories and concluded that Forest's drug Lexapro was better than placebo, but omitted data from the same study that showed that Lexapro is no better than counseling.^{1,3} In response, the Editor of *JAMA* called Leo a "nobody and a nothing," tried to intimidate the Dean of his medical school, and banned him for life from publishing anything in *JAMA*.¹ *JAMA* then let the perpetrators of the misrepresentation explain away their misconduct in a letter to the editor and denied they had maligned Leo.^{4,5}

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These incidents remind us that the peer review process does not end with publication. This is true not only for published papers, but also for scientific argument and evidence presented as testimony offered for purposes of public policy-making and litigation. Azuma et al.'s paper in this issue, as well as letters from Hessel and Welch and colleagues, have motivated this commentary, which reviews the presentation of epidemiology- and pathology- based testimony in asbestos litigation and regulation.⁶⁻⁸ The comments are designed to address general issues, but of necessity are comments on statements and/or publications of particular individuals. This commentary was reviewed by four experts, two of whom do not participate in U.S. asbestos litigation.

In this issue, Azuma et al. use real, although limited, exposure data to correlate environmental "background" asbestos exposures with mesothelioma incidence in Japan. "Background" has no universal definition.* Azuma et al. correlated mesothelioma cases with environmental exposure data and the weighted average number of asbestos ferruginous bodies detected in the lungs of the people with no identifiable point source of exposure either occupational, para-occupational or known environmental. Their data roughly confirm the U.S. Environmental Protection Agency's (EPA's) dose-response equation, which is consistent with a no threshold-effect level for asbestos-induced mesothelioma. Azuma et al. show that many, if not most, "background" mesothelioma cases are caused by ambient levels of asbestos which are attributable to asbestos released during building construction and from automobile and truck brakes, among other sources. Sprayed chrysotile and amphibole asbestos was used in the United States as well as Japan and other countries.

In addition to the Azuma paper, there is significant evidence that asbestos causes most mesotheliomas. Mark

*It is important to distinguish between occupational exposures (direct and bystander), non-occupational but clearly above-background exposures (e.g., neighborhood and residential exposures as well as "handyman" and "shade tree" mechanic type of exposures, both direct and indirect) and "environmental" exposures. "Background" exposures, as I use the term, refers to exposures with no identifiable point source that would elevate airborne respirable asbestos fiber concentrations in excess of those recorded for the environment at large. Azuma et al. refer to these exposures as "environmental."

and Yokoi reviewed all autopsies at Massachusetts General Hospital from 1896 onward, and failed to find any mesothelioma case before 1940.⁹ They concluded that “the background level of diffuse malignant mesothelioma in Europe and in the United States prior to 1930 was extremely low,” and that, “current cases in Boston are not attributable to any significant background level [non-asbestos cause] of the disease.” In addition, Camus et al. reported seven “environmental” mesothelioma cases in women who lived near Canadian asbestos mines.¹⁰ Camus et al. concluded that the EPA risk formula overestimated the risk of asbestos lung cancer 10-fold. They reported, but did not analyze, the mesothelioma risk. Unfortunately, Camus et al. relied on particle counting techniques that were inversely related to actual asbestos fiber counts.¹¹ (The higher the particle count, the lower the exposure.) In contrast, Swedish researchers who relied on fiber counts and controlled for smoking found that “low exposure” (10 fiber-years) relative risks ranged from 1.5 to 4.5, and argued the EPA model underestimated the risk at 1.10.¹² Gustavsson et al. found a non-linear dose-response relationship indicating that per-fiber risks were higher at low exposures than at high exposures. Pan et al. found a relationship between distance from natural outcroppings of chrysotile (occasionally containing tremolite) in California and concluded that the findings supported “the hypothesis that residential proximity to naturally occurring asbestos [NOA] is significantly associated with increased risk of mesothelioma mortality in California.”¹³

Despite this rather consistent evidence of real risk of mesothelioma from “background exposures,” some industry consultants have assumed in testimony and publication that background exposures are benign. In this commentary, I review these and related assertions on chrysotile potency and lung fiber counting, examining how they have been put to use in litigation and public policy hearings.

SEER DATA CANNOT BE USED TO ESTABLISH A THRESHOLD FOR ASBESTOS INDUCTION OF MEOTHELIOMA

Recent papers by Teta et al. and Price and Ware claim to establish a “safe threshold” below which asbestos does not cause mesothelioma.¹⁴⁻¹⁶ These authors have attempted to use the National Cancer Institute’s Surveillance, Epidemiology and End Results (SEER) data to estimate the “background” rate of mesothelioma in human populations.^{14,15} They define “background” cases as mesotheliomas that occur in individuals who have no history of exposure to asbestos. From a scientific perspective, this approach is problematic since it is based on the unreferenced assumption and assertion that certain cohorts were never exposed to sufficient amounts of asbestos to develop asbestos-caused mesotheliomas, based on the false premise that there

were constant rates of mesothelioma over time. They base this assertion on mesothelioma rates—not exposure data, interviews, medical record reviews or a search of medical literature.

In fact, scientists have published contrary information for more than a century and as recently as 2008.¹⁷⁻²² The Swedish Family-Cancer Database is the largest cancer data base in the world that links job and other factors and cancer incidence. Using this data, Hemminki and Li reported that a comparatively “low [mesothelioma] risk among farmers [who have likely occupational exposures] suggests that the population at large is at a risk of mesothelioma from undefined sources in urban areas.” They concluded that “Background exposures do cause mesothelioma and epidemiologic data on excess risk should use the lowest rates for the least exposed as controls. Occupational and para-occupation exposures are added to ‘background’ rates which have their own real risk.”

The UK Health and Safety Executive (HSE) has also agreed that “background” exposures cause mesothelioma in adopting the position that:

A PMR of 100 does not represent the ‘background’ risk of mesothelioma (the level that would be expected in the absence of asbestos exposure), A hypothetical group of men with zero exposure to asbestos would record” PMR of approximately 6. . . . An occupational group with a PMR greater than 100 indicates that the level of mesothelioma mortality is higher than average for all occupations.²³

Disregarding this evidence, Teta et al. review SEER data and make the circular argument that mesotheliomas that occur in this cohort are, by definition, not caused by asbestos because the subjects were by definition not exposed, and therefore all cases are unrelated to asbestos.¹⁵ But if the mesothelioma cases were not exposed to asbestos why look at any death data? Everyone agrees that absent exposure, asbestos is not a cause of mesothelioma. Teta et al. attempt to use mesothelioma rates to “prove” there were no exposures. SEER data cannot answer this question; exposure information can only come from patient histories and/or pathologic studies.

These papers are an example of using the wrong tool (epidemiology) and the wrong data (SEER) set to obtain a desired answer to a question.²⁴ Since all citizens in developed countries have lung asbestos burdens, there is no unexposed control group. There are many case reports of patients who developed mesothelioma after short, low-dose exposure. Most experts believe asbestos caused these cases.^{18,25-38} Epidemiology based on the SEER data cannot answer the question about the effects of low-dose exposure to asbestos because it includes no exposure data, and because the pathologic diagnosis of mesothelioma can be confused with other cancers (such as lung or ovarian), has changed over time, and can be