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LETTER TO THE EDITOR

Editorial Note. Letters to the Editor are peer reviewed to ensure that the arguments are reasonable and clearly expressed. However, letters may express a particular opinion rather than a balanced interpretation. Authors of papers commented on are invited to reply, but neither the journal nor peer reviewers should be assumed to support the arguments made.

Thinking about Occupation–Response and Exposure–Response Relationships: Vehicle Mechanics, Chrysotile, and Mesothelioma

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The 2015 paper by Garabrant *et al.* (2016), Mesothelioma among Motor Vehicle Mechanics: An Updated Review and Meta-analysis, includes our 1997 paper (Teschke *et al.*, 1997) as a 'tier 1' study in the meta-analysis.

About a decade after our paper (Teschke *et al.*, 1997) was published, it came to my attention that it had been used regularly in litigation related to mesothelioma in people who had worked as vehicle mechanics or in brake repair. I do not normally accept legal work, but agreed to take part as an expert witness in one case to point out some problems in interpretation of epidemiological evidence such as ours in these cases. It seems possible that this new meta-analysis will be used in the same way as our individual paper, so I thought it may be useful to present the issues in a more public forum. I will focus on two questions.

The first question addresses the statement at the beginning of the review paper (Garabrant *et al.*, 2016): are studies of motor vehicle repair activities and brake repair activities appropriate settings to examine the risks of mesothelioma from chrysotile exposure?

The issue of interest is whether chrysotile asbestos causes mesothelioma. It may be reasonable to study jobs or tasks to investigate this question, but note that the jobs or tasks are being used as surrogates of chrysotile exposure. It is important to consider whether they are good surrogates. Some occupations are synonymous with extensive exposure to certain agents. For example, it would be a rare wood furniture maker who did not have daily high exposure to hard wood dust and an exceptional asbestos insulator without daily high exposure to amphibole asbestos. For such jobs, the association between the occupation and a disease

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may be virtually equivalent to the association between its predominant exposure and that disease. Many jobs have much more variable exposures. For example, some nurses are regularly exposed to anesthetic gases and others are rarely or never exposed. Examining the relationship between nursing and spontaneous abortion is not equivalent to examining exposure to anesthetic gases and that outcome. Because exposures are so variable within the occupation, any true 'exposure–response' relationship will be attenuated or not observable when examined instead via an 'occupation–response' analysis.

In the case of vehicle mechanics, brake repair work is not consistently performed. Three studies (Woitowitz and Rödelsperger, 1994; Teschke *et al.*, 1997; Rake *et al.*, 2009) cited in the meta-analysis (Garabrant *et al.*, 2016) included information on subjects' brake repair work separately from vehicle mechanic occupation; at least 34% of the vehicle mechanics reported no brake repair work. Yet of the 16 studies included in the meta-analysis (Garabrant *et al.*, 2016), 12 examined only the vehicle mechanic job or even broader job categories such as garage workers, auto repair and related services, and auto engineers. It is reasonable to expect that many in these categories had chrysotile exposures similar to background levels in the population.

What about brake repair work itself? Four studies (Woitowitz and Rödelsperger, 1994; Teschke *et al.*, 1997; Hessel *et al.*, 2004; Rake *et al.*, 2009) in the meta-analysis reported on brake repair. The era of potentially etiologic exposure in these studies was dominantly long prior to 1980, a period when vehicle mechanics largely worked in gas stations and brake work was one possible task of many within the job. The frequency of exposure was likely to be intermittent, though it is possible that rare subjects may have worked in specialized brake shops and done this task repeatedly every day all day for most of their careers.

Interpretation of the results of the studies included in the meta-analysis (Garabrant *et al.*, 2016) should acknowledge the likelihood that many vehicle mechanics had done no brake repair work and that of those who had, most would have done so infrequently as part of a broad array of activities. This means that both the vehicle mechanic occupation and the brake repair task are unlikely to be good surrogates of chrysotile exposure. Associations between the occupation or task and mesothelioma were likely attenuated by subjects with background or low exposure levels. Other occupational groups, such as chrysotile textile workers, may be more appropriate occupations to study. The most reliable epidemiological study would measure chrysotile exposure and assess the 'exposure–response' relationship, not count on an occupation or task to act as an exposure surrogate. Even with 'exposure–response' analyses, data quality can make a profound difference in the strength of an observed relationship; for example, a 9-fold stronger relationship between chrysotile and mesothelioma was observed with better exposure data (Burdorf and Heederik, 2011).

The second question addresses an issue that is raised in litigation and workers' compensation: is it appropriate to require evidence of elevated associations between an occupation and a disease to ascertain whether someone incurred the disease as a result of exposures in that occupation?

The answer must be 'no'. Answering 'yes' requires that every person who has a disease arising from workplace exposure provide epidemiological evidence that their specific job has an elevated risk of that disease. Of course, it is impossible to study every occupation–disease relationship. In addition, even where a job has been studied, the potential for variable exposures within a job to dilute the relationship is probable for many jobs, and would preclude a person with high exposures from having their occupational disease recognized, simply because others in the same job were not similarly exposed. The question is whether the exposure caused the disease. A job cannot cause disease, its exposures may.

It may be helpful to think of this in another way. Studies of chrysotile miners and textile workers have found elevated risks of mesothelioma (International Agency for Research on Cancer, 2012), whereas studies of vehicle mechanics and brake repair workers typically have not (Garabrant *et al.*, 2016). Does this mean that vehicle mechanics and brake repair workers are somehow immune to the effects of asbestos, that they are especially resistant, superhuman? No, they simply work in a job that has very varied exposures, so detecting occupation–disease relationships is difficult. In other words, the effects of chrysotile are not properly assessed via the surrogate measures of exposure 'vehicle mechanic' or 'brake repair'.

For people with mesothelioma who have been exposed to chrysotile in their job, the first question to ask is whether chrysotile causes mesothelioma

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(International Agency for Research on Cancer, 2012). If so, the next question is whether they had sufficient exposure to cause mesothelioma. For some the answer will be yes, and for others the answer may be no. The question of what constitutes sufficient exposure is not simple to answer. In some jurisdictions, workers' compensation boards have a presumption in favor of compensation where a person has any workplace exposure to asbestos and a diagnosis of mesothelioma. Others consider duration of exposure and/or intensity of exposure. Note that exposure, appropriately, is the focus.

DECLARATION

I was the first author of one of the studies reviewed in the Garabrant *et al.* article. In 2011–2012, I acted as an expert witness at the request of the Ruckdeschel Law Firm in a mesothelioma case to explain problems with interpretation of epidemiological studies such as ours. This is also the motivation for this letter. I wrote the letter, its contents are solely mine, and I received no funding related to it. No one other than reviewers and editors of the *Annals of Occupational Hygiene* saw this letter prior to it being accepted for publication.

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