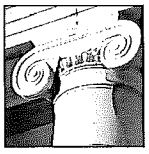


The Causation of Lung Cancer:
How Much Does Asbestos Really Contribute?

A Commentary by Mark G. Zellmer of Husch Blackwell LLP
Author bio on page 10

In his book with Douglas Lee, Irving Selikoff states that often-forgotten truism that among a group of people who have been exposed to asbestos and develop lung cancer, many of those cases of lung cancer would have occurred even if the people had never been exposed.[1] In fact, of all lung cancer cases, tobacco smoking is the cause 85 to 90 percent of the time.[2] What is the standard of causation for asbestos exposure in lung cancer cases and how is it to be applied?

Because trials and appeals are more frequent in mesothelioma than lung cancer cases, much of the case law on specific causation relates to mesothelioma rather than lung cancer. This should not matter, as the principles of causation should be the same regardless of the disease; only the conclusions reached from application of those principles to the specific facts should change. The case law on causation can be classified into a few categories.

Some courts allow plaintiff experts to testify and send the case to the jury based only on testimony that "each and every" exposure above background is a substantial cause of the plaintiff's disease.[3] This view has become distinctly the minority view for courts that have recently examined this issue. The courts that utilize this approach find that the issue of causation is a question of fact exclusively within the province of the jury.

Other courts follow the "substantial factor" test more strictly and refuse to allow plaintiff experts to opine that "each and every" exposure is causative of the plaintiff's disease.[4] These courts have a number of reasons for ruling in this manner:

- Such testimony is contrary to the nature of the substantial factor test because it allows the jury to conclude that any exposure, no matter how insubstantial has caused the plaintiff's disease.

- No peer-reviewed scientific literature provides a basis for this view of disease causation — as the late Kevin Browne, as well as others, have observed, the lungs have defenses which the exposure must overcome to cause disease.

- Testimony that "each and every" exposure substantially contributes is inconsistent with the concept that asbestos-associated diseases are dose-response diseases, i.e. the risk of disease increases with increasing dose.

A number of courts have followed the "*Lohrmann*" test of causation, also known as the "frequency, proximity and regularity" standard. In general, these courts have not defined exactly what exposures meet the standard of "frequency, proximity and regularity," and, instead, have left such questions to adjudication on a case-by-case basis.[5] Testimony that "each and every" exposure contributes would seem to be just as much inconsistent with a requirement of "frequency, proximity and regularity," as such testimony is inconsistent with "substantial factor" causation. Exposures that are infrequent or remote cannot meet a standard of "frequency, proximity and regularity," even if an expert is willing to opine that "each and every" exposure contributes.

Certain courts have taken the issue a step further, requiring that in order to submit the case to the jury, a plaintiff must show that the exposure for which a defendant is responsible is sufficient to cause the plaintiff's disease. Most of these cases have not defined well what may be a sufficient exposure.[6]

At least one court has professed to follow "but for" causation even though plaintiff experts admitted that they could not say that plaintiff would have suffered his disease but for the exposure that he had sustained. The court held that the parties were reading Missouri's standard of "but for" causation too strictly and that the plaintiff could submit the case to the jury even under "but for" causation because the plaintiff had proven exposure sufficiently as to one defendant. The court noted that more than one cause including exposure for which a defendant is responsible may combine to cause an injury. Whether other Missouri courts

will follow "but for" causation more strictly is an open question, but this decision in its reasoning and result seems rather similar to other decisions that have required proof of sufficient exposure by a defendant to cause the plaintiff's disease.[7]

Sufficient Dose and Asbestosis

If the courts are asking plaintiffs to prove a sufficient dose to prove causation, then what is a sufficient dose?

The answer begins with a historical note. In 1955, Richard Doll published his seminal work about lung cancer among the workers at Turner & Newall. He found an excess of lung cancer incidence among the workers in this asbestos product manufacturing facility. All of those with lung cancer also had asbestosis. He concluded that the regulations intended to prevent exposures causative of asbestosis would also prevent lung cancer.[8]

Further epidemiological research confirmed that lung cancer from asbestos occurs only in the presence of asbestosis.[9] As a result, asbestosis is a prerequisite to the diagnosis of an asbestos-related lung cancer.[10] In fact, the only consistently reliable marker for an asbestos-related lung cancer is asbestosis, especially in asbestos workers who smoke.[11]
Kevin Browne, referring to asbestosis, opines that heavy exposure to asbestos is necessary to cause lung cancer.[12]
Although certainly not unanimous on the exact cumulative exposure, the scientific literature indicates that cumulative exposure of 25 f/cc-years can be causative of asbestosis.[13] Another researcher recently found that both cumulative exposure and lung fiber burden are strongly correlated with severity of asbestosis. According to that research, the least cumulative exposure in a subject with asbestosis was 23.1 f/cc-years.[14]

A different school of thought suggests a somewhat similar but alternative theory of lung cancer caused by asbestos exposure. Under this theory, it is not the asbestosis but rather the dose of asbestos at a level high enough to cause asbestosis that actually causes an asbestos-related lung cancer even though the dose does not in fact cause asbestosis.[15] This would be a cumulative dose of asbestos of 25 f/cc-years, whether or not the plaintiff actually had asbestosis.

"The importance of this data cannot be understated. In any case of a person suing for lung cancer, defendants must focus not just on the amount of smoking, but the age at which the smoking habit began."

In *Mobil Oil Corporation v. Bailey*, the plaintiffs claimed that the decedent died of lung cancer due to asbestos exposure on the premises of the defendant.[16] The court examined the issue of whether asbestosis was a prerequisite for proof of causation of lung cancer by asbestos. The court apparently left open the possibility of such a ruling. The court found it unnecessary to reach that precise issue, rather, finding that plaintiffs had failed to offer any "scientifically reliable evidence" to show that asbestos exposure on the defendant's premises had caused the decedent's lung cancer. Noting that the decedent had a smoking history, the court held that the plaintiff had failed to exclude other possible causes of lung cancer. In particular, the court found that neither of the plaintiff experts had shown general acceptance of the theory that the effects of asbestos and cigarette smoking are synergistic. Without defining what more may be necessary, the court clearly thought that more evidence was needed than just testimony about decedent's history of exposure at the defendant's premises.[17]

This view of the causation of lung cancer is not unanimous. For example, Dr. Murrary Finkelstein opines that there is an increased risk of lung cancer among those without radiographc evidence of asbestosis and that the risk of lung cancer increases at "doses" below which radiographically evident fibrosis does not occur.[18] Finkelstein overstates his findings. Finkelstein notes that the mean cumulative exposure to asbestos among the subjects of the study is 101-137 f/cc-years.[19] This is well in excess of the 25 f/cc-years that is often cited as the amount of exposure necessary to cause asbestosis. His findings fail to support the view that asbestos-related lung cancer occurs at doses below which asbestosis will not be visible on radiography. And this is not the only problem with such research.

The Effect of Smoking Duration

The risk of lung cancer increases "far more strongly with each additional year of smoking than with each additional cigarette per day."[20] The risk of death from lung cancer is related more strongly to duration of smoking than to smoking

intensity.[21] Men between the ages 40-49 with an average smoking duration of 29 years show lung cancer mortality of 24/100,000 persons while men aged 70-79 with average smoking duration of 51 years show lung cancer mortality of 933/100,000 persons.[22]

Richard Peto's epidemiology on the effects of cigarette smoking demonstrates the same conclusions. He finds that a three-fold increase in the amount of smoking can increase lung cancer risk by three times while a three-fold increase in the duration of smoking can increase the incidence of lung cancer 100 times.[23] Specifically, for men who start smoking between ages 15-24, Peto's data shows that 20 years duration of smoking is associated with less than 10 deaths from lung cancer per 100,000 men while duration of 60 years leads to more than 1000 deaths from lung cancer per 100,000 men.[24]

The importance of this data cannot be understated. In any case of a person suing for lung cancer, defendants must focus not just on the amount of smoking, but the age at which the smoking habit began.

The data also has unexpected implications for the validity of research on the causes of lung cancer by asbestos, i.e. when smoking needs to be excluded as a confounder. Epidemiological studies that attempt to determine the degree to which asbestos causes lung cancer compare lung cancer rates of the group of asbestos-exposed workers with the lung cancer rates in the general population.[25]

Studies often merely cite a comparison to the general population without further assurance that the issue of smoking duration has been properly controlled in the calculations of risk of lung cancer.[26] This is the problem. If one group smokes in similar proportion to another group, but one of the groups has people who started smoking earlier, that group will have the higher lung cancer rate. That is the inescapable consequence of the fact that duration of smoking multiplies the risk of lung cancer 100-fold over 50 to 60 years. If the group of asbestos-exposed workers is, on average, older and smoked longer than the general population, the increasing risk from the duration of smoking will make the lung cancer rates among the asbestos-exposed workers appear larger; hence, asbestos may erroneously appear to have a larger effect in causing any elevated lung cancer rates. Even if the ages of the people in the control group are similar to the group of asbestos-exposed workers under study, differences in smoking habits between the general population and the studied group particularly affecting a difference in the duration of smoking can seriously impair the ultimate conclusions about the health effects of asbestos separate from cigarette smoking.

A short journey illustrating the methods used to calculate relative risk will show the potential impact of this problem. The following formula is used to calculate relative risk:

$$a/(a+b)/c/(c+d)=RR$$

a = smokers with lung cancer in the asbestos-exposed cohort
a+b = the entire asbestos-exposed cohort who also smokes
c = smokers with lung cancer in the control group
c+d = the entire control group of smokers

The general risk of lung cancer in the smoking population is approximately 100 out of 100,000 person years.[27] Assuming 35 persons with lung cancer in the cohort of 10,000 and 100 persons with lung cancer in the control group of 100,000 (risk lung cancer of 100 out of 100,000), the formula calculates a relative risk of 3.5:[28]

$$35/(35+9965)/100/(100+99,900)=$$
$$.0035/.001=3.5$$

Assuming that (1) the proportion of long duration smokers in the subject cohort is 1 percent greater than in the control group and (2) 25 percent of the long duration smokers contract lung cancer (a conservative number for a group potentially 100 times more likely to contract lung cancer), when the confounders are excluded, the numbers in the formula change as follows:

$$10/(10+9890)/100/(100+99,900)=$$
$$.0010101/.001=1.01$$

When the formula is corrected for duration of smoking, relative risk changes from 3.5 to 1.0101. The apparent risk from asbestos exposure has virtually disappeared.[29] In addition, for this relative risk, the 95 percent confidence interval is 0.8097 to 1.2457 which, not surprisingly, crosses one and is thereby not statistically significant.[30]

Calculation of relative risk for exposure to asbestos is not accurate unless the confounding effects of smoking are fully removed, including any confounding effects from smoking of long-term duration among the cohort subject to study.

Multiplicative or Additive Risk

For any lung cancer case involving a long-term smoker, defendants must face the argument that asbestos exposure and cigarette smoking cause lung cancer through a synergistic effect on the human lungs. Having heard this concept, authors today repeat the argument without critical analysis or without appropriate citation to scientific literature. At best, the argument badly stretches the science. At worst, the science itself is suspect.

Peto, a member of the Imperial Cancer Research Fund in Great Britain, cites the usual numbers. Relative risk of lung cancer without smoking or asbestos exposure is, of course, 1. Relative risk of lung cancer among smokers is 11, while such risk

among the population exposed to asbestos without smoking is 5. Risk of lung cancer among smokers obviously varies greatly based on a number of factors, e.g. longevity of smoking, amount of smoking per day, total cumulative dose of cigarette smoke. The relative risk of lung cancer is 53 for smokers also exposed to asbestos. Peto emphasizes that this multiplicative effect is only found among those who experience "high asbestos exposure" which means "prolonged employment as a lagger before 1968." Such conditions seldom exist in other occupations or later time frames.[31] Wanton application of the multiplicative risk of smoking and asbestos to workers not similarly exposed simply lacks scientific basis.

More recent research has even called into question whether there is in fact even any synergistic risk from smoking and asbestos; rather, such research has shown that risk for smoking and asbestos exposure is additive.[32] Irving Selikoff, whose studies helped grow the idea of a synergistic or multiplicative effect from smoking and asbestos, admitted in 1978 that evidence of a relationship between asbestos and lung cancer, even among smokers, is "not strong."[33]

This is not just an academic exercise. When the risk is only additive, a five-week exposure to a particular product may not appear to have substantial consequence compared to a 40-year smoking habit. Assuming that asbestos is less carcinogenic than cigarette smoke for the induction of lung cancer in a ratio of 5/11, the following calculation demonstrates the comparative contribution to risk from asbestos exposure over five weeks as compared to 40 years of smoking:

(5/11)(5 weeks/50 work weeks per year)/(40 years x 52 weeks per year) =0.00002185.

Considering such a miniscule, comparative risk, it is little wonder that plaintiff counsel presses the claim of the synergistic effects from asbestos and smoking.

Lung Cancer without Cigarette Smoking

Obviously, mesothelioma cases differ from lung cancer cases. The difference most highlighted is that smoking will cause lung cancer. Without cigarette smoking, the difference between a mesothelioma and lung cancer is still substantial. The advantage in a mesothelioma case for plaintiffs is that their experts argue that most cases of mesothelioma studied in epidemiology involve a history of asbestos exposure. They cite that, regardless of the percentage of mesothelioma cases that are expected to occur without asbestos exposure or even without any known cause, the percentage of mesothelioma occurrences with exposure to asbestos outnumber the percentage of cases occurring without asbestos exposure.

The situation is the reverse for lung cancer. In research that identifies increased lung cancer among asbestos exposed workers, more than twice as many instances of lung cancer occur without asbestos exposure and without cigarette smoking than occur among persons exposed to asbestos.[34]

In fact, the degree to which asbestos causes lung cancer among non-smokers is in doubt. "In the absence of smoking, there may be an increase in the prevalence of [lung cancer] but it is not significant."[35] To understand this more fully, the effects of asbestos can be studied among persons who cease smoking or never smoked. Hammond, Selikoff and Seidman performed such work.[36] The results of their study of deaths among asbestos-exposed workers 20 years after the onset of exposure are highlighted at the bottom of this page.

Once the effects of smoking are removed, deaths from lung cancer among asbestos exposed workers are substantially less than expected. It is little wonder that Selikoff always emphasized the need for asbestos workers to quit smoking.[37]

Plaintiffs should not be allowed to imply, and juries should be reminded that they should not presume, that a person's lung cancer came from asbestos exposure just because such person claims a history of asbestos exposure.[38] For non-smoking lung cancer cases, the court should still be require proof that plaintiff has asbestosis and that defendant exposed plaintiff to products that would sufficiently cause his or her disease.

Declining or Disappearing Risk

In his 2010 article on lung cancer among cement workers, Dr. Finkelstein a follow-up of the cohort. Based upon a study period of 1968-1985, he had originally calculated the risk of lung cancer in the cohort among those without radiographic evidence of asbestosis, alternatively after latencies of 20 and 25 years from first exposure. He recalculated lung cancer risk based upon the follow up during 1986-1997. The results can be seen on page 8.

Smoking History	Lung cancer	
	Observed deaths	Expected deaths
Ex-smoker, 5-9 yrs	5	9.8
Ex-smoker, 10+ yrs	3	24.2
Never smoked	5	35.5

Period of follow up	SMR for subjects w/o radiographic asbestosis at 20 years latency	SMR for subjects w/o radiographic asbestosis at 25 years latency
1968-1985	5.6 (2.9-9.8)	3.76 (1.03-9.66)
1986-1997	2.18 (0.71-5.1)	3.6 (0.98-9.23)

Interestingly, the data in the 1986-1997 follow-up period is not statistically significant. Dr. Finkelstein offers no explanation. The decline in risk to a level not statistically significant calls into question his conclusions about asbestos as a cause of lung cancer in those without radiographic evidence of asbestosis.

The statistically non-significant risk of lung cancer in the later follow-up period could be due to cessation of smoking. The data has already been presented in this paper showing the precipitous decline in risk among former smokers even when exposed to asbestos. If cessation of smoking explains Dr. Finkelstein's results, any risk would likely be the result of tobacco use and not asbestos.

Another explanation may be supportable. After a certain number of years from exposure, the increased risk of lung cancer from asbestos exposure may disappear. Some authors suggest a three phase model for carcinogenesis of lung cancer from environmental carcinogens:

- *Initiation*: a susceptible stem cell transforms into an intermediate stage with one or more mutations and possibly accompanied by epigenetic changes without loss of relevance of the model form.
- *Promotion*: if there is clonal expansion of the intermediate cells, probability is increased that initiated cells will undergo an additional genetic change leading to malignant transformation.
- *Progression*: malignant conversion actually occurs.

Consistent with this model, these researchers find strong evidence that asbestos appears to act early in the process of lung carcinogenesis and that there is no evidence of a later-stage effect. Epidemiology adds weight to this conclusion, demonstrating that the risk of lung cancer is strongly associated with exposures occurring 20-24 years before lung cancer death with little or no risk associated with exposures at any other time.[39] In other words, when a person's exposure is more than 24 years before his lung cancer death, his asbestos exposure is not likely the cause of his lung cancer. Dr. Finkelstein's statistically non-significant risk of lung cancer in the later follow up period could be due to this disappearance of risk following a certain period after exposure, that being more than 24 years.

Sufficient Cause

If a defendant's conduct exposes plaintiff to asbestos and raises his or her risk of lung cancer by 0.00001 percent, should a defendant be held responsible to plaintiff if he or she gets lung cancer? If a defendant releases asbestos that exposes plaintiff in a small amount ten miles, or even five miles from the source of exposure, should defendant be held responsible to plaintiff if he or she gets lung cancer? If a defendant's conduct increases plaintiff's cumulative exposure to asbestos by 0.0001 f/cc-years, should defendant be held responsible to plaintiff if he or she gets lung cancer? There must be some limit to a plaintiff's right to submit the case to the jury. None of these hypothetical situations comport either the "substantial factor" test or the "*Lohrmann*" test of frequency, regularity and proximity. None of these hypothetical situations comport with a need for plaintiff to prove that the exposure was sufficient to cause the plaintiff's lung cancer.

The Court's decision in *Wannall v. Honeywell International Inc.* found that a plaintiff's proof of exposure was not sufficient to support lung cancer claims.[40] One court has provided definite guidelines; in *Borg-Warner Corp. v. Flores*, the Texas Supreme Court finds that plaintiff, to submit his case to the jury, must prove that the exposure for which defendant is responsible doubled plaintiff's risk of his disease.[41] *Borg-Warner* is a particularly instructive opinion because the underlying disease of plaintiff was asbestosis. It is asbestosis that is in turn related to the risk of lung cancer.

Some may disagree with the standard that is set in *Borg-Warner*. Maybe it should be higher or lower. Maybe it should be set as some number of fibers per cubic-centimeter-years. Maybe the standard should be set in some other manner. But, make no mistake — the standard should be set so that plaintiff may go to the jury only when he has proven sufficient exposure, an exposure in fact that is sufficient to cause his disease.

Conclusion

As a practical matter, defendants should take one or more steps in lung cancer cases:

❖ The Court should be urged to require that plaintiff prove that he has asbestosis and that the defendant exposed the plaintiff at a level sufficient to cause asbestosis, a cumulative dose of 25 f/cc-years. Plaintiff studies on the cause of lung cancer should be the subject of objections unless smoking as a confounder is properly eliminated.

❖ Through motion *in limine* or objection, plaintiff should not be allowed to argue that smoking and lung cancer are multiplicative or synergistic risks, especially if plaintiff is not a lagger exposed before 1968.

❖ The Court should be urged to require the same proof from plaintiff in a non-smoking lung cancer case, as plaintiff's claim of causation does not improve just because he does not smoke. The Court should be asked for a directed verdict or summary judgment if the exposure was too long ago to present a risk of lung cancer to plaintiff.

Footnotes

[1] Selikoff, I.J. et al. *Asbestos and Disease.* (Academic Press: 1978) at 309.

[2] Williams, M.D., et al. "The Epidemiology of Lung Cancer." *Cancer Treatment and Research.* 105: 31 (2001).

[3] *Wolfinger v. 20th Century Glove Corporation of Texas*, No, 1393 EDA 2011 (Pa. Super. Ct..2013); *Robertson v. Doug Ashy Building Materials, Inc.*, 77 So.3d 323 (La.App. 2011).

[4] *Betz v. Pneumo Abex LLC*, 44 A.3d 27 (Pa. 2012); Smith v. Ford Motor Company, Case No. 2:08-cv-630 (Utah Dis.Ct. 2013); *Lindstrom v. A-C Prod. Liab. Trust*, 424 F.3d 488 (6th Cir. 2005); *Wills v. Amerada Hess Corporation*, 379 F.3d 32, 40, 53 (2d Cir. 2004); *Georgia Pacific Corporation v. Stephens*, 239 S.W.3d 304, 321 (Tex.App. 2007); *Smith v. Kelly Moore Paint Company*, 307 S.W.3d 829, 839 (Tex.App. 2010); *Butler v. Union Carbide Corporation*, 310 Ga.App. 21, 712 S.E.2d 537 (2011); *Sclafani v. Air & Liquid Systems Corporation*, No. 12-3013 (Cal.Dis.Ct. 2012).

[5] *Lohrmann v. Pittsburgh Corning Corporation*, 782 F.2d 1156 (4th Cir. 1986); *Chism v. W.R. Grace & Company*, 158 F.3d 988, 992 (8th Cir. 1998).

[6] *Wannall v. Honeywell International Inc.* No. 10-351 (D.C. Dis.Ct. 2013); *Dixon v. Ford Motor Company*, Md.Ct. Spec.App. 2012WL2483315); Moeller v. *Garlock Sealing Technologies, LLC*, 660 F.3d 950, 952 (6th Cir. 2011).

[7] *Wagner v. Bondex International Inc.*, 368 S.W.2d 340 (Mo.App. 2012).

[8] Doll, R. "Mortality from Lung Cancer in Asbestos Workers." *British Journal of Industrial Medicine.* 12: 81, 86 (1955).

[9] Browne, K. "The Quantitative Risks of Mesothelioma and Lung Cancer in Relation to Asbestos Exposure (letter to the editors)." *Annals of Occupational Hygiene* 45:327-329 (2001).

[10] Cagle, P. T. "Criteria for Attributing Lung Cancer to Asbestos Exposure." *American Journal of Clinical Pathology.* 117:9, 14 (2002).

[11] *Id.*

[12] Browne, *supra.*

[13] Henderson, Douglas W. "Letter to the Editor – Commentary regarding the Article by Fischer et al.: Fibre Years, Pulmonary Asbestos Burden and Asbestosis. Int. J. Hyg. Environ. Health 205: 245-248 (2002)." *International Journal of Hygiene and Environmental Health,* 206: 249, 250 (2003) (citing various sources including the Ontario Royal Commission, greater than 25 f/cc-years; South Carolina chrysotile textile cohort, greater than 20 f/cc-years; Helsinki Criteria requiring 25 f/cc-years or more to attribute lung cancer to asbestos).

[14] Mastrangelo, G. et al. "Asbestos Exposure and Benign Asbestos Diseases in 772 Formerly Exposed Workers: Dose-Response Relationships." *American Journal of Industrial Medicine.* 52: 596, 598 (2009).

[15] Henderson, D.W. et al. "Asbestos, Asbestosis, and Cancer: the Helsinki Criteria for Diagnosis and Attribution." *Scandanavian Journal of Work and Environmental Health.* 23: 311-316 (1997); Roggli, V. et al. *Pathology of Asbestos- Associated Diseases* 2d ed. (Springer, New York: 2003) at 197.

[16] 187 S.W.3d 265 (Tex. App. 2006).

[17] *Id.*

[18] Finkelstein, M. "Radiographic Asbestosis Is Not a Prerequisite for Asbestos-Associated Lung Cancer in Ontario Asbestos-Cement Workers." *American Journal of Industrial Medicine.* 53: 1065, 1069 (2010).

[19] Finkelstein, M. "Radiographic Asbestosis Is Not a Prerequisite for Asbestos-Associated Lung Cancer in Ontario Asbestos-Cement Workers." *American Journal of Industrial Medicine.* 32:341 (1997).

[20] Flanders, W. D. et al, "Lung Cancer Mortality in Relation to Age, Duration of Smoking, and Daily Cigarette Consumption: Results from Cancer Prevention Study II." *Cancer Research* 63: 6556, 6559 (2003).

[21] *Id. at 6561.*

[22] The term "persons" includes both smokers and non-smokers.

[23] Peto, R., "Influence of Dose and Duration of Smoking on Lung Cancer Rates." *Tobacco: A Major International Health Hazard* 23, 24 World Health Organization/International Agency for Research on Cancer: 1986.

"Plaintiffs should not be allowed to imply, and juries should be reminded that they should not presume, that a person's lung cancer came from asbestos exposure just because such person claims a history of asbestos exposure."

[24] Id. at 25. The term "men" includes both smokers and non-smokers.

[25] See Finkelstein, M. "Radiographic Asbestosis Is Not a Prerequisite for Asbestos-Associated Lung Cancer in Ontario Asbestos-Cement Workers." *American Journal of Industrial Medicine* 32:341 (1997) (comparison of a group of asbestos cement workers with the general population).

[26] *Id.*

[27] Thun, J.M. et al. "Age and the Exposure-Response Relationships Between Cigarette Smoking and Premature Death in Cancer Prevention Study II." *Changes in Cigarette-Related Disease Risks and Their Implication for Prevention and Control* 383, 396 (National Cancer Institute: 1995).

[28] Calculations based upon person years actually reflect a different level of risk than calculations based upon persons. For ease of this illustration, the fraction 100/100,000 is used.

[29] These input numbers were selected to show how relatively small changes may have a substantial effect on the outcome. On the other hand the numbers were not selected at random. For example, the relative risk of 3.5 is close to the relative risk that Finkelstein determines in his 2010 article.

[30] One method to calculate the 95 percent confidence interval is the following: (1) determine the lognormal of the relative risk; (2) apply the formula ((b/a)/(a+/b))+((d/c)/(c+d)); (3) the formula result is multiplied by 1.96 (standard deviation of 2 or 2.0-(0.05-0.01); (4) the result in #3 is added to and subtracted from the lognormal of the relative risk; and (5) the antilog of the two numbers in #4 are determined to provide the upper and lower limits of the confidence interval.

[31] Peto, R., "Influence of Dose and Duration of Smoking on Lung Cancer Rates." *Tobacco: A Major International Health Hazard* 23, 31 World Health Organization/International Agency for Research on Cancer: 1986.

[32] Liddell, F.D. and B.G. Armstrong. "The Combination of Effects on Lung Cancer of Cigarette Smoking and Exposure in Quebec Chrysotile Miners and Millers." *Annals of Occupational Hygiene,* Volume 46, No. 1, January 2002: 5-13 (the multiplicative hypothesis is untenable and the data favors an additive model); Gustavsson P, Nuberg F. "Low-Dose Exposure to Asbestos and Lung Cancer: Dose-Response Relations and Interaction with Smoking in a Population-Based Case Referent Study in Stockholm, Sweden." *American Journal of Epidemiology.* 2001; 155:1016-1022 (exposure to both asbestos and cigarette smoke have a joint effect that is only slightly in excess of additive and is not a synergistic/multiplicative risk).

[33] Selikoff, I.J. et al. *Asbestos and Disease.* (Academic Press: 1978) at 336.

[34] Kishimoto, T. et al. "Clinical Study of Asbestos-related lung cancer in Japan with Special Reference to Occupational History." *Cancer Science.* 101: 1194, 1195 (2010) (20.4 percent of lung cancer without either asbestos exposure or smoking and 9.9 percent of the lung cancer subjects with asbestos exposure who did not smoke).

[35] Selikoff, I.J. et al. *Asbestos and Disease.* (Academic Press: 1978) at 336; Selikoff, I.J. et al. "Asbestos Exposure, Smoking and Neoplasia." *Journal of the American Medical Association.* 204:106, 109 (1968)(exposure to asbestos not an extremely high risk of lung cancer among non-smokers).

[36] Hammond, E.C., et al, "Asbestos Exposure, Cigarette Smoking and Death Rates." *Annals of the New York Academy of Sciences* 473, 483 (1979).

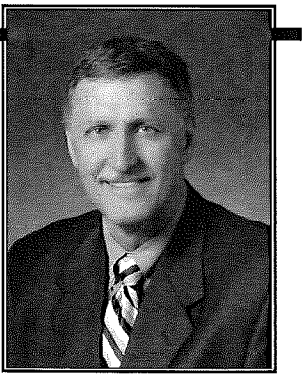
[37] Selikoff, I.J. et al. "Asbestos Exposure, Smoking and Neoplasia." *Journal of the American Medical Association.* 204:106, 109 (1968).

[38] *Mobil Oil Corporation v. Bailey,* 187 S.W.3d 265 (Tex. App. 2006).

[39] Zeka, A. et al. "The Two-Stage Clonal Expansion Model in Occupational Cancer Epidemiology: Results from Three Cohort Studies." *Occupational and Environmental Medicine.* 68: 618, 623 (2011)(the two phases to which the authors refer are initiation and promotion).

[40] No. 10-351 (D.C. Dis.Ct. 2013)

[41] 232 S.W.3d 765 (Tex. 2007); *Merrell Dow Pharm. Inc. v. Havner,* 953 S.W.2d 706 (Tex. 1997); *Robinson v. Crown Cork & Seal Co. Inc.,* 335 S.W.3d 126 (Tex. 2010).



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