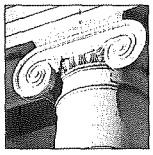



# Still Not Probable:
## A Reply to Impossible Not To Be Probable

*A Reply from Mark G. Zellmer of Husch Blackwell LLP*
*Author bio on page 8*

As presented in this publication in October 2019, Bayes' Theorem provides a format to determine the probability that a particular exposure to asbestos caused, or materially contributed to cause, mesothelioma.[1] Studies suggesting that significant exposure to asbestos causes mesothelioma do not prove or even imply that lower exposure causes the disease. Indeed, it is distinctly improbable that low exposures are causative. This determination is key as the law requires a finding that causation is more probable than not.

An article in the November 2019 issue of this publication presents a position to the contrary. The effort to address the assertions of the November 2019 article in this present article will hopefully provide insight about the usefulness of Bayes' Theorem in assessing causation in toxic tort cases. At the start of each section of this article, an assertion made in the November 2019 article will be quoted or summarized. A response then follows along with an explanation of that response.

**Assertion #1 from the November article: application of probability theory to causation in mesothelioma cases is an effort to prove that nothing causes mesothelioma.**

**Response to #1: Bayes' Theorem shows that low-dose exposures are highly unlikely to have caused mesothelioma.**

The November 2019, article contains a number of misstatements about what was intended to be shown in the effort to apply Bayes' Theorem to causation in asbestos cases. For example, according to the November article, the October article was intended to show that:

- "absolutely no exposures are probable to cause an individual's disease" or
- "numerous equations prove that *nothing* causes mesothelioma"

Such misstatements could not be further from the substance of what is stated in the October article. Quoting from the October article:

> Even accepting the "no threshold" concept, the result of an asbestos-associated disease from some exposures is so improbable that plaintiffs cannot meet appropriate legal standards for proof of causation. (*emphasis added*)

In fact, the October article contains a section discussing that doses of exposure incurred by insulation workers were highly probable to have caused their mesothelioma. Such misstatements in the November article stem from at least two sources.

First, the November article refers to the Selikoff insulator cohort stating that "only 8.33 percent of workers develop the disease."[2] It is true that only a "small" percentage of insulators contracted mesothelioma. Published reports of various cohorts do not show that the occurrence of mesothelioma reached anywhere near a majority of the deaths in any cohort even among the most highly exposed workers. The November article misconstrues what the October article examined, namely what was the probability that a particular low dose of exposure to asbestos caused a person's mesothelioma. This misconstruction is central to the problem with the November 2019 article. Nowhere in that November article does the author ever address the probability of particular doses of exposure as the cause of mesothelioma.

Second, the November article misapplies the theory of probability, to-wit: "an individual *actually* has the disease (thus, in hindsight, has 100 percent probability of getting the disease)." Probability simply does not work in this manner. This statement is the same as saying that a coin turning up heads was in hindsight 100 percent likely to be heads once it was flipped. Probability is applied to events and the relationships between events about which there are aspects that are not or cannot be completely known. Assuming by definition that every exposure materially contributes to cause a disease simply defines and assumes a situation in which probability has no role. Doctors and other experts testifying for plaintiffs cannot opine that a person would or would not have contracted mesothelioma depending on whether that person had a particular dose of exposure to asbestos. They simply know that it may contribute in some amount to the overall risk of disease; however, that

somewhat begs the question. It is more appropriate to ask: what is the probability of having contracted mesothelioma from a particular exposure?

**Assertion #2 from the November article: asbestos exposure is the only known cause of mesothelioma, irrelevant theories of exposures to therapeutic radiation and Turkish erionite excepted.**[3]

**Response to #2: asbestos exposure is not the only known cause of mesothelioma.**

Plaintiffs have long attempted to use such a statement to justify the claim that every exposure to asbestos contributes to cause mesothelioma. Even if asbestos was the only cause of mesothelioma, it is not logical to assume that every exposure contributes to that causation.[4] Even wrongly assuming that asbestos is the only cause of mesothelioma does not change the value of a calculation of the probability that a particular exposure to asbestos caused mesothelioma. Hypothetically, person A is an insulator exposed to dust from work with amosite asbestos insulation made by two manufacturers, B & C, all on the same premises of company D for twenty years. The insulator, person A, can remember that, for a total of eight hours, he was a bystander to removal and installation of asbestos packing in a pumps manufactured by company E. Companies B, C, and D are all bankrupt or out of business. What is the probability that exposure to the packing as opposed to the exposure to insulation caused his mesothelioma? Bayes' Theorem is not needed to know that the likelihood is very low—in fact, too improbable to justify a judgment against company E. Yet, plaintiffs will argue that company E should alone be liable for person A's mesothelioma.

Any analysis of this claim requires an understanding of the causes of cancer.

***"Plaintiffs have long attempted to use such a statement to justify the claim that every exposure to asbestos contributes to cause mesothelioma. Even if asbestos was the only cause of mesothelioma, it is not logical to assume that every exposure contributes to that causation.***

Certainly, environmental exposures such as asbestos can cause cancer; however, random errors in replication of DNA when cells divide cause cancer. In addition to environmental exposure and erroneous DNA replication, heredity causes cancer. Mesothelioma is not a unique cancer with asbestos as its only cause.

Heredity as a cause of cancer, of course, refers to inherited genetic conditions. That genetic conditions cause mesothelioma independent of any asbestos exposure is now without dispute. A number of genetic pathways, unrelated to asbestos exposure, have been identified as the cause of mesothelioma. Among those is the recent example of the genetic condition known as Lynch Syndrome.[5] Lynch Syndrome is not alone as an inherited cause of mesothelioma. Researchers at Brigham and Women's Hospital found rearrangement of the ALK gene in young women with peritoneal mesothelioma.[6]

Random errors in replication of DNA when cells divide are responsible for two-thirds of all cancer.[7] Cells of human organs that divide more frequently are more subject to the occurrence of malignancy from these random errors in DNA replication.[8] Although less frequently than the cells of many other organs of the human body, mesothelial cells divide and, hence, replicate DNA, with the resulting risk of error and malignancy.[9] The lesser rate of replication likely explains why the background rate of spontaneous mesothelioma is low, particularly when compared to other cancers.

This claim that only asbestos causes mesothelioma is surprising. Dr. Arnold Brody, a frequent expert witness for plaintiffs, agrees that "any cancer can develop spontaneously from inherited genetic defects or from endogenous mutations . . ."[10]

Radiation and erionite as causes of mesothelioma are neither theoretical nor irrelevant. Therapeutic radiation as a cause of mesothelioma is well established. As one example, researchers studying a statistically robust number of patients (40576) treated with radiation for testicular cancer had a relative risk of pleural mesothelioma equal to four.[11] No one seriously disputes that erionite is a cause of mesothelioma. Even NIOSH has raised concerns about the risk of mesothelioma from deposits of erionite in the western United States.[12]

**Assertion #3 from the November article: application of Bayes' Theorem applied to medical screening tests can illustrate its application in a legal context**

**Response to #3: this is true, but Bayes Theorem must be applied correctly and its results must be interpreted correctly.**

The November article runs the numbers through Bayes' Theorem for a medical screening test for a hypothetical disease. That article does not contain all of the necessary data to apply Bayes' Theorem to a hypothetical medical screening test. Most prominently, for the application of Bayes' Theorem to medical screening tests, the calculations must include the percentage of people who do and do not have the disease in the relevant population. If cancer occurs in 5.2 percent of the relevant population and the test detects the cancer in 92 percent of the tests, but the test provides a false positive in 13 percent of the tests, what is the probability that a person who tests positive actually has this cancer? Applying those values, the following is an accurate application of Bayes' Theorem to a medical screening test:

| | Cancer = 5.2% | No Cancer = 94.8% |
|---|---|---|
| Positive Test | 92% | 13% |
| Negative Test | 8% | 87% |

| True Positive Test | False Positive Test |
|---|---|
| 0.92 x 0.052 = 0.04784 | 0.948 x 0.13 = 0.12324 |

| Test accuracy for cancer x % of population with cancer/ (True positive rate + False positive rate) |
|---|
| 0.92 x 0.052/(0.04784 + 0.12324) = 0.04784/0.17108 = 0.0279 = 27.9% |

Now, the value of Bayes' Theorem in a legal context becomes clear.[13] Assuming that a plaintiff's attorney needs to prove that his client has this cancer and has no other evidence that his client has this cancer, should plaintiff be allowed to go to the jury on the issue that he has this cancer? Of course not. A 27.9 percent probability that plaintiff has this cancer fails to meet the burden of proof and cannot justify a jury verdict.

The November article also posits that the probability that a person has a disease increases multiple times when the hypothetical test is rerun by a second doctor and again shows a positive result. This is not necessarily true. The hypothetical confuses what is a positive result and what is the meaning of a positive result. Indeed, a second, positive test increases the odds that the positive test result is correct. The degree to which various conditions can cause a positive result mean that the odds that a person has the relevant disease may not change at all or may not change much. Again, this is a function of the false positive rate and the degree to which the disease is found in the general population. In a legal context, when the rate of false positives and the rate of the disease in the population are considered, the resulting percentage may well not be in excess of 50 percent and thereby below the standard of proof.

This is exactly the lesson of the October article. The determination of the probability of an occurrence should not justify a verdict if the probability is less than the burden of proof (50 percent or less).

**Assertion #4 from the November article: "The P(A) should be .85, not the outrageously small .00049. What does the Court or Jury care about the millions and millions of people NEVER exposed to asbestos? . . . Why discard or ignore the relevant statistics reflecting specific causation in individuals in favor of population-based noise?"[14]**

**Response to #4: P(A) is the number of all cases of mesothelioma over the period studied divided by the U.S. population of 328 million. The inclusion of the United States population, including those millions not exposed, ultimately does not change the probability determined by the equation because that population figure of 328 million is included in both the numerator and the denominator. Statistics of this nature are of necessity based on populations, not individuals.**

To review, the equation from Bayes' Theorem is the following:

$$P(A/B) = \frac{P(B/A)P(A)}{P(B)}$$

The variables as explained and justified in the October article are the following:

P(B/A) = 0.85(1 f/cc-year/468.5 f/cc-years) = 0.0018142

P(A) = 163,000 being the number of cases of mesothelioma divided by 328 million

P(B) = 0.6138(29,000,000) divided by 328 million

The November article asserts that P(A) was ".00049." Although true, the rhetorical question from the November article ("[w]hat does the Court or Jury care

about the millions and millions of people NEVER exposed to asbestos") reflects a misunderstanding of the equation. The U.S. population of 328 million is included in both the numerator and the denominator. Those numbers then divide into each other and do not affect the final answer.

The November article also asserts that P(A) should be 0.85. That number, 0.85, is not part of P(A), but rather part of P(B/A). If the November article is actually a criticism intended to be directed at the calculation of P(B/A), the November article misconstrues the thesis of the October article, to-wit: a low dose exposure, e.g. 1 f/cc-yrs., is not a probable cause of mesothelioma and, hence, not consistent with the burden of proof. In other words, Bayes' Theorem was used to determine the probability of contracting mesothelioma from exposures of 1 f/cc-yrs, not from any and all exposures. If the calculation of P(B/A) was simply 85 percent, the percentage of persons with mesothelioma known to be exposed to asbestos, P(B/A) would include all exposures and would not be limited to the effects of exposures from a low dose such as 1 f/cc-yrs.[15]

The final part of assertion #4 suggests that decisions about causation should be based upon "statistics reflecting specific causation in individuals" rather than epidemiology. This is hard to understand. What are these statistics reflecting specific causation in individuals? No such statistics are cited in the November article. Epidemiological statistics are necessarily based on findings from the study and comparison of populations.

**Assertion #5 from the November article: causation of mesothelioma is assumed for any exposure to asbestos in any amount.**

**Response to #5: this is neither consistent with the law on causation nor an accurate determination of probability.**

The original article in October contains numerous citations about causation and probability in various states. Most importantly, causation is an issue at trial subject to the same jury instructions on burden of proof as every other issue. Those instructions on burden of proof are written in terms of probability stating that the finding must be essentially more probable or more likely than not.

The November article states that "an individual exposed to asbestos at any level is at a much higher probability of contracting cancer than a never-exposed individual." There are no calculations in the November article to justify the statement of a "much higher probability" of mesothelioma from exposures "at any level." There are not even citations to medical or scientific literature. Simply stating that there is no known safe level of exposure is not enough to prove that causation is probable. Even if it is assumed that the probability is "much higher," is it enough to meet the burden of proof?

The November article states that "the increase in probability, whatever the size, is where liability lays." In this manner plaintiffs attempt to eliminate causation as an issue in mesothelioma cases. This is really the crux of what plaintiffs want—recovery for all exposures, no matter how small, no matter what is the law. Yet, no law is cited in support of this statement. This statement is akin to taking the "substantial factor" test for causation and saying "no matter how small, it is still substantial." Before rejecting probabilistic calculations out of hand, everyone should consider the following hypothetical facts: the probability of getting a disease without exposure is 0.0001 and the exposure increases the probability by 10%. That is not enough to justify a finding of causation.

There is little dispute that the risk of mesothelioma increases with increasing dose.[16] Of course, dose response also implies decreasing risk with decreasing dose. Tellingly, the November 2019 article makes no meaningful mention of dose response and mesothelioma. Despite agreement with the concept of a dose response for mesothelioma, plaintiff's attorneys and their experts are loath to admit that the probability of the occurrence of mesothelioma from an exposure can be sufficiently low that it will not justify a finding of causation. Probability theory and Bayes' Theorem provide needed answers, but plaintiffs are resistant. For plaintiffs' attorneys, it is simply too inconvenient because causation becomes complicated to prove. For plaintiffs' attorneys, it is just not "right" for some recoveries against some defendants to slip away because some exposures are just too low to justify a recovery.

## Endnotes

[1] The definition of probability according to Wikipedia: "Probability is a numerical description of how likely an event is to occur or how likely it is that a proposition is true. Probability is a number between 0 and 1, where, roughly speaking, 0 indicates impossibility and 1 indicates certainty." (emphasis added)

[2] In fact the last numbers from Selikoff and co-authors show that approximately 9.3 percent of the deceased workers contracted mesothelioma. Selikoff, I. J. et al. "Asbestos-Associated Deaths among Insulation Workers in the United States and Canada, 1967-1987." *Annals of the New York Academy of Sciences.* Vol. 643 (1991) at 1, 7.

[3] Interestingly, the November article contains no citation to scientific or medical literature for this statement.

[4] Put in another way, why does the statement that asbestos is the only cause of mesothelioma mean that every exposure to asbestos causes the disease?

[5] Latham, A. et al. "Microsatellite Instability Is Associated With the Presence of Lynch Syndrome Pan-Cancer." *Journal of Clinical Oncology*. 107.012.191.158 (2018); Lu, Y. et al. "Metachronous Uterine Endometrioid Adenocarcinoma and Peritoneal Mesothelioma in Lynch Syndrome: A Case Report." *International Journal of Surgical Pathology*. Vol 25 (3) (2017) at 1.

[6] This is far more important than simply the basis for causation of mesothelioma as this discovery may lead to improved methods of treatment. https://www.sciencedaily.com/releases/2017/09/170914152347.htm

[7] Tomasetti, C. et al. "Stem Cell Divisions, Somatic Mutations, Cancer Etiology, and Cancer Prevention." *Science* Vol. 335(6331) (2017) at 1330. Doi: 10.1126/science.aaf9011.

[8] *Id.*

[9] Mutsaers, S. E. "The Mesothelial Cell." *The International Journal of Biochemistry and Cell Biology*. Vol. 36(1) (January, 2004) at 9-16.

[10] Brody, A.R. "How Inhaled Asbestos Causes Scarring and Cancer." *Current Respiratory Medical Reviews*. Vol. 14 (2018) at 204-217. He admittedly still wants to classify any exposure as causative.

[11] Travis, L.B. et al. "Second Cancers Among 40576 Testicular Cancer Patients: Focus on Long-term Survivors." *Journal of the National Cancer Institute*. Vol. 97(18) (September 21, 2005) at 1354, 1362.

[12] https://blogs.cdc.gov/niosh-science-blog/2011/11/22/erionite/

[13] The results for a true negative test and a false negative test are interesting:

| True negative test | False negative test |
|---|---|
| 0.948 x 0.87 = 0.82476 | 0.08 x 0.052 = 0.00416 |

This suggests that only 0.4 perecent of the time is the test negative when the patient actually has cancer.

[14] Before expressing these criticisms, the November article analogizes the use of Bayes' Theorem in this context to a man who emerges from a cave to see his first sunrise, i.e. the cave man has only a limited database from which to make a Bayesian calculation. The cave man analogy is extreme. It is true that there is much that we do not know about the causation of mesothelioma, but there is also much that we do know. What is known provides the opportunity to make calculations of the probable effect of an exposure to asbestos.

[15] In footnote 3, the November article discusses that "idiopathic" mesothelioma is often due to an "inaccurate and incomplete" work history. How is it known that the work history was incomplete or inaccurate? How is it known that a "better" work history would have found a credible history of exposure to asbestos? This appears to be speculation or assumption, namely that, if there is mesothelioma, asbestos must have caused it.

[16] Even government publications that plaintiffs cite agree that mesothelioma is a dose response disease. DDHS (NIOSH). *Workplace Exposure to Asbestos*, Publication No. 81-103 (April 1980) at 30-31. The document contains various errors about the sequelae of asbestos exposure, including the assumption of equal effect of amphiboles and chrysotile, but it confirms the concept of dose response.

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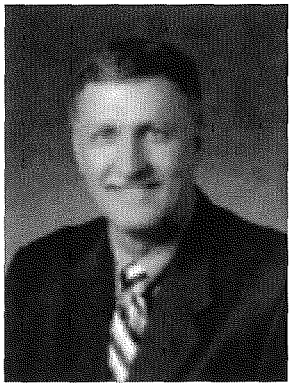

Zellmer speaks and writes extensively on products liability law and asbestos litigation. Such writing and presentation on asbestos litigation include subjects such as premises liability, application of statutes of limitations, medical causation, the litigation in historical context, and exclusivity of remedies under workers' compensation.

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