

Teratology, Toxicity, and Torts

MICHAEL SEAN QUINN

Michael D. Green, *Bendectin and Birth Defects: The Challenges of Mass Toxic Substances Litigation* (Philadelphia: The University of Pennsylvania Press, 1996), 368 pages, \$29.95

Marcia Angell, M.D., *Science on Trial: The Clash of Medical Evidence and the Law in the Breast Implant Case* (New York: W.W. Norton & Co., 1996), 256 pages, \$27.50

***Hall v. Baxter Health Care Corp.*, 947 F. Supp. 1387 1996 WL 730693 (D. Ore. 1996)**

Tort-based exposures to toxic substances are one of the key dimensions of private environmental litigation. Asbestos, sandblasting, DES, and Agent Orange claims are probably the most famous of these cases, but there are others. The Bendectin series of suits is extraordinary because it may have been the first case of mass tort litigation where the plaintiffs had it wrong. Bendectin was a "cocktail" of several medications which, in combination, proved useful in combating morning sickness in pregnant women. Worldwide, 36 million women took Bendectin. No one ever developed any proof that Bendectin caused birth defects. (At the same time, it is well to remember that no one ever developed any proof that it was perfectly safe either, and it is now off the market.) The breast implant cases may be even more interesting. Evidence is building which suggests that silicone-based breast implants do not cause substantial bodily disorders. At the same time, millions upon millions of dollars have changed hands in breast implant lawsuits.

Bendectin and Birth Defects

Professor Green's well-written and thoroughly researched book on Bendectin falls, roughly, into three parts. In the first one, Green

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describes the state of American tort law at the beginning of the 1980s. The theory of strict liability for product defects had arrived on the scene and was well established. Several mass tort cases involving drugs had been processed through the system, and proof based on toxicology was becoming more sophisticated all the time. Green goes to some length to explain these sources of proof:

In the science of toxicology, there are five different types of evidence that may contribute to an inference of causation: epidemiology, animal toxicology, in vitro testing, chemical structural analysis, and case reports. In addition, some limited information may be available based on what is known about the mechanisms by which the disease develops—the field of molecular biology—but this evidence is almost always incomplete and of limited utility in causal assessments. The most desirable evidence is epidemiological, because it can be better generalized to those outside the study group, supporting inferences about the effect of an agent in causing diseases in humans.

Professor Green describes each of these types of evidence at some length, but his discussion of epidemiological evidence is particularly instructive. Such evidence is an ingenious lawyer's dream.

Professor Green juxtaposes a chapter on the science of determining toxic causation with a chapter on the Food and Drug Administration. Much of the testing done on drugs is conducted in the context of pharmaceutical manufacturers making applications to the FDA for permission to market new drugs. The drug manufacturers, which have an incentive to sell their drugs, are in charge of running the safety tests and then reporting them to the government. Obviously, this is a situation fraught with temptation.

Indeed, Merrell, the company which manufactured Bendectin, had a history of being a bad actor. It was the North American licensee for Thalidomide, and it was the manufacturer of MER/29, an anti-cholesterol drug. Thalidomide was clearly teratogenic, since it caused birth defects in up to 12,000 children in 46 countries. Merrell eventually paid \$50 million damages for its role in distributing it. There is apparently continuing controversy as to whether, given the times, the Thalidomide manufacturers were culpable for "failing to conduct fetal toxicity studies[.]" There is no controversy, however, as to whether drug companies should ghost-write scientific papers for ostensibly independent researchers. Unfortunately, Merrell did just that. A medical director for Merrell wrote an article bearing the name of an apparently independent physician. The article was published in a respectable medical journal, and it claimed to provide evidence that

Thalidomide was safe when taken during pregnancy. When this unseemly affair came to light, the evidence suggested Merrell may have fabricated some of the data.

The same sort of unethical conduct occurred in conjunction with MER/29. In fact, in that case, the corporation and several of its senior officials were indicted for providing false information to the government. They pleaded *nolo contendere*. In conjunction with MER/29, it turned out that several senior scientific officials at Merrell ordered scientific data to be fabricated.

Between them, Thalidomide and MER/29 cost Merrell in the neighborhood of \$100 million in settlements. These events also suggested to the plaintiffs' bar that Merrell was a company that could not be trusted—a target, a pigeon. That general frame of mind probably contributed substantially to the course of the Bendectin litigation.

The middle section of Professor Green's book tells the story of the Bendectin lawsuits. Green recounts one case in Florida—the first major battle—in some detail. Lawrence E. Walsh, later a famous federal special prosecutor, headed up the defense for Merrell, and his law firm billed Merrell approximately \$12 million in the process. The plaintiffs' lawyers, who were largely penniless—certainly after the trial, if not before—approached the case quite differently and learned the true meaning of frustration, as did the plaintiffs themselves. After the case was over, Merrell moved for costs and asked for a shade over \$200,000. Eventually, the court reduced Merrell's cost recovery to \$6,000. Although "Merrell never attempted to collect on the \$6,000 cost award . . . , it did file its judgment as a lien on the [plaintiffs'] home." This is not the finest hour of American industry. Vindictiveness is seldom to the credit of anyone.

In the central portion of the middle section of his book, Professor Green describes the consolidation of many, if not most, Bendectin cases in the federal district court in Cincinnati. Stanley Chesley, along with a few others, led the plaintiffs' committee, whereas Frank Woodside, a lawyer-physician, led the defense. The story of the development of the multi-district case is well-told and very instructive for lawyers who think about complex litigation.

Perhaps the most interesting feature of the multi-district case is the amount of scientific research that took place during its preparation. Most of the research suggested that Bendectin did not cause birth defects. At the same time, some of the research suggested that Bendectin might cause some problems, such as pyloric stenosis and perhaps some heart valve anomalies. These studies were not without methodological problems, however, as Green demonstrates. In the

end, the evidence that Bendectin caused birth defects was quite weak, and the plaintiffs lost on that issue. At the same time, as Green's account makes it clear, Merrell was not without fault. For example, "Merrell was well aware of the inadequacy of the Bendectin teratology studies of the 1970s." In other words, Merrell knew that they did not have evidence that Bendectin did not cause birth defects, although no one had any evidence that it did. Apparently, an independent consultant advised Merrell in the early 1970s to conduct further teratology studies, but Merrell failed to do so for some ten years—until after the Bendectin litigation began. It also turned out that Merrell had once again ghost-written an article laudatory of one of its own products.

The tale of the multi-district case is fascinating. Merrell settled with the plaintiffs for \$120 million. In order to make the settlement work, a mandatory class action had to be created. The district judge entered an order doing that, but the Sixth Circuit reversed the district judge, finding that the certification of the mandatory class was improper. The settlement obviously failed. Chesley's attempting to sell other lawyers and plaintiffs on the class action was not to his credit, according to Professor Green. "One neutral observer who [attended at least one relevant meeting] and had obtained a confidential copy of the settlement agreement was 'blown away' at the misrepresentations made by Chesley about the settlement. Moreover, according to Green, Chesley's firm has very substantial conflicts of interest. According to Martindale-Hubbell, Chesley's firm represented Lloyds of London, which was a high excess carrier for Merrell.

After the appellate court undermined the settlement, the district judge in Cincinnati divided the case into stages, and the jury heard causation issues first. The question was quite simple. As the judge said to the jury: "Does Bendectin cause birth defects, yes or no?" In retrospect, Professor Green thinks it is clear that the plaintiffs were winning until Merrell presented its third witness, Dr. James Goddard, "a former head of the FDA and the Centers for Disease Control." Dr. Goddard was an outspoken administrator, a strict regulator, and a critic of the drug industry in the past. However, in this context, Dr. Goddard relied on the testimony of a statistical epidemiologist, Steven Lamm, hired by the guardian ad litem, who had been appointed by the district judge to protect the interest of the child plaintiffs. Dr. Lamm demonstrated that, in the aggregate, birth defects around the world did not decline as the sales of Bendectin declined, due to adverse publicity. Lamm's studies showed that there was virtually no correlation between any of the types of birth defects alleged by the plaintiffs and the sales of Bendectin. Lamm prepared a number of compelling graphic

exhibits. "The exhibits and the evidence were a strategical tour de force." The district judge wrote to Professor Green years after the trial that "The most telling single piece of evidence I have ever seen after 23 years on the Federal Bench is the [Lamm] exhibit." Jurors who were interviewed after the trial agreed. Professor Green is somewhat critical of this evidence, however. Most significantly, according to Professor Green, "time-line analyses may be useful for generating hypotheses about causal factors or even providing strong evidence of powerful toxins, but they are not very useful in determining small effects." Subject to critique or not, the jury deliberated only four-and-a-half hours before delivering a verdict for Merrell.

After the conclusion of the multi-district litigation, most plaintiffs' lawyers lost interest in Bendectin. A few more cases were tried, but the judiciary became ever more critical of the evidence on causation. Merrell also, quite correctly, pursued without mercy the expert witnesses relied on by the plaintiffs. One significant witness from Australia, who had codiscovered Thalidomide's teratogenicity, eventually lost his medical license for deliberately falsifying scientific data. (It was not data used in the Bendectin cases.) Another expert, Dr. Alan Done, was pushed out of his medical school for his involvement in the plaintiffs' case, disgraced as a scientist, and eventually found to be a perjurer in a Bendectin case, although no criminal charges were filed.

Eventually, the fire storm over the use of scientific experts created by the Bendectin cases reached the Supreme Court of the United States. It is perfectly clear, according to Professor Green, that the Supreme Court cared nothing about the specific issues in the Bendectin cases. Rather, it cared about the general contours of scientific expert evidence. Of course, this is exactly how the landmark case of *Daubert v. Merrell Dow Pharmaceuticals Inc.*, 509 U.S. 579 (1993), reads.

The third, and last, major section of Professor Green's study focuses on the more general socio-legal problems that the Bendectin litigation raised but did not solve. In the end, the tort system worked. It was a long way, however, from beginning to end, and many argue that the tort system permitted the Bendectin fiasco to go on much too long. Lamm has actually argued that the net aggregate utility has declined as the result of the attack on Bendectin. For example, he has found a decrease in the use of anti-emetic drugs (including Bendectin) that correlates with an increase in hospitalizations. Thus, Green concluded:

the attempt to treat morning sickness with more conservative non-drug therapy has resulted in an increase of hyperemesis that requires hospitalizations. Lamm's data appear correct and it is implausible that

there is some other change during the 1980 to 1984 period when Bendectin use was dropping and ultimately ended that is responsible for the increased hospitalizations. Thus it seems reasonable to conclude that an indirect cost of the Bendectin litigation and its impact on obstetricians' treatment of morning sickness is an increase in hospitalizations for hyperemesis. Of course, this conclusion assumes that Bendectin truly was effective in reducing the incidence of severe cases of hyperemesis, a proposition for which none of the efficacy studies of Bendectin provides proof.

Nevertheless, it is doubtful that the Bendectin case is fully emblematic of the tort system. After all, says Professor Green, "Bendectin is the Taj Mahal of horror stories about the tort system[.]" One wonders if Professor Green's qualified optimism about the tort system is fully justified. This is especially true when we reflect on breast implant litigation, not to mention environmental litigation.

Science on Trial

The series of lawsuits known as the breast implant litigation are largely predicated upon the hypothesis that silicone-gel-filled implants are causally responsible for "a constellation of disorders known as connective tissue diseases." These diseases include systemic lupus erythematosus, rheumatoid arthritis, scleroderma, and polymyalgia, among others. These diseases are thought to involve disturbances in the immune system that turn the body's protective defenses against itself. "The result is an autoimmune disease—that is, a prolonged civil war within the body that can produce profound weakness and fatigue, along with variable damage to the joints, skin, and internal organs." The idea behind the breast implant litigation was that when silicone gel leaked out of the implants, it set off an autoimmune response that thereby created an autoimmune disease.

The breast implant litigation was in some ways like, and in some ways different from, the Bendectin litigation. The most striking similarity between the two was the fact that the scientific evidence on causation was weak in both cases. The cases are quite different in the ways they have been handled. Much more money has changed hands from defendant to plaintiff in the breast implant cases than in the Bendectin cases. Arguably, this results from one or more of the lawyers appearing for the plaintiffs. Perhaps it also results from pre-tort reform venue manipulation in Texas.

Science on Trial is a much more readable book than *Bendectin and Birth Defects*. Marcia Angell is a physician and the executive editor of the *New England Journal of Medicine*, probably the most distinguished

medical journal in America. She is harshly critical of both implant manufacturers and plaintiffs' lawyers. She accuses them both of avarice, for example. At the same time, she is unequivocal in her opinion that there is no evidence to support the proposition that breast implants cause autoimmune diseases or connective tissue disorders. Interestingly, Dr. Angell goes far out of her way to claim that she is not a person normally sympathetic to corporate interests, such as those of the breast implant manufacturers. She identifies herself as a feminist, a liberal Democrat, a quick critic of the inequities of large corporations, and so forth. Thus, as befits a Boston intellectual and scientist, Dr. Angell is painfully correct, politically speaking. Nevertheless, even though she believes that "women should have political, economic, and social rights equal to those of men," and even though she is "alert to discriminatory practices against women, which some feminists believe lie at the heart of the breast implant controversy," as a scientist she simply does not believe that the evidence supports causation.

Another similarity between breast implants and Bendectin is the evidence of corporate wrongdoing. Dow Corning knew that the implants leaked. It even advised its sales personnel on how to conceal this fact from physicians. Moreover, Dow Corning employees falsified manufacturing data; for example, "some of the employees doctored the automatic recordings of failures in the heat-curing process for the implants."

Silicone-gel-filled implants and Bendectin suffered the same fate in the market: There came a time when neither was available for purchase. There was a difference, however. Merrell withdrew Bendectin from the market, whereas the FDA ordered breast implants to be removed. (Dow Corning, however, had left the market approximately a month before.)

Dr. Angell describes the litigation following the FDA ban of breast implants as a "frenzy." She also describes the tort system as a "runaway," and characterizes virtually all mass tort litigation as disastrous. Her central point appears to be that neither the tort system nor American culture understands scientific evidence or takes its strictures seriously. According to Dr. Angell, science is not simply a "bottom-line" enterprise. Studies must be designed; study designs must be reviewed. Data must be collected, which means that something must be measured or counted. This process must be accurate, free from guess-work, and free from prejudice. Conclusions must be drawn strictly within the evidence. At every step, what the researcher does must be verifiable by others, and in the end it must be reviewed by peers. All scientific conclusions are tentative and subject to revision.

According to Dr. Angell, the logic of scientific discourse always proceeds on the basis of falsification. Every truly scientific hypothesis must be empirically falsifiable, and scientific procedures must be able to falsify.

According to Dr. Angell, at the time the implants were marketed, and at the time lawsuits were filed and even settled, there was no canonically acceptable scientific data proving or disproving the hypothesis that silicone breast implants caused autoimmune disorders or connective tissue diseases. Such information cannot be obtained experimentally, for obvious reasons. The only way to determine whether breast implants are associated with connective tissue diseases is through observational epidemiological studies. According to Dr. Angell, no such reliable study was published until June 16, 1994, when the so-called Mayo Clinic study was published in the *New England Journal of Medicine*. (That study examined a group of 749 women living in a county near the Mayo Clinic. They received breast implants between 1964 and 1991.) The second study appeared in 1996 in the *Journal of the American Medical Association*. This study was called the Women's Health Cohort Study, and it was a retrospective cohort study of approximately 400,000 American women in the health professions, of whom approximately 11,000 had breast implants. This study found a slight increase in reports of connective tissue diseases among women with breast implants. However, it did not attempt to verify the diagnosis by examining medical records. Since the survey was done after the 1992 FDA ban and the resultant publicity and legal activity, it is difficult to know how much to rely on the self-reports. A third major study appeared in the *New England Journal of Medicine* in June 1995. It examined 90,000 nurses, of whom nearly 1,200 had breast implants. It could find no association between implants and connective tissue disease.

A different kind of research focused on whether silicone is capable of causing an immune reaction. Some scientific observers, and certainly many lawyers, hypothesized that silicone could cause autoimmune disorders, because "silica (a dust that is the cause of silicosis in miners) is associated in epidemiological studies with a high incidence of autoimmune disease." According to Dr. Angell, however, the inclination which forms the basis of this hypothesis has no basis in fact: Silica dust is quite different from silicone (although a different type of silica is a constituent of the silicone envelope). "The weight of evidence indicates that silicone probably is not capable of acting as an antigen and causing an immune reaction. Nor is there evidence that women with breast implants are more likely to have antibodies against their

own tissues (autoantibodies)." Thus, there is no evidence linking alleged cause to alleged effect, and the hypothesized causal mechanism is improbable as well.

The remainder of Dr. Angell's book focuses on two issues. First, she savages lawyers and the legal system at some length. The plaintiffs' lawyers pushing breast implant cases are a bad bunch, she says, and Texas is the worst place of all. The legal system betrays science by asking for educated opinions, rather than insisting on scientifically proved hypothesis. Legal doctrine is essentially incoherent in key places, because it encourages significant confusions. The phrase "by a preponderance of the evidence" is problematic, Dr. Angell says, because it encourages confusion between (1) the degree of probability a body of evidence endows upon a conclusion and (2) the size of the effect which some cause may have. Her critique, of course, is correct, but it is directed at a straw man, in that it confuses logical probability, a concept at home in the law of evidence, with causal chains, which are part of the law of torts. Dr. Angell also underestimates the extent to which cross examination can limit the effect of expert witness testimony which strays too far from solid science. This point, like many others, reveals Dr. Angell's profound contempt for any sort of activity short of the strictly scientific. Dr. Angell has no appreciation for the fact that social systems are political. She completely fails to understand that decisions have to be made now, not when perfect science arrives.

The second major concluding theme in Dr. Angell's book concerns American culture. She believes that as Americans become more health conscious, they have become more susceptible to manipulation by the media, quacks, gurus, and greedy lawyers. Dr. Angell implies that there needs to be a paradigm shift in the culture. Science needs to be taken more seriously. Citizens need to become less prone to the turbulent and multidirectional winds of pseudo-scientific babble. And the populace needs to become more grounded in the rigors of scientific epistemology.

Hall

The *Hall* opinion of Judge Richard Jones of the United States District Court for the district of Oregon is a fitting supplement to Dr. Angell's book. The history behind his opinion is as follows. A number of breast implant cases in Oregon were transferred to the judge supervising the multi-district litigation. He remanded a number of the cases to Oregon for trial, and they were all assigned to Judge Jones. They were divided into groups for trial, and the defense filed a "motion in limine to exclude testimony by plaintiff experts concerning any causal connection between silicone breast implants and the alleged

systemic disease or syndrome." Judge Jones evoked his inherent authority and appointed independent advisors to the court. These advisors reviewed a variety of materials submitted by the parties. The courts held "four intense days" of hearings. At these hearings, experts from both sides were questioned by counsel, the court, and the technical advisors. The parties then submitted videotape summations, which the court and all technical advisors reviewed. Following the hearings, the court asked for reports from its technical advisors. The reports were to concern several questions: (1) Is the scientific reasoning and methodology of the experts consistent with federal evidentiary standards? (2) Is the expert's opinion based upon scientifically reliable data? (3) If epidemiological studies have not been done or are inconclusive, what other data, such as animal studies, biophysical data, clinical experience in the field, medical records, differential diagnoses, preliminary studies, general scientific knowledge, and medical literature can justify, to a reasonable degree of medical probability, a conclusion concerning the cause of the syndrome or disease at issue? (4) Are the experts' conclusions supported by proper data and proper methodology? (5) Did the experts use relevant scientific data? (In addition, the court provided its technical advisors with other questions from the parties and invited advisors to consider them.)

The court's technical advisors submitted reports, and the court turned them over to the parties. Thereafter, the court gave counsel from both sides an opportunity to examine the technical advisors. The court preliminarily found that the plaintiffs' experts did not survive the *Daubert* test and asked for proposed findings and conclusions from the defense, as well as written objections from the plaintiffs. Following this exchange, the court granted defendant's motions in limine.

During this process, the district judge managing the multi-district case appointed a national panel of experts to review the scientific data. Because of the ongoing national proceeding, and because of the potential for further scientific developments, Judge Jones deferred the effective date of his order until the findings of the national panel were available. During that period of time, Judge Jones ordered that the plaintiffs might move for reconsideration. Nevertheless, Judge Jones wrote an elaborate opinion and attached as appendices the reports of his technical experts. The significant point of Judge Jones' opinion may be summarized very quickly: The scientific evidence does not support the proposition that breast implants are injurious. The expert reports—fascinating reading for the thoughtful lawyer—are to the same effect.

SIGNIFICANT BOOKS

To a considerable extent, these books concern complex litigation of the same type faced in environmental disputes. One glaring omission in these writings is the total absence of any discussion of the role of insurance in these disputes. Such a discussion should have been in Dr. Angell's book, and it is hard to imagine that Professor Green can tell the whole story of Bendectin without an extended discussion of insurance issues. This omission is common enough, unfortunately. Until it is included in such books, the whole story of complex tort litigation cannot be told.



