Lessons from Litigation over Silicone Breast Implants: A Call for Activism by Scientists

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What constitutes good science? Many researchers ask themselves this on a regular basis. It may not, however, seem like a question that is appropriately addressed by a court of law. Yet it is sometimes essential that courts address exactly this question. This is vividly illustrated by litigation to determine whether silicone breast implants cause autoimmune disease. I present a review of the nature of that controversy, summarize the conclusions of a recent federal court ruling that limited the testimony of "scientists," and offer recommendations to improve the availability, reliability, and independence of scientific expert testimony in a courtroom.

The Nature of the Debate

Silicone is a synthetic polymer consisting of silicon, oxygen, and carbon side chains (*1*). It may exist as a solid, liquid, or gel, depending on the nature of chemical cross-links. Medical uses of silicone include components of cardiac pacemakers, intraocular lenses, syringes, ventricular shunts, antacids, artificial joints, and implantable contraceptives. A breast implant usually consists of a silicone envelope that encases either saline or a combination of silicone oil and gel. The use of silicone implants for breast augmentation began in 1962. An estimated 800,000 to 2 million women have undergone implantation in the United States, either for reconstruction after mastectomy or for cosmetic purposes.

In 1991, a jury awarded a litigant more than $7 million on her claim that her autoimmune disease, mixed connective tissue disease, was caused by silicone breast implants (*2*). Some of the trial testimony indicated that her disease had begun before she received the implants (*2*). As the national media began to report and foster public concern about breast implants, the commissioner of the U.S. Food and Drug Administration (FDA) in 1992 declared a moratorium that severely limited the use of silicone breast implants (*3*). An avalanche of product liability litigation followed.

Currently, silicone breast implants are the subject of a staggering amount of litigation. Approximately 400,000 women are participants in a class action lawsuit against implant manufacturers, including 3M, Bristol-Myers Squibb, Dow Corning, and Baxter Healthcare. The registrants claim that the implants cause various diseases. A proposed settlement of $4 to $5 billion could be distributed among these individuals. An additional 20,000 to 30,000 others have elected to litigate individually. A recent tally of litigation found that 16 of 50 plaintiffs had won jury decisions with total awards exceeding $100 million (*4*). Legal defense can cost as much as $1 million. Assuming an average award of $2 million on the basis of verdicts for either the plaintiff or defense, $40 to $60 billion is at stake in this litigation, independent of the legal fees and in addition to the class action settlement. One manufacturer, Dow Corning, has entered into bankruptcy reorganization.

Although implants are accused of causing autoimmune disease, the American Cancer Society, the American Society for Clinical Oncology (*5*), the American Medical Association (*6*), the American Society of Plastic and Reconstructive Surgeons, the British Council on Medical Devices (*7*), and the board of directors of the American College of Rheumatology, as well as the commissioner of the FDA (*3, 8*), have concluded that there is currently no evidence that silicone breast implants induce such a disease.

Plaintiffs' experts argue that silicone can stimulate the immune system (that is, act as an adjuvant); that the implants are associated with a localized inflammatory process; and that case reports and series have linked silicone to a variety of immunologically mediated diseases, including scleroderma (*9, 10*). Silicone is alleged to cause a newly recognized autoimmune disease (*11, 12*) sometimes called atypical connective tissue disease. The diagnostic criteria for this disease have not achieved consensus (*13*), but common manifestations include fatigue, dizziness, myalgia, arthralgia, ocular dryness, and forgetfulness. Defense experts counter that the adjuvant effects require emulsification; that the clinical criteria for atypical connective tissue disease are vague, subjective, and inclusive of "symptoms" that are common in healthy individuals; and that epidemiologic studies have failed to show an association between silicone breast implants and various rheumatologic diseases (*14–26*), breast cancer (*27–31*), specific symptoms (*32, 33*), or autoantibodies (*34*).

The Role of Science in the Courtroom

If one accepts the premise that silicone breast implants do not cause systemic disease, what is the future of biomedical product development when billions of dollars must be spent to defend a product that has been in clinical use for 35 years and has no proven ability to induce disease? How can a judge or jury optimally evaluate immunology, epidemiology, biochemistry, and other technical issues?

The saga of Bendectin has many parallels with silicone litigation (*35*). Bendectin was an antinausea medication used primarily for morning sickness. It had been taken by 17.5 million women when case reports began to appear suggesting that Bendectin might be teratogenic. Thirty epidemiologic studies had failed to show an association between Bendectin and birth defects. The manufacturer, Merrell Dow, spent in excess of $100 million defending itself against lawsuits alleging that Bendectin had been responsible for fetal abnormalities. In *Daubert* v. *Merrell Dow Pharmaceuticals*, eight "well-credentialed experts" testified on behalf of two plaintiffs that the drug had caused limb defects (*36*). The scientists based their opinions on in vitro testing, animal studies, and analysis of prior epidemiologic reports. In 1993, the U.S. Supreme Court directed a lower court to determine whether this scientific testimony was admissible under the Federal Rules of Evidence. Justice Blackmun wrote that "whether the theory or technique in question can be (and has been) tested, whether it has been subjected to peer review and publication, . . . and whether it has attracted widespread acceptance within a relevant scientific community" are some of the criteria used in determining the admissibility of scientific testimony.

The Ninth Circuit Court applied these guidelines in determining that plaintiffs' expert testimony was not admissible in

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Daubert v. *Merrell Dow* (*37*). The lower court further admonished that admissible scientific testimony could not be developed solely for litigation. The court also noted that "a relative risk of less than two may suggest teratogenicity, but it actually tends to disprove legal causation." The relative risk refers to the increased chance of developing a given disease as determined in an epidemiologic study. If the relative risk is 2, the disease is twice as likely to develop after exposure. A relative risk of 1.5 would mean a 50% increase in likelihood, but it would also mean that for a given individual who developed the disease, there would be a two-thirds probability that the illness was not caused by the exposure. The standard in civil court is "more probable than not"; therefore, only conclusions from a study finding a relative risk greater than 2 can be used to argue that it is more probable than not that exposure caused illness.

This legal standard differs from the scientific question of whether the exposure ever causes or even contributes to the illness. It also has no relation to the separate issues of statistical significance, reproducibility, confounding variables, or biologic plausibility. Although victorious in *Daubert*, the manufacturer had already found the cost of legal defense to be prohibitive. Since Bendectin was withdrawn from the market in June 1983, hospital admissions for morning sickness have doubled and the rate of limb defects has remained unchanged.

The Precedent in Oregon

In August 1996, U.S. District Court Judge Robert E. Jones heard arguments on the scientific admissibility of evidence relative to alleged silicone disease in federal district court in Oregon. The Ninth Circuit *Daubert* opinion had noted, "Though we are largely untrained in science and certainly no match for any of the witnesses whose testimony we are reviewing, it is our responsibility to determine whose experts' proposed testimony amounts to 'scientific knowledge,' constitutes 'good science,' and was derived from the scientific method." With the aid of a scientific adviser, Richard Jones, Judge Jones enlisted four neutral panelists to advise on the admissibility of opinions offered by plaintiffs' experts for lawsuits involving silicone breast implants pending in his jurisdiction.

Using the report from this panel, Judge Jones ruled that plaintiffs' "scientific" experts could not offer opinions on causation issues. In reaching this conclusion, he noted that the opinions of the scientists hired by the plaintiffs were not based on tested hypotheses; their analyses of experimental studies involved an extrapolation that represented a "leap of faith"; no study had found an increase in relative risk greater than 2 for any disease; the proposed experts had relied on differential diagnosis, a process that is not reliable in establishing causation; and their opinions differed from the prevailing consensus (*38*, *39*). Although this opinion is having a far-reaching effect, it is not binding on state courts where the vast majority of implant cases are being tried. Nor does the ruling bind other federal district courts. One other federal judge who has been assigned breast implant litigation is also seeking advice from a similar panel (*40*). In two other federal cases (*Nyitray* v. *Baxter* in Brooklyn and *Kelley* v. *Baxter* in San Antonio), courts have limited the testimony on causation by plaintiffs' experts.

The proceedings before Judge Jones demonstrate the appropriate use of a scientific advisory panel. Although this approach entails some expense, the cost is trivial in comparison to the billions at stake. Juries need unbiased guidance to fathom immunology, epidemiology, biochemistry, and the pathogenesis of autoimmune disease.

One solution to the challenge of evaluating science is to allow the courts to appoint experts to testify. A second approach is to empanel a group of experts to advise the court. In either case, the experts need to have appropriate credentials, including knowledge, neutrality, and diligence. The National Institutes of Health (NIH) now maintain a roster of potential scientific reviewers who are checked for conflicts of interest. The NIH, universities, the American Association for the Advancement of Science (AAAS), the National Academy of Sciences (NAS), and other neutral organizations are existing resources to provide scientific guidance in the courtroom.

Scientific bodies should not wait for the court to seek advice; as scientists we should ensure that every court has at its disposal a listing of neutral experts with specified areas of expertise and acknowledgment of potential conflicts. In an amicus brief filed in connection with the *Daubert* decision, the AAAS and the NAS wrote, "Science is not an encyclopedic body of knowledge about the universe. Instead, it represents a process for proposing and refining theoretical explanations about the world that are subject to further testing and refinement." Although scientific "truth" is not immutable, the courts have recognized that scientific arguments for causation must meet definable standards and that scientists themselves, either as experts appointed by the court or as advisers to the court, are best qualified to judge science.

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