

Proof Of Causation In Recent Product Liability Cases

Law360, New York (April 30, 2008) -- There is fairly widespread agreement that proof of causation in a toxic tort case requires three steps: first, the plaintiff must prove that the alleged toxin can cause an injury of the sort he alleges (general causation); second, the plaintiff must prove that he was exposed to the toxin in amounts sufficient to have caused his injury; and third, the plaintiff must prove that his exposure to the toxin did in fact cause his injury (specific causation).

But despite this general agreement, courts are still grappling with what each step demands of a plaintiff.

For example, while there is no doubt that epidemiological evidence can be probative of general causation, there is no clear consensus on quite what epidemiological evidence can be admitted – for example, what relative risks are probative of general causation, and what role confidence intervals and other measures of statistical significance play.

There are also unresolved issues concerning how a plaintiff can meet his burden of showing he was sufficiently exposed to the toxin.

And, except for short (and often misleading) discussions of differential diagnosis, courts have said little to clarify what a plaintiff has to do to show his injury was in fact caused by the toxin.

We here discuss some recent decisions that have addressed these issues. Not all of these cases are important for their precedential value; nevertheless, each affords some helpful insight into these issues.

Proving General Causation

Courts typically require that a plaintiff alleging injury from a toxic substance first prove general causation. For example, the New York Court of Appeals recently confirmed that “[i]t is well-established [under Frye] that an [expert’s] opinion on causation should set forth ... that the [alleged cause] is capable of causing the particular illness (general causation).” *Parker v. Mobil*

Oil Corp., 7 N.Y.3d 434, 447 (N.Y. 2006); see also Grant v. Boccia, 133 Wash. App. 176, 183 (Wash. Ct. App. 2006) (excluding expert opinion testimony when general causation was not proven); In re Lockheed Litigation Cases, 115 Cal. App.4th 558, 565 (Cal. Ct. App. 2004) (affirming exclusion of expert testimony for failure to produce evidence of general causation).

Courts in Daubert jurisdictions likewise require proof of general causation. See, e.g., National Bank of Commerce v. Associated Milk Producers, Inc., 22 F. Supp. 2d 942, 963 (E.D. Ark. 1998) (requiring plaintiff provide expert opinion about general causation based on scientifically valid methodology); Raynor v. Merrell Pharms., Inc., 104 F.3d 1371, 1376 (D.C. Cir. 1997) (holding that testimony about specific causation is admissible only given evidence of general causation).

Why does a plaintiff have to prove general causation in order to establish that the plaintiff's injuries were in fact caused by the toxin?

The answer derives, it appears, from a model of reasoning well-entrenched within the law – that an expert, in any particular case, reasons deductively from established principles to conclusions about the plaintiff.

This model is at the heart of Frye itself, which held that “while courts will go a long way in admitting expert testimony deduced from a well-recognized scientific principle or discovery, the thing from which the deduction is made must be sufficiently established to have gained general acceptance.” Frye v. United States, 293 F. 1013, 1014 (D.C. Cir. 1923).

But this deductive model probably has little to do with how experts actually reason.

So, for example, the thought process of a radiologist interpreting an image is not likely to commence with the radiologist calling to mind general principles about the differential absorption rates of various organs or tissues, and reasoning from those principles to conclusions about the particular patient.

Rather, an experienced radiologist is more likely to look at the image and “just see” the patient's condition.

A recent decision from the Florida Supreme Court rejected the scientific-deductive model and allowed an expert to testify about causation more in line with the reasoning he might adopt in his professional practice.

In Marsh v. Valyou, No. SC06-118 (Fla. Nov. 21, 2007) (r'hg denied Mar. 10, 2008), plaintiff alleged that a series of car accidents had caused her fibromyalgia.

The court held that plaintiff's expert did not have to testify about general causation, but could give "pure opinion testimony" – testimony based on his expertise and experience – about what caused plaintiff's injury.

The court did not identify anything particular to the case before it that caused it to reject the usual requirement of proving general causation, leading the dissent to conclude that the court had "in effect render[ed] specific causation testimony always admissible as the 'pure opinion' of the expert." *Id.*

It remains to be seen whether the Florida Supreme Court's conclusion is as sweeping as the dissent suggests. (A report on the effect of an analogous ruling on expert opinion testimony under Frye in Kansas, *Kuhn v. Sandoz Pharmaceuticals Corp.*, 270 Kan. 443 (2000), found "no indication that Kuhn's holdings on expert testimony have become the source of new or different practices with regard to Kansas rules of evidence." Report of the Judicial Council Civil Code Advisory Committee on *Kuhn v. Sandoz Pharmaceuticals Corp.* and "Pure Opinion" Testimony 6 (Feb. 15, 2006).)

Still, Marsh illuminates the question of why it should matter that an expert need not give his testimony in the scientific-deductive form, but may instead testify in much the same way as he might reach a conclusion in his professional practice.

The answer is that it matters because even though an experienced expert might not, in practice, follow the deductive model, the deductive model must be used when the expert's conclusions are put to the test.

So even if the radiologist "just sees" what is wrong with the plaintiff based on his experience and expertise, if called on to justify his conclusion, he should be able to explain how it is supported by established principles from which his conclusions follow.

This is particularly important in the courtroom, where an expert is required to defend his conclusion, not just state it.

And this is what is worrying about the Florida Supreme Court's opinion in Marsh – it seems to relieve an expert from the burden of having to justify his opinion by reference to underlying scientific principles that are themselves justified.

Even when there is no question that proof of general causation is required, courts face potentially difficult issues concerning the method of proof used.

Very often, this proof turns on epidemiological evidence, and there has been a long-running

debate about the level of relative risk a study must show for the study to be admissible. Compare *In re Hanford Nuclear Reservation Litigation*, 292 F.3d 1124, 1137 (9th Cir. 2002) (holding relative risk of 2.0 sufficient for proof of general causation), *DePyper v. Navarro*, 1995 WL 788828 (Mich. Cir. Ct. Nov. 27, 1995) (suggesting relative risk of 2.0 required to prove general causation), and *Manko v. United States*, 636 F. Supp. 1419 (W.D. Mo. 1986) (holding relative risk greater than 2.0 sufficient to prove vaccination caused injury), with Restatement (Third) of Torts: Liability of Physical Harm § 28 cmt. c(4) (Tentative Draft No. 5) (stating “any judicial requirement that plaintiffs must show a threshold increase in risk or a doubling in incidence in a group study in order to satisfy the burden of proof of specific causation is usually inappropriate”); see also *id.* at § 28 Rptrs’ Note to cmt. c(4) (reporting on split in courts with respect to 2.0 threshold).

But few courts have studied the equally important notion of a confidence interval, which makes a recent decision in the *Celebrex* multidistrict litigation of particular interest. *In Re: Bextra and Celebrex Marketing Sales Practices and Product Liability Litigation*, 524 F. Supp. 2d 1166, 1174 (N.D. Cal. 2007).

Plaintiffs in that case proposed that an expert would testify that a daily 200 mg dose of *Celebrex* can cause heart attack or stroke. Defendant moved to exclude such testimony, and the court granted the motion. The court’s decision identified two factors that courts should consider when interpreting epidemiological evidence.

First, the court held that, whatever level of the relative risk was required for admitting epidemiological testimony, a court must also examine the confidence interval associated with the relative risk. *Id.* at 9.

A relative risk is an estimate drawn from the study of a sample population; like all estimates drawn from samples, it is subject to random sampling error.

Confidence intervals account for this randomness, and only if the lower bound of the interval excludes a relative risk of 1 does the result warrant the claim that the increased risk is due to the exposure, rather than chance.

Thus, an otherwise unimpressive relative risk of 1.4 with a 95% confidence interval of 1.2 to 1.7 might be probative of the claim that the exposure increases the risk, whereas a relative risk of 2.1 with a 95% confidence interval of 0.8 to 3.2 is not statistically significant, so not probative.

The court held that the plaintiffs’ expert’s failure to describe the confidence intervals for his

relative risk estimates of risks at 200 mg doses required the exclusion of the expert's testimony. Id. at 18-19.

The court also emphasized that a correct interpretation of statistical evidence requires knowing the processes used to arrive at that evidence.

One expert testified that a 200 mg/day dose significantly increased the risk of heart attack, but reached this conclusion by observing the (statistically significant) relative risk of a 400 mg/day dose and dividing that number by two, apparently assuming that risk is directly proportional to dose.

The court excluded the testimony, holding correctly that such a crude extrapolation could not take the place of evidence of the real dose-response relationship.

Proving Sufficient Exposure

Exposure is the bridge linking general causation and specific causation. A toxin has injurious effects only at a certain dose, and the plaintiff must show he has received such a dose in order to prove specific causation.

In many cases, the plaintiff's exposure to a toxin will be very hard to quantify with any accuracy. So, for example, in *Parker v. Mobil Oil*, 857 N.E.2d 1114 (N.Y. 2006), the plaintiff alleged he had been exposed to benzene in gasoline, and that the benzene caused his leukemia.

The plaintiff's experts testified that benzene can cause leukemia and that the plaintiff's exposure was sufficient to cause for his injury. Id. at 1121. But the plaintiff's experts had a hard time quantifying his exposure. One expert opined that the plaintiff's exposure was "far more" than that of refinery workers, but was unable to state the level of refinery workers' exposure; another expert said his exposure was "frequent" and "excessive."

The court concluded that these opinions were insufficient for they "cannot be characterized as a scientific expression of [plaintiff's] exposure level." Id. at 1122.

What would a "scientific expression" of exposure be? A plaintiff need not quantify exposure levels "precisely," the court held. Rather, the court said, an expert might use such techniques as "mathematical modeling" to estimate exposure based on the plaintiff's work history, or might make a comparison with exposure levels with subjects in other studies.

But it is unclear how these suggestions might work in practice, for, without some initially quantifiable exposure, it is hard to see what "mathematical modeling" might achieve, and also

difficult to see how a comparison might be made with other subjects' exposure levels.

New York courts are beginning to explore these issues, but few helpful guidelines have yet emerged. See, e.g., *Nawrocki v. Coastal Corp.*, 845 N.Y.S.2d 896 (4th Dep't 2007); *Jackson v. Nutmeg Tech, Inc.*, 842 N.Y.S. 2d 588 (3rd Dep't 2007).

One approach plaintiffs sometimes use to prove sufficient exposure is to argue that there is no safe level of exposure to the substance in question. This was the tactic used by the Parker plaintiff, who sought to avoid having to quantify his benzene exposure by contending that any amount of exposure could cause cancer.

The intermediate appellate court rejected this argument, finding the linear non-threshold dose-response model on which plaintiff's claim rested to be "flatly rejected as a mere hypothesis." *Parker v. Mobil Oil Corp.*, 793 N.Y.S.2d 434, 438 (2d Dep't 2005). Other courts have also rejected such a theory. See, e.g., *Willis A. Amerada Hess Corp.*, 2002 WL 140542, at *23 (S.D.N.Y. Jan 31, 2002), *aff'd*, 379 F.3d 32 (2d Cir. 2004); *Sutera v. Pemer Group*, 986 F. Supp. 655, 666 (D. Mass. 1997).

There is good reason to be skeptical of such arguments. A plaintiff's burden is to show that his or her exposure was sufficient to cause the injury; all that the "no safe exposure" claim implies is that any increase in exposure increases the risk of injury.

But that says nothing about how great the increase is, nor does it imply that the exposure-related increase is significant when compared to the background risk of the injury.

There are, of course, contexts in which it is wise to assume there is no safe level of exposure to a particular substance; such assumptions are often made in the regulatory context when the data are not sufficient to determine the true dose-response relationship. See, e.g., EPA, *Guidelines for Carcinogen Risk Assessment* 3-21 to 3-22 (2005) (adopting policy of using a linear non-threshold model as the default for known carcinogens, "because linear extrapolation generally is considered to be a health-protective approach" in the absence of sufficient data to conclude the substance is not mutagenic at very low doses).

But while this may be a prudent policy decision, it should not be confused with evidence that there is in fact no threshold. So, for example, when the Surgeon General recently concluded that "[t]he scientific evidence indicates that there is no risk-free level of exposure to secondhand smoke," *The Health Consequences of Involuntary Exposure to Tobacco Smoke: A Report of the Surgeon General* 11 (2006), the Report was widely criticized for confusing regulatory policy with good science.

It is also unclear how much it matters to a plaintiff's case even if in fact a toxin has no safe exposure level. Such thresholds are clearly relevant in a regulatory context, since even very small risk increases at low doses can cause more injuries or deaths at the population level.

In litigation, however, the issue is typically not whether the exposure added to plaintiff's risk of injury.

Rather, the plaintiff needs to show her exposure was sufficient to meet the standard of proof for causation – i.e., that it is more likely than not that the exposure caused the injury.

If there is any background risk of the injury, then proof that there is no safe level of exposure will not, in itself, be enough to prove sufficient exposure.

Proving Specific Causation

Proof of general causation and the plaintiff's exposure to a sufficient amount of the toxin does not yet prove that the plaintiff's injury was in fact caused by the toxin. But what further proof can be mustered to show specific causation?

It is often said that epidemiological evidence is not probative of specific causation. See, e.g., Reference Manual on Scientific Evidence at 336 ("Epidemiology focuses on the question of general causation ... rather than that of specific causation ...").

On this view, all that epidemiology can show is that exposure to a toxin can cause injury; it can say nothing about whether a particular plaintiff's injury resulted from his exposure to toxin.

But the recent opinion in the Celebrex case cites to a 2004 case, *In re Silicone Gel Breast Implant Prod. Liab. Lit.*, 318 F. Supp. 2d 879, 892 (C.D. Cal. 2004), which holds that an epidemiological study can be probative of general causation if the study shows a relative risk greater than 2:

When the relative risk is 2.0, the alleged cause is responsible for an equal number of cases of the disease as all other background causes present in the control group. Thus a relative risk of 2.0 implies a 50% probability that the agent at issue was responsible for a particular person's disease.

This means that a relative risk that is greater than 2.0 permits the conclusion that the agent was more likely than not responsible for a particular individual's disease.

But this argument is flawed. A relative risk is simply the ratio of the proportion of persons in the exposed population who have the disease to the proportion of persons in the unexposed

population who have the disease.

The *In re Silicon Gel* court presumed that these proportions tell us something about the individuals involved.

But these proportions are properties of populations, not the individuals that comprise them, and it is a mistake to assume that what applies to one must also apply to the other.

No one would conclude that because, say, half of all New Yorkers were born elsewhere that there is anything indeterminate about where a particular New Yorker was born.

A similar fallacy underlies the inference that the proportion of the exposed group who get the disease tells us that that person's disease was caused by the exposure, or even that the exposure probably caused that person's disease.

A further analogy highlights the effect of this error. Suppose a study of truck drivers on a highway over a one-week period shows that 51% of truck drivers exceed the speed limit.

A plaintiff injured in a collision with a truck on this highway argues that the study is probative of the fact that the defendant was speeding.

But while the study tells us about truckers in general, it says nothing about the defendant in particular; he was either speeding when he struck the plaintiff or he wasn't, and the study doesn't tell us which of those two states he was in.

It may seem reasonable to infer that because a majority – be it 51% or even 99% – of drivers were speeding that it was more likely than not that the defendant was speeding as well.

But that can be said of every driver, which would justify holding every driver liable, despite our knowing that at least some drivers were not speeding at all.

Inferring that a person's exposure to a toxin caused her injury because the relative risk is at least 2 is fallacious for the same reason.

The relative risk indicates a relationship between two populations.

To infer from that that the toxin caused some particular person's injury would justify inferring that every exposed person's injury was caused by the toxin.

Relative risks do provide evidence of causation, since a relative risk that is significantly greater than 1 tells us that the incidence of the injury in the exposed population is greater than the incidence in the unexposed population.

This, however, goes to the issue of general causation, or the capacity of the exposure to cause the injury.

It does not justify an inference that any particular person's injury was caused by her exposure.

A Minnesota trial court recently diagnosed the confusion in a plaintiff's argument that epidemiology is probative of specific causation. In *Zandi v. Wyeth*, slip op., No. 27-CV-06-6744 (4th Dist. Minn. Oct. 15, 2007), the plaintiff sought to rely on epidemiological data to establish that her breast cancer was caused by hormone replacement therapy.

The court held that plaintiff's experts could not "deduce the specific cause of breast cancer in Plaintiff" from epidemiological studies. *Id.* at 17. Epidemiology, the court held, is at best evidence of "prospective risk"; it does not indicate the "retrospective probability ... that an already-existing event was influenced by a particular factor." *Id.*

But if epidemiology is not relevant to proving specific causation, what can be used to prove that an exposure which can cause injury did in fact cause the plaintiff's injury?

The favored answer is differential diagnosis. See, e.g., *James C. Westberry vs. Gislaved Gummi A.B.*, 178 F. 3d 257 (4th Cir. 1999) (holding reliable differential diagnosis is a valid foundation for expert opinion); *U.S. Sugar Corp. v. Henson*, 823 So. 2d 104, 110 (Fla. 2002) ("[T]here is no question that the differential diagnosis technique ... is generally accepted in the scientific community.").

This method involves identifying a set of possible diagnoses for a patient's condition and using test results and the patient's history to eliminate these possibilities until (ideally) only one remains.

Differential diagnosis has become a standard part of expert testimony, yet few courts have explored precisely how differential diagnosis is supposed to function.

In particular, differential diagnosis is often treated by courts and litigators as a general method of identifying the external causes of a plaintiff's injury. Reference Manual on Scientific Evidence 443-44. In fact, it is more accurately seen as a method of identifying the internal physical condition or disease responsible for a patient's symptoms. *Id.* at 443.

This process is distinct from that of determining the ultimate cause of the disease, since an expert may be very good at determining that a person has a particular kind of cancer from her symptoms without having any idea of what in turn caused that cancer.

And, to the extent that the expert has an opinion about that external cause, it is likely based on the very same kind of statistical evidence the Zandi court held to be an inadequate foundation for inferences to specific causes.

This is not to say that differential diagnosis is useless for proving specific causation.

Identifying the specific cause of an injury often involves the same pattern of reasoning used in differential diagnosis, such as the identification and elimination of likely causes.

Indeed, diagnoses of infections or acute poisoning necessarily involve identifying the external cause of the disorder.

But this is not generally true, for diagnoses of slowly-developing conditions or those with a long latency period are, like the breast cancer discussed in Zandi, ones that do not generally involve an inference to an external cause at all.

Consequently, there is no reason to think an expert capable of diagnosing a disease is equally adept at determining the cause of the disease.

The cases discussed above indicate some of the complexities involved in proving causation, particularly when epidemiological evidence is used.

While they also suggest that courts across the country have reached a consensus on some issues (such as the requirement that general causation be proved prior to proving specific causation), they also reveal important unsettled matters.

Individual judges and courts will likely have different views on the appropriate interpretation of statistical evidence, and there is likely to be variation on what individual courts demand of plaintiffs when it comes to proving exposure and specific causation as well.

It is, therefore, important for attorneys to be alert to these differences and to be able to educate courts about the proper use of the fundamental concepts.

--By Stephen Blacklocks and Michael Kruse, Hunton & Williams LLP

Stephen Blacklocks, D.Phil., and Michael Kruse, Ph.D., are attorneys in Hunton & Williams' New York office.