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Got **Epidemiology?**

Interpretations of 'Parker' general causation in mass tort cases vary.

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IN MASS TORT litigation, plaintiffs must prove not only that the defendant's product can cause the alleged injury (general causation) but also that it did cause their injury (specific causation). One method of proving specific causation is through "differential diagnosis" in which medical experts consider possible causes of a disease, and, through a scientifically rigorous process, rule out each possibility.

However, before a defendant's product can appear on a list of possible causes, plaintiffs must show that the product can cause the disease generally (general causation). This article compares two recent New York Supreme Court decisions interpreting *Parker v. Mobil Oil,*[1] which provides guidance about the type of epidemiological evidence needed to support general causation.

General Causation Must Come First

Courts consider "differential diagnosis" the method by which experts "establish specific causation by ruling out other causative factors, leaving the exposure to the harmful agent as the likely explanation for plaintiff's harm."[2]

Experts create a "working list of possibilities"[3] to establish what caused the injured plaintiff's disease. The list of possibilities is comprised of external factors for which there are studies demonstrating that the factor can cause the disease. In order to make it onto that list, there must be strong studies demonstrating that a factor can cause the disease generally.

Any differential diagnosis that includes the factor in the list of possibilities without background studies is flawed and unreliable.

For example, the U.S. Court of Appeals for the Second Circuit examined whether an expert's reliance on differential diagnosis could lead to an admissible opinion that the diabetes medication Rezulin could cause cirrhosis.[4] The circuit determined that plaintiff was required to prove that Rezulin *could* cause cirrhosis (general causation) before proving that Rezulin *did* cause the plaintiff's cirrhosis:

> A differential diagnosis is "a patient-specific process of elimination that medical practitioners use to identify the 'most likely' cause of a set of signs and symptoms from a list of possible causes." …As the district court observed, this method does not (necessarily) support an opinion on general causation, because, like any process of elimination, it assumes that "the final, suspected cause remaining after this process of elimination must actually be *capable* of causing the injury." …Here, Dr. Dietrich may have used a differential diagnosis to rule out competing causes of cirrhosis without establishing Rezulin is among them.[5]

New York state courts agree that a differential diagnosis can determine specific causation of a disease only after general causation has been proven. For example, the First Department rejected differential diagnosis without general causation in *Fraser v. 301-52 Townhouse Corp.*[6]

Plaintiff in *Fraser* tried to prove that his respiratory illness was caused by mold and dampness in his apartment.[7] When plaintiff's experts could not point to any scientific proof that the amount of mold and dampness in his apartment could cause his injury, the court found that differential diagnosis was not "an adequate substitute for quantitative proof."[8] Clinical studies and, at times, epidemiological studies, provide the basis for the inclusion of an item in a differential diagnosis checklist.

Epidemiology Under 'Parker'

Epidemiology is the "study of factors determining and influencing the frequency and distribution of disease[s]…and their causes in a defined human population…"[9]

Epidemiological studies compare two populations: one that is exposed to the agent being studied, e.g., patients using a pharmaceutical drug, and the second population that is not exposed to the agent (e.g., patients not on the drug). Measure is then taken of the incidence of disease in each population. The results of epidemiological studies are expressed in terms of "relative risk," which measures the strength of the association between the agent and the disease in a given study.[10]

Relative risk of 1.0 means that the incidence of disease in the exposed group (e.g., the group that took the drug) in the study was the same as the incidence of disease in the control group.[11] Relative risk of less than 1.0 means that, in that study, those exposed to the agent had lower incidence of the disease than those in the control group.[12] Relative risk of greater than 1.0 means that there was greater incidence of disease in the exposed group in that study.

For example, a relative risk of 1.25 means that there is a 25 percent greater incidence of the disease in the exposed group in that study. New York courts have held that "association is not equivalent to causation,"[13] but depending on the strength of the association, epidemiological studies can, at times, contribute to a determination of general causation.[14]

The New York Court of Appeals in *Parker v. Mobil Oil Corp.*[15] required epidemiological evidence to prove general causation in complex injury cases. Plaintiff in *Parker* alleged that his exposure to gasoline containing benzene caused his acute myelogenous leukemia (AML).[16] The Court rejected defendant's argument that plaintiff was required under *Frye* to show exactly how much benzene exposure took place. On the other hand, the court struck plaintiff's causation testimony because it was "lacking in epidemiologic evidence" that benzene in gasoline could cause AML. The Court refused to allow plaintiff to rely on studies demonstrating an association between benzene (but not gasoline containing benzene) and AML:

> [Plaintiff's expert] concentrates on the relationship between exposure to benzene

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> and the risk of developing AML—an association that is not in dispute. Key to this litigation is the relationship, if any, between exposure to *gasoline* containing benzene as a component and AML… Plaintiff's experts were unable to identify a single epidemiologic study finding an increased risk of AML as a result of exposure to gasoline.[17]

The *Parker* decision sets forth two rules governing causation in complex injury cases, such as mass tort litigation.

First, plaintiffs must proffer strong epidemiological proof of general causation; failure to do so results in dismissal.

Second, the epidemiological proof must concern the precise product alleged to be defective, i.e., epidemiology concerning exposure to benzene (but not exposure to gasoline containing benzene) was not sufficient. An expert armed with epidemiological evidence that the defendant's product can cause the plaintiff's injury can then insert that product onto the list of possible causes in a differential diagnosis.

Courts in New York have an uneven record of applying *Parker*'s two requirements, however.

Courts Have Different Interpretations

New York Supreme Court, Nassau County. in *Barbaro v. Eastman Kodak Co.*[18] recently scrutinized a plaintiff's epidemiological evidence under *Parker*.

There, the plaintiff sued for lung cancer allegedly due to exposure to the defendant's liquid cleaners. The liquid cleaners contained the chemical sodium dichromate, a known carcinogen. The court demanded that the plaintiff "submit epidemiologic evidence to support [his] claim that the product at issue caused his injuries" under *Parker*.[19] Plaintiff did submit epidemiological studies linking sodium dichromate to lung cancer, but this was not enough to satisfy *Parker*'s second requirement that the epidemiology tie defendant's product to the injury:

> While there is indisputably evidence that sodium dichromate causes lung cancer, that alone is not adequate: Evidence that the product itself causes cancer is required [citation to *Parker*.] …Kodak has also established that there are no epidemiological studies that demonstrate that sodium dichromate in the form used by plaintiff causes lung cancer. …While the studies in the chromate production, chromate pigment production and the chromium plating industries demonstrated an increase in the risk of lung cancer, Kodak has demonstrated that the use of sodium dichromate was markedly different there in the form, manner and quantity. Those studies are simply incomparable.[20]

The subsequent differential diagnosis, in the absence of epidemiological studies tying the defendant's product to the injury, therefore was unreliable.[21]

The *Barbaro* court's interpretation of *Parker* stands in contrast to the decision by Supreme Court, New York County in *In re: Neurontin Product Liability Litig.*[22]

The *Neurontin* plaintiffs alleged that defendant's antiepileptic drug Neurontin® (also known as gabapentin) caused suicide-related events. Plaintiffs argued that Neurontin® can cause suicide-related events (general causation) because of an epidemiological study conducted by the Food and Drug Administration (FDA Study).[23]

The FDA Study, however, looked at a group of 2,903 patients using Neurontin® (gabapentin) and found only two patients with suicide related events, a risk of 0.069 percent. The control group (given placebo and not gabapentin) included 2,029 patients using placebo, with one patient experiencing a suicide related event, a risk of 0.049 percent. Thus, the odds ratio[24] of gabapentin for suicide related events was 1.40 (risk of exposed group divided by risk of control group).[25] Accordingly, the FDA Study lacked statistical significance with respect to Neurontin®. Had but one of the two patients experiencing a suicide-related event after exposure to Neurontin® dropped out of the study, the odds ratio would have dropped to 0.69.

The *Neurontin* court acknowledged that the plaintiffs lacked "statistically significant information about gabapentin alone"[26] but excused this omission by observing that data about suicide was difficult to obtain.[27] The court then approved "pooling and extrapolation" from data on other antiepileptic drugs, many of which had significantly higher risk for suicide related events.[28] Based on this data, the court held that plaintiffs proffered enough evidence on general causation "to raise a triable issue of fact as to whether Neurontin causes suicide-related events."[29]

The *Neurontin* court interpreted *Parker* very differently than the court in *Barbaro*.

First, there was no statistically significant epidemiology linking Neurontin® and suicide-related events. The lack of "epidemiologic evidence to support the claim"[30] doomed the plaintiff in *Parker*, but was excused in *Neurontin*.

Second, the *Neurontin* court allowed plaintiffs to use epidemiological studies demonstrating increased risk in other products, a method rejected in both *Parker* and then *Barbaro*.

Attorneys litigating mass tort claims should closely examine both the *Barbaro* and *Neurontin* decisions. While some trial courts read *Parker* as requiring epidemiological proof linking the defendant's product to the plaintiff's injury, at least one court does not agree. Until New York appellate courts issue further guidance on exactly what kind of epidemiological proof can be considered, courts may continue to interpret *Parker v. Mobil Oil* in different ways.

1. 7 N.Y.3d 434 (2006).
2. Manual for Complex Litigation (Fourth) §23.273 (Thomson Reuters, 2009). Medical professionals, however, do not use the term "differential diagnosis" to describe a method of determining causation of a patient's disease. Instead, medical practitioners refer to differential diagnosis as the process by which a physician determines only what disease the patient has among a list of possible diseases, not the cause of that disease. See Dorland's Illustrated Medical Dictionary 507 (30th ed., Elsevier Health Sciences, 2003) (defining differential diagnosis as "the determination of which one of two or more diseases or conditions a patient is suffering from, by systematically comparing and contrasting their clinical findings"); see also Federal Judicial Center, Reference Manual on Scientific Evidence 444 (2d ed. 2000) ("[f]or the sake of clarity and consistency, this reference guide uses the term 'differential diagnosis' in its traditional medical sense, that is, referring to the diagnosis of disease, and refers to the process of identifying external causes of diseases and conditions as 'determining cause'…").
3. Philip E. Karmel and Peter R. Paden, "Differential Diagnosis and Proof of Toxic Injury," 229 NYLJ, 3 (2003).
4. *Ruggiero v. Warner-Lambert Co.*, 424 F.3d 249 (2d Cir. 2005).
5. Id. at 254 (citations omitted) (emphasis in original). The court in *Ruggiero*, however, stopped short of saying that differential diagnosis can "never provide a sufficient basis for an opinion as to general causation." Id.
6. 57 A.D.3d 416 (1st Dept. 2008).
7. Id. at 417.
8. Id. at 420; see also *Marso v. Novak*, 42 A.D.3d 377, 377 (1st Dept. 2007) (even though plaintiff's expert excluded "all other possibilities for causation of the [plaintiff's] stroke," court holds that it was "not generally accepted in the scientific community that bradycardia is a risk factor").
9. Dorland's Illustrated Medical Dictionary 626 (30th ed. 2003).
10. Federal Judicial Center, Reference Manual on Scientific Evidence 348 (2d ed. 2000).
11. Id. at 349.
12. Id.
13. *Fraser*, 57 A.D.3d at 417, quoting Reference Manual on Scientific Evidence 336.
14. Reference Manual on Scientific Evidence 336.
15. 7 N.Y.3d 434 (2006).
16. 7 N.Y.3d at 434.
17. Id. at 449 (emphasis in original).
18. 2010 WL 597204, at *1 (Sup. Ct. Nassau Cty. Jan. 28, 2010).
19. Id. at *3.
20. 2010 WL 597204, at *10.
21. Id. at *15.
22. 2009 WL 1979936, at *1 (Sup. Ct. N.Y. Cty. May 15, 2009).
23. Id. at *4. The "FDA Study" was the Statistical Review and Evaluation: AntiEpileptic Drugs and Suicidality, available at http://www.fda.gov/ohrms/dockets/ac/08/briefing/2008-4372b1-01-FDA.pdf.
24. The concepts of "relative risk" and "odds ratio" are related. Relative risk cannot be used to study disease incidence from case control studies because those studies involve patients that already have the disease studied. In those situations, an "odds ratio" compares the number of patients with the disease to the number of patients not having the disease and accounting for exposure in each group. Reference Manual on Scientific Evidence 350 (2d ed. 2000).
25. FDA Study, Table 13.
26. 2009 WL 1979936, at *4.
27. Id. ("no large scale, randomized, placebo-controlled studies, designed specifically to test for an association between gabapentin and suicidality have been performed").
28. Id. at *5.
29. Id. at *6.
30. *Parker*, 7 N.Y.3d at 449.