

Differential Diagnosis - Trending Toward Exclusion?

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The recent decisions of *Perry v. Novartis*^[1] and *Zandi v. Wyeth*^[2] signify a trend towards courts excluding unreliable expert witness testimony based on differential diagnosis in toxic tort cases. Each of these courts concluded that, although differential diagnosis can be a generally accepted method for determining causation, the proffered expert witnesses improperly and unreliably applied the methodology in these cases by failing to account for unknown causes of the plaintiffs' alleged injuries.

Introduction and Background

Differential diagnosis (more accurately "differential etiology")^[3] is a two-step process whereby scientifically plausible causes of an injury are "ruled in," then the expert "rules out" the least plausible causes until reaching the one that cannot be ruled out.

In the context of toxic torts, expert testimony based on differential diagnosis is frequently proffered in two categories of cases. The first category involves cases where the medical community recognizes the toxicity of the drug or chemical at issue. The second category includes cases in which the medical community has not widely recognized that the drug or chemical is capable of causing the kind of harm alleged by the plaintiff.

In the first category of cases, the plaintiff may establish causation by demonstrating that the agent caused this specific plaintiff's injury ("specific causation"). In the second category, as a practical matter, the plaintiff must first establish that the agent is generally capable of causing the kind of injury the plaintiff alleges ("general causation"). Then, the plaintiff may move on in the hope of establishing specific causation.

Although expert witnesses have been proffered to give testimony based on differential diagnosis even though general causation has not been established, courts have generally recognized that such testimony is unreliable. In other words, courts in most jurisdictions acknowledge that the proffered expert must have a sufficient basis to "rule in" the drug or chemical at issue as a plausible cause of plaintiff's injury.^[4] Conversely, many courts have been reluctant to exclude expert testimony that fails to reliably "rule out" plausible causes of the injury, especially when its causes are largely unknown. Recently, however, several courts have taken a closer look at the reliability/unreliability of specific causation testimony reached by differential diagnosis where the injuries alleged have unknown causes.

Perry v. Novartis: Differential Diagnosis and Disease with Unknown Causes

After developing non-Hodgkin lymphoma, Perry brought suit against the pharmaceutical company Novartis, claiming that a Novartis-manufactured emollient named Elidel caused Plaintiff's lymphoma. The plaintiff proffered two experts, arguing that their specific causation testimony based on differential diagnosis was reliable. The *Perry* Court disagreed and held that the proffered testimony was inadmissible under *Daubert*

because the experts' differential diagnosis analysis could not rule out unknown causes of non-Hodgkin lymphoma.

Each expert "ruled out" various known risk factors, but admitted that most patients who are diagnosed with non-Hodgkin lymphoma are categorized as idiopathic, meaning that the lymphoma has no known cause. However, neither expert "ruled out" the possibility that the plaintiff's lymphoma was idiopathic. The failure to exclude the most likely scenario—which is that Perry's lymphoma had no known cause—rendered the experts' testimony unreliable.

In holding the proffered testimony inadmissible, the court noted:

This is not to say that where most diagnoses of a disease are idiopathic it is impossible to prove specific causation. But in those cases, analysis beyond a differential diagnosis will be required.^[5]

The *Perry* Court excluded the testimony and went on to grant summary judgment for Novartis.

Zandi v. Wyeth: Similar testimony inadmissible under Frye-Mack

Several months after the *Perry* decision, the *Zandi* Court affirmed a trial court ruling that expert testimony similar to that proffered in *Perry* was inadmissible, based on a *Frye-Mack* analysis. In *Zandi*, the plaintiff brought suit against several manufacturers of hormone replacement therapy drugs ("HRT"), claiming that ingestion of HRT drugs caused her to develop breast cancer. Plaintiff's evidence of specific causation consisted of the testimony of two proffered expert witnesses, Dr. Layfield and Dr. Bender. The district court held the testimony of both experts inadmissible.

Dr. Layfield proposed to testify regarding causation based on differential diagnosis and the results of a Ki-67 test. The *Zandi* Court found that the plaintiff did not introduce any evidence tending to show that the medical community generally accepts differential diagnosis as a method for diagnosing breast cancer. The Court went on to note that even if such evidence existed, Dr. Layfield's testimony would nonetheless be inadmissible because he failed to "rule out all other hypotheses, or at least explain why the other conceivable causes are excludable."^[6] Dr. Layfield's use of the Ki-67 test was also found to be unreliable since the Ki-67 test is not generally used to determine etiology.

The plaintiff's second expert, Dr. Bender, professed to base her opinion regarding causation on differential diagnosis. However, she did not faithfully "rule out" plausible risk factors. Instead, Dr. Bender testified that she did not "think that it's a matter of ruling in or ruling out...[She thinks that] different causes can work independently or they can work synergistically" to cause breast cancer. The court excluded her testimony as unreliable since she failed to faithfully apply the methodology that forms the basis of differential diagnosis—ruling out plausible causes.

In upholding the district court's decision excluding the testimony of both experts, the *Zandi* Court noted:

Breast cancer does not lend itself to differential diagnosis because the scientific community has not accepted that breast cancer has a limited number of discrete and recognized possible causes such that ruling out one cause would implicate another.^[7]

The proffered expert witness testimony in *Zandi*, like that in *Perry*, was unreliable and thus inadmissible because the testimony was based on faulty differential diagnosis analysis. Specifically, the experts could not "rule out" plausible causes of plaintiff's injury since the alleged injury could be idiopathic. Thus, differential diagnosis alone is an unreliable method to determine specific causation where the plaintiff's alleged injury has unknown causes. Such testimony is inadmissible, regardless of whether the court analyzes admissibility under the *Daubert* or *Frye-Mack* standards.

Conclusion

Although not universally followed, *Perry* and *Zandi* evince a trend of excluding specific causation testimony based solely on differential diagnosis (or testimony based on differential diagnosis in conjunction with another unreliable method) when the plaintiff's injury could be idiopathic. More significantly, the *Perry* and *Zandi* decisions clearly articulate the inherent unreliability of differential diagnosis analysis when the injury the plaintiff alleges likely arises from unknown causes.

[1] *Perry v. Novartis*, 564 F. Supp.2d 452 (E.D. Penn. 2008).

[2] *Zandi v. Wyeth*, 2009 Minn. App. Unpub. LEXIS 785 (Minn. Ct. App. July 21, 2009), *petition denied*, 2009 Minn. LEXIS 648 (Minn. Sept. 29, 2009).

[3] *Hendrix v. Evenflo*, 255 F.R.D. 568, 596 (N.D. Florida, 2009).

[4] See e.g., *Ervin v. Johnson & Johnson*, 492 F.3d 901, 904 (7th Cir. 2007) (excluding expert testimony when the basis of the expert's decision to rule in a particular potential cause was based on temporal proximity); *Jazairi v. Royal Oaks Apts.*, 217 Fed. Appx. 895 (8th Cir. 2007) (same); *McClain v. Metabolife*, 401 F.3d 1233, 1241 (11th Cir. 2005) (rejecting witness's testimony regarding general causation when the proffered expert failed to consider a dose-response relationship in concluding that the agent was toxic).

[5] *Perry*, 564 F. Supp.2d at 470.

[6] *Zandi*, 2009 Minn. App. Unpub. LEXIS 785 at *18, citing *McDonough v. Allina Health Sys.*, 685 N.W.2d 688, 695 (Minn.App. 2004).

[7] *Zandi*, 2009 Minn. App. Unpub. LEXIS 785 at *17.