MEDICAL CAUSATION AND RELIABILITY

Recent cases concerning Parlodel, a lactation suppressant, demonstrate the *Daubert* issues associated with admission of scientifically reliable medical evidence necessary to prove causation. Some courts have allowed expert opinions into evidence to establish a causal link between Parlodel and acute myocardial infarction (AMI);[i] others have refused admission of expert medical evidence claiming a link between Parlodel and seizures or strokes.[ii] Analysis of one of the Parlodel cases, *Globetti v. Sandoz Pharmaceutical Corporation,*[iii] is helpful in evaluating a court's determination of how it approached compliance with its *Daubert* "gatekeeping" requirements.

Mrs. Globetti suffered an AMI about six days after delivering her sixth child, having taken Parlodel twice daily after the child's birth to suppress lactation. Her overall health was good, she was not a smoker or overweight, and had "protective" (very low) cholesterol levels. She had no history of high blood pressure and had never experienced hypertension during pregnancy nor delivery. Angiography of her heart wall failed to reveal any thrombus, dissection, or occlusion of the coronary artery that could account for the AMI. Her initial treating cardiologist concluded her heart event had been caused by a spasm of the coronary artery. This cardiologist knew of the possible association between Parlodel and AMI but opined Mrs. Globetti's heart spasm was spontaneous. Other treating cardiologists and retained experts expressed medical opinions the Parlodel contributed to the arterial spasm that caused the AMI. The defendant pharmaceutical company (Sandoz) challenged these causation opinions by summary judgment motion.

Sandoz contended the medical expert opinion of the plaintiff's treating and retained doctors was nothing more than unscientific speculation, excludable under *Daubert*. According to Sandoz, plaintiffs needed an epidemiological study showing an increased risk of AMI associated with Parlodel use for a sufficiently reliable scientific opinion to be admissible. Plaintiffs opposed the motion, arguing that epidemiological evidence was not needed since there was plenty of scientifically reliable data from which a medical expert could conclude Parlodel can cause vasoconstriction sufficiently severe to cause AMI: animal studies, case reports, Food and Drug Administration Adverse Drug Reaction Reports (ADRs) and the generally accepted opinion of the medical community that Parlodel is a risk factor for AMI since it causes vasoconstriction.

The *Globetti* opinion began its analysis by noting the four *Daubert* factors[iv] were neither exclusive nor exhaustive, that it remains for the trial court to determine what procedures are necessary for it to analyze the admissibility of an expert's opinion[v] and *Daubert* supplemented the old *Frye*[vi] standard with a more "flexible" approach. Thus, the "gatekeeping" role of the trial court requires a practical recognition of what can be known and how it is known. The gatekeeping role is to separate opinions supported by appropriate validation based on "good grounds" from simple subjective speculation masquerading as scientific knowledge. The court wrote:

It is not part of the trial judge's gatekeeping role to determine whether the

> proffered opinion is scientifically *correct* or *certain* in the way one might think of the law of gravity. The gatekeeping role is addressed to mere evidentiary admissibility; it is the fact-finder's role (usually a jury) to determine whether the opinion is correct or worthy of credence. For the trial court to overreach in the gatekeeping function and determine whether the opinion evidence is correct or worthy of credence is to usurp the jury's right to decide the facts of the case. All the trial judge is asked to decide is whether the proffered evidence is based on "good grounds" tied to the scientific method.[vii]

Three of plaintiffs' experts used the differential diagnostic technique, wherein the physician lists the known possible causes of a condition or disease, usually from most likely to least likely, then utilizes diagnostic tests eliminating causes from the list until left with the most likely cause. Diagnostic tests typically include physical examination, medical history, testing of blood and other body fluids, MRIs, CAT scans, X-rays and other techniques for "falsifying" a hypothesis the disease came from a particular listed cause. The court recognized tests such as these performed on Mrs. Globetti are scientifically accepted techniques for confirming or eliminating specific causes for her AMI. Thus, the court considered the doctors' conclusion the AMI was caused by an arterial spasm to be well-supported.

The court then considered the quality of the next part in the causation opinion that the spasm was caused by plaintiff's ingestion of Parlodel. Experts for plaintiffs reasoned Parlodel has vasoconstrictive characteristics and is capable of causing a coronary artery spasm and was the most likely cause of AMI in the absence of any other reasonable explanation. Sandoz attacked this reasoning by claiming there was no reliable evidence Parlodel can cause vasconstriction and plaintiffs' experts were incorrect in concluding there were no other causes for Mrs. Globetti's AMI.

The court concluded plaintiffs' experts based their opinion Parlodel can cause vasoconstriction sufficiently severe to cause an AMI on sound scientific evidence and methodologies. As foundation for their opinions plaintiffs' experts cited animal studies of ergot alkaloids similar to Parlodel to have a vasoconstrictive effect; Sandoz acknowledged and relied upon these studies in internal documents. Case reports and ADRs reported to the FDA were consistent with literature reviews that identified Parlodel as a risk factor for AMI in the postpartum period. Also, several medical textbooks state that bromocriptine (the chemical compound from which comes Parlodel) is a risk factor for AMI in the postpartum period. These sources and others were more than adequate evidence from which a reliable conclusion could be drawn about the association between Parlodel use, arterial spasm and AMI. Sandoz pointed out there is no epidemiological study showing an increased risk of AMI associated with bromocriptine. This lack of study, according to defendant, was fatal to plaintiffs. The court disagreed. Plaintiffs argued and the court agreed that an epidemiological study of the association between Parlodel and AMI is not practical because of the relative rarity of AMIs among postpartum women. The court wrote:

> To gather a population of postpartum women with a sufficient sub-population of those who have suffered an AMI to be statistically significant would require hundreds of thousands, if not millions, of women. The evidence suggests that

> AMI occurs in postpartum women at the rare rate of 1 to 1.5 per 100,000 live births. Thus, even in a study of one million women, the sub-population of those suffering an AMI would be only ten to fifteen women, far from enough to allow drawing any statistically significant conclusions. In short, the best scientific evidence available *as a practical matter* is that presented by plaintiffs' experts.[viii]

The court also commented on the ethical problems associated with experimenting on human beings just to satisfy an evidentiary standard. A control-group study would require administering Parlodel to women and exposing them to the possibility of strokes and heart attacks. Thus, for the association between Parlodel and AMI or stroke to be scientifically established, a scientist must expect a number of deaths to occur among the test subjects.

The court further noted although one can question the adequacy of the scientific evidence relied upon by plaintiffs' experts, the validity of the methodologies is adequate. Thus, the court denied the defendant's motion for summary judgment on medical causation since there is reliable scientific information from which a reasonable scientific inference can be drawn that Parlodel can cause vasoconstriction under circumstances of low vascular resistance and that such vasoconstriction can cause arterial spasm to occlude a coronary artery leading to a myocardial infarction.

i *Globetti v. Sandoz Pharmaceutical Corporation,* 111 F.Supp. 2d 1174 (N.D. Alabama 2000); *Anderson v. Sandoz Pharmaceutical Corporation*, 77 F.Supp. 2d 804 (S.D. Texas 1999).

ii *Hollander v. Sandoz Pharmaceutical Corporation*, 95 F.Supp. 2d 1230 (W.D. Okla. 2000); *Glastetter v. Novartis Pharmaceutical Corporation*, 107 F.Supp. 2d 1015 (E.D. Mo. 2000); *Brumbaugh v. Sandoz Pharmaceutical Corporation*, 77 F.Supp. 2d 1153 (D. Mont. 1999)

iii 101 F.Supp. 2d 1174 (N.D. Alabama 2000).

iv These factors were testability, peer review and publication, assessing the known or potential rate of error of the proposition, and whether it has found general acceptance in the scientific community.

v See *Kumho Tire Company, Ltd. v. Carmichael,* 526 U.S. 137, 119 S.Ct. 1167, 143 L.Ed. 2d 238 (1999).

vi *Frye v. United States*, 293 F. 1013 (1923).

vii *Globetti,* 101 F.Supp. 2d at 1177.

viii *Id.* at 1179.