

In the United States Court of Federal Claims

No. 99-212V
Filed Under Seal April 22, 2009.¹
Reissued May 7, 2009.

**JOHN DOE/11 and JANE DOE/11,
as representatives of the Estate of
CHILD/DOE/11, Deceased,**

Petitioners,

v.

**SECRETARY OF THE DEPT. OF
HEALTH AND HUMAN SERVICES,**

Respondent.

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* **National Vaccine Injury**
* **Compensation Program, 42 U.S.C.**
* **§ 300aa-1, et seq.; Hepatitis B**
* **Vaccine; Burden of Proof; Prima**
* **Facie Case; Expert Witness**
* **Credibility.**
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Richard Gage, Richard Gage, P.C., Cheyenne, WY, for Petitioners.

Glenn MacLeod, Torts Branch, Civil Division, U.S. Department of Justice, Washington, DC, for Respondent.

OPINION AND ORDER

WILLIAMS, Judge

This matter comes before the Court on Petitioners' Motion for Review of the Special Master's Decision on Remand, which denied Petitioners' claim that the Hepatitis B vaccine caused the death of their daughter, Monica.

¹ This opinion was filed under seal on April 22, 2009, in accordance with the Rule 18(b) of the Rules of the United States Court of Federal Claims (RCFC), Appendix B. Each party was afforded 14 days from the date of sealed filing to object to the public disclosure of any information supplied by that party. No redactions having been received, the Court publishes this opinion *in toto*, correcting errata.

In the original Decision on Entitlement, the Special Master ruled that Petitioners did not establish that the vaccine caused Monica's death, and instead found that a "factor unrelated" to the Hepatitis B vaccination, Sudden Infant Death Syndrome (SIDS), which the Special Master characterized as asphyxiation, overlaying or wedging, caused her death. This Court vacated the original decision and remanded the petition, finding inter alia that the Special Master had improperly allocated and applied the burden of proof.

On remand, the Special Master found that Petitioners failed to establish a prima facie case that the Hepatitis B vaccination caused Monica's death and did not reach the issue of whether Defendant established that an unrelated factor caused her death. In the instant Motion for Review, Petitioners argue that the Special Master failed to follow this Court's instructions on remand, issued arbitrary and capricious findings of fact on Monica's brain weight, and erroneously considered evidence of SIDS as a factor unrelated in analyzing Petitioners' prima facie case. Because Petitioners have not demonstrated that their asserted legal or factual errors warrant reversal or remand, this Court upholds the Special Master's Decision on Remand.

Background²

On December 21, 1994, Monica, a healthy infant of seven and one-half weeks of age, received her second Hepatitis B vaccination at approximately 2:00 p.m.³ The vaccination was administered in Monica's thigh. After Monica's appointment, the family went holiday shopping at a mall for several hours. Monica's father carried her in a transportable car seat, and she slept during the entire shopping trip and did not cry or interact with her parents. Monica's mother tried to feed Monica a bottle on several occasions towards the end of the shopping trip, but Monica did not drink from the bottle. Monica's parents did not take her temperature. The family returned home between approximately 5:00 and 5:30 p.m. that evening and took a nap. Monica's father laid Monica on a futon next to him, face up and propped up on a pillow. He slept from approximately 5:30 until 6:00 p.m. beside Monica, and upon awakening, discovered that Monica, who was still propped up on a pillow face up, was "blue in the face" and not breathing.

Monica's mother called paramedics at 6:49 p.m., and her father performed CPR until the paramedics arrived via ambulance at 6:54 p.m. The paramedics "found [Monica] supine on couch."

² The background is set forth in the Special Master's decisions and this Court's earlier decision and will be briefly summarized here. See Doe/11 v. Sec'y of HHS (Doe I), No. 99-212V, 2008 WL 649065 (Fed. Cl. Spec. Mstr. Jan. 31, 2008); Doe/11 v. Sec'y of HHS (Doe II), 83 Fed. Cl. 157 (2008); Doe/11 v. Sec'y of HHS (Doe III), No. 99-212V, 2008 WL 4899356 (Fed. Cl. Spec. Mstr. Oct. 29, 2008).

³ The Hepatitis B vaccine is "a noninfectious viral vaccine derived by recombination from Hepatitis B surface antigen and cloned in yeast cells [and] administered intramuscularly for immunization of children and adolescents and of persons at increased risk for infection." Dorland's Illustrated Medical Dictionary 2044 (31st ed. 2007).

Pet'rs' Ex. 4 at 2. The paramedics determined that Monica had no heartbeat, pulse, or respiration, and she did not respond to CPR. Id. The emergency room records listed Monica's diagnosis as "cardiopulmonary arrest, unknown participant." Pet'rs' Ex. 5 at 6. The paramedics also noted that Monica's "skin was warm, dry and extremit[ies] were mottled and chest and abd[omen] was white . . . and [patient's] abd[omen] was distend[ed]." Pet'rs' Ex. 4 at 1. Shortly after her arrival at the emergency room, Monica was diagnosed as having suffered cardiopulmonary arrest of an unknown cause, and she was pronounced dead at 8:00 p.m.

Forensic pathologist Robert M. Anthony M.D/Ph.D. performed an autopsy on Monica on December 22, 1994, the day after her death.⁴ Dr. Anthony recorded Monica's weight as 12 pounds 12 ounces and her length as 25 inches. Dr. Anthony noted that Monica's bladder and stomach were both empty and that her lungs revealed "moderate pulmonary congestion and edema." Pet'rs' Ex. 6 at 4-5.⁵ Dr. Anthony determined the condition of Monica's brain to be "grossly unremarkable" with "no evidence of edema or herniation." Id. at 5. The autopsy report did not indicate that any of Monica's visceral organs, other than her lungs, showed the presence of edema. Id. at 3-5. Dr. Anthony recorded the cause of Monica's death as SIDS.⁶

⁴ Dr. Anthony did not testify at the hearing, and his credentials are not in the record.

⁵ As the Special Master noted, edema is "the presence of large amounts of fluid in the intercellular tissue spaces of the body, usually referring to demonstrable amounts in the subcutaneous tissues." Doe III, 2008 WL 4899356 at *5 n.15 (quoting Dorland's Illustrated Medical Dictionary 589 (30th ed. 2003)).

⁶ The Special Master described SIDS as follows:

SIDS is "the sudden and unexpected death of an apparently healthy infant, typically occurring between the ages of three weeks and five months, and not explained by careful postmortem studies." *Dorland's Illustrated Medical Dictionary* 1833 (30th ed. 2003). Additionally, "sudden infant death syndrome" has been defined by a panel convened by the National Institute of Child Health and Human Development as "the sudden death of an infant under 1 year of age which remains unexplained after a thorough case investigation, including performance of a complete autopsy, examination of the death scene, and review of the clinical history." Ps' Ex. 20 at 2 (Ramzi S. Cotran, et al., *Robbins Pathologic Basis of Disease* (6th ed.1997) The death usually occurs while the infant is asleep. *Id.* As a diagnosis of exclusion, SIDS is the rendered diagnosis when neither the autopsy, the examined death scene nor the clinical history yields an explanation for the death. *See id.*; *see also* R's Ex. FF (Marie Valdes-Dapena, M.D., *Sudden Infant Death Syndrome: Pathologic Findings*, Vol. 19, No. 4 Clinics in Perinatology, at 703 (Dec.1992).

The Althen Factors

In Althen v. Secretary of Health & Human Services, 418 F.3d 1274, 1278 (Fed. Cir. 2005), the Federal Circuit set forth a three-pronged test a petitioner must meet in order to establish causation under the Vaccine Act. Under Althen, a petitioner must prove by a preponderance of the evidence:

- (1) a medical theory causally connecting the vaccination and the injury;
- (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and
- (3) a showing of a proximate temporal relationship between vaccination and injury.

Althen, 418 F.3d at 1278.

The Special Master's First Decision, Vacatur and Remand

In the original Decision on Entitlement, the Special Master ruled that Petitioners did not establish that the vaccine caused Monica's death, and instead found that a "factor unrelated" to the Hepatitis B vaccination, Sudden Infant Death Syndrome (SIDS) -- which the Special Master characterized as asphyxiation, overlaying or wedging -- caused her death.

The Court vacated the Special Master's decision and remanded the matter, finding that the Special Master had misallocated the burden of proof and effectively required Petitioners to disprove that SIDS was the cause of death as part of their prima facie case. The Court further ruled that, to the extent the Special Master had concluded that an idiopathic condition either defeated Petitioners' prima facie case of causation or constituted an unrelated factor that caused Monica's death, the decision was contrary to the Vaccine Act's definition of a "factor unrelated" as a cause that "does not include any idiopathic, unexplained, unknown, hypothetical or undocumentable cause, factor, injury, illness or condition" 42 U.S.C. § 300aa-13(a)(2) (emphasis added). The Court instructed the Special Master to clarify what unrelated factor caused Monica's death and to assess whether such factor was idiopathic.

The Court also held that the Special Master placed an overly onerous burden of proof on Petitioners under Althen's prong one by requiring them to prove that the medical theory linking the Hepatitis B vaccine with edema and an adverse reaction known as "cytokine storm" was "more likely than not," instead of establishing that the theory was medically plausible. Finally, the Court found that the Special Master had not considered the totality of the evidence in finding that Monica's brain weight of 570 grams was within the normal range. The Court found that the Special Master did not address Petitioners' evidence of normal brain weight and appeared to rely on a study whose subjects suffered moderate to severe edema as a marker of normal brain weight. The Court instructed the

Doe III, 2008 WL 4899356 at *5 n.12 (emphasis in original omitted).

Special Master to reevaluate the totality of evidence on brain weight and reconsider her conclusion that Monica's brain weight was within the normal range.

The Special Master's Decision On Remand

In her Decision on Remand, the Special Master again determined that Petitioners were not entitled to compensation under the Vaccine Act, applying the Althen test and finding that Petitioners had not established a prima facie case. On remand, the Special Master concluded that Petitioners had satisfied their burden under Althen's first prong, in that they proffered a biologically plausible medical theory causally connecting the vaccination and the injury. However, the Special Master found that Petitioners failed to satisfy their burden of proof as to Althen's second and third prongs.

With respect to Althen prong two -- "logical sequence of cause and effect showing that the vaccination was the reason for the injury" -- the Special Master concluded that "in the absence of other evidence that would support a finding that Child Doe/11 suffered an encephalopathic injury," she was not persuaded that Monica's somnolence represented the "significantly decreased level of consciousness" indicative of encephalopathy. Doe III, 2008 WL 4899356 at *9-13. The Special Master noted that Monica's medical records contained no references to any other standard symptoms of encephalopathy, such as "irritability, fever, vomiting, or seizures." Id. at *13.

In assessing whether Monica's brain weight at autopsy was significantly heavy and edematous, the Special Master considered all the record evidence on brain weight. The Special Master credited the expert opinion of pediatric neuropathologist Dr. Enid Gilbert-Barness that Monica's brain was not significantly heavy or edematous and concluded that Monica's body length and body weight, which were in the 95th and 90th percentile respectively, were not out of proportion with Monica's brain weight "and not much beyond, if at all beyond, the range of normal brain weight." Id. at *17.

In the context of assessing Petitioners' evidence under Althen's prong-two causation, the Special Master also considered the competing experts' views on whether Monica's death was a SIDS death. The Special Master credited the testimony of Respondent's expert, Dr. Gilbert-Barness, that most deaths attributable to SIDS actually resulted from asphyxiation and that Monica's nap environment placed her at risk of accidental asphyxiation. The Special Master also cited studies that correlate SIDS diagnoses with a heavy brain at autopsy. The Special Master clarified that she considered evidence regarding potential alternative causation for the limited purpose of evaluating Petitioners' "proposed causal sequence for a vaccine injury." Id. at *22.

In continuing to assess prong two, the Special Master weighed the competing expert testimony on whether Monica's Hepatitis B vaccination had triggered a cytokine storm. The Special Master credited the testimony of Respondent's expert, pediatric immunologist Dr. Christine McCusker, who concluded that a cytokine storm and life-threatening inflammation in Monica's brain would not have resulted from a vaccination administered in her thigh because such a cytokine

reaction would occur locally, not over long distances, and because cytokine-induced cerebral edema has only been shown where brain tissue is infected or compromised by viruses. Dr. McCusker also found a disconnect in the causal chain between vaccination and death because Monica did not exhibit the symptoms of a cytokine reaction -- headache, restlessness, vomiting, nausea, diarrhea, rapid heartbeat, drop in blood pressure, respiratory failure or renal impairment. The Special Master concluded that Petitioners' proposed sequence of events leading from vaccine to encephalopathy did not "appear to be supported by the facts of the case," based primarily on her determination that the evidence, in particular the testimony of Petitioners' pathology expert Dr. John J. Shane, did not establish that Monica's brain was significantly heavy or edematous, which left an "absence of clinical symptoms of the type and severity that would be expected" Id.

Examining Althen's prong three, the Special Master determined that Petitioners failed to establish a temporal relationship between Monica's vaccination and her injury. The Special Master credited Dr. McCusker's testimony that Monica's death occurred too soon to have resulted from a cytokine storm in lieu of the contrary testimony of Petitioners' immunology expert, Dr. Alan S. Levin. In weighing the testimony and credibility of Petitioners' expert, the Special Master observed that Dr. Levin first testified that a cytokine storm could develop in seven hours, incorrectly believing that Monica's death occurred "eight hours or something like that" after vaccination. Id. at *28-29; see Tr. at 308, 310-11. He lowered his assessment ("[t]hree hours is also reasonable") when counsel and the Special Master pointed out that Monica had died within three to four and one-half hours after vaccination. Tr. at 311-12. Dr. Levin also distinguished the study cited by Dr. McCusker -- Respondent's Exhibit DD -- because it involved healthy adults, one of whom "passed out" only 2.5 hours after injection. Id.⁷ However, the Special Master viewed this study differently, noting that all of the study's subjects suffered symptoms during the first two to three hours after injection that Monica did not exhibit. The Special Master concluded that the record did "not support the compressed time frame that Dr. Levin proposed . . . [or] a finding in petitioners' favor regarding the causal relationship between Child Doe/11's vaccination and her death." Doe III, 2008 WL 4899356 at *29-30.

Discussion

Jurisdiction And Standard Of Review

Jurisdiction lies in this Court pursuant to 42 U.S.C. § 300aa-12(e). In reviewing a decision of the Special Master, this Court may (1) uphold the findings of fact and conclusions of law, (2) set aside any of the Special Master's findings of fact or conclusions of law "found to be arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law," or (3) "remand the petition to the Special Master for further action in accordance with the court's direction." 42 U.S.C.

⁷ This study, Ganesh Suntharalingam et al., Cytokine Storm in Phase 1 Trial of the Anti-CD28 Monoclonal Antibody TGN1412, 355 New Eng. J. Med. 1018, 1018-28 (2006), described a cytokine storm induced in otherwise healthy trial subjects by the intravenous injection of an experimental drug.

§ 300aa-12(e)(2)(A)-(C); Althen, 418 F.3d at 1277-78; Saunders v. Sec’y of HHS, 25 F.3d 1031, 1033 (Fed. Cir. 1994). Findings of fact of the Special Master are reviewed under the arbitrary and capricious standard, legal questions are reviewed under the “not-in-accordance-with-law” standard, and discretionary rulings are reviewed under the abuse of discretion standard. Saunders, 25 F.3d at 1033 (quoting Munn v. Sec’y of HHS, 970 F.2d 863, 870 n.10 (Fed. Cir. 1992)).

This Court must uphold the Special Master’s findings unless it concludes that those findings are arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law. See 42 U.S.C. § 300aa-12(e)(2)(B). Reversible error is “extremely difficult to demonstrate” if the Special Master “has considered the relevant evidence of record, drawn plausible inferences and articulated a rational basis for the decision.” Hines v. Sec’y of HHS, 940 F.2d 1518, 1528 (Fed. Cir. 1991). As the Federal Circuit recognized, it is not the role of a court reviewing a special master’s decision to reweigh the factual evidence or to assess whether a special master correctly evaluated the evidence. Lampe v. Sec’y of HHS, 219 F.3d 1357, 1360 (Fed. Cir. 2000) (citing Munn, 970 F.2d at 871).

A decision is arbitrary and capricious if it relied on factors that Congress has not intended, entirely failed to consider an important aspect of the problem, offered an explanation for its decision that runs counter to the evidence, or is so implausible that it could not be ascribed to a difference in view or the product of the Special Master’s expertise. Motor Vehicle Mfrs. Ass’n v. State Farm Mut. Auto. Ins. Co., 463 U.S. 29, 43 (1983); Hines, 940 F.2d at 1527-28.

Elements And Burden Of Proof

The Vaccine Act provides two methods for a petitioner to establish causation. See 42 U.S.C. § 300aa-13(a)(1); Walther v. Sec’y of HHS, 485 F.3d 1146, 1149 (Fed. Cir. 2007); Capizzano v. Sec’y of HHS, 440 F.3d 1317, 1319-20 (Fed. Cir. 2006); Althen, 418 F.3d at 1278. First, causation of an injury due to a vaccination is presumed if a petitioner demonstrates, through medical records or expert testimony, that the injury is one listed in the Vaccine Injury Table, 42 U.S.C. § 300aa-14(a), and shows by a preponderance of the evidence that the injury occurred within the time provided by the Table. Capizzano, 440 F.3d at 1319-20; Munn, 970 F.2d at 865.

Second, in a case such as the instant action where the alleged injury is not listed in the Vaccine Injury Table, a petitioner must establish causation-in-fact. Walther, 485 F.3d at 1149; Pafford v. Sec’y of HHS 451 F.3d 1352, 1355 (Fed. Cir. 2006); Shyface v. Sec’y of HHS, 165 F.3d 1344, 1350-51 (Fed. Cir. 1999). The Act provides:

Compensation shall be awarded under the Program to a petitioner if the special master or court finds on the record as a whole--

(A) that the petitioner has demonstrated by a preponderance of the evidence the matters required in the petition by section [300aa-11(c)(1)], and

(B) that there is not a preponderance of the evidence that the illness, disability, injury, condition, or death described in the petition is due to factors unrelated to the administration of the vaccine described in the petition.

The special master or court may not make such a finding based on the claims of a petitioner alone, unsubstantiated by medical records or by medical opinion.

42 U.S.C. § 300aa-13(a)(1).

A petitioner can establish a prima facie case on causation by providing: ““(1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of a proximate temporal relationship between vaccination and injury.”” De Bazan v. Sec’y of HHS, 539 F.3d 1347, 1351-52 (Fed. Cir. 2008), (quoting Althen, 418 F.3d at 1278); see also Walther, 485 F.3d at 1150; Capizzano, 440 F.3d at 1324. A petitioner must show that the vaccine was a “substantial factor” in bringing about the harm, not merely a “non-negligible” factor. De Bazan, 539 F.3d at 1351 (citing Shyface, 165 F.3d at 1352 and the Restatement (Second) of Torts § 432(1)).

If the petitioner establishes a prima facie case, the burden of proof shifts to the respondent to prove by a preponderance of the evidence that the “illness, disability, injury, condition, or death described in the petition is due to factors unrelated to the administration of the vaccine described in the petition.” 42 U.S.C. § 300aa-13(a)(1)(B); Walther, 485 F.3d at 1151.

The Act defines a “factor unrelated” as follows:

(A) does not include any idiopathic, unexplained, unknown, hypothetical, or undocumentable cause, factor, injury, illness, or condition, and

(B) may, as documented by the petitioner’s evidence or other material in the record, include infection, toxins, trauma (including birth trauma and related anoxia), or metabolic disturbances which have no known relation to the vaccine involved, but which in the particular case are shown to have been the agent or agents principally responsible for causing the petitioner’s illness, disability, injury, condition, or death.

42 U.S.C. 300aa-13(a)(2).

The separate “factor unrelated” inquiry is to be made only after the Special Master has determined that a petitioner has successfully put forward a prima facie case of causation. Walther,

485 F.3d at 1151-52; Grant v. Sec’y of HHS, 956 F.2d 1144, 1149 (Fed. Cir. 1992). If the Government fails to rebut the petitioner’s prima facie showing of causation by a preponderance of evidence, the petitioner is entitled to compensation under the Act. De Bazan, 539 F.3d at 1352; Walther, 485 F.3d at 1151; 42 U.S.C. § 300aa-13(a)(1)(B).

If the record evidence is in equipoise on any requisite element of proof, the party bearing the burden of proof with respect to such element cannot prevail because that party has not marshaled a preponderance of the evidence in its favor. See Knudsen v. Sec’y of HHS, 35 F.3d 543, 550 (Fed. Cir. 1994) (recognizing with regard to alternative causation that “[i]f the evidence is seen in equipoise, then the government has failed in its burden of persuasion and compensation must be awarded”).

The Special Master Properly Applied The Althen Factors In Her Decision On Remand

Petitioners argue in their Motion for Review that the Special Master committed several legal errors in her decision following remand. First, although Petitioners applaud the Special Master’s conclusion under Althen’s prong one that the Hepatitis B vaccine can cause cytokine storm, edema, and death, they fault her failure to articulate a sufficient rationale for this conclusion. Because this is the first case in which the Hepatitis B vaccine has been found capable of causing this reaction, Petitioners contend that the Special Master was required to explain her reasoning to impart sufficient precedential value to the decision. They further argue that the Special Master’s failure to do so prejudiced them in building their case and urge this Court to step in and articulate a rationale in support of this admittedly proper legal conclusion. The Court declines, as such action is unwarranted under the circumstances here.

In its earlier decision, this Court concluded that the Special Master had erred in her prong-one analysis by requiring Petitioners to demonstrate that their medical theory of causation be “more likely than not” and instructed the Special Master to apply a different legal standard on remand, i.e., whether Petitioners’ theory of causation was biologically plausible. Doe II, 83 Fed. Cl. at 173-74. This Court quoted Althen’s statement that a “possible link” between a vaccination and injury may permit a finding of causation even though the link involved a “sequence hitherto unproven in medicine.” See id. at 174 (quoting Althen, 418 F.3d at 1280).⁸ The Special Master followed this instruction, concluding that Petitioners had satisfied prong one based upon the testimony of Petitioners’ experts Dr. Levin and Dr. Shane, and the literature they cited.

Nor have Petitioners demonstrated that the Special Master’s failure to set forth an expansive rationale for this conclusion prejudiced their case. In attacking the Special Master’s prong-two analysis, Petitioners contend that the Special Master erred by conflating her Althen prong-one and prong-two analyses. The Special Master did not conflate these analyses in her remand decision, but

⁸ Accord Nussman v. Sec’y of HHS, 83 Fed. Cl. 111, 118 (Fed. Cl. 2008) (stating a petitioner is not required to prove the proffered medical theory, citing the special master’s decision in that case which cited Knudsen, 35 F.3d at 549).

properly separated prong one from prong two. Legal error cannot be demonstrated simply because the Special Master concluded that Petitioners satisfied Althen prong one but failed to prove prong two. As the Federal Circuit articulated in Capizzano:

The second prong of the *Althen III* test is not without meaning. There may well be a circumstance where it is found that a vaccine *can* cause the injury at issue and where the injury was temporally proximate to the vaccination, but it is illogical to conclude that the injury was actually caused by the vaccine. A claimant could satisfy the first and third prongs without satisfying the second prong when medical records and medical opinions do not suggest that the vaccine caused the injury, or where the probability of coincidence or another cause prevents the claimant from proving that the vaccine caused the injury by preponderant evidence.

440 F.3d at 1327 (emphasis in original).

Petitioners argue that the Special Master, after conceding Petitioners had satisfied their burden under Althen's "can cause" prong, "appears to denigrate her own . . . finding that Hepatitis B vaccine can cause cytokine storm" by ultimately favoring Dr. McCusker's testimony denying Althen's "did cause" prong. Pet'rs' Mot. for Review at 18. While Dr. McCusker did espouse generalized principles disputing the medical plausibility of a cytokine storm resulting from a Hepatitis B vaccination, Dr. McCusker articulated specific reasons demonstrating why she concluded Monica did not experience a cytokine storm: the vaccine was given too far away from the locus of the cytokine storm (in the thigh) and none of the symptoms associated with cytokine storm in a study -- headache, fever, vomiting, bowel distress and hypotension -- appeared in Monica. In short, Petitioners have not demonstrated error in the legal framework of the Special Master's prong-one and prong-two analyses.

The Special Master's Fact-Finding On Brain Weight Was Not Arbitrary And Capricious

Petitioners next argue that Monica's brain weight is the determinative factor for assessing whether the Hepatitis B vaccine caused Monica's death and take issue with the Special Master's fact-finding on brain weight. Petitioners allege two errors in the Special Master's fact-finding on brain weight: her reliance on the same skewed study the Court cautioned against when it remanded the case, and her determination that Monica's height was 23 inches -- a measurement not in the record -- which informed the Special Master's analysis of brain weight. Id. at 35-36.⁹

⁹ Petitioners also argue that the Special Master should have regarded Monica's somnolence as a symptom of encephalopathy. Pet'rs' Mot. for Review at 20-22. However, Petitioners' expert, Dr. Shane, stated that he would defer to a pediatrician on whether somnolence was a normal reaction to a vaccination. Tr. at 87. Respondent's experts, both of whom are pediatricians, testified that Monica's somnolence was a normal reaction to the vaccine. Tr. at 139, 251, 288-89. It was

Before turning to these specific allegations of error, the Court notes that Petitioners' contention that brain weight is the dispositive indicator of causation is flawed. Petitioners posit that Monica's significantly heavy brain weight demonstrates a high degree of edema which demonstrates that a cytokine storm, triggered by the Hepatitis B vaccine, erupted. Two considerations refute this argument. First, as the Special Master recognized, the evidence of edema is not confined to brain weight alone. Rather, there is other evidence apart from evidence of brain weight that establishes that Monica's brain was not significantly edematous. The autopsy report found no edema except in the lungs, and expressly noted that the condition of Monica's brain was "grossly unremarkable" with "no evidence of edema or herniation." Pet'rs' Ex. 6 at 5. The Vaccine Act directs special masters to consider the "relevant medical and scientific evidence contained in the record," including the "autopsy or coroner's report" in determining whether to award compensation. 42 U.S.C. § 300aa-13(b)(1). The autopsy slides do not establish severe edema either -- the evidence of what the slides show is in equipoise. While Petitioners' expert, Dr. Shane, claimed to have seen halo formation -- or clear spaces around the glial cells and the blood vessels of the brain -- in the autopsy slides, which he attributed to cerebral edema, Respondent's expert, Dr. Gilbert-Barnes, who examined the same slides, did not observe such phenomena; she did "not see the changes that Dr. Shane described." Compare Pet'rs' Ex. 11 at 1-2, and Tr. at 61, with Tr. at 122.

Second, there is a further problem with Petitioners' evidence on causation independent of the issue of brain weight -- the lack of evidence that a cytokine storm occurred. Dr. McCusker, an expert in pediatric immunology, disagreed with Petitioners' contention that Monica died as the result of a "cytokine storm" caused by the Hepatitis B vaccination. Tr. at 243. While Dr. McCusker agreed with Petitioners' expert, Dr. Levin, that a vaccination induces a cytokine response from the immune system to counter the antigens released by the vaccination, she noted that only in rare cases does a cytokine storm occur. Id. at 251-53. Further, Dr. McCusker testified that a cytokine storm begins with symptoms that Monica did not display -- headache, fever, vomiting, bowel distress, and hypotension. In addition, Dr. McCusker testified that while a cytokine storm frequently results in vascular collapse and multi-organ failure, Monica's autopsy results showed no signs of inflammation consistent with multi-organ failure. Tr. at 254-55, 260-61; Resp't's Ex. E. Dr. McCusker further testified that the inflammatory effects of a cytokine reaction are primarily local, and because Monica received her Hepatitis B vaccination in the leg, "there's no way to connect that with a life-threatening encephalitis or encephalopathy." Tr. at 249, 257-58, 291. Thus, according to Respondent's expert, Monica did not exhibit the expected symptoms of a cytokine storm.

Importantly, the Special Master's conclusion that Petitioners had not proven that Monica's brain was severely edematous or that a cytokine storm had occurred was dependent upon her assessment of the credibility of conflicting experts -- determinations that are "virtually unreviewable" on appeal. Bradley v. Sec'y of HHS, 991 F.2d 1570, 1575 (Fed. Cir. 1993). For example, while Dr. Shane observed "halos" indicative of edema in Monica's brain, Dr. Gilbert-Barnes testified that she did "not see the changes that Dr. Shane described." Compare Pet'rs' Ex.

therefore reasonable for the Special Master to discount Monica's somnolence as a symptom of encephalopathy.

11 at 1-2, with Tr. at 122. While Petitioners' experts testified that Monica's heavy organs were consistent with their cytokine storm theory, Respondent's experts attributed this heaviness to blood congestion. Tr. at 142, 144-46. In short, the expert testimony that the Special Master credited militated against a finding of severe edema resulting from a cytokine storm.

Nor can this Court conclude that the Special Master's findings on brain weight were arbitrary and capricious. On remand the Special Master followed this Court's instructions and assessed all of the evidence on brain weight. In attacking the Special Master's fact-finding on brain weight, Petitioners argue that the Special Master continued to rely on the skewed study "Brain Weight of Danish Children," Respondent's Exhibit LL.¹⁰ While Petitioners are correct that this study should not have been used in establishing a baseline for normal brain weight since 83% of the subjects had edematous brains, this error -- mention of the flawed study -- does not undermine the Special Master's conclusion that Petitioners failed to prove that Monica's brain was significantly heavy and edematous. It is Petitioners who have the burden of proving that Monica's brain weight of 570 was significantly heavy and edematous as a result of a cytokine storm triggered by the vaccine.¹¹ Even removing this study from the analysis, the remaining evidence of record does not, as Petitioners posit, establish that Monica's brain weight was significantly heavy and edematous.

The Special Master did not depend exclusively on Exhibit LL for her conclusion that Monica's brain at autopsy "reflected a marginally increased brain weight beyond the heaviest listed brain weights . . . within the normal range for her age group." Doe III, 2008 WL 4899356 at *15. Petitioners' own expert considered a brain weight of 555 grams (accounting for error) on the high side of normal, and Petitioners' experts did not explain why Monica's brain weight of 570 grams was "significantly" heavy in light of the fact that 555 grams represented the top of the purported normal range. Tr. at 68-69, 105-06. All of the experts agreed that Monica's brain was heavy; what was disputed was whether it was "significantly" heavy or so heavy as to be severely edematous resulting from a cytokine storm.¹²

¹⁰ The Special Master had accepted Dr. Gilbert-Barnes' two estimates of normal brain weight -- 516 grams and 560 grams -- without considering the totality of the evidence. In addition, the brain weight chart from which Dr. Gilbert-Barnes drew her high-end estimate of 560 grams for a normal brain weight was taken from a study in which 83% of the subjects suffered from moderate to severe edema -- a fact that the authors of that study recognized contributed to a "systematically higher" mean weight. Resp't's Ex. LL at 11.

¹¹ The Special Master observed that Monica's brain weight was within the normal range in the context of assessing whether Petitioners had met their burden of establishing that Monica's brain was both significantly heavy and edematous.

¹² According to the 490-gram mean and 51-gram standard deviation relied on by Petitioners' expert, Dr. Shane, Monica's brain at autopsy was 570 grams -- 80 grams heavier than Petitioners' proffered mean of 490 grams. Her brain weight was within approximately 1.57 standard deviations of Petitioners' mean. Petitioners did not address whether this deviation was significant in this

Second, Petitioners claim that the Special Master improperly calculated Monica's body length at 23 inches, a measurement not in the record, and used that measurement to inform her assessment of brain weight. The record regarding Monica's length is contradictory. While Dr. Shane relied on Monica's growth chart to conclude that she was in the 50th percentile for height, other records indicated that Monica was in the 95th percentile for height. Compare Pet'rs' Ex. 3 at 7, with Pet'rs' Ex. 2 at 2, 3. The Special Master's decision to credit hospital records from the day of Monica's birth that indicate she was in the 95th percentile for height was not arbitrary and capricious. Doe III, 2008 WL 4899356 at *16; Pet'rs' Ex. 2 at 2, 3. The Court also finds reasonable the Special Master's reliance upon "the length at autopsy [as] the proper measurement" because of the absence of "the difficulties associated with measuring the length of a squirming baby." Doe III, 2008 WL 4899356 at *16 n.29. Monica's autopsy report stated that she measured 25 inches in height at death -- which would place Monica well above the 95th percentile in height according to Monica's pediatric growth chart. Pet'rs' Ex. 3 at 7. Petitioners argue that the 25-inch measurement is "clearly wrong" because it would have required Monica's pediatrician "to be wrong by 3 and 1/4 inches," and would have required her to grow at the rate of "3/4 of an inch a week" from birth. Pet'rs' Mot. for Review at 35. The Special Master extrapolated a shorter length from other evidence in the record, and there is no basis to overturn the Special Master's decision to credit one set of height measurements over another.¹³ Given the contradictions in the record, the Special Master did not err in extrapolating that Monica's height approximated 23 inches and using that measurement to inform her decision that Monica's height was consistent with a heavy brain weight. There is evidence indicating that Monica was a long baby -- medical records indicating she was in the 95th percentile at birth and above the 95th percentile at autopsy.

Given the totality of the evidence on brain weight, Petitioners have not established that the Special Master's conclusion that Monica's brain weight was not significantly heavy or edematous was arbitrary and capricious. The Special Master's reference to the flawed study and extrapolation of Monica's body length were at most harmless error as they were not critical to this result. Even removing consideration of the skewed study and the Special Master's extrapolation of Monica's length, substantial evidence supports the Special Master's conclusion that Petitioners failed to prove a prima facie case on prong two. See, e.g., Hines v. Sec'y of HHS, 940 F.2d 1518, 1526 (Fed. Cir. 1991) ("[E]ven if it was error, it was harmless because . . . the special master's decision was based on a number of factors and she has not shown that reliance on the judicially noticed incubation period . . . was likely critical to the result.").

context as requested by the Court. See Tr. at 23 and Order dated January 16, 2009.

¹³ Petitioners question how the Special Master arrived at her estimate that Monica was nearly 23 inches in height at death. Pet'rs' Mot. for Review at 35. It appears that the Special Master extrapolated this number by taking the height of 21.75 inches listed in Monica's hospital records and increasing it by the "growth differential" listed in Monica's growth charts over a period of seven weeks. See Doe III, 2008 WL 4899356 at *16.

The Special Master Properly Considered Evidence of Alternative Causation in Assessing Petitioners' Prima Facie Case

Petitioners also argue that the Special Master ignored the Court's remand instructions by including within her prong-two analysis a discussion of SIDS, a potential "factor unrelated." Pet'rs' Mot. for Review at 18-20. Because the Special Master determined on remand that Petitioners did not establish a prima facie case, it was unnecessary for her to shift the burden of proof and reach the issue of whether respondent demonstrated that a factor unrelated caused Monica's death. Nevertheless, the Special Master did assess the conflicting expert testimony on SIDS in her decision on remand. See Doe III, 2008 WL 4899356 at *19-22. Petitioners argue that the Special Master's intermingling of the SIDS discussion in the prong-two analysis constituted legal error. The Court disagrees.

The Special Master cited testimony from Dr. Shane and Dr. Gilbert-Barnes, who agreed that SIDS, a term once used to describe unexplainable infant deaths, has "become a definable disease process." Id. at *19 (quoting testimony of Dr. Shane, Tr. at 77-78). Dr. Shane stated that SIDS deaths often are connected with upper respiratory problems. Id. Dr. Gilbert-Barnes testified that most deaths attributed to SIDS actually resulted from asphyxiation caused by "the [sleeping] position . . . and . . . the hazards of mattresses, beds and bedding." Id. at *20 (quoting Tr. at 123 (alteration in original)). Dr. Gilbert-Barnes testified that "examination of the death scene" is one of the most important steps in clarifying a SIDS diagnosis, and that Monica's nap environment put her at risk of accidental asphyxiation. Id. (citing Tr. at 123-24, 126). The Special Master credited testimony from Dr. Gilbert-Barnes describing "overlying" and "wedging" as methods of accidental asphyxiation and cited studies submitted by Respondent that correlate SIDS diagnoses with heavy brain weights at autopsy. Id. at *21, *22 n.32; see Resp't's Ex. MM at 1 (study reporting that 57 percent of brains from SIDS victims were above the 99th percentile in brain weight); Resp't's Ex. KK at 9 (study reporting that 81 percent of SIDS victims were above the 95th percentile in brain weight).

In the context of assessing Althen's prong two, the Special Master determined that:

Many of the classic findings in a post mortem examination of a SIDS case were present in Child Doe/11 at autopsy. She was a long, weighty baby with a large brain. Although there was evidence of some edema in her brain, because edema of the degree that Dr. Shane asserted was present in Child Doe/11 is accompanied generally by clinical symptoms of a severity and type that were not present in this case, . . . the undersigned is not persuaded that the edema was as severe as Dr. Shane described.

2008 WL 4899356 at *21.

The Special Master, however, did not go so far as to conclude that the cause of Monica's death was SIDS. Rather, the Special Master simply considered the evidence that "many of the classic findings" of a SIDS death were present in Monica in the course of assessing whether Petitioners had met their burden of proving their prima facie case that the Hepatitis B vaccine caused Monica's death. The Special Master explained:

The undersigned considered, as a whole, the testimony of petitioners and of the parties' experts regarding Child Doe/11's clinical and pathological presentation (including the experts' discussion about the expected pathological findings in an explained SIDS death), the filed medical literature and the medical records in evaluating whether petitioners' medical theory reflected a logical sequence of cause and effect supported by a reliable medical explanation. The testimony of respondent's experts and the literature filed by respondent's experts exposed the difficulties with petitioners' proposed theory. . . . Although some of the testimony and literature supplied by respondent might also have advanced a claim of alternate causation by respondent if petitioners had prevailed in proving a prima facie case, the undersigned considered the aspects of the offered evidence (including that offered by respondent) for the limited purpose of evaluating carefully the reliability of the medical underpinnings of petitioners' proposed causal sequence for a vaccine injury.

Here, petitioners' proposed sequence of post-vaccinal events that led to an encephalopathy does not appear to be supported by the facts of the case. Dr. Shane's opinion of causation rested heavily on his view that Child Doe/11's brain was heavy and that heaviness necessarily indicated that Child Doe/11 had moderate to moderately severe edema, . . . and the opinion of petitioners' expert, Dr. Levin, rested as well on a finding of significant edema in Child Doe/11's brain based on Dr. Shane's opinion of Child Doe/11's pathology In the absence of clinical symptoms of the type and severity that would be expected medically in circumstances in which the pathological picture was as dire as petitioners' experts described, however, the undersigned is not persuaded that Child Doe/11's pathological presentation was, in fact, as critical as petitioner's experts have asserted. Because the undersigned finds that petitioners have not carried their burden of proving that Child Doe/11's brain was significantly edematous, an important aspect of petitioners' proposed sequence of cause and effect, petitioners do not prevail on the second prong of the Althen standard.

Id. at *22. The Special Master did not require Petitioners to eliminate SIDS as an alternative cause. Rather, the Special Master simply weighed the SIDS evidence as part of the totality of the evidence in considering Althen's prong two. The Special Master weighed the evidence of Monica's brain weight and edema and compared it with similar indicators of SIDS deaths to assess whether the severity of Monica's edema and the heaviness of her brain comported with Petitioners' claim that the Hepatitis B vaccine had induced a cytokine storm, edema and death. Petitioners have not demonstrated that the Special Master's review of the SIDS evidence for this limited purpose was error.

The Special Master's consideration of SIDS is consistent with the Federal Circuit's recent guidance in De Bazan v. Secretary of Health and Human Services, 539 F.3d 1347, 1353 (Fed. Cir. 2008), which was issued after this Court's decision remanding this case. There, the Federal Circuit held that a special master may consider proof relating to alternative causes in assessing whether the petitioner established a prima facie case. The Federal Circuit explained that the respondent "is permitted to offer evidence to demonstrate the inadequacy of the petitioner's evidence on a requisite element of the petitioner's case-in-chief." De Bazan, 539 F.3d at 1353. The Federal Circuit clarified:

While a failure of proof that the vaccine was the cause of the petitioner's injury suggests that some other cause was responsible, that is not equivalent to having proven by preponderant evidence that a *particular* agent or condition (or multiple agents/conditions) unrelated to the vaccine was in fact the sole cause (thus excluding the vaccine as a substantial factor).

Id. at 1354 (emphasis in original). Here, consistent with De Bazan, the Special Master properly considered the record as a whole in evaluating Petitioners' prima facie case -- including respondent's expert's characterization of overlaying or wedging as a method of accidental asphyxia or SIDS and a potential alternative cause of Monica's death.

The Federal Circuit in Pafford, 451 F.3d at 1359, also approved the special master's consideration of potential alternative causes in assessing whether a petitioner had proven a prima facie case of causation in fact. The Pafford court stated:

Without a link between Still's disease and the vaccinations, the Special Master properly introduced the presence of the other unrelated contemporaneous events as just as likely to have been the triggering event as the vaccinations. . . . Hence, petitioner did not show it was *more* likely that the vaccinations were a but-for cause of and a substantial factor in her contracting Still's disease.

Id.; cf. Walther, 485 F.3d at 1151 (stating that "a petitioner is certainly permitted to use evidence eliminating other potential causes to help carry the burden on causation and may find it necessary

to do so when the other evidence on causation is insufficient to make out a prima facie case, as was true in Pafford.”).

By considering the record in its entirety, the Special Master followed the directive of the Vaccine Act, which states that “[c]ompensation shall be awarded . . . if the special master or court finds on the record as a whole . . . that the petitioner has demonstrated by a preponderance of the evidence” the claims of the petition. 42 U.S.C. § 300aa-13(a)(1) (emphasis added). Moreover, because the autopsy report listed SIDS as the cause of Monica’s death, and both Petitioners and Respondent introduced evidence on SIDS as a potential cause of Monica’s death, it was proper for the Special Master to consider evidence relating to SIDS as a potential alternative cause in assessing Petitioners’ prima facie case. The Vaccine Act directs special masters to consider the “relevant medical and scientific evidence contained in the record,” including the “autopsy or coroner’s report” in determining whether to award compensation. 42 U.S.C. § 300aa-13(b)(1).

The Special Master Correctly Determined That Petitioners Failed to Prove Temporal Proximity Under Althen’s Prong Three

Petitioners must establish each prong of the Althen test independently in order to make out a prima facie case of causation. Failure to satisfy any of the three prongs prevents Petitioners from making their prima facie showing. Thus, even if Petitioners had demonstrated that the Special Master wrongly assessed the evidence of brain weight, cytokine storm and edema, and that they had in fact satisfied Althen’s prong two, they still must establish a proximate temporal relationship between the vaccination and injury under prong three in order to prevail. Petitioners’ Motion for Review does not point to any discrete reversible error in the Special Master’s prong-three analysis. Instead, Petitioners state that the Special Master’s decision:

makes it clear that she views the pathology in this case as integral to answering the question posed by *Althen* step 3. This actually makes some sense. If Hepatitis B vaccine can cause wide spread edema, and cerebral edema, because it is a superantigen, and Monica had the pathological findings the petitioners claim . . . then one would logically look for an exposure to a superantigen. Hepatitis B is the only superantigen we have to choose from in this case. Therefore, the answer to *Althen* step 3 is intertwined with the answer to *Althen* step 2.

Pet’rs’ Mot. for Review at 27.

Contrary to Petitioners’ characterization, the Special Master did not make it clear that she viewed “the pathology in this case as integral to answering the question posed by *Althen* step 3.” Id. Instead, she relied upon Dr. McCusker’s testimony that Monica did not exhibit the symptoms of a cytokine storm, symptoms that should have appeared within 50-90 minutes of the injection.

Further, while Petitioners endeavor to characterize the Special Master’s decision as intertwining the analysis of Althen steps two and three, making her conclusion on step three wholly dependent upon her conclusion on step two, the Special Master properly segregated the proof on each step. As required by precedent, the Special Master separately considered Althen prongs two and three. See Pafford, 451 F.3d at 1360 (“[T]he Special Master did not err in requiring specific evidence about a medically acceptable time frame linking the [injury] to the vaccinations at issue.”). In her prong three analysis, the Special Master determined that Petitioners failed to establish a proximate temporal relationship between vaccination and injury because Monica’s death occurred some four hours after her vaccination. In so ruling, the Special Master credited the testimony of Dr. McCusker that Monica’s death occurred “too soon” to have resulted from the Hepatitis B vaccine. Tr. at 258. Dr. McCusker testified: “[T]he progression occurs over days. It doesn’t happen over hours. It takes days for there to accumulate enough edema . . . for the final event to occur.” Id. at 258. Dr. McCusker cited a study, Respondent’s Exhibit DD, that demonstrated the effects of a cytokine storm on a group of healthy adults, all of whom suffered early symptoms, such as restlessness, nausea, vomiting and diarrhea, that Monica did not display. Id. at 252-55, 259-61; Doe III, 2008 WL 4899356 at *29. This study’s subjects all began to show symptoms of an excessive cytokine reaction within the first 50 to 90 minutes after their injections; however, Monica did not show any such symptoms during that time. Resp’t’s Ex. DD at 2; Doe III, 2008 WL 4899356 at *30.¹⁴

Petitioners have not articulated any basis for overturning the Special Master’s decision to credit the testimony of Dr. McCusker. So too, the Special Master reasonably discounted the testimony of Dr. Levin. This expert first opined that a cytokine storm could develop in seven hours, but then, after being reminded that Monica’s father discovered that Monica was blue in the face and not breathing four to four and one-half hours after the vaccination, instead opined that a cytokine storm could develop in just three hours. Tr. at 308, 310-12. This Court sees no reason to disturb the Special Master’s credibility determination. As the Federal Circuit has recognized, the Special Master’s determinations about the credibility of expert witnesses are “‘virtually unreviewable’” on appeal. Bradley, 991 F.2d at 1575 (quoting Hamsch v. Dept. of the Treasury, 796 F.2d 430, 436 (Fed. Cir. 1986)); Munn, 970 F.2d at 871 (stating that a reviewing Court should not “examine the probative value of the evidence or the credibility of the witnesses. These are all matters within the purview of the fact finder.”); see also Nordwall v. Sec’y of HHS, 83 Fed. Cl. 477, 491 (stating when referring to expert testimony that “[i]t is not the job of the Court to second guess the Special Master’s credibility determination”).

Moreover, no other persuasive evidence supports the conclusion that a cytokine storm developed in Monica in the abbreviated time frame of three to four hours. Rather, other evidence on temporal proximity suggests that Monica’s death did not result from a cytokine storm in such a short timeframe. In addition, no persuasive evidence directly addressed how a child of Monica’s

¹⁴ The one symptom Petitioners identified in Monica -- somnolence -- does not establish a cytokine storm. Dr. McCusker testified that Monica’s somnolence was a normal reaction to a vaccination. Tr. at 288-89.

age could die from a cytokine storm before exhibiting any of the documented symptoms of such a reaction.

In sum, there is no basis to disturb the Special Master’s reasonable conclusion under Althen’s prong three that Monica’s death occurred too soon to have been caused by the vaccine. See De Bazan, 539 F.3d at 1352 (stating “we see no reason to distinguish between cases in which onset is too soon and cases in which onset is too late; in either case, the temporal relationship is not such that it is medically acceptable to conclude that the vaccination and the injury are causally linked”).

Conclusion

1. This Court upholds the findings of fact and conclusions of law of the Special Master.
2. The Petition for Review is DENIED.
3. The Clerk shall not disclose this decision publicly for 14 days.

s/Mary Ellen Coster Williams _____
MARY ELLEN COSTER WILLIAMS
Judge