

In the United States Court of Federal Claims

No. 99-212V

(Filed Under Seal: July 31, 2008)

**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.; Burden of**
* **Proof; Prima Facie Case;**
* **Unrelated Factor; Hepatitis B**
* **Vaccine; Sudden Infant Death**
* **Syndrome.**
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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 ORDER¹

WILLIAMS, Judge

This matter comes before the Court on Petitioners’ Motion for Review of the Special Master’s decision denying compensation for the death of their daughter, Monica, under the National Vaccine Injury Compensation Program. Petitioners assert that a hepatitis B vaccination, administered when Monica was seven weeks old, triggered an adverse reaction known as a “cytokine storm” which caused cerebral edema and led to her death approximately four-and-a-half hours after she received the vaccination.

¹ In accordance with the Rule 18(b) of the Rules of the United States Court of Federal Claims (RCFC), Appendix B, this opinion is filed under seal. Each party is afforded 14 days from the date of sealed filing to object to the public disclosure of any information supplied by that party.

The Special Master found that Petitioners did not satisfy their burden of establishing a prima facie case that the vaccine caused Monica's death. Instead, the Special Master determined that Monica's death was caused by a "factor unrelated" to the hepatitis B vaccination -- Sudden Infant Death Syndrome (SIDS). In so ruling, the Special Master did not allocate the burden of proof as required by the Vaccine Act. Rather, the Special Master required Petitioners to disprove that SIDS was the cause of death as part of their prima facie case. This analytical construct runs counter to the Vaccine Act. Under the statute, Petitioners initially have the burden to prove their prima facie case by a preponderance of the evidence. If they are successful, the burden shifts to the respondent to prove by a preponderance of the evidence that Monica's death was caused by some factor other than the vaccine. The Special Master's failure to allocate the burden of proof properly warrants a remand so that the Special Master, who heard the testimony and assessed the witnesses' credibility, may reweigh the evidence in accordance with the proper legal standard.

However, this Court's review of this matter does not end here. The Special Master determined that SIDS, not the vaccine, caused Monica's death without considering the Vaccine Act's proscription against relying upon an unknown factor as the cause of injury. The Act defines 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). Yet SIDS appears to be a label for precisely such an unknown, hypothetical condition. As this Court has held, "SIDS is an idiopathic, unexplained diagnosis, and as such cannot defeat a petitioner's established case." Davis v. Sec'y of HHS, 54 Fed. Cl. 230, 235 (2002). Further, the decision is unclear as to what the Special Master deemed the unrelated factor to be -- relying upon Respondent's expert, Dr. Enid Gilbert-Barness, the Special Master appeared to equate SIDS with "asphyxia," "overlay," and "wedging" by Monica's father, who slept next to her on a futon for approximately 30 minutes prior to her death. To the extent that the Special Master's decision concluded that an idiopathic or hypothetical condition either defeated Petitioners' prima facie case of causation or constituted an unrelated factor which caused Monica's death, the decision is contrary to law. On remand, the Special Master should clarify precisely what unrelated factor, if any, caused Monica's death, and assess whether such factor is idiopathic.

Finally, the Special Master determined that Monica's brain weight of 570 grams fell within the normal range and was not edematous, crediting the testimony of Dr. Gilbert-Barness, who relied upon two studies. Eighty-three percent of the subjects in one study suffered from moderate to severe edema and consequently had brain weights that were higher than normal. Nonetheless, Dr. Gilbert-Barness and the Special Master accepted those weights as normal in comparison to Monica's. In citing the second source, Dr. Gilbert-Barness relied upon the brain weight for a child two to three months old -- when Monica was only seven weeks old. In concluding that Monica's brain weight was within the normal range, the Special Master credited testimony which relied upon inapposite studies and failed to consider other record evidence suggesting that Monica's brain was heavy. As such, on remand, the Special Master is directed to reevaluate the totality of the evidence on brain weight.

Factual Background²

Medical History

Monica was born on October 31, 1994, in Sacramento, California. Joint Stipulation of Uncontested Facts (Joint Stip.) ¶ 1. Although her mother's pregnancy was classified as "at risk," both the pregnancy and Monica's birth were uneventful. Doe/11 v. Sec'y of HHS, No. 99-212V, 2008 U.S. Claims LEXIS 71 at *4-5 (Fed. Cl. Jan. 31, 2008). Monica weighed 9 pounds, 10 ounces at birth and was 55.2 centimeters long. Pet'rs' Ex. 2 at 2. Monica's Apgar scores at birth and her newborn examination were normal. Joint Stip. ¶ 2. Monica received her first hepatitis B vaccination on the date of her birth, and she was discharged from the hospital the following day. Id. ¶ 3.³ On November 9, 1994, nine days after her birth, Monica was examined by her pediatrician who reported that she was developing normally. Id. ¶ 4.

The Vaccine And Monica's Death

On December 21, 1994, at approximately seven weeks of age, Monica returned to her pediatrician for a well-baby examination, and her pediatrician again reported that her condition and development were normal. Joint Stip. ¶ 5. Monica received her second hepatitis B vaccination that same day at approximately 2:00 p.m. Id. ¶ 6. According to the testimony of her father, Monica received this vaccination in the thigh. Tr. 36. After Monica's appointment, the family went holiday shopping at a mall for several hours. Tr. 29-36. Monica slept during the shopping trip and did not cry or interact with her parents during that time. Tr. 30-31, 37. Monica's father carried her in a transportable car seat during the entire shopping trip. Tr. 37. 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 which was "very unusual [as] she was a good eater . . ." Tr. 15. Monica's parents were not overly concerned about her inactivity or lack of appetite as they had been informed by Monica's pediatrician that the vaccine would make her drowsy. Tr. 29, 31. Monica did not vomit or display any abnormal jerking or movement after receiving the vaccination. Monica's parents did not take her temperature and did not notice any signs that she had a fever. Tr. 15, 37-38.

The family returned home between approximately 5:00 and 5:30 p.m. that evening, and the family took a nap. Tr. 11-12, 30-31. Monica's father laid Monica on a futon next to him, face up

² The factual background is derived from the Special Master's Decision, the Joint Stipulation of Uncontested Facts dated October 4, 2006, the exhibits submitted by the parties, and the transcript of the one-day hearing held on October 12, 2006.

³ The hepatitis B vaccine is "a noninfectious viral vaccine derived by recombination from hepatitis B surface antigen and cloned in yeast cells; administered intramuscularly for immunization of children and adolescents and of persons at increased risk for infection." Dorland's Illustrated Medical Dictionary 1999 (30th ed. 2003). According to Petitioners' expert and medical literature, this vaccine is classified as a superantigen. Tr. 214; Pet'rs' Ex. 28.

and propped up on a pillow. Tr. 18-19, 31-32. 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. Tr. 19, 33, 188; Joint Stip. ¶ 7. Monica’s father described the baby’s sleeping position when he woke up as follows:

Q: You looked over -- if you can sort of describe the position that you were in with Monica on the futon -- was she in your arms?

A: No. She -- there’s a pillow going across -- we’re both laying -- you know -- we’re both laying on the back of the pillow, and like her head’s right next to mine.

...

We were both laying on a pillow, and the futon is -- it’s like a mattress that like slopes -- and we’re just kind of laying on a pillow, and she’s like even with me. And I look over, and she’s blue.

Tr. 40. Monica’s mother testified that the baby’s father “was laying down on the couch. Monica was right next to him, propped up on a pillow.” Tr. 18. Both parents testified that Monica was sleeping “face-up.” Tr. 18-19.

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. Joint Stip. ¶ 7. The paramedics “found [Monica] supine on couch.” Pet’rs’ Ex. 4 at 1. The ambulance records indicate that Monica “was last checked on 30 minutes ago and was fine.” *Id.* The paramedics determined that Monica had no heartbeat, pulse, or respiration, and she did not respond to CPR. *Id.* The ambulance records listed Monica’s diagnosis as “cardiopulmonary arrest, unknown participant.” *Id.* 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].” *Id.* at 1. Shortly after her arrival at the emergency room that evening, Monica was diagnosed as having suffered cardiopulmonary arrest of an unknown cause, and she was pronounced dead at 8:00 p.m. Joint Stip. ¶ 8.

The Autopsy

Dr. Robert M. Anthony, M.D.-Ph.D., a forensic pathologist with the Sacramento Coroner’s Office performed an autopsy on Monica on December 22, 1994, the day after her death, and issued the Report of Autopsy on January 25, 1995. Joint Stip. ¶ 9; Pet’rs’ Ex. 6 at 2.⁴ Dr. Anthony recorded Monica’s weight as 12 pounds 12 ounces and her length as 25 inches. Pet’rs’ Ex. 6 at 2. Dr. Anthony recorded the following organ weights:

⁴ Dr. Anthony did not testify at the hearing.

heart	28 grams
right lung	71 grams
left lung	69 grams
liver	225 grams
spleen	28 grams
right kidney	22 grams
left kidney	22 grams
brain	570 grams

Id. at 4-5. Dr. Anthony noted that Monica’s bladder and stomach were both empty and that her lungs revealed “moderate pulmonary congestion and edema.” Id.⁵ When describing Monica’s cardiovascular system, Dr. Anthony noted that there were “rare epicardial petechiae,” and that “[t]he epicardial surface is smooth and glistening.” Id. at 4.⁶ Dr. Anthony determined the condition of Monica’s brain to be “grossly unremarkable” with “no evidence of edema or herniation.” Id. at 5.⁷ The autopsy report did not indicate that any of Monica’s visceral organs, other than her lungs, showed the presence of edema. See id. at 3-5. Nor did the report state whether the weight of Monica’s visceral organs and brain were within the normal range for an infant of her age. Id. The autopsy report, under “Pathological Diagnoses,” recorded the following:

I. Well-developed, well-nourished female infant without evidence of congenital anomalies. A. Rare epicardial petechiae.

Id. at 6. Dr. Anthony recorded Monica’s cause of death as SIDS. Id.⁸

⁵ Edema is “the presence of abnormally large amounts of fluid in the intercellular tissue spaces of the body, usually referring to demonstrable amounts in the subcutaneous tissues.” Dorland’s Illustrated Medical Dictionary 589 (30th ed. 2003).

⁶ Petechiae are “pinpoint, nonraised, perfectly round, purplish red spot[s] caused by intradermal or submucous hemorrhage.” Dorland’s Illustrated Medical Dictionary 1411 (30th ed. 2003). Epicardial pertains to “the epicardium,” which is “the lower portion of the esophagus, extending from the hiatus esophagi to the cardia.” Dorland’s Illustrated Medical Dictionary 625 (30th ed. 2003).

⁷ Herniation is the “abnormal protrusion of an organ or other body structure through a defect or natural opening in a covering, membrane, muscle or bone.” Dorland’s Illustrated Medical Dictionary 844 (30th ed. 2003).

⁸ 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). The Special Master further stated that SIDS “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 one year of age which remains

Petitioners' Experts

Dr. Alan S. Levin, M.D., J.D., board certified in clinical pathology and allergy-immunology, testified for Petitioners. Dr. Levin was a professor of immunology from 1972 to 1988 at the University of California, San Francisco, and worked in private practice in clinical pathology and allergy-immunology from 1974 to 1995. Dr. Levin sold his allergy-immunology practice in 1995 and currently sees patients with serious immunologic problems on a referral-only basis. The Special Master accepted Dr. Levin as an expert in immunology.

Dr. Levin disputed Dr. Anthony's determination that Monica died from SIDS, and opined that Monica died of cerebral edema caused by an excessive release of cytokines triggered by the hepatitis B vaccine. Pet'rs' Ex. 12.⁹ Dr. Levin testified that the intended use of vaccinations, including the hepatitis B vaccination, is to cause a controlled cytokine reaction resulting in inflammation to which the body can react by mustering protective cells to counter the inflammation. Tr. 200-01.

Dr. Levin opined that the hepatitis B vaccination administered to Monica caused the release of an excessive amount of cytokines, known as a "cytokine storm," that caused cerebral edema and led to Monica's death. Pet'rs' Ex. 12. Dr. Levin explained that a cytokine storm, once triggered, attacks healthy cells and causes those cells to lose water and create edema in the surrounding areas:

What [you are] dealing with is cytokines that are provoked by the hepatitis-B that are now attacking vascular endothelium. Those are the cells that line the capillaries, and they attack those cells, kill them, and all of a sudden, those cells' capacity to keep the water that's in the blood vessels away from the other tissues -- so the water gets pumped out into the other tissues -- into the surrounding tissues.

Tr. 208. In support of this testimony, Dr. Levin cited T. Esch and G. Stefano, Proinflammation: A Common Denominator or Initiator of Different Pathophysiological Disease Processes, 8(5) Med. Sci. Monitor HY1-9 (2002) (available at http://www.MedSciMonit.com/pub/vol_8/no_5/2686.pdf), which describes the proinflammatory effects of excessive cytokine activity on human tissue. Tr.

unexplained after a thorough case investigation, including performance of a complete autopsy, examination of the death scene, and review of the clinical history." Doe/11, 2008 U.S. Claims LEXIS 71 at *14 n. 12 (quoting Ramzi S. Cotran, et al., Robbins Pathologic Basis of Disease 454-55 (5th ed. 1994)).

⁹ Cytokines are defined as "nonantibody proteins released by one cell population . . . on contact with [a] specific antigen, which act as intercellular mediators, . . . in the generation of an immune response." Dorland's Illustrated Medical Dictionary 469 (30th ed. 2003). Dr. Levin explained that cytokines are "actually hormones . . . [that] regulate the growth and differentiation of cells" and they "control the body, and they're necessary for life." Tr. 198-99.

207-08; Resp.'s Ex. H.

Dr. Levin offered documentary evidence in support of his contention that the hepatitis B vaccine, specifically, can cause cytokine storm and encephalopathy. First, he relied upon a medical study measuring cytokine release in response to hepatitis B vaccine, I. Couillin, et al., Specific Vaccine Therapy in Chronic Hepatitis B: Induction of T Cell Proliferative Responses Specific for Envelope Antigens, 180 J. Infectious Diseases 15 (1999). Pet'rs' Ex. 18. Second, he noted that hepatitis B is a superantigen and cited a report by the Institute of Medicine, K. Stratton, et al., Immunization Safety Review: Hepatitis B Vaccine and Demyelinating Neurological Disorders, Nat'l Acad. Press (2002), stating that:

Superantigens can also lead to the release of inflammatory mediators such as cytokines, which could participate in demyelinating processes. It is conceivable that antigenic stimulation from vaccines generally, and from hepatitis B vaccine in particular could trigger any of these three potentially damaging mechanisms. Thus, there is a theoretical basis for an association between vaccine-induced immune response and demyelination.

Pet'rs' Ex. 28.¹⁰ Finally, Dr. Levin provided a hepatitis B vaccine data sheet which listed "encephalopathy" as a reported "undesirable event" following the hepatitis B vaccine. Pet'rs' Ex. 23.

Dr. Levin further testified that the somnolence that Monica displayed after receiving the hepatitis B vaccine indicated that she was suffering from a cytokine storm caused by the hepatitis B vaccine. Tr. 204-05.¹¹ Dr. Levin testified that a cytokine storm could be triggered in an infant in seconds and that three to seven hours was a "reasonable" amount of time for the hepatitis B vaccination to have caused Monica's death. Tr. 307, 311-12.

Dr. John J. Shane, M.D., a neuropathologist, also testified for Petitioners. Dr. Shane served as the Chairman of the Department of Pathology and Director of Laboratory Medicine at Lehigh Valley Hospital, Lehigh, Pennsylvania, for 26 years. After stepping down from that position in 2000, Dr. Shane entered private practice where he performs 30 to 60 autopsies a year. The Special Master accepted Dr. Shane as an expert in pathology.

Dr. Shane disputed Dr. Anthony's determination that Monica died from SIDS, instead

¹⁰ Demyelination is the "destruction, removal, or loss of the myelin sheath of a nerve or nerves." Dorland's Illustrated Medical Dictionary 488 (30th ed. 2003).

¹¹ According to Dr. Levin, the record indicated Monica's somnolence as she slept for approximately four hours after receiving the hepatitis B vaccine and did not cry, interact with her parents, or eat during that time. Tr. 30-31, 37.

concluding that Monica died from encephalopathy triggered by the hepatitis B vaccination. Pet'rs' Ex. 11. Dr. Shane concurred with Dr. Levin's theory that the hepatitis B vaccination caused a "cytokine-induced encephalopathy," citing the heavy weight of Monica's brain and visceral organs, as well as microscopic findings from the autopsy slides of the brain tissue. Tr. 103; Pet'rs' Ex. 11. Dr. Shane testified that Monica's brain at the time of the autopsy was significantly heavier than the median brain weight of an infant of similar age -- which he viewed as evidence of brain edema. Tr. 68-69, 97-98; Pet'rs' Ex. 11. Dr. Shane proffered a median normal brain weight of 490 grams for a two-month-old female, citing a chart of organ weights from I. Damjanov, et al., Anderson's Pathology, 10th ed., 2905. Tr. 68-69; Pet'rs' Ex. 19.

Dr. Shane also testified that Monica's visceral organs were significantly heavier than those of an infant of similar age, indicating edema:

- The median lung weight for an infant similar in age to Monica is 74 grams, and Monica's lungs were 140 grams;
- The median liver weight for an infant similar in age to Monica is 159 grams, and Monica's liver was 225 grams;
- The median spleen weight for an infant similar in age to Monica is 14 grams, and Monica's spleen was 28 grams; and
- The median kidney weight for an infant similar in age to Monica is 36 grams, and Monica's kidneys were 44 grams.

Tr. 103-04, 108-11, 162-66.

When examining the autopsy slides of Monica's brain, Dr. Shane found other pathological markers that he deemed proof of encephalopathy caused by the hepatitis B vaccination. Dr. Shane stated:

The brain has perivascular and periglial halo formation. The formation of clear spaces around the glial cells and the blood vessels of the brain and is due to cerebral edema which accounts for the increased brain weight. In addition, I find unequivocal early neuronal necrosis with shrinkage of the neurons and neuronal cytoplasmic basophilia with some degree of nuclear fragmentation. There is prominent gliosis which is an increase in the number of glial cells indicative of an inflammatory process.

Pet'rs' Ex. 11 at 1-2. Dr. Shane explained:

[W]hen [the] brain swells, when it becomes edematous, the oxygen

supply to the brain, to these neurons, is diminished, and they will begin to undergo degenerative change, and it's those changes that I found in these neurons in this particular brain.

Tr. 61.

Dr. Shane testified that it would have taken a “matter of hours” for the degenerative neuronal pathological changes he observed in Monica’s autopsy slides to occur. Tr. 61. Dr. Shane concluded that the edema affecting Monica’s brain and organs was evidence of encephalopathy and that the most probable cause of the encephalopathy was the hepatitis B vaccine. Pet’rs’ Ex. 11.

Respondent’s Experts

Dr. Christine McCusker, M.D., certified by the Royal College of Physicians and Surgeons in Canada in pediatrics and allergy-immunology, testified for the Respondent. Dr. McCusker is an Assistant Professor of Pediatrics at McGill University, Montreal, an Associate Member of Medicine at McGill University, and a Research Director at the Meakins-Christie Laboratories of McGill. Additionally, Dr. McCusker is the Director of the Clinical Immunology Lab at Montreal Children’s Hospital where she has an active pediatric practice in allergy-immunology. The Special Master accepted Dr. McCusker as an expert in pediatric immunology.

Dr. McCusker disagreed with Petitioners’ theory that Monica died as the result of a “cytokine storm” caused by the hepatitis B vaccination and testified that such a theory is not supported by the immunological literature. Tr. 243; Resp.’s Ex. E. Dr. McCusker agreed with Dr. Levin that a vaccination induces a cytokine response from the immune system to counter the antigens released by the vaccination and that in rare cases, a cytokine storm can occur. Tr. 251-53. Dr. McCusker testified that a cytokine storm begins with headache, fever, vomiting, bowel distress, and hypotension, and frequently results in vascular collapse and multi-organ failure. Tr. 254-55; Resp.’s Ex. E. Dr. McCusker testified that Monica did not experience these symptoms and that, in her opinion, the autopsy results showed no signs of inflammation consistent with multi-organ failure. Tr. 260-61; Resp.’s Ex. E.

While Dr. McCusker conceded that the hepatitis B vaccine induces a cytokine reaction, and that cytokine reactions can cause edema, she could find no medical literature in which the hepatitis B vaccine, specifically, was reported to cause either a cytokine storm or encephalopathy. Tr. 251, 279-81; Resp.’s Ex. E. Dr. McCusker opined that “viral infections caused by hepatitis viruses are not associated with systemic cytokine storm.” Resp.’s Ex. E at 3.¹² She testified that the extant

¹² Dr. McCusker cited two medical articles in support of this proposition. The first, M. Heydtman, et al., Cytokines and Chemokines in the Immune Response to Hepatitis C Infection, 14 Current Opinion in Infectious Diseases 279 (2001), details cytokine reaction to hepatitis C virus, not hepatitis B. Resp.’s Ex. F. The second article, A. Frodsham, Host Genetics and the Outcome of Hepatitis B Viral Infection, 14 Transplant Immunology 183 (2005), discusses genetic predisposition

medical literature demonstrated no connection between the hepatitis B vaccine and cerebral edema, stating: “[i]mmune responses to bacteria and viruses, not directly infecting the brain tissue, such as hepatitis B have neither been shown to cause cytokine storm nor cerebral edema.” Resp.’s Ex. E at 4-5. Dr. McCusker 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. 249, 257-58, 291.

Dr. McCusker opined that Monica’s death occurred too soon to have been caused by cerebral edema:

Reports of cerebral edema following infection of nervous tissues is accompanied by fever as noted above and requires several days (3-5 in one report) to develop to the point of significant symptom development. Thus while Monica did receive HBV on the day of her death, if a cytokine storm could develop, studies noted earlier would suggest that cytokine induced cerebral edema would have required days to manifest.

Id. at 5.¹³ Dr. McCusker further testified:

Additionally, when you look at the case reports of encephalopathy induced by different organisms, you realize that the progression occurs over days. It doesn’t happen over hours. It takes days for there to accumulate enough edema for the immune -- for the final event to occur.

Tr. 258.

Dr. McCusker concluded that Monica’s death was caused by “Sudden Infant Death Syndrome not related to hepatitis B vaccination.” Resp.’s Ex. E at 6. In so concluding, Dr. McCusker

to hepatitis B infection. Resp.’s Ex. P.

¹³ Dr. McCusker did not specify to which “studies noted earlier” she was referring in this report. It appears from the reference to “3-5 days in one report” that Dr. McCusker was referring to a study she described earlier in her report where she stated: “[i]n an experimental model of influenza encephalitis, symptoms of severe brain edema did not occur until 3-5 days after infection (Yao et al., 2003).” Resp.’s Ex. E at 4. Though Dr. McCusker parenthetically cited this study in the text as “Yao et al., 2003,” in the footnote accompanying this text she instead cited a 1998 Yao study -- Y.M. Yao, et al., The Inflammatory Basis of Trauma/Shock-Associated Multiple Organ Failure, 47 Inflammatory Research 201 (1998), Respondent’s Exhibit N. This 1998 Yao study does not discuss influenza encephalitis or suggest a 3-5 day period for edema to develop. There is no 2003 Yao article or study in the record.

employed the traditional definition of SIDS as a death due to a cause unknown, stating: “[i]f you are a purist and you can come up with a mechanism of death, then it is not Sudden Infant Death . . .” Tr. 293. She further testified:

Q: So smothering a baby is not SIDS, is it?

A: Not -- then you have a mechanism of action, so theoretically you would not -- you would say that that is not SIDS. But that would imply that every baby who was put prone . . . who died was smothered.

Tr. 294. When asked whether it was SIDS or smothering that caused Monica’s death, Dr. McCusker testified, “I don’t know why Monica died. I can tell you that there isn’t evidence that she had cytokine storm.” Tr. 292-93.

Dr. Enid Gilbert-Barness, M.D., a professor of pathology and laboratory medicine, pediatrics, and obstetrics and gynecology at the University of South Florida, Tampa, testified for the Respondent. Dr. Gilbert-Barness has conducted approximately 10,000 pediatric autopsies, has been a member of a National Institute of Health panel tasked with studying SIDS, and has written 30 to 40 articles on SIDS. Tr. 114-15. The Special Master accepted Dr. Gilbert-Barness as an expert in pediatric neuropathology.

Dr. Gilbert-Barness concurred with Dr. Anthony’s assessment that Monica died from SIDS, which Dr. Gilbert-Barness characterized as being related to a death by asphyxia. Tr. 121, 123, 126. Specifically, Dr. Gilbert-Barness testified:

I think Monica’s death was related to what we have called Sudden Infant Death Syndrome. I would prefer to call it Sudden Infant Death, and I believe this was very likely in this case related to an asphyxia death.

Tr. 121.¹⁴ Dr. Gilbert-Barness explained her conclusion:

She was on a couch with her father who was many times her size, and there were pillows on the couch, and actually I have emphasized this in some of my writings, and I’ve written a paper on the hazards of mattresses, beds and bedding in the Sudden Infant Death Syndrome. So I think that she was in an ideal situation to suffer from Sudden Infant Death in that environment. And one of the most important things in defining SIDS is examination of the death scene. That has

¹⁴ Asphyxia is pathological change “caused by lack of oxygen in respired air, resulting in hypoxia and hypercapnia.” Dorland’s Illustrated Medical Dictionary 165 (30th ed. 2003).

really not been emphasized in this case.

Tr. 123-24 (emphasis added).

Dr. Gilbert-Barness continued:

I don't like using the term Sudden Infant Death Syndrome because it's really not a syndrome, and I've emphasized it in much of my writings. In fact, it is Sudden Infant Death, cause not determined, if you can call it SIDS -- or what the cause actually is. I think as we know now because of the change in the sleeping position that most of these deaths are due to lying in the prone position and actually related to an asphyxial death.

...

I don't believe she was necessarily in the prone position, but she was lying on a pillow. She was on a sofa with her father, and she certainly could have rolled to the side and then asphyxiated.

Tr. 126. Dr. Gilbert-Barness testified that the blanching and mottled appearance of Monica's skin noted by paramedics was consistent with a finding that Monica was lying in a prone position indicative of SIDS/asphyxia. Tr. 126-28; Resp.'s Ex. OO.¹⁵

Dr. Gilbert-Barness testified that Monica's autopsy results displayed pathological changes in her organs that were consistent with SIDS. Tr. 124. Specifically, Dr. Gilbert-Barness testified that Monica's organs -- the lungs, liver, spleen, kidneys, and adrenal glands -- were "for the most part heavy," which she attributed to congestion that occurs in a SIDS or asphyxia death. Tr. 125-26, 141, 145-46. Additionally, Dr. Gilbert-Barness determined that the "small, pinpoint hemorrhages from the membrane that covers the heart" (epicardial petechial hemorrhages), the over-distinction of the alveoli of the lungs, and the mild increase in the smooth muscle of the pulmonary arteriole in the brain were consistent with a SIDS-related death. Tr. 124; Resp.'s Ex. OO.

Dr. Gilbert-Barness did not believe Monica's death was caused by the hepatitis B vaccination or encephalopathy. Dr. Gilbert-Barness testified that if encephalopathy were the cause of death, one would expect the autopsy results to show "considerable brain edema" and "herniation of the brainstem," which she concluded were not present in Monica's case. Tr. 122. Citing the brain weight charts in Respondent's Exhibits EE and LL, Dr. Gilbert-Barness proffered two estimates of normal brain weight for an infant similar in age to Monica -- 516 grams and 560 grams. Tr. 129-30. Dr. Gilbert-Barness further testified that because Monica's body weight was in the 90th percentile for her age group, her brain and other organ weights would be expected to be "on the high side of

¹⁵ The Special Master made a finding that Monica was not in the prone position, but rather was lying on her back. Doe/11, 2008 U.S. Claims LEXIS 71 at *44-45.

normal.” Tr. 135-36.

Despite her conclusion that Monica’s brain weight was normal, Dr. Gilbert-Barness acknowledged that “[t]here may have been a minimal degree of edema”-- but maintained that in cases of Sudden Infant Death, it is not unusual to find some degree of cerebral edema -- “you usually do see a brain that is slightly heavier than normal.” Tr. 122, 133.

Additionally, Dr. Gilbert-Barness testified that encephalopathy would have been accompanied by symptoms such as vomiting, seizures, crying, somnolence, or coma, which, in her view, Monica did not display. Tr. 136-38.¹⁶

The Special Master’s Decision

The Special Master determined that Petitioners failed to demonstrate by a preponderance of the evidence that the hepatitis B vaccination was more likely than not the cause of Monica’s death. Specifically, the Special Master determined that Petitioners failed to satisfy their burden of proof by demonstrating: “(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 the vaccination and injury.” Doe/11, 2008 U.S. Claims LEXIS 71 at *17 (quoting Althen v. Sec’y of HHS, 418 F.3d 1274, 1278 (Fed. Cir. 2005)).

With regard to the first prong of Althen -- “a medical theory causally connecting the vaccination and the injury”-- the Special Master determined that the hepatitis B vaccine could not cause cytokine storm and subsequent edema as Dr. Levin and Dr. Shane posited.¹⁷ The Special Master concluded: “Nor does the medical literature report a causal association between hepatitis B vaccine and encephalopathy, and subsequent death.” Id. at *60. The Special Master acknowledged that Petitioners cited medical literature which, based upon reports to the Vaccine Adverse Events Reporting System (VAERS), indicated 36 reported deaths due to hepatitis B vaccine. Id. at *61.¹⁸

¹⁶ Somnolence is “drowsiness or sleepiness, particularly in excess.” Dorland’s Illustrated Medical Dictionary 1723 (30th ed. 2003). Monica’s mother testified that Monica was “very tired” and “lethargic,” and would not drink from her bottle. Tr. 15. She noted that there was “no crying,” adding that “[s]he usually cries, and she wasn’t even making a sound, really.” Id. Despite this testimony, Dr. Gilbert-Barness opined, without elaborating, that these symptoms did not rise to the level of somnolence. Tr. 139.

¹⁷ However, the Special Master made this determination not in her analysis of Althen’s prong one, but rather in her analysis of prong two.

¹⁸ The Special Master described VAERS as a government-sponsored vaccine safety surveillance program which collects and analyzes information from reports of adverse events following immunization. Doe/11, 2008 U.S. Claims LEXIS 71 at *60-61.

This article stated, “In conclusion, the present study, in conjunction with emerging biological plausibility, case-reports, case-series, positive re-challenge or significant exacerbation of symptom reports, and population epidemiological studies, suggests that adult [hepatitis B vaccine] is associated with a significant increased risk for serious autoimmune disorders.” Resp.’s Ex. AA at 4, 6. The Special Master found this study unpersuasive, stating that “any person can file a report with VAERS” and noting that although the article found a connection between the vaccine and reported deaths, it did not indicate that those deaths were specifically associated with encephalopathy. Doe/11, 2008 U.S. Claims LEXIS 71 at *61.

In purporting to address prong one, “can cause,” the Special Master actually addressed prong two, “did cause,” -- whether the hepatitis B vaccine actually caused Monica’s injury -- stating:

. . . [T]he undersigned finds Dr. McCusker’s testimony which challenged Dr. Levin’s “theory” that Child Doe/11's death was the result of a cytokine-induced cerebral edema, or “cytokine storm” caused by the hepatitis B vaccine, more persuasive on the facts of this case. Dr. Levin’s theory requires, as a predicate to support his theory that Child Doe/11 suffered an acute encephalopathy after her vaccination, a pathological finding that Child Doe/11's organ were significantly edematous at her death. The necessary pathological findings to support Dr. Levin’s theory, however, are lacking in this case.

Id. at *58. In reaching this conclusion, the Special Master determined that Monica’s brain weight fell within the normal range, accepting two estimates of normal brain weight from Dr. Gilbert-Barness’ testimony and the medical literature she cited -- an excerpt from a book she authored, Handbook of Pediatric Autopsy Pathology, and a 1983 study, “Brain Weight of Danish Children.” Id. at *40-41; Resp.’s Exs. EE and LL.

Continuing under the rubric of analyzing Althen’s first prong, the “medical theory,” the Special Master determined that Monica’s death was caused by SIDS, stating:

The factual evidence in this case does not support petitioner’s theory of causation implicating Monica’s hepatitis B vaccine as the cause of her death. Rather, the presented evidence by respondent supports a finding of death by a factor unrelated, specifically, that the probable cause of Monica’s death was SIDS, and was very likely a death by inadvertent asphyxiation.

Doe/11, 2008 U.S. Claims LEXIS 71 at *58-59.

With regard to Althen’s second prong -- “a logical sequence of cause and effect showing that the vaccination was the reason for the injury”-- the Special Master found that the record evidence

did not support Petitioners' claim of encephalopathy, noting that Monica's clinical presentation was inconsistent with Dr. McCusker's personal experience with encephalopathic children, and that Dr. Shane's conclusion that Monica's behavior and condition were symptomatic of encephalopathy was not supported by the facts of this case.

In concluding that Petitioners failed to satisfy Althen's second prong, the Special Master again found that an unrelated factor -- "overlying" or "wedging" -- caused Monica's death:

. . . [W]ithout more, the undersigned does not view the VAERS reports of suspected adverse events as sufficient evidence to satisfy petitioners' statutory burden of proving by a preponderance of the evidence that the suffered injury was more likely than not caused by the received immunization. Rather, the factual record and the testimony of Child Doe/11's parents suggests that the more likely cause of Child Doe/11's death was an inadvertent overlying or wedging of Child Doe/11 in the futon where she napped with her father.

Id. at *61.

With regard to Althen's third prong -- a "proximate temporal relationship"-- the Special Master credited Dr. McCusker's testimony that the death occurred too soon to be a cytokine-storm mediated edema. In analyzing temporal proximity, the Special Master did not discuss Dr. Levin's testimony that "three to seven hours" was a reasonable amount of time for the hepatitis B vaccine to have caused Monica's death or Dr. Shane's opinion that it would have taken a "matter of hours" for the degenerative neuronal changes to occur in Monica's brain -- changes he detected on the autopsy slides.

Instead, the Special Master concluded that SIDS was the cause of death, stating:

Although Child Doe/11's death occurred several hours after her vaccination, the evidence militates in favor of a finding that Child Doe/11's death was a SIDS death, quite likely to have resulted from inadvertent asphyxiation while her father napped beside her on the family's futon after returning home from holiday shopping, rather than a vaccine-related death.

Id. at *64.

Discussion

Jurisdiction And Standard Of Review

Jurisdiction lies in this Court pursuant to 42 U.S.C. § 300aa-12(e). In reviewing a decision rendered by the Special Master, this Court may: (1) uphold the findings of fact and conclusions of law of the Special Master; (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. § 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 or capricious. 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 decision] to reweigh the factual evidence, or to assess whether the 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). Nor should this Court "examine the probative value of the evidence or the credibility of the witnesses. These are all matters within the purview of the fact finder." Id. A decision is arbitrary and capricious if it relied on factors which 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. Assn. 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, 485 F.3d at 1149; Capizzano v. Sec'y of Health & Human Servs., 440 F.3d 1317, 1319-20 (Fed. Cir. 2006); Althen, 418 F.3d at 1277-78. 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 865.¹⁹ Second, in a case such as the

¹⁹ The Vaccine Injury Table lists only the following as "covered" illnesses, disabilities, injuries, or conditions resulting from the hepatitis B vaccine:

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 the vaccination and injury.” Althen, 418 F.3d at 1278; see also Walther, 485 F.3d at 1150; Capizzano, 440 F.3d at 1324. Petitioner must show that the vaccination was a “but-for” cause of the harm, i.e., that the harm would not have occurred but for the vaccine. Walther, 485 F.3d at 1151; Pafford, 451 F.3d at 1356. A petitioner is not required to show that the vaccine at issue was the sole or predominant cause of the injury, nor does a petitioner need to

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- A. Anaphylaxis or anaphylactic shock.
 - B. Any acute complication or sequela (including death) of an illness, disability, injury, or condition referred to above which illness, disability, injury, or condition arose within the time period prescribed.

42 C.F.R. § 100.3. Anaphylaxis is “a general term originally applied to the situation in which exposure to a toxin resulted not in development of immunity (prophylaxis) but in hypersensitivity.” Dorland’s Illustrated Medical Dictionary 73 (30th ed. 2003). The time period for hepatitis B-related anaphylaxis or anaphylactic shock to manifest under the Table for a petitioner to be entitled to compensation is 4 hours. 42 C.F.R. § 100.3.

produce particular types of evidence or prove causation as a matter of scientific or medical certainty. Shyface, 165 F.3d at 1353; Althen, 418 F.3d at 1279; Bunting v. Sec’y of HHS, 931 F.2d 867, 873 (Fed. Cir. 1991).

As the Federal Circuit recognized in Knudsen v. Sec’y of HHS, 35 F.3d 543 (Fed. Cir. 1994):

The determination of causation in fact under the Vaccine Act involves ascertaining whether a sequence of cause and effect is “logical” and legally probable, not medically or scientifically certain. Thus, for example, causation can be found in vaccine cases based on epidemiological evidence and the clinical picture regarding the particular child without detailed medical and scientific exposition on the biological mechanisms.

Furthermore, to require identification and proof of specific biological mechanisms would be inconsistent with the purpose and nature of the vaccine compensation program.

Knudsen, 35 F.3d at 548-49 (citations omitted).

Once a petitioner establishes its prima facie case, the burden of proof shifts to 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 Vaccine Act defines a “factor unrelated” as follows:

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

(A) 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

(B) 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; Whitecotton, 17 F.3d at 376; 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 Vaccine Act. 42 U.S.C. § 300aa-13(a)(1)(B); Walther, 485 F.3d at 1151.

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 it has not marshaled a preponderance of the evidence in its favor. See Knudsen, 35 F.3d at 550 (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 Misallocated The Burden of Proof

In denying entitlement, the Special Master found that Petitioners failed to establish a theory of causation connecting the hepatitis B vaccination with Monica’s death, and that her death was instead caused by a “factor unrelated, specifically . . . SIDS, and was very likely a death by inadvertent asphyxiation.” Doe/11, 2008 U.S. Claims LEXIS 71 at *59. In reaching these conclusions, the Special Master properly recited the three-part test articulated by the Federal Circuit in Althen to prove a prima facie case of causation. Doe/11, 2008 U.S. Claims LEXIS 71 at *29. In analyzing whether Petitioners satisfied Althen, the Special Master considered not only Petitioners’ evidence that the hepatitis B vaccine caused a cytokine-induced cerebral edema which led to Monica’s death, but also Respondent’s evidence that Monica’s death was caused by an unrelated factor, SIDS. This consideration of the evidence was appropriate, as the Act directs the Special Master to consider “the record as a whole” in determining whether compensation is warranted.²⁰ However, the Special Master erred when she proceeded to make a legal conclusion that an “unrelated factor” caused Monica’s death in the context of evaluating whether Petitioners had established a prima facie case, without stating which party had the burden of proving the unrelated factor. The

²⁰ The Act, 42 U.S.C. § 300aa-13(a)(1), is somewhat unusual in that it requires the Special Master to examine the “record as a whole” in ascertaining whether a petitioner has put forward a prima facie case. See 42 U.S.C. § 300aa-13(a)(1) (requiring the Special Master to consider the “record as a whole” when making determinations regarding compensation); Bunting, 931 F.2d at 872 (stating that “causation must be established by a preponderance of the evidence as a whole.”). In other areas of the law implicating a prima facie case and burden shifting, a court is to consider only the evidence of the moving party when determining whether a prima facie case has been established. See, e.g., Tex. Dep’t of Cmty. Affairs v. Burdine, 450 U.S. 248, 252-253 (1981) (under Title VII of the Civil Rights Act of 1964, “the plaintiff has the burden of proving by the preponderance of the evidence a prima facie case of discrimination. Second, if the plaintiff succeeds in proving the prima facie case, the burden shifts to the defendant to articulate some legitimate, nondiscriminatory reason for the employee’s rejection.”); Corning Glass Works v. Brennan, 417 U.S. 188, 196 (1974) (In Equal Pay Act cases, “once the Secretary has carried his burden of showing that the employer pays workers of one sex more than workers of the opposite sex for equal work, the burden shifts to the employer to show that the differential is justified under one of the Act’s four exceptions.”).

decision suggests that the Special Master erroneously required Petitioners to prove that SIDS was not the cause of Monica's death, instead of shifting the burden to Respondent to demonstrate that SIDS did cause Monica's death.

SIDS appeared to be a paramount consideration in the Special Master's conclusion that Petitioners did not put forward a prima facie case of causation-in-fact. In discussing all three elements of the Althen test, the Special Master concluded Petitioners failed to establish causation because she found SIDS to be the more likely cause of Monica's death. Although the SIDS diagnosis has no relevance to the determination as to whether a medical theory connects the hepatitis B vaccine to a cytokine storm and cerebral edema, the Special Master considered SIDS in analyzing that factor. So too, in weighing the testimony of the pathologists, the Special Master expressly considered the fact that Dr. Shane had no experience in SIDS, while Dr. Gilbert-Barness was a recognized expert in SIDS, in deciding to credit Dr. Gilbert-Barness' opinions. Finally, in considering a proximate temporal relationship, the Special Master weighed SIDS in determining there was an insufficient showing of proximate temporal relationship. The Special Master stated, "Although [Monica's] death occurred several hours after her vaccination, the evidence militates in favor of finding [Monica's] death was a SIDS death" Id. at *63.²¹

The Federal Circuit's opinions in Pafford and Walther provide guidance on the proper allocation of the burden of proof. In Pafford, the Federal Circuit affirmed the Special Master's and Court of Federal Claims' conclusions that the petitioner did not prove that her DtaP, MMR and OPV vaccines caused systemic juvenile rheumatoid arthritis. The petitioner in Pafford received vaccinations on March 24, 1998, and had a fever and neck pain on April 4, 1998. By April 7, the neck pain continued and was accompanied by limb pain and a rash. On April 13, she was hospitalized with fever, vomiting, pain and a rash, and tested positive for a bacterial infection, mycoplasma. On April 20, Pafford was seen by a doctor for a recurrence of these symptoms and was diagnosed with the juvenile rheumatoid arthritis also known as Still's disease. 451 F.3d at 1354.

Applying the three Althen factors, the Special Master in Pafford found that the vaccines could cause Still's Disease but that Pafford failed to prove they "did cause" the disease or that there was a proximate temporal relationship between the vaccinations and onset of Still's disease. The

²¹ The Special Master did not discuss Dr. Levin's or Dr. Shane's respective opinions that the edema could have developed between three to seven hours or within a matter of hours. In support of his temporal proximity assessment, Dr. Levin pointed to a study, G. Suntharalingam, et al., Cytokine Storm in a Phase 1 Trial of the Anti-CD28 Monoclonal Antibody TGN1412, 355 New Eng. J. Med. 1018 (Sept. 7, 2006), which described a cytokine storm induced in six healthy adult males upon injection of a monoclonal antibody during a clinical trial. Tr. 312; Resp.'s Ex. DD. Within a median of 60 minutes from injection, these patients all displayed severe headaches; within 77 minutes, they all displayed back pain; five patients suffered short bouts of amnesia in the early stages and severe fever; four patients suffered rigors (an indication of shock) within 58 to 120 minutes. At 300 minutes after injection, one patient suffered signs of respiratory failure. Over several days, the patients began to suffer signs of multi-organ failure.

Special Master in Pafford was particularly troubled by the lack of evidence demonstrating “any defined time period in which one would expect to see the onset of Still’s disease subsequent to a triggering event.” Id. at 1356. The absence of temporal linkage prevented the Special Master from finding that a vaccine rather than unrelated, contemporaneous, documented conditions -- a positive test for mycoplasma, a sinus infection, tonsillitis and an earlier cold accompanied by diarrhea -- caused Still’s disease.

On appeal, the Pafford petitioner argued that the Special Master erred in imposing a heightened burden requiring petitioners to rule out other potential causes in proving vaccine-related causation. The Federal Circuit rejected this argument, finding that because petitioners had not established a temporal link between Still’s disease and the vaccinations, there was inadequate evidence to show but-for causation. The Federal Circuit held:

Without credible testimony . . . on the medically acceptable time frame, the record contains little evidence linking Still’s disease to the vaccinations in this particular case and leaves Pafford without adequate evidence to show “but-for” causation 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.

Id. at 1359. Thus, in Pafford, the Federal Circuit approved the Special Master’s consideration of alternative causes in the context of addressing the adequacy of a petitioner’s prima facie case.

However, subsequently in Walther, the Federal Circuit clarified this aspect of Pafford, stating:

While our recent decision in Pafford held that a petitioner as a practical matter may be required to eliminate potential alternative causes where the petitioner’s other evidence on causation is insufficient, 451 F.3d at 1359, we conclude that the Vaccine Act does not require the petitioner to bear the burden of eliminating alternative causes where the other evidence on causation is sufficient to establish a prima facie case.

485 F.3d at 1149-50. The petitioner in Walther alleged she suffered from acute disseminated encephalomyelitis (“ADEM”) as a result of receiving the tetanus diphtheria (“Td”) vaccine. On the same day, the petitioner received the yellow fever, typhoid and meningitis vaccinations in addition to the Td, and six days later she received a rabies vaccination. Roughly four months later, Walther was diagnosed with ADEM. The Special Master found that the petitioner had failed to prove causation for a number of reasons including that “Walther has not adequately eliminated the other vaccines she received [at the same time] as causative agents for her condition.” Id. at 1148. The

Federal Circuit in Walther concluded that the Special Master’s decision was erroneous to the extent it placed a requirement on the petitioner to establish a lack of alternative causation. The Walther Court explained:

the government bears the burden of establishing alternative causation by a preponderance of the evidence once the petitioner has established a prima facie case. . . . [T]he text and structure of “[t]he Vaccine Act separates the inquiry for alternative etiologies from the inquiry for causation. These are two separate inquiries under the statute.”

Id. at 1151 (quoting Grant, 956 F.2d at 1149). In parsing the Vaccine Act, the Federal Circuit in Walther explained:

The alternative causation issue is addressed in [42 U.S.C. § 300aa-13(a)(1)(B)]. That provision does not specifically place the burden on the petitioner with respect to alternative causation. When juxtaposed with [42 U.S.C. § 300aa-13(a)(1)(A)]’s clear statement as to the burden of proof under that prong, the absence of any such language in [42 U.S.C. § 300aa-13(a)(1)(B)] suggests that the petitioner does not bear the burden as to alternative causation under the second prong. Moreover, it would be unusual to require a party to prove that “there is not a preponderance of the evidence,” as our legal system rarely requires a party to prove a negative. A plain reading of the statutory text more naturally places the burden on the government to establish that there is an alternative cause by a preponderance of the evidence. Indeed, placing the alternative causation burden on the petitioner would essentially write [42 U.S.C. § 300aa-13(a)(1)(B)] out of the statute. On the one hand, if the petitioner did not successfully eliminate other causes, then the petition would fail and the second prong would not be reached. On the other hand, if the petitioner did eliminate alternative causes, the second prong would not be reached because the question of alternative causation would already have been resolved. Thus, construing the statute in such a way would make [42 U.S.C. § 300aa-13(a)(1)(B)] “redundant or largely superfluous, in violation of the elementary canon of construction that a statute should be interpreted so as not to render one part inoperative.” Colautti v. Franklin, 439 U.S. 379, 392 (1979).

Id. at 1150.

The Walther Court, in the wake of Pafford, clarified that the petitioner does not “bear the

burden of eliminating alternative causes where the other evidence on causation is sufficient to establish a prima facie case.” 485 F.3d at 1150 (emphasis added). In Pafford, the majority appeared to view the lack of evidence of the requisite temporal proximity as a gaping hole, definitively preventing “sufficient” evidence of causation. In such a case, the Walther Court held 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.” Walther, 485 F.3d at 1151. Nevertheless, the Walther Court made clear that petitioner does not have the burden of eliminating other causes in establishing a prima facie case where the other evidence suffices to establish a prima facie case of causation.

In the instant case, the Special Master did not assess whether Petitioners’ evidence unrelated to alternative causes sufficed to establish a prima facie case of causation. Without making this assessment, the Special Master nonetheless required Petitioners to eliminate SIDS, asphyxiation, overlay and/or wedging as alternative causes of Monica’s death as part of their prima facie case, contrary to Walther. As such, the proper course for this Court is to vacate the Special Master’s decision and remand “for a new causation determination that applies the correct legal standard.” Walther, 485 F.3d at 1152. As the Federal Circuit recognized:

Since we conclude that the special master appeared to apply an erroneous legal standard, we must set aside the decision and remand for further proceedings. Insofar as a finding is derived from the application of an improper legal standard to the facts, it cannot be allowed to stand. In such a circumstance, this court must remand for new factual findings in light of the correct legal standard.

Id. at 1152 (citations omitted).²²

The Special Master Applied An Overly Onerous Burden Of Proof On Petitioners To Establish That The Hepatitis B Vaccine “Can Cause” The Claimed Injury And Death

In order to establish Althen’s first prong, the “can cause” step, a petitioner “must show a medical theory causally connecting the vaccine and the injury.” 418 F.3d at 1278 (emphasis added). The Althen Court clarified that such a “theory” could be demonstrated on the basis of expert testimony alone and did not require “confirmation of medical plausibility from the medical community or literature” or proof of “an injury recognized by the medical plausibility evidence and literature.” 418 F.3d at 1279. In so ruling, the Federal Circuit expressly rejected the Special Master’s imposition of such requirements in Stevens v. Sec’y of HHS, 2001 WL 387418 (Fed. Cl.

²² Petitioners also allege that “[t]he Special Master applied a legally erroneous ‘compelling proof’ standard to reject petitioners’ proof of causation” because the Special Master cited Kennedy v. Collagen Corp., 161 F.3d 1226, 1230 (9th Cir. 1998). Pet’rs’ Mot. for Review at 22. The Court does not interpret the Special Master’s decision to have required Petitioners to marshal compelling proof of causation.

Sp. Mstr. Mar. 30, 2001). Althen, 418 F.3d at 1281. The Special Master in Stevens had ruled that “without some objective confirmation that the vaccine administered is potentially associated with the injury alleged, petitioner’s causal claims are mere speculation and thus insufficient.” Stevens, 2001 WL 387418 at *12. The Althen Court struck down this requirement and further held that “by requiring medical literature,” the Stevens test contravened the Vaccine Act’s allowance of medical opinion as proof of causation. Althen, 418 F.3d at 1280. The Althen court explained:

This prevents the use of circumstantial evidence envisioned by the preponderance standard and negates the system created by Congress, in which close calls regarding causation are resolved in favor of injured claimants (citing Knudsen, 35 F.3d at 549 (explaining that “to require identification and proof of specific biological mechanisms would be inconsistent with the purpose and nature of the vaccine compensation program’’)). While this case involves the possible link between TT vaccination and central nervous system injury, a sequence hitherto unproven in medicine, the purpose of the Vaccine Act’s preponderance standard is to allow the finding of causation in a field bereft of complete and direct proof of how vaccines affect the human body.

Id. (emphasis added).

In analyzing Althen’s first prong in the decision sub judice, the Special Master stated:

To prove causation, petitioners must offer a medical theory causally connecting Child Doe/11's receipt of her hepatitis B vaccination and her death. Althen, 418 F.3d at 1278. The causal connection must be more likely than not. 42 U.S.C. §§ 300aa-11(c)(1)(C)(ii)(I) and (II). See Shyface, 165 F.3d at 1352-53.²³

Doe/11, 2008 U.S. Claims LEXIS 71 at *29-30 (emphasis added).

Nothing in the case law requires that the medical theory be “more likely than not.” As the Althen Court stated in fashioning the inquiry:

²³ Neither the cited sections of the Vaccine Act nor Shyface elucidate the requisite showing necessary for establishing a medical theory. The sections of the Vaccine Act cited by the Special Master in this passage do not support the conclusion that the medical theory must be “more likely than not.” Rather, they simply delineate the requirements for the contents of the petition stating that a petition shall contain supporting documentation that the injured party sustained or significantly aggravated an injury caused by the vaccine. See 42 U.S.C. §§ 300aa-11(c)(1)(C)(ii)(I) and (II). So too, the cited passage in Shyface does not require that a medical theory be “more likely than not,” but simply that a medical theory be shown. Shyface, 165 F.3d at 1352-53.

Concisely stated, Althen's burden is to show by preponderant evidence that the vaccination brought about her injury 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.

Althen, 418 F.3d at 1278 (emphasis added).

Indeed, a "theory" intrinsically has yet to be proven and puts forth a hypothesis. A "theory" is defined to be "a hypothetical . . . structure explaining or relating an observed set of facts", "a judgment, conception, proposition or formula . . . formed by speculation or deduction or by abstraction or generalization from facts", or "a working hypothesis given probability by experimental evidence or by factual or conceptual analysis but not conclusively established or accepted as a law." Webster's Third New International Dictionary 2371 (3d ed. 2002).

Consistent with this definition, Walther and Pafford, as well as several Special Master decisions, have interpreted Althen's first prong to require a medical theory that has "biological plausibility," not one that is "more likely than not." See Walther, 485 F.3d at 1148 ("The government conceded that the Td vaccine was a biologically plausible cause of Walther's ADEM"); Pafford, 451 F.3d at 1356 (discussing Special Master's finding that it was "biologically plausible" for the vaccinations at issue to cause Still's disease); see, e.g., Perez v. Sec'y of HHS, 2008 WL 763301, *30 (Fed. Cl. Sp. Mstr. Mar. 4, 2008) (asking whether petitioner had established a "biologically plausible" theory).

As such, the Special Master erred in requiring petitioner to demonstrate that the causal connection between the hepatitis B vaccine with cytokine storm and edema in their medical theory had to be "more likely than not." Such a requirement finds no support in the Vaccine Act and conflicts with Althen's statement that a "possible link" between a vaccination and injury may still permit a finding of causation even though that "link" involved a "sequence hitherto unproven in medicine." Althen, 418 F.3d at 1280. On remand, the Special Master shall assess whether Petitioners' medical theory of causation is biologically plausible.

The Special Master Failed To Consider Whether SIDS Is An Idiopathic Condition Which Cannot Be Deemed A Factor Unrelated

Petitioners' second allegation of error is that the Special Master erred in concluding that Monica died of SIDS -- which is internally inconsistent with a conclusion that Monica died by being inadvertently smothered by her father. Pet'rs' Mot. for Review at 26.

The Special Master concluded that SIDS constituted a "factor unrelated" and relied upon this factor to conclude that Petitioners failed to establish a prima facie case of causation, without addressing whether SIDS or other purported unrelated factors -- asphyxia, wedging, or overlay --

may constitute factors unrelated within the meaning of the Vaccine Act and this Court's case law. Specifically, the Special Master concluded that Monica's death "was a SIDS death, quite likely to have resulted from inadvertent asphyxiation . . . rather than a vaccine-related death." Doe/11, 2008 U.S. Claims LEXIS 71 at *64. The Special Master further concluded that "the factual record and the testimony of Child Doe/11's parents suggests that the more likely cause of Child Doe/11's death was an inadvertent overlaying or wedging of Child Doe/11 in the futon where she napped with her father." Id. at *61.

A "factor unrelated" is defined by 42 U.S.C. § 300aa-13(a)(2) as a theory of causation that "does not include any idiopathic, unexplained, unknown, hypothetical, or undocumentable cause, factor, injury, illness, or condition . . ." An "idiopathic illness is an illness of unknown origin." Koston v. Sec'y of HHS, 974 F.2d 157, 161 (Fed. Cir. 1992). Idiopathic conditions have "no known etiology, which means simply that there is no known cause." Wagner v. Sec'y of HHS, 37 Fed. Cl. 134, 139 (1997).

This Court has previously held that, because SIDS is an idiopathic condition for purposes of the Vaccine Act, SIDS can neither prevent petitioners from establishing a prima facie case of causation nor serve as an alternative theory of causation. Davis, 54 Fed. Cl. at 230; Hossack v. Sec'y of HHS, 32 Fed. Cl. 769 (1995); see also Perez, 2008 WL 763301 at *37 (Fed. Cl. Sp. Mstr. Mar. 4, 2008) (stating, "To find that, firstly, SIDS is a diagnosis, and secondly, that it may be relied upon as more persuasive than Petitioners' theory of causation is an act of casuistry: it is to place faith certain in a diagnosis of uncertainty. It is also reversible error.").

In Davis, the petitioner's son died two days after receiving his first diphtheria-pertussis-tetanus (DPT) vaccination at the age of approximately eight weeks. The autopsy report identified the cause of death as "crib death," otherwise known as SIDS. Davis, 54 Fed. Cl. at 231. In reversing and remanding the Special Master's decision denying compensation, the Court stated: "the Vaccine Act's plain language and settled case law make clear that the special master's consideration of evidence of SIDS in evaluating whether petitioner established a prima facie case of a Table Injury contravenes the statute's bar against idiopathic evidence and is contrary to law." Id. at 236. The Davis Court explained:

As the Court noted in Hossack, 32 Fed. Cl. at 771 n.4, 'although HHS continues to raise the SIDS diagnosis as a tool to thwart petitioners' case, such a diagnosis can neither prevent petitioners from establishing their prima facie case, nor serve as any kind of defense or alternative cause of injury due to factors unrelated to the administration of the vaccine. Special masters have consistently held that SIDS is an idiopathic, unexplained diagnosis, and as such cannot defeat a petitioner's established case.' By considering respondent's proof of an unexplained, idiopathic alternative cause for plaintiff's injury (in this case, SIDS), the special master shifted the burden to the petitioner by 'forcing her to disprove the causal effects of a condition

... that the government could not rely on as a defense.’ Wagner, 37 Fed. Cl. at 139.

Id. at 235.

Further, the Special Master equivocated in determining whether two potential unrelated factors -- overlay or wedging -- actually caused Monica’s death, stating:

In this case, Child Doe/11 napped near her father in the family's futon prior to her death. It appears that this sleeping position would have permitted an accidental overlay either by Mr. Doe/11 or by the futon material or alternatively, would have permitted an unintentional wedging of Child Doe/11.

Doe/11, 2008 U.S. Claims LEXIS 71 at *42-43 (emphasis added) .

Because the Special Master did not articulate precisely what she deemed to be the unrelated factor which caused Monica’s death, the Court remands this matter for clarification. Further, if on remand, the Special Master considers whether asphyxiation, overlay, or wedging might constitute factors unrelated, the Special Master should examine the record as a whole and assess whether any of these proffered causes fits within the Act’s prohibition against an “unexplained, unknown, hypothetical or undocumentable cause” serving as a “factor unrelated.” 42 U.S.C. § 300aa-13(a)(2).

The Special Master Failed To Consider The Totality of the Evidence In Concluding That Monica’s Brain Weight Was In The Normal Range

Petitioners also attack as arbitrary and capricious the Special Master’s finding that Monica’s brain weight of 570 grams was within the normal range for an infant similar in age to Monica. The Special Master cited two estimates of normal brain weight from Dr. Gilbert-Barness -- 516 grams and 560 grams -- and concluded that Monica’s brain weight fell within the normal range. Doe/11, 2008 U.S. Claims LEXIS 71 at *40-41. Petitioners claim that the Special Master only relied on the testimony of Respondent’s expert, Dr. Gilbert-Barness, for this conclusion and ignored the testimony of Petitioners’ expert, Dr. Shane, and evidence that pointed to the contrary.

The brain weight chart from which Dr. Gilbert-Barness 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 which the authors of that study recognized contributed to “rather high mean weight.” Resp.’s Ex. LL at 10. Although Petitioners pointed out this anomaly, the Special Master nonetheless credited Dr. Gilbert-Barness’ testimony and this exhibit without addressing this circumstance.

Dr. Gilbert-Barness derived her low-end estimate of normal brain weight, 516 grams, from a chart in her textbook, Respondent’s Exhibit EE. This chart lists 516 grams as the median brain

weight of a child, male or female, in the two-to-three month age range. However, Monica was younger -- approximately seven weeks old at the time of her death. Dr. Gilbert-Barness' chart lists 489 grams as the normal median brain weight for the seven-to-nine week age group -- a number akin to the estimate of 490 grams proffered by Petitioners. Resp.'s Ex. EE at 3. Thus, neither exhibit supports Dr. Gilbert-Barness' normal brain weight estimates for a child of Monica's age.²⁴

Petitioners cited a brain weight chart from a standard pathology textbook, Anderson's Pathology, which listed the median brain weight for a two-month-old female as 490 grams and argued that Monica's brain weight of 570 grams fell above the normal range. However, the Special Master did not address Petitioners' evidence of normal brain weight in her decision.

Given the questionable estimates of normal brain weight on which Dr. Gilbert-Barness and the Special Master relied and Petitioners' other evidence of normal brain weight, the Court directs the Special Master to reevaluate the evidence of Monica's brain weight and reconsider her conclusions that Monica's brain weight was within the normal range.

Conclusions

1. The Special Master's decision is **VACATED** and **REMANDED**.
2. Although the Special Master did not articulate whether or how she was allocating the burden of proof, this Court interprets the decision to have placed the burden on Petitioners, in the context of establishing their prima facie case, to disprove that a factor unrelated to the vaccine caused Monica's death. On remand, the Special Master is directed to allocate the burden of proof in the manner set forth in Walther, 485 F.3d at 1149-52, and reweigh the evidence in accordance with that allocation. In remanding this matter, the Court does not dictate any particular determination on causation.
3. Because the Special Master misapplied the prongs of the Althen test by meshing the "can cause" analysis with the "did cause" analysis and by determining that a "factor unrelated" caused Monica's death in her analysis of all three prongs, the Special Master is directed to address each Althen prong and the considerations pertinent to each prong separately.
4. In analyzing Althen's first prong—whether Petitioners put forward a medical theory causally connecting the vaccine to cytokine storm and cerebral edema—the Special Master shall not require Petitioners to prove their theory is "more likely than not," but rather that their medical theory is biologically plausible.

²⁴ The Special Master also cited a second chart from Respondent's Exhibit EE which listed 560 grams as the normal brain weight for a two-month-old female. However, this chart is merely a reprint of the earlier referenced Exhibit LL, in which 83% of the participants suffered from moderate to severe edema. Compare Resp.'s Ex. EE at 4 with Resp.'s Ex. LL at 7.

5. If the Special Master proceeds to determine whether a factor unrelated to the hepatitis B vaccine caused Monica's death, she shall clarify what such factor unrelated was -- SIDS, asphyxia, overlay, or wedging -- and articulate why such an unrelated factor can be deemed to have caused Monica's death in light of the definition of unrelated factor in the Vaccine Act, 42 U.S.C. § 300aa-13(a)(2), and Davis, 54 Fed. Cl. 230 (2002), Wagner, 37 Fed. Cl. 134 (1997) and Hassock, 32 Fed. Cl. 769 (1995), as well as the physical and medical evidence of record.

6. In assessing whether Monica's brain weight fell within normal ranges for purposes of assessing Petitioners' prima facie case, the Special Master shall consider the totality of the evidence.

7. In assessing whether Petitioners have put forward a prima facie case with respect to Althen's third prong, temporal proximity, the Special Master shall consider the totality of the evidence.

8. Pursuant to the Vaccine Act, the remand proceedings shall be completed within 90 days of the date of this decision. 42 U.S.C. § 300aa-12(e)(2); Vaccine Rule 28.

9. The Clerk shall not disclose this decision publicly for 14 days.

MARY ELLEN COSTER WILLIAMS
Judge