In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

No. [Redacted]V

(Filed: January 31, 2008; Re-filed Redacted: March 5, 2008)

JOHN DOE/11 and JANE DOE/11 as Representatives of the Estate of Child Doe/11 Deceased, Petitioners, v. SECRETARY OF HEALTH AND HUMAN SERVICES, Respondent.	TO BE PUBLISHED Sudden Infant Death Syndrome; Death Within Hours Of Vaccination; No Entitlement to Program Compensation

Richard Gage, Cheyenne, WY, for petitioner.

Glenn A. MacLeod, with whom were Jeffrey S. Bucholtz, Acting Assistant Attorney General, Timothy P. Garren, Director, Mark W. Rogers, Deputy Director, and Gabrielle M. Fielding, Assistant Director, Department of Justice, Civil Division, Torts Branch, Washington, DC, for respondent.

DECISION ON ENTITLEMENT[1]

[1] Vaccine Rule 18(b) provides that all decisions of the special masters will be made available to the public unless an issued decision contains trade secrets or commercial or financial information that is privileged or confidential, or the decision contains medical or similar information, the disclosure of which clearly would constitute an unwarranted invasion of privacy. Special masters afford the parties a fourteen day time period from the issuance of a decision to move for the redaction of privileged or confidential information before the document's public disclosure.

Campbell-Smith, Special Master

On April 8, 1999, petitioners John and Jane Doe/11, as representatives of the Estate of Child Doe/11, filed a petition pursuant to the National Vaccine Injury Compensation Program[2] (the Act or the Program). Petitioners allege that on the afternoon of December 21, 1994, Child Doe/11 received a Hepatitis B vaccination.[3] Petition (Pet.) ¶ 4. Petitioners further allege that "[a]fter receiving her hepatitis B vaccination[,] Child Doe/11 was weak and less responsive and slept more than usual." Id. ¶ 5. Petitioners assert that "[a]s a result of the Hepatitis B vaccine which Child Doe/11 received on December 21, 1994, she died that same evening." Id. ¶ 9.

Petitioners rely on a theory of causation in fact. Among the documents that were filed in support of their claim were: (1) [Jane Doe/11's] prenatal records,[4] see Petitioners' Exhibit 1 (Ps' Ex. 1); Child Doe/11's birth and newborn records; see Ps' Ex 2; (3) Child Doe/11's pediatric records (Ps' Ex. 3); (4) ambulance records dated December 21, 1994, see Ps' Ex. 4; (5) emergency room records, see Ps' Ex. 5; and (6) the coroner's report, see Ps' Ex. 6. Petitioners also offered the expert opinions of Alan S. Levin, M.D., J.D., an immunologist, and John J. Shane, M.D., a pathologist, together with medical literature supporting the respective opinions of petitioners' experts.

Challenging petitioners' theory of causation, respondent presented the expert opinions of Christine McCusker, M.D., a pediatric immunologist, and Enid Gilbert-Barness, M.D., a pathologist. Respondent also filed a number of medical articles in support of the opinions proffered by its experts.

During a recorded proceeding in Eugene, Oregon, on October 12, 2006, the

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[2] The National Vaccine Injury Compensation Program is set forth in Part 2 of the National Childhood Vaccine Injury Act of 1986, Pub. L. No. 99-660, 100 Stat. 3755, codified as amended, 42 U.S.C.A. § 300aa-10-§ 300aa-34 (West 1991 & Supp. 2002) (Vaccine Act or the Act). All citations in this decision to individual sections of the Vaccine Act are to 42 U.S.C.A. § 300aa.

[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).

[4] [Redacted] was Mrs. Doe/11's maiden name. Petitioners have since married, and Ms. [Redacted] changed her surname to Doe/11.

undersigned heard fact testimony from petitioners, and testimony from the parties' respective expert witnesses. The parties filed post-hearing briefs to address issues that were raised during the hearing. Based on the factual record, the testimony of petitioners, the testimony of the parties' experts, and the supporting medical literature, and for the reasons more fully addressed in this decision, the undersigned finds that petitioners failed to meet their evidentiary burden and therefore, are not entitled to compensation for the death of Child Doe/11.

I. Facts[5]

Mrs. Doe/11's medical records identified her pregnancy with Child Doe/11 as an "at risk" one due to her "maternal age[, and a] surgically scarred uterus." Petitioners' Exhibit (Ps' Ex.) 1 at 2. Additionally identified as a prenatal risk during Mrs. Doe/11's pregnancy with Child Doe/11 was Mrs. Doe/11's prescription use of Haldol.[6] Id. at 1-4. Notwithstanding her identified risk factors, Mrs. Doe/11's pregnancy appears to have proceeded uneventfully. Id.

Child Doe/11 was born on October 31, 1994, in Sacramento, California. Joint Stipulation of Uncontested Fact filed October 4, 2006 (Joint Stip.) ¶ 1. Her Apgar scores at birth were 7 and 9.[7] Id. Her newborn examination was normal. Id. On the date of her

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[5] Included in the parties' pre-hearing submissions are certain "[a]greed [u]pon [f]acts," which were proposed by respondent and agreed to by petitioners, and were set forth in the Joint Stipulation filed on October 4, 2006. These facts are cited as Joint Stip. (Joint Stipulation of Uncontested Fact filed 10/4/06). The undersigned cites to the record for all other facts.

[6] Haldol is a trade name for haloperidol, and is an antipsychotic drug. See Physician's Desk Reference (PDR), 2005 WL 4061863 (definition of haldol). Cases of sudden and unexpected death have been reported for persons taking this drug. Id. Because haloperidol is excreted in human breast milk, infants should not be nursed during maternal drug treatment with haloperidol decanoate. See id. Mrs. Doe/11's medical records indicate that she was taking haldol for a period of time during her pregnancy with Child Doe/11. Ps' Ex. 1 at 2, 3, 4; Ps' Ex. 7. A social work assessment at the time of Mrs. Doe/11's hospital discharge after giving birth to Child Doe/11 reflects that she was no longer taking haldol and was scheduled to return to her psychiatrist in December 1994, one month after Child Doe/11's birth. Ps' Ex. 7.

[7] An Apgar score is "a numerical expression of the condition of a newborn infant . . . , being the sum of points gained on assessment of the heart rate, respiratory effort, muscle tone, reflex irritability, and color." Dorland's Illustrated Medical Dictionary 1670. The Apgar score, developed in 1952 by anesthesiologist Virginia Apgar, "is a numerical expression of the condition of a newborn infant, usually determined 60 seconds after birth." Dorland's Illustrated

birth, she received her first hepatitis B vaccination. Id. ¶ 3. She was discharged from the hospital on November 1, 1994, the day following her birth. Id.

Among the notes on Child Doe/11's hospital newborn profile under "maternal data" were Mrs. Doe/11's age ("[over] 35 [years old]") and her status as a "smoker." Ps' Ex. 2 at 2.[8] Mrs. Doe/11's age and her smoking habit also were noted on another hospital document, in particular, the newborn birth summary, under the subsection titled "risk assessment" under the section titled "Admission Data." Id. at 3.

On November 9, 1994, nine days after Child Doe/11's birth, Carl C. Hsu, M.D., Child Doe/11's pediatrician, examined Child Doe/11 and reported appropriate development. Ps' Ex. 3 at 1. Dr. Hsu's records indicate that he drained Child Doe/11's right eye during the office visit and subsequently treated both of her eyes with antibiotic

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Medical Dictionary 1670; The Apgar Score, http://www.babycenter.com/refcap/3074.html (November 19, 2007). The score reflects a combined numerical measurement of a newborn's appearance (color), pulse (heart rate), grimace (reflex irritability or responsiveness), activity (muscle tone), and respiration. Id.; see also Neil M. Davis, Medical Abbreviations 51 (12th ed. 2005). Each of these five indicators is assigned a number between zero and 2 (2 being the strongest rating), and the numbers are totaled to yield the Apgar score. A perfect score is 10. The Apgar Score, http://www.babycenter.com/refcap/3074.html (last visited November 19, 2007).

[8] On September 18, 2006, petitioners' counsel filed a status report (Ps' SR) wherein he reported that "Child Doe/11's mother, Jane Doe/11, did not smoke while she was pregnant with Child Doe/11. Nor[] did she smoke during Child Doe/11's life." Ps' SR at 1. Mrs. Doe/11 gave similar testimony during the hearing. Mrs. Doe/11's testimony conflicts with the medical records contemporaneous to Child Doe/11's birth. Whether or not Child Doe/11's mother was a smoker during her pregnancy with Child Doe/11 or thereafter is of some interest in this case because maternal smoking is an identified risk factor for Sudden Infant Death Syndrome (SIDS).

The case law provides that in circumstances where the testimony of a witness conflicts with the medical records, contemporaneous medical records generally are afforded more weight than later given witness testimony. See Cucuras v. Dept. of Sec'y of Health and Human Servcs., 993 F.2d 1525, 1528 (Fed. Cir. 1993). Here, more than one of the hospital's records of Child Doe/11's birth identified Mrs. Doe/11 as a smoker. While it is possible that the hospital could have perpetuated an error in the records, the undersigned noted that the maternal risk factors listed on the birth records from the same hospital for Mrs. Doe/11's son, [redacted], Child Doe/11's older brother, do not include smoking. See Ps' Ex. 9 at 4. Considering "the record as a whole," 42 U.S.C. § 300aa-13(1), the undersigned declined to credit as accurate Mrs. Doe/11's later recollection of her smoking status at the time of Child Doe/11's birth.

eye drops. Id.

On December 21, 1994, Child Doe/11 returned to Dr. Hsu's office for a well-child visit and for the receipt of her second hepatitis B immunization. Id. at 3. Child Doe/11 was nearly two months old. Her scheduled appointment was at half past one o'clock. Id. She received her second hepatitis B immunization at approximately two o'clock. Id.; see Transcript of October 12, 2006 hearing (Tr.) at 11 (mother's testimony).

After Child Doe/11's appointment, the family went holiday shopping at the mall. Tr. at 11. During the period of time immediately following Child Doe/11's immunization, Mrs. Doe/11 testified that Child Doe/11's affect was unusual, and that although Child Doe/11 was awake during the shopping trip, there was "[n]o crying. . . . She usually cries, and she wasn't even making a sound . . . ." Id. Mrs. Doe/11 testified that "[at] first we didn't notice [any reaction to the immunization], but towards the end, when we were getting home . . . [Child Doe/11] wasn't drinking from her bottle, which [was] very unusual . . . and she was very tired – lethargic." Id. at 15.

Mr. Doe/11's testimony conflicted with the recollection of Mrs. Doe/11 that Child Doe/11 was awake. According to Mr. Doe/11, Child Doe/11 was asleep the whole time the family was holiday shopping. Tr. at 37. Mr. Doe/11 testified that Child Doe/11 had no interaction with the family while they shopped and that she did not feed during that time. See Tr. at 30-31, 37. Mr. Doe/11 also testified that while the family shopped, he carried Child Doe/11 in a transportable car seat and he did not notice Child Doe/11 to have a fever or to have any abnormal jerking. Tr. at 437-38. Furthermore, Child Doe/11 did not cry between the time that she received her vaccination and the time that Mr. Doe/11 found her turning blue on the couch at home. Tr. at 38. Mr. Doe/11 testified that Dr. Hsu, Child Doe/11's pediatrician, had told the Doe/11s "that [the vaccination] would make Child Doe/11 drowsy." Tr. at 36-37. Because Mr. Doe/11 carried Child Doe/11 during the shopping trip, the undersigned found his testimony more likely to be accurate than his wife's testimony on this point.

Mrs. Doe/11 testified that when the family returned home from shopping around 5:00 p.m., they ". . . all laid down for a nap – me and the two boys laid in the bedroom, and John Doe/11, my husband, and Child Doe/11 laid [down] outside on the couch." Id. at 12. Mrs. Doe/11 indicated that her husband "was laying down on the couch. Child Doe/11 was right next to him, propped up on a pillow." Id. at 18, 19. Child Doe/11 "was face-up." Id. at 18.

Mr. Doe/11 fell asleep beside Child Doe/11 between 5:30 and 6:00 p.m. Tr. at 32-33. He testified at the hearing that he had placed Child Doe/11 next to himself,

propped up on a pillow, on the family's futon on her back with her face up. See Tr. at 31-33. When he woke up about 30 minutes later, Mr. Doe/11 noticed Child Doe/11 was "blue in the face." Tr. at 33, 188. Mr. Doe/11 called to his wife in the bedroom, awakened her and told her that something was wrong with Child Doe/11. Id. Mrs. Doe/11 came out of the bedroom to see Child Doe/11, who was face-up on the pillow on the couch. Tr. at 19. She appeared "bluish." Id. at 19-20. Child Doe/11 was not breathing, and Mr. Doe/11 called 911 at approximately 6:49 p.m. Joint Stip. ¶ 7; Tr. at 20. Mr. Doe/11 tried to administer cardiopulmonary resuscitation ("CPR") to Child Doe/11. Tr. at 34-35. He breathed into her mouth and applied compressions to her chest. Tr. at 41. The ambulance arrived at
6:54 p.m., within five minutes of the placed call to 911. Tr. at 21; Joint Stip. ¶ 7.

According to the records prepared by the emergency response team, Mrs. Doe/11 gave the report: "[Child Doe/11] was last checked on 30 minutes [prior to ambulance arrival] and was fine. [Child Doe/11] has no medical h[istory] . . . . [C]hild did have a hep[atitis] B vaccine today." Ps' Ex. 4 at 1. The filed records indicate that on December 21, 1994, an emergency medical technician arrived by ambulance at the Doe/11's home at 6:54 p.m. and found Child Doe/11 lying supine on the couch with a fire department emergency responder administering CPR. Id. She had no heart beat or respiration. Id. She did not respond to CPR. Id. The emergency responders recorded in their patient care report Child Doe/11's "skin was warm, dry, and extremit[ies] were mottled and chest and abdomen was (sic) white . . . and [Child Doe/11's] abdomen was distended." Id.

At 7:18 p.m., Child Doe/11 arrived at the University of California Emergency Room where she remained unresponsive. Id. Child Doe/11 was diagnosed as having suffered cardiopulmonary arrest of unknown cause. Ps' Ex. 5 at 6. She was pronounced dead by the emergency room doctor at 8:00 p.m. on December 21, 1994. Id. at 6.

Robert M. Anthony, M.D., a forensic pathologist in the Sacramento Coroner's office, performed an autopsy on Child Doe/11 on December 22, 1994, the day after her death. Joint Stip. ¶ 9. Dr. Anthony's autopsy report records his findings on inspection of each of Child Doe/11's individual organs. Dr. Anthony reported "[Child Doe/11's] heart weighs 28 grams." Ps' Ex. 6 at 4. "There are rare epicardial petechiae noted.[9] The epicardial surface is smooth and glistening." Id. Dr. Anthony reported that "[Child

[9] Petechiae are "pinpoint, nonraised, perfectly round, purplish red spots caused by intradermal or submucous hemorrhage." Dorland's Illustrated Medical Dictionary 1411. Epicardial is "pertaining to the epicardium or to the epicardia." Id. at 625. The epicardia is "the lower portion of the esophagus, extending from the hiatus esophagi to the cardia." Id.

Doe/11's] right lung weighs 71 grams. The left lung weighs 69 grams." He noted that "[t]he cut surfaces reveal moderate pulmonary congestion and edema." Id. Dr. Anthony reported that "[Child Doe/11's] stomach is empty." Id. He further reported that Child Doe/11's "liver weighs 225 grams." Id. Child Doe/11's brain weighed 570 grams at autopsy. Id. at 5; Joint Stip. at ¶ 10. Dr. Anthony's autopsy report indicated that "[t]he meninges[10] are clear, glistening, and intact; and there is no blood in any meningeal compartment." Ps' Ex. 6 at 5. Dr. Anthony also noted that "[t]he bladder is empty." Id. After describing his particular findings, Dr. Anthony concluded in the autopsy report that "[t]here is no evidence of edema or herniation."[11] Id. (emphasis added). He recorded the official cause of Child Doe/11's death as Sudden Infant Death Syndrome (SIDS).[12] Joint Stip. ¶ 11; Ps' Ex. 5 at 7.

II. Discussion

A. Legal Standards

The Vaccine Injury Table lists particular injuries and conditions which, if found to have occurred within a prescribed time period, create a rebuttable presumption that an administered vaccine caused the injury or condition. 42 U.S.C. § 300aa-14(a). With respect to adverse events related to the administration of the hepatitis B vaccine, the Vaccine Injury Table lists "[a]naphylaxis or anaphylactic shock" within four hours as an "[i]llness, disability, injury or condition covered." 42 C.F.R. § 100.3(a)(8)(A). The Table also lists "[a]ny acute complication or sequela (including death) of an illness, disability, injury, or condition referred to above [specifically, the anaphylaxis or anaphylactic shock]

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[10] The meninges are "the three membranes that envelop the brain and spinal cord . . . ." Dorland's Illustrated Medical Dictionary 1124.

[11] Herniation is the "abnomral 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.

[12] Sudden infant death syndrome is "the sudden and unexpected death of an apparently healthy infant, typically occurring between the ages of three weeks and five months, and [the death is] not explained by careful postmortem studies." Dorland's Illustrated Medical Dictionary 1833. 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 one 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." Ramzi S. Cotran, et al., Robbins Pathologic Basis of Disease 454-55 (5th ed.1994) (emphasis added).

which illness, disability, injury, or condition arose within the time period prescribed." 42 C.F.R. § 100.3(a)(8)(B). Dorland's Medical Dictionary defines anaphylaxis as "a type [of] hypersensitivity reaction . . . in which exposure of a sensitized individual to a specific antigen . . . results in urticaria, pruritus, and angioedema, followed by vascular collapse and shock and [is] often accompanied by life-threatening respiratory distress." Dorland's Medical Dictionary 73.

Petitioners here do not allege that Child Doe/11 suffered a Table injury presumptively caused by her received vaccination. Neither does the fact testimony of petitioners nor the testimony of the parties' expert witnesses appear to support such a contention. Accordingly, petitioners must prove that Child Doe/11's death was caused by the administration of the hepatitis B vaccine.

A claim for which causation is not presumed under the Act, such as petitioners' claim in this case, is known as an "off-Table" case. To demonstrate entitlement to compensation in an off-Table case, petitioners must demonstrate by a preponderance of the evidence that the vaccination in question more likely than not caused the injury alleged. 42 U.S.C. §§ 300aa-11(c)(1)(C)(ii)(I) and (II). Petitioners satisfy their burden 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." Althen v. Sec'y of Health and Human Servs., 418 F.3d 1274, 1278 (Fed. Cir. 2005)

A persuasive medical theory offers "proof of a logical sequence of cause and effect showing that the vaccination was the reason for the injury." Hines v. Sec'y of Health and Human Servs., 940 F.2d 1518, 1525 (Fed. Cir. 1991) (citations omitted); Knudsen v. Sec'y of Health and Human Servs., 35 F.3d 543, 548 (Fed. Cir. 1994) (same); Grant, 956 F.2d at 1148 (same). A logical sequence of cause and effect requires the support of "[a] reputable medical or scientific explanation" that petitioner may offer "in the form of scientific studies or expert medical testimony." Grant, 956 F.2d at 1148.[13] See also H.R.

[13] The Federal Rules of Evidence do not apply in Program proceedings. See 42 U.S.C. § 300aa-12(d)(2)(B) (stating that the Vaccine Rules "shall . . . include flexible and informal standards of admissibility of evidence"); Vaccine Rule 8(c), Rules of the Court of Federal Claims, Appendix B ("In receiving evidence, the special master will not be bound by common law or statutory rules of evidence."). Hines v. Sec'y of Health and Human Servs., 940 F.2d 1518, 1525-6 (Fed. Cir. 1991). The United States Court of Federal Claims, however, has stated that in vaccine cases, the Supreme Court's decision in "Daubert[v. Merrell Dow

Rep. No. 99-908, Pt. 1, at 15 (1986), reprinted in 1988 U.S.C.C.A.N. 6344, 6356.

Petitioners need not show that the vaccine was the sole or even the predominant cause of the injury. See Shyface v. Sec'y of Health and Human Servs., 165 F.3d 1344, 1353 (Fed. Cir. 1999). But petitioners bear the burden of establishing "that the vaccine was not only a but-for cause of the injury but also a substantial factor in bringing about the injury." Id. at 1352; see also Pafford v. Sec'y of Health and Human Servs., 451 F.3d 1352, 1355 (Fed. Cir. 2006) (reiterating that petitioner must prove by preponderant evidence both that the received vaccination was a substantial factor in causing her injury and that the harm would not have occurred in the absence of the vaccination). Petitioners do not satisfy their burden by merely showing a proximate temporal association between the vaccination and the injury. Grant, 956 F.2d at 1148 (quoting Hasler v. United States, 718 F.2d 202, 205 (6th Cir. 1983), cert. denied, 469 U.S. 817 (1984) (stating "inoculation is not the cause of every event that occurs within the ten day period [following it]. . . . Without more, this proximate temporal relationship will not support a finding of causation")).

_____ The Federal Circuit has stated that there is no requirement in the Vaccine Act's preponderant evidence standard that petitioners submit particular types of evidence as "objective confirmation" to support their theory of causation. Althen, 418 F.3d at 1279. The Court of Appeals for the Federal Circuit has explained that requiring particular types of evidence "prevents the use of circumstantial evidence envisioned by the preponderance standard and negates the system created by Congress, in which close calls regarding

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Pharmaceuticals, Inc., 509 U.S. 579, 594 (1993)] is useful in providing a framework for evaluating the reliability of scientific evidence." Terran v. Sec'y of Health and Human Servs., 41 Fed. Cl. 330, 336 (1998), aff'd, 195 F.3d 1302, 1316 (Fed. Cir. 1999), cert. denied, Terran v. Shalala, 531 U.S. 812 (2000). The Supreme Court in Daubert noted that scientific knowledge "connotes more than subjective belief or unsupported speculation." Daubert, 509 U.S. at 590. Rather, some application of the scientific method must have been employed to validate an expert's opinion. Id. An expert's "testimony must be supported by appropriate validation . . . based on what is known." Id. Factors relevant to evaluating an expert's theory may include, but are not limited to:

> [W]hether the theory or technique employed by the expert is generally accepted in the scientific community; whether it's been subjected to peer review and publication; whether it can be and has been tested; and whether the known potential rate of error is acceptable.

Daubert v. Merrell Dow Pharmaceuticals, Inc., 43 F.3d 1311, 1316 (9th Cir. 1995) (citations omitted), on remand, 509 U.S. 579 (1993); see also Daubert, 509 U.S. at 592-94.

causation are resolved in favor of the injured claimants." Id. at 1280 (citing Knudsen, 35 F.3d at 549); see also Capizzano v. Secretary of Health and Human Services, 440 F.3d 1317, 1325 (Fed. Cir. 2006) (denouncing the requirement of "either epidemiologic studies, rechallenge, the presence of pathological markers or genetic disposition, or general acceptance in the scientific or medical communities to establish a logical sequence of cause and effect"). The expressed "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.

The Federal Circuit's decisions in Althen and Capizzano make clear that petitioners need not produce particular types of evidence to satisfy their burden of proof. But the Federal Circuit's decisions do not preclude courts from considering presented medical literature when evaluating expert testimony.

Under the Act, petitioner's showing of entitlement is rebuttable. Thus, if respondent establishes, by a preponderance of the evidence, that petitioner's injury is "due to factors unrelated to the administration of the vaccine described in the petition," petitioner's claim must fail. 42 U.S.C. § 300aa-13(a)(1)(B); Shalala v. Whitecotton, 514 U.S. 268, 270-71 (1995) ("The Secretary of Health and Human Services may rebut a prima facie case [established by petitioners] by proving that the injury or death was in fact caused by 'factors unrelated to the administration of the vaccine. . . .' [But,] [i]f the Secretary fails to rebut, the claimant is entitled to compensation.) (citations omitted); see also Walther v. Secretary of Health and Human Services, 485 F.3d 1146, 1151 (Fed. Cir. 2006) (stating that the petitioner does not bear the burden of eliminating alternative independent potential causes") .

B. The Parties' Experts' Opinions of Causation

Four medical experts offered opinions in this case regarding what caused Child Doe/11's death.

1. Petitioners' Experts' Opinions

a. Dr. Shane

John J. Shane, M.D., a neuropathologist, testified for petitioners. Dr. Shane served as the Chairman of the Department of Pathology and Director of Laboratory Medicine at Lehigh Valley Hospital in Lehigh, Pennsylvania for twenty-six years. Stepping down from that post in August of 2000, Dr. Shane began a private consultation practice in which he continues to work full-time. As a private consultant, he "performs anywhere

between 30 and 60 autopsies a year." Id. at 53. Dr. Shane, by his own admission, "is not a pediatric pathologist." Id. at 56. The undersigned accepted Dr. Shane as an expert in the area of pathology.

Based on his review of Child Doe/11's medical records, which include the autopsy report and slides from the Sacramento County Coroner's Office, Dr. Shane opined in his report that: "The organs at autopsy were grossly unremarkable with no evidence of apparent disease process or congenital defect or anomaly. The only abnormality was a brain weight of 570 g[ra]ms and rare epicardial petechiae." Ps' Ex. 11 at 1. His opinion rests primarily on his view that Child Doe/11's brain weight of 570 grams was "abnormal." Dr. Shane believes that contrary to the reported findings in Child Doe/11's autopsy report, Child Doe/11's brain weight at autopsy is evidence of significant brain edema[14] that resulted from a brain injury. See Ps' Ex. 11 at 1-2. Dr. Shane stated in his expert report that "the sections of [Child Doe/11's] brain are pro[of] positive of an encephalopathy." Id. at 2. Further, Dr. Shane stated that "in the absence of other etiologic factors and with the timing of the Hepatitis B vaccination, the Hepatitis B is the obvious[,] probable and preferred etiologic mechanism for the encephalopathy which caused this child's death." Id. During the hearing, Dr. Shane testified that Child Doe/11 suffered a "respiratory death" secondary to her hepatitis B vaccination. Tr. at 89-90.

b. Dr. Levin

Alan S. Levin, M.D., J.D., also testified for petitioners. Dr. Levin is board certified in allergy and immunology and in clinical pathology. Dr. Levin sold his allergy-immunology practice and became a lawyer, graduating from law school in 1995. Id. at 193. He currently sees patients only on referral, and by his own testimony, sees only two or three children a year. Id. 195-197. He no longer maintains an active clinic or practice. Id. at 196. Additionally, Dr. Levin currently has a relationship with a pharmaceutical company, in which he is a seven-percent stakeholder and a board member. Id. at 193-195. Dr. Levin testified that this pharmaceutical company is a "Chinese biotech company, [which is] developing certain cytokines for treatment, one of which is [interleukin] IL-22 . . . .so [he is] very, very conversant with cytokines."[15] Tr. at 193-94.

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[14] 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." Dorland's Medical Dictionary 589.

[15] Cytokine is "a generic term for 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 Medical Dictionary 469.

Dr. Levin concurs with Dr. Shane that Child Doe/11's death was caused by her receipt of the hepatitis B vaccination. Dr. Levin opined in his report that Child Doe/11's vaccination led to an "excessive cytokine release followed by cerebral edema." Ps' Ex. 12 at 4. According to Dr. Levin's cytokine theory, "[i]ncreased cytokine levels cause neutrophils[16] to migrate from the bloodstream to the CSF, causing neutrophilic pleocytosis (an increased number of cells in the CSF) and contributing to vasogenic edema (increased water content in the brain). Eventual cerebral edema results in a decreased cerebral blood [flow]." Id. In Dr. Levin's opinion, "[t]his process can lead to death or permanent neuronal dysfunction." Id.

Dr. Levin testified during the hearing that the purpose of the hepatitis B vaccination is "to cause a cytokine reaction." Tr. at 202. Dr. Levin explained that "pediatricians warn parents about the somnolence, the reaction, the fever [that may follow the administration of a vaccine] – that's cytokines. That's what the pediatricians are talking about." Id. Dr. Levin described the difference between cytokine activation and cytokine storm as a matter of degree. See Tr. at 225. He explained that a cytokine storm is a significantly enhanced process because "[cytokine] activation can be a normal phenomenon." Id.

2. Respondent's Expert's Opinions

a. Dr. Gilbert-Barness

Enid Gilbert-Barness, M.D., testified for respondent. Dr. Gilbert-Barness is a Professor of Pathology and Laboratory Medicine, Professor of Pediatrics, and Professor of Obstetrics and Gynecology at the University of South Florida. Id. at 113. She estimates that she has personally conducted "about 10,000" pediatric autopsies. Id. at 115. She has served on the "National Institutes of Health[] panel to examine the Sudden Infant Death Syndrome." Id. at 115. Dr. Gilbert-Barness teaches medical students on the subject of pediatric pathology. Id. at 115. The undersigned accepted Dr. Gilbert-Barness as an expert in the field of pediatric neuropathology. Id. at 116.

Dr. Gilbert-Barness disputed that Child Doe/11's death was related to the hepatitis

[16] A neutrophil is "a mature granular leukocyte (white blood cell) that is polymorphonuclear [having a deeply-lobed nucleus or a nucleus so divided that it appears to be more than one]." Dorland's Medical Dictionary 1261, 1481. Neutrophils can "adhere[] to immune complexes, and [cause] phagocytosis [cell death]." Id. at 1261.

B vaccination. In her opinion, Child Doe/11's death was related to "Sudden Infant Death . . . [which] was very likely in this case related to an asphyxia[l] death." Id. at 121. Dr. Gilbert-Barness stated that Child Doe/11's internal organs were congested. However, she testified that she did not "think that there was a significant increase in brain weight. . . [nor did she] think there was significant brain edema." Id. at 122. Addressing her review of the autopsy slides, she stated that "[she] saw very little abnormality. There may have been a minimal degree of edema, but I did not see the changes that Dr. Shane has described." Id. at 122. Dr. Gilbert-Barness further opined that "if it were an encephalopathy, one would expect to see considerable brain edema. One would also very likely – as the cause of death – see herniation of the brainstem, which was not present in this case." Id. at 122.

b. Dr. McCusker

Christine McCusker, M.D., testified for respondent. Certified by the Royal College of Physicians and Surgeons in Canada in general pediatrics[17] as well as in allergy and immunology, Dr. McCusker is an Assistant Professor of Pediatrics at McGill University, Associate Member of Medicine at McGill University, and a Research Director at the Meakins-Christie Laboratories of McGill. Additionally, as Director of the Clinical Immunology Lab for the Montreal Children's Hospital, Dr. McCusker has an active pediatric practice at Montreal Children's Hospital primarily in the area of allergy and immunology. Dr. McCusker has served on peer review committees for evaluating research dossiers and determining who is eligible for research grants with the Fonds de Recherche en Sante du Quebec (FRSQ).[18] Dr. McCusker also has served as an examiner for the Royal College Allergy-Immunology Qualification Boards. The undersigned accepted Dr. McCusker as an expert in the area of pediatric immunology.

Dr. McCusker disagreed with Dr. Levin's theory that a cytokine storm led to "an immune-mediated encephalopathy, [a] cytokine-induced encephalopathy," which led, in turn, to the death of Child Doe/11 Doe/11. Tr. at 243. Dr. McCusker agreed with Dr. Levin that cytokine activation is a normal response to vaccination. Dr. McCusker testified that "[w]hen you vaccinate, you induce an immune response. That's the purpose." Id. Dr. McCusker further testified that the evidence of a proper immune

[17] Dr. McCusker has previously been certified by the American Board of Pediatrics. Dr. McCusker stated during her testimony that she has let her American certification lapse due to the expense of maintaining several certifications. See Tr. at 239-240.

[18] FRSQ is the Research Funds in Health for the province of Quebec. Tr. at 240. It provides "sort of the regional equivalent of what would be NIH grants." Id.

response is "the active inflammation at the [injection] site[,] . . . the redness and swelling . . . at the site, and . . . the effects of the [vaccination] acting over distances [in the body, specifically]: the fever [and] the malaise." Id. at 251.

C. Evaluating the Presented Evidence

To establish entitlement to compensation, petitioners must satisfy the prongs of the Althen standard.

1. A Medical Theory Causally Connecting the Vaccination and the Injury

To prove causation, petitioners must offer a medical theory causally connecting Child Doe/11's receipt of her hepatitis B vaccination and her death.[19] 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. The mere "possibility" of a causal relationship between an injury and a particular vaccine does not permit a finding of actual causation. Duncan v. Sec'y of Health and Human Servs., No. 90-3809V, 1997 WL 75429 *4 (Fed. C1. Spec. Mstr. Feb. 6, 1997). That the alleged injury may be "consistent with" a possible vaccine injury is likewise inadequate to establish the necessary causal association. Cain v. Sec'y of Health and Human Servs., No. 91-817V, 1992 WL 183202, *9 (Cl. Ct. Spec. Mstr. July 15, 1992).

Dr. Shane, petitioners' expert in forensic pathology, opined that Child Doe/11's death was the result of an acute encephalopathy[20] caused by her receipt of the hepatitis B

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[19] While the law does not require absolute precision in identifying the medical mechanism of injury, there must be "sufficiently compelling proof that the agent must have caused the damage somehow." Kennedy v. Collagen Corporation, 161 F.3d 1226, 1230 (9th Cir. 1998)(quoting Daubert v. Merrell Dow Pharmaceuticals. Inc., 43 F.3d 1311, 1314 (9th Cir.), cert. denied, 516 U.S. 869 (1995)).

[20] Within the Vaccine Program, a vaccinee is deemed to have suffered an encephalopathy if the vaccinee manifests, within the applicable period, an injury that is an acute encephalopathy, and that persists as a chronic encephalopathy for more than 6 months beyond the date of vaccination. 42 C.F.R. §100.3(b)(2) (qualifications and aids to interpretation of the Vaccine Injury Table). The qualifications and aids to interpretation of the Vaccine Injury Table, which are set forth at 42 C.F.R. §100.3, describe an acute encephalopathy as one that is sufficiently severe that, whether or not hospitalization occurs, the condition requires hospitalization. Id.

For children less than 18 months of age who present without an associated seizure event,

vaccination. Ps' Ex. 11 at 1-2; Tr. at 88. In his submitted written opinion, Dr. Shane stated "that this case represents an excephalopathic death with unequivocal microscopic findings of an encephalopathy; [and] microscopic central nervous system findings that are inconsistent with a SIDS death." Ps' Ex. 11 at 2. Dr. Shane offered that these findings "followed by the expected [clinical] signs and symptoms [] of an encephalopathy namely weakness, somnolence, and a reduced level of responsiveness[,]" made the cause of death unequivocally an encephalopathy. Id.

Dr. Shane's opinion is predicated on his belief that Child Doe/11's brain weight of 570 grams, measured at autopsy, was abnormally "heavy" and was indicative of a significant brain edema, which occurred as a result of a brain injury suffered prior to her death.[21]

Petitioners' expert, Dr. Levin, opined that the administration of Child Doe/11's hepatitis B vaccination produced an excessive release of cytokines, which caused, in turn, brain edema, encephalopathy and death. Ps' Ex. 12 at 4; Tr. at 201-215.

Dr. Levin explained that in Child Doe/11's situation, the release of two cytokines, particularly IL-1 and TNG, was "provoked by the hepatitis B," and the release of the cytokines began to have a cytotoxic effect on the vascular endothelium (the cellular lining

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an acute encephalopathy is indicated by a significantly decreased level of consciousness lasting for at least 24 hours. Id. For those children less than 18 months of age who present following a seizure, the children shall be viewed as having suffered an acute encephalopathy if their significantly decreased level of consciousness persists beyond 24 hours and cannot be attributed to a seizure or medication. Id.

A "significantly decreased level of consciousness" is indicated by the presence of at least one of the following clinical signs for at least 24 hours or greater: (1) decreased or absent response to environment (responds, if at all, only to a loud voice or painful stimuli); (2) decreased or absent eye contact (does not fix gaze upon family members or other individuals); or (3) inconsistent or absent responses to external stimuli (does not recognize familiar people or things). Id.

The following clinical features, whether alone or in combination, do not demonstrate an acute encephalopathy or a significant change in either mental status or level of consciousness: sleepiness, irritability (fussiness), high-pitched and unusual screaming, persistent inconsolable crying, and a bulging fontanelle. Id. In the absence of other evidence of an acute encephalopathy, seizures shall not be viewed as the first symptom or manifestation of the onset of an acute encephalopathy. Id.

of Child Doe/11's capillaries) by attacking it. The cytokines "attack[ed] th[e] cells [of the capillaries' lining], kill[ed] them, and all of a sudden [impaired] 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." See Tr. at 207-208. Dr. Levin further explained:

> And that's why you have water around the vessels, and that's why, when you fix those vessels – fix that tissue – you see what they call halos, and that's precisely what's going on.
>
> The endothelium is being destroyed, the water's getting pumped out because the patient now has blood pressure – the water's being pumped out – and there's water surrounding these nerves, these glial cells[22] . . . and also the vessels.
>
> So that's diagnostic of cytokine-induced endothelial damage . . . . There's nothing else in the human body that does that.

Tr. at 207-208 (footnote added).

During the hearing, Dr. Levin relied on an excerpt from Nelson's Textbook of Pediatrics to explain how cytokines cause brain edema:

> Increased ICP [intercranial pressure] due to cell death (cytotoxic cerebral edema), cytokine-induced increased capillary vascular permeability (vasogenic cerebral edema), [and that's what everybody is talking about] and, possibly, increased hydrostatic pressure (interstitial cerebral edema) after obstructive reabsorption of CSF [cerebrospinal fluid] in the arachnoid villus or obstruction of the flow of fluid to [sic] the ventricles.

Tr. at 203-204 (brackets in original). Dr. Levin clarified for the court that "basically, what [Nelson's Textbook of Pediatrics] says is edema begets edema. The edema shuts down the [body's] drainage system, and then the pressure goes up." Petitioners' Exhibit 17 at 204.

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[22] Glial cells or neuroglia refers to the "supporting structure of nervous tissue. It consists of a fine web of tissue made up of modified ectodermal elements, in which are enclosed peculiar branched cells known as neuroglial cells or glial cells." Dorland's Illustrated Medical Dictionary 1254.

Dr. Levin submitted literature in support of his theory that hepatitis B is a superantigen that is capable of triggering a cytokine storm. In particular, Dr. Levin provided an excerpt from the Institute of Medicine Report filed as Petitioners' Exhibit 28 (Kathleen Stratton et al., Immunization Safety Review: Hepatitis B Vaccine and Demyelinating Neurological Disorders, at 8-9 (The National Academies Press 2002). The excerpt described superantigens as one of three posited mechanisms by which "immunization of any kind (either through infection or vaccination) could cause the development of demyelinating diseases of the central and peripheral nervous systems." Ps' Ex. 28 at 3-4. The excerpt provided:

> Superantigens are proteins that are produced by viruses and bacteria and that activate T cells either by direct activation of auto-reactive T cells (regardless of antigen specificity) or activation of humoral responses. 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 [one of which is superantigen stimulation]. Thus, there is a theoretical basis for an association between vaccine-induced immune response and demyelination. Biological evidence exists regarding some components of this.

Ps' Ex. 28 at 3-4 (emphasis added). The IOM report on which Dr. Levin relies, however, postulates a theoretical basis for an association between a vaccine-mediated immune response and demyelination, not an association between a mediated-immune response and sudden death.

Respondent's two expert witnesses rebutted petitioners' theory. Specifically, Dr. Gilbert-Barness disputed Dr. Shane's finding of cerebral edema in Child Doe/11, and Dr. McCusker disputed the plausibility of Dr. Levin's proposed biological mechanism. Both Dr. Gilbert-Barness and Dr. McCusker opined that the symptoms that Child Doe/11 exhibited after her immunization were not encephalopathic. Tr. at 139, 264-265.

Dr. Gilbert-Barness, reviewed the autopsy slides in this case as well as Child Doe/11's clinical history prior to her death. Dr. Gilbert-Barness testified that there is no reliable evidence linking the hepatitis B immunization to Child Doe/11's death, and that Child Doe/11's death is, in fact, consistent with SIDS.[23] See Tr. at 121-41; Respondent's

[23] At trial, Dr. Gilbert-Barness clarified her opinion, stating that "I think Child Doe/11's death was related to what we have called Sudden Infant Death Syndrome. I would prefer to call it

Report (R's Report) at 3; R's Ex. OO (Dr. Gilbert-Barness' rebuttal opinion to Dr. Shane's testimony and opinions). According to Dr. Gilbert-Barness, Child Doe/11's brain did not show evidence of an acute encephalopathy at autopsy. Id. Child Doe/11's brain weight at her death was not abnormal for her age, and her brain weight and "heavy" internal organs, as measured at autopsy, are consistent with a finding of SIDS. R's Ex. A at 2; Tr. at 122, 125-26, 128-130, 133-138.

The typical autopsy of a SIDS death reveals no process that accounts for the death, and very little pathologic change in the organs can be detected by ordinary means. See Marie Valdes-Dapena, et al., Sudden Death in Infants, in Vol. 1, Ch. 12 Potter's Pathology of the Fetus and Infant 433, 439 (Enid Gilbert-Barness ed., 1997) (filed as R's Ex. GG). Nevertheless, there are "gross and microscopic features [that] are apt to be observed in the course of a typical postmortem examination in a case of SIDS." Marie Valdes-Dapena, M.D., Sudden Infant Death Syndrome: Pathologic Findings, in Vol. 19, No. 4 Clinics in Perinatology, 701-16 at 703 (December 1992) (filed as R's Ex. FF).

On internal postmortem examination, certain lesions, are commonly encountered. Id. These are said to be "classical findings or typical of SIDS and include "thymic, pleural, and epicardial petechiae . . . pulmonary congestion . . ., and pulmonary edema." Id. Among other findings noted on internal examination is an "empty urinary bladder." R's Ex. FF at 703. Not all of the classic or typical findings occur in each case, and none of the findings are required for the diagnosis of SIDS. Id. SIDS remains a diagnosis of exclusion. See id. "One cannot find in [SIDS cases] any pathologic lesion sufficiently grave to be the cause of the baby's death–and it is that, combined with an equally negative medical history and scene investigation, that makes it SIDS." Id. On external examination, it is common for the coroner to observe that the infant's "[b]ody [is] apparently well developed and well nourished." Id. On autopsy, Child Doe/11 was found to be a "well-developed, well-nourished, female infant." Ps' Ex. 6 at 2. Child Doe/11 was also found to have "rare epicardial petechiae[,]" "moderate pulmonary congestion and edema" and "[her] bladder [was] empty." See Ps' Ex. 6 at 4-5. These internal and external findings appear to be the classic findings typically associated with a SIDS death and are supportive of Dr. Anthony's finding of SIDS as the cause of Child Doe/11's death. Ps' Ex. 6 at 6.

The medical literature indicates that children who die from SIDS often have increased brain weight at death, and cerebral edema is found in "a small proportion of

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Sudden Infant Death, and I believe this was very likely in this case related to an asphyxia[l] death." Tr. at 121.

SIDS victims." R's Ex. FF at 710; accord F. J. Aranda, et al., Assessment of Growth in Sudden Infant Death Syndrome, in Vol. 9 Neuroepidemiology 95-105 at 95 (1990) (filed as R's Ex. KK)(finding the brain weight of children who died from SIDS to be "heavier" than normal); Kadhim, H., et al., Incongruent Cerebral Growth in Sudden Infant Death Syndrome, Vol. 20, No. 3 Journal of Child Neurology 244-246 at 244 (March 2005) (filed as R's Ex. MM) (describing a recent neuropathologic study in which the brain weight of infants who died from SIDS were found to be "invariably heavier in comparison with those of a group of age-matched controls. . . issuing from the same population" and the weights of the other organs, such as the liver, lungs and heart, in the infants who died from SIDS were noted to be elevated as well). A standard text on pediatric pathology documents that the normal brain weight for a two-month-old infant ranges from 516 grams to 609 grams, and lists 560 grams as a normal brain weight for girls at two months of age. E. Gilbert-Barness, et al., Ch. 2 Handbook of Pediatric Autopsy Pathology, 57, 61 (Humana Press 2005) (filed as R's Ex. EE); see also Jorgen Voigt, et al., Brain Weight of Danish Children, Vol. 116 Acta Anat. 290-301 at 299 (1983) (filed as R's Ex. LL) (listing, without reporting the standard deviation, the normal "mean" brain weight for a two-month-old female as 560 grams and finding, on average, a nine percent increase in brain weight within 12 hours after the child's death). Child Doe/11's brain on autopsy weighed 570 grams. She was two months old at the time of her death. Her brain weight at death would appear to fall within the normal range of brain weights for infants of her age.

Additionally, Dr. Gilbert-Barness testified that in SIDS cases when the baby is not found in the prone position, the death was likely to have resulted from an asphyxial death caused by an accidental overlay on the child either by a larger person or by bedding material. See Tr. at 123, 126. The article filed as Respondent's Exhibit NN describes death by overlaying as a form of "mechanical asphyxia [that] occurs when a bigger person rolls on top of a smaller person - usually a child less than five months of age." Kim Collins, M.D., Death by Overlaying and Wedging, a 15 Year Retrospective Study, Vol. 22 The American Journal of Forensic Medicine and Pathology 155 at 1, (2001) (filed as R's Ex. NN).[24] The article also describes the circumstances in which an infant might be overlain inadvertently by an adult or an older child. Specifically, a bigger person might: (1) smother an infant by pressing the infant's face into the bedding; (2) prevent an infant's respiration by putting pressure on the infant's thorax and abdomen; or less likely, (3) compress the infant's neck and thereby prevent blood flow to and from the brain." Id. at 5. Similarly, death by wedging, "another form of accidental mechanical

[24] Because this article was paginated manually and the original page numbers were not reflected on the filed copy of the document, the undersigned relied on the consecutively inserted page numbers when referencing this article.

asphyxia," may result "when an infant's body or face is compressed within a narrow space, resulting in asphyxia from interference with chest wall movements or obstruction of the airway." Id. at 6. 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.

An examination of the "pattern of livor" and blanching of the infant's skin after death may indicate the position of the infant or the points of pressure unintentionally applied by the bed sharer. R's Ex. NN at 6; see also Joseph A. Perper, Time of Death and Changes After Death: Anatomical Considerations, Ch. II, Part 1 Medicolegal Investigation of Death 23-25 (2002) (filed as R's Ex. II) (text excerpt discussing post-mortem lividity and the nature and extent of "blanching" of the skin after death); Sannohe, Seiya, M.D., Change in Postmortem Formation of Hypostasis in Skin Preparations 100 Micrometers Thick, Vol. 23(4) The American Journal of Forensic Medicine and Pathology 349-354 (2002) (filed as R's Ex. JJ) (additional article addressing the timing of post-mortem lividity and the occurrence of blanching).

Indeed, during the hearing, there was much discussion about blanching and lividity for the apparent purpose of establishing the position of Child Doe/11's body at death, a fact that might provide information regarding the likely cause of her death. In the filed records, Tracy Brown, the emergency medical technician (EMT) who completed the patient care report on arrival at the Doe/11 house, noted that an inspection of Child Doe/11 revealed that her skin "was warm, dry, and extremet[ies] were mottled and [her] chest and abd[omen] [were] white (no color at all). . . Ps' Ex. 4 at 1. Dr. Shane testified that "the pallor [of Child Doe/11's abdomen] . . . [was] indicative of her being on her back [at the time of death.]" See Tr. at 171-175. Dr. Shane's testimony and Ms. Brown's report are consistent with Mr. Doe/11's testimony that at the time Child Doe/11's body went into shock, "[Child Doe/11] was on her back . . .propped up on the pillow right next to him." Tr. at 31. The pathology findings also noted a "moderate amount of fixed purple livor mortis over the posterior aspects of the body surfaces."[25] Ps' Ex. 6 at 2. The record amply supports a finding that Child Doe/11 was not in the prone position at the time of her death, but was lying on her back.

The age of an infant is a factor in SIDS cases. SIDS usually occurs in the second

[25] Petitioner's Exhibit 24, an excerpt from Pathophysiology: The Biological Basis for Disease in Adults & Children 80 (2002), provides further elucidation on this point. "Gravity causes blood to settle in the most dependent, or lowest, tissues, which develop a purple discoloration called livor mortis." Id.

to fourth month of life. Marie Valdes-Dapena, M.D., Sudden Infant Death Syndrome: Pathologic Findings, in Vol. 19, No. 4 Clinics in Perinatology, 701-16 at 709 (December 1992) (filed as R's Ex. FF). At the time of Child Doe/11's death, she was a little more than seven weeks old, nearly two months old. Additionally, maternal smoking during pregnancy is a risk factor for SIDS. Here, the undersigned afforded greater evidentiary weight to the contemporaneous medical record notes that Mrs. Doe/11 was a smoker at the time of Child Doe/11's birth than she afforded to Mrs. Doe/11's later offered, contrary testimony at hearing that she was not a smoker when Child Doe/11 was born.

In support of Dr. Gilbert-Barness's opinion that the more likely cause of Child Doe/11's death was SIDS, and not an encephalopathy, she pointed to the absence of significant edema in Child Doe/11's brain and to the presence of petechiae reported in Child Doe/11's autopsy report. Dr. Gilbert-Barness also pointed to the risk factor of Mrs. Doe/11's smoking. Although the mere presence of risk factors is not dispositive of the question of what caused Child Doe/11's death, the presence of a risk factor does create an increased risk that the condition will occur. And yet, as the literature supplied by Dr. Gilbert-Barness indicates, there are a number of infants who have died from SIDS and have "had no risk factors" at all. R's Ex. GG at 439.

Respondent's expert Dr. McCusker challenged the aspect of petitioner's theory advanced by Dr. Levin, specifically, his theory that a cytokine storm had occurred. Dr. McCusker explained that cytokines are "loosely divided into different groups." Tr. at 248. Proinflammatory cytokines are "designed to ramp up the system and call the effector cell[s] – the cells and the proteins that are going to do something to that antigen – to that bacteria that you're infected with." Id. Proinflammatory cytokines "open up the spaces . . . between the blood vessels so that cells that are sitting in the tissue can come into the blood vessel[s] and be directed to the site of inflammation or to the site of attack." Id. at 249. Cytokines "can increase temperature, [t]hey can give you a sense of malaise, that sense of 'I feel lousy.'" Id. at 250. Dr. McCusker testified that "[e]verything else . . . increasing vascular permeability, the cerebral edema . . . [these] are effects that can only occur locally . . . [but] do not occur over long distances." Id. at 250.

Dr. McCusker stated that cytokines that can "act across distances are really tightly regulated." Id. at 249. Dr. McCusker provided the following example:

> [I]f [a] gentleman that ha[s] [an] abscess in his toe [also] has a headache, . . . it may be an effect of the cytokine, but his headache is not cerebral edema. His headache is the malaise and the fever that's being induced by the cytokine.

> [But] if that gentleman has an abscess in his brain, then the effects of . . . the proinflammatory cytokines can operate [locally], and you can get those bad outcomes that are secondary to cytokines acting in a place or acting in a way they're not supposed to.

Tr. at 250.[26]

In addition to the fact that cytokines are tightly regulated, Dr. McCusker testified that one of the factors involved in the tight regulation of cytokines in the body is the limited period of time within which cytokines act. "[C]ytokines . . . don't hang out in the body for very long." Tr. at 251-52. Dr. McCusker explained that:

> The half-life of TNF-Alpha,[27] for example, is 15 minutes. So it comes, it's released, it starts to do its job, but it's gone within 15 minutes, and unless there's . . . continued stimulus, its activity decreases over time and very quickly because the immune system says, 'You know what? I really don't want these things operating for very long if we can't control them.'

Tr. at 252.

Dr. McCusker explained further that "the other thing [the immune system] does . . . [at] the same time it turns up these proinflammatory cytokines, [is] also start[] to turn up the anti-inflammatory cytokines or the regulatory cytokines, and those cytokines' job is to say, 'You know what? You guys are too busy. Turn it down.'" Id. The result under most circumstances, is that . . . you minimize what you would call immunopathology or side effects as a result of the immune response. See id.

Dr. McCusker testified, "When an immune response is induced . . . whether [] by

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[26] Dr. McCusker's testimony on this point was similar to Dr. Levin's who testified that "cytokines in the periphery can cause central nervous system problems." Tr. at 210. He explained that "anything that induces cytokines in the periphery – even in the big toe – can cause symptoms in the head." Id. He described, as "one of the classic situations – if you have an abscess in the big toe, you can get a headache. The reason for that is the cytokines from the big toe – IL-1 primarily – is getting into the central nervous system and causing symptoms." Id.

[27] TNF-[Alpha] is tumor necrosis factor-Alpha, an "alarm" cytokine "which signal[s the immune system] that an invasion has begun." Lauren Sompayrac, How the Immune System Works (2d ed.) at 20.

natural infection or by a vaccination . . . the body is introduced to a protein that is [foreign], and the body has to respond to that protein, and it can respond in several ways." Tr. at 244. Dr. McCusker explained that one response by the immune system is to ignore the protein, and another response is to develop a tolerance to the protein. Id. To develop tolerance, "requires the activation of an immune response . . . that require[s] the formation of T-cells or the proliferation – the division of T-cells that are specific for this protein and, as well, the formation or the activation of B-cells to ultimately form antibodies."[28] Id. Dr. McCusker observed that "the purpose of vaccination is to generate memory and antibodies." Id. at 247.

While Dr. McCusker acknowledged that cytokines do participate in the development of cerebral edema, Tr. at 257, she testified that cytokine-induced cerebral edema has been shown only to develop in situations where nervous tissue has been infected or compromised. See Expert Report of Christine McCusker, M.D., (filed as R's Ex. C) ¶ 4; Tr. at 255; Shumpei Yokoto et al, Hypothetical Pathophysiology of Acute Encephalopathy and Encephalitis related to Influenza Virus Infection and Hypothermia Therapy, 42 Pediatrics International 197 (2000)(filed as R's Ex. Q). Immune responses to bacteria and viruses, not directly infecting the brain tissue, have not been shown to cause either cytokine storm or cerebral edema. R's Ex. C ¶ 5; Tr. at 258. Nor has a cytokine-induced cerebral edema been reported following either wild hepatitis B infection or the administration of the hepatitis B vaccine. R's Ex. C ¶ 5; Tr. at 279-80, 282.

Dr. McCusker testified that what has been observed and reported in the literature, however, indicates that any significant release of pro-inflammatory mediators that is sufficient to create a cytokine storm results first, in the onset of fever, as an initial symptom, and then, frequently leads to multi-organ failure. R's Ex. C ¶ 5; Tr. at 254-55, 259-60, R's Ex. DD. As Dr. McCusker pointed out in her testimony, no fever was reported in this case, and Dr. Anthony's examination of Child Doe/11's internal organs at autopsy were unremarkable for inflammation.[29] R's Ex. C ¶ 5; Tr. at 260-61.

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[28] Among the multiple functions of the T cells is the generation of cytokines. Lauren Sompayrac, How the Immune System Works at 8-9 (2d ed. 2003). The B cells of the immune system produce antibodies. Id. at 28.

[29] In Petitioners' Post Hearing Memorandum (Ps' PHM), petitioners' counsel moved to have the undersigned disregard paragraph 8 of Dr. Gilbert-Barness's supplemental opinion, which was filed on February 15, 2007. In this paragraph, Dr. Gilbert-Barness states that "[t]here is no scientific evidence [in Child Doe/11's case] for cytokines – no fever or infection to initiate [the] release of cytokines." R's SR ¶ 8. Petitioners' counsel argues that this statement is an offered opinion pertaining to immunology, not pathology, and that the expressed opinion is

In support of her testimony regarding the cascade of events that would be indicative of a cytokine storm, Dr. McCusker cites an article describing a cytokine storm induced by the intravenous administration of an experimental drug in six healthy persons. The article details the progression of symptoms and the clinical presentation that a cytokine storm provokes. See Suntharalingam, et al., Cytokine Storm in Phase I Trial of the Anti-CD28 Monoclonal Antibody TGN1412, Vol. 255(10) New England Journal of Medicine 1018 (2006) (filed as R's Ex. DD). The observations reported in the article are consistent with Dr. McCusker's testimony. Five of the six patients first developed severe headaches. Id. at 1019. All six developed lumbar myalgia within a median of 77 minutes after receiving the injection. Id. Then the patients developed hypotension followed by vascular collapse. Id. Within days, the patients experienced multi-organ failure. Id. at 1018. The volunteers experienced fevers, as evidenced through body temperatures of 39.5 to 40.0 degrees Celsius within a median of 280 minutes. As Dr. McCusker observed in her testimony, "Interestingly, none of the[] [patients] had encephalitis or encephalopathy. They all had systemic effects not related to an encephalopathy leading to death[,and] [n]one of them died, fortunately." Id. at 254.

Dr. McCusker testified that in her work in the emergency room, she had seen approximately ten or fifteen children who were encephalopathic. Tr. at 261. Based on her clinical experience, she agreed with Dr. Shane's assessment of the symptoms that a two-month-old child who had suffered an acute encephalopathy would present clinically. Dr. McCusker stated that "[i]t's a child who's very, very sleepy, difficult to rouse – usually impossible to rouse. We would use what's called the Glasgow Coma Scale,[30] so you look at whether or not they respond to voice, whether or not they respond to minor stimulus or major stimulus, [whether] they respond to pain." Tr. at 262. "If they don't respond to pain but they're still alive, that's severe somnolence." Id.

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beyond the scope of Dr. Gilbert-Barness's accepted area of expertise in this case. The undersigned deems petitioners' counsel's motion to **BE MOOT** because she does not rely on this portion of Dr. Gilbert-Barness's opinion. The undersigned notes that Dr. McCusker, who is an immunologist, opined on this matter independently and agreed with Dr. Gilbert-Barness's expressed opinion on this point.

[30] The Glasgow Coma Scale is a "standardized system for assessing response to stimuli in a neurologically impaired patient; reactions are given a numerical value in three categories (eye opening, verbal responsiveness, and motor responsiveness), and the three scores are then added together. The lowest scores are the worst clinical scores." Dorland's Illustrated Medical Dictionary 1660.

Dr. McCusker acknowledged that "it is difficult to assess the degree of somnolence that [Child Doe/11] had. It wasn't assessed clinically in any way." Id. Dr. McCusker stated "[t]he father said that she was sleeping, and it was unlike her – so that's certainly a change in her normal behavior pattern."[31] Id. But, Dr. McCusker observed that "most pediatricians would say [somnolence] occurs when you take a child out to the doctor's and you agitate them with a vaccine and you bring them home, and they tend to be a little bit tired after that." Id. Dr. Gilbert-Barness concurred with Dr. McCusker and opined that Child Doe/11's sleepiness, unresponsiveness, and lack of appetite were consistent with a reaction that could be anticipated after receipt of a vaccination. Id. at 139.

In addition to the opinions of Dr. Shane and Dr. Gilbert-Barness, the undersigned considered the opinion of Dr. Anthony, the pathologist who performed the autopsy on Child Doe/11 Doe/11, that he expressed in Child Doe/11's autopsy report. In the autopsy report, Dr. Anthony concluded that Child Doe/11's death was consistent with SIDS in the absence of any significant findings of neurologic pathology. Ps' Ex. 6 at 5-6; Tr. at 137-42. Because a SIDS diagnosis indicates the absence of any clinical or pathological evidence of an alternative cause of death, Dr. Anthony's diagnosis of SIDS is relevant and probative evidence in considering whether Child Doe/11 suffered an encephalopathy prior to her death. Both the opinions of Dr. Anthony and Dr. Gilbert-Barness regarding the pathological significance of Child Doe/11's autopsy findings find ample support in the filed medical literature.[32]

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[31] As addressed earlier in the decision, see p. 5, although Mrs. Doe/11's testimony differed from that of Mr. Doe/11 regarding whether Child Doe/11 was awake or not during the family's shopping trip prior to Child Doe/11's death, Mrs. Doe/11 told the emergency responders that Child Doe/11 was "fine" until thirty minutes before they arrived. Ps' Ex. 4 at 1; Ps' Ex. 5 at 1. Her account is reflected in the Patient Care Report completed by emergency responders who arrived at the Doe/11's home on December 21, 1994 to attend to Child Doe/11. The Patient Care Report prepared by the emergency responders indicates in the narrative section that "[p]er mother [Child Doe/11] was last checked on 30 minutes ago and was fine. Child has no medical [history], mother stated that child did have a hepatitis B vaccine today." Ps' Ex. 4 at 1. And Mrs. Doe/11's account to the emergency responders regarding Child Doe/11's well-being is not inconsistent with Mr. Doe/11's testimony about Child Doe/11's condition prior to his finding her turning blue while lying on the family's living furniture.

[32] Dr. Anthony found no evidence of brain edema or herniation at autopsy. Ps' Ex. 6 at 5. Dr. Gilbert-Barness found Child Doe/11's brain only mildly edematous. She concluded, however, that the degree of edema is no more severe than that which is usually associated with SIDS deaths. This anatomical finding, therefore, is not diagnostically significant. See R's Ex. A at 2.

An additional consideration by the undersigned in evaluating the testimony of the pathologists, in particular, in this case, is the respective experience and areas of expertise of the expert witnesses. Dr. Shane does not specialize in pediatric pathology, and he has no expertise in SIDS. Tr. at 56, 57. In contrast, Dr. Gilbert-Barness, is board certified in pediatrics, clinical and anatomical pathology and pediatric pathology, has practiced pediatric pathology for over 40 years, Tr. at 113-114, is a recognized expert in SIDS, and has performed over 10,000 pediatric autopsies. Tr. at 113-116. Based on the presented evidence, Dr. Shane's own acknowledged lack of expertise in pediatric pathology and with SIDS cases, the undersigned finds the opinions of Dr. Gilbert-Barness, a pediatric neuropathologist, and Dr. Anthony, the pathologist who performed Child Doe/11's autopsy, more persuasive regarding the significance of the pathological findings at Child Doe/11's death and the unlikelihood that Child Doe/11 suffered an acute and fatal encephalopathy. Therefore, the undersigned accords greater weight to the opinions expressed by Dr. Gilbert-Barness and Dr. Anthony than to the expressed opinion of Dr. Shane.

Additionally, the 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 organs were significantly edematous at her death. The necessary pathological findings to support Dr. Levin's theory, however, are lacking in this case.

The factual evidence in this case does not support petitioner's theory of causation implicating Child Doe/11'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 Child Doe/11's death was SIDS, and was very likely a death by inadvertent asphyxiation.

2. A Logical Sequence of Cause and Effect Showing that the Vaccination was the Reason for the Injury

Althen also requires petitioners to show a logical sequence of cause and effect between the vaccination and the injury. Althen, 418 F.3d at 1278. Here, however, petitioners have failed to show a sequence of cause and effect between Child Doe/11's hepatitis B vaccination and her subsequent death. The record evidence does not support petitioners' claim that Child Doe/11 exhibited symptoms of encephalopathy. The testimony by each of Child Doe/11's parents is inconsistent with the other's recollection

of whether Child Doe/11 was awake or sleeping. Nonetheless, neither of the parents' narratives describe a clinical presentation in Child Doe/11 that Dr. McCusker, a pediatrician who personally has examined approximately ten to fifteen encephalopathic children, would expect in a child who had suffered an encephalopathy.

The medical opinion offered by petitioners' expert, Dr. Shane, that Child Doe/11's behavior and described condition after her immunization were symptomatic of an encephalopathy is not supported by the facts of this case. Nor does the medical literature report a causal association between hepatitis B vaccine and encephalopathy, and subsequent death. Tr. at 133, 278-79.

Petitioners point to an article, filed by respondent as Respondent's Exhibit AA, in an effort to show that deaths have been reported following a hepatitis B immunization. See David A. Geier and Mark R. Geier, A Case-Control Study of Serious Autoimmune Adverse Events Following Hepatitis B Immunization, 38(4) Autoimmunity 295-301 (June 2005). That particular article describes various adverse events following hepatitis B vaccinations that have been reported in the Vaccine Adverse Event Reporting System ("VAERS"). VAERS is

> a national vaccine safety surveillance program co-sponsored by the Centers for Disease Control and Prevention (CDC) and the Food and Drug Administration (FDA). VAERS collects and analyzes information from reports of adverse events following immunization. . . . By monitoring such events, VAERS helps to identify any important new safety concerns and thereby assists in ensuring that the benefits of vaccines continue to be far greater than the risks.

Frequently Asked Questions About VAERS, at http://vaers.hhs.gov/vaers.htm (last visited November 15, 2006). Any person can file a report with VAERS. Id. The article indicates that VAERS contains reports of 36 deaths in relation to the hepatitis vaccine. The article does not, however, indicate that the reported deaths were related in any way to a vaccine-caused encephalopathy. And without 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 overlaying or wedging of Child Doe/11 in the futon where she napped with her father. The facts of this case simply do not correspond to petitioners' proposed sequence of events.

3. Proximate Temporal Relationship Between the Vaccination and Child Doe/11's Death

Althen also requires petitioners to establish an appropriate temporal association between the vaccination and the injury. Althen, 418 F.3d at 1278. When the undersigned asked Dr. Levin to provide a time frame for his hypothesis, Dr. Levin responded that "[Child Doe/11] was well until she got an injection with something that can and does – is supposed to cause cytokine release, and then she developed the typical symptoms of a cytokine-induced disease process and eventually died from it." Tr. at 204-05. The undersigned later posed the question again to Dr. Levin, "if you vaccinated a child who screamed upon receipt of the vaccination, [and] the child then became somnolent and for a period of three or four hours became somnolent – [and this is] the report that you receive from [the] parents – would that information alone cause you to think that there was something unusual about the child's response?" Id. at 316. Dr. Levin responded that "Me, yes, and that's because I'm very old-fashioned, and I'm very nervous about vaccinations." Id.

Challenging Dr. Levin's testimony, Dr. McCusker testified that the timing of Child Doe/11's death from a cytokine-storm mediated edema was "too soon." R's Ex. C at 75. Reports of cerebral edema following infection of nervous tissue generally are accompanied by fever and significant symptom development usually requires several days to occur. Id. Although Child Doe/11 received a hepatitis B vaccine on the day of her death, Dr. McCusker opined that a cytokine-induced cerebral edema would have required days to manifest. Id.; Tr. at 258-59. Dr. McCusker observed that whenever an event is temporally associated with the administration of a vaccine "whether or not [the event is] related to the vaccine or [something] else . . . going on with the child is a difficult question. The parents always remember the vaccine." Tr. at 289.

"Temporal rationalization" is not accepted as reliable evidence of causation in Program cases. Fricano v. Sec'y of Dept. of Health and Human Servcs, 22 C1. Ct. 796, *800 (1991). In short, the temporal association alone between the hepatitis B vaccination and Child Doe/11's death does not establish that the vaccine caused her death. Althen v. Sec'y of Dept. of Health and Human Servcs., 418 at 1278 (Fed. Cir. 2005) (citing Grant, 956 F.2d at 1149); Abbott v. Sec'y of Dept. of Health and Human Servcs., 27 Fed. Cl. 792 (1993) ("Clearly a vaccination is not the cause of every adverse event that occurs following it."). In this case, Child Doe/11's reported condition prior to her death was not inconsistent with the sleepiness that ordinarily occurs after a child receives a vaccination. 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.

III. Conclusion

For the foregoing reasons, the undersigned finds that petitioners have not established, by a preponderance of the evidence, that Child Doe/11's death was causally connected to her second hepatitis B vaccination. Petitioners have failed to establish entitlement to compensation. The Clerk of the Court shall **ENTER JUDGMENT** accordingly.[33]

IT IS SO ORDERED.

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Patricia E. Campbell-Smith
Special Master

[33] Pursuant to Vaccine Rule 11(a), entry of judgment is expedited by the parties' joint filing of notice renouncing the right to seek review.