IN THE UNITED STATES COURT OF FEDERAL CLAIMS
OFFICE OF SPECIAL MASTERS
No. 98-817V
Filed: August 29, 2007
To be Published

ENRIQUE M. ANDREU, a Minor Child by his Parents and Natural Guardians, ENRIQUE C. ANDREU and SONIA C. ANDREU,	*	
Petitioners,	*	Entitlement; DTP; Afebrile Seizures; Encephalopathy
v.	*	
SECRETARY OF THE DEPARTMENT OF HEALTH AND HUMAN SERVICES,	*	
Respondent.	*	

Clifford Shoemaker, Esq., Shoemaker & Associates, Vienna, VA, for Petitioners
Nathaniel J. McGovern, Esq., U. S. Department of Justice, Washington, DC, for Respondent

VOWELL, Special Master

DECISION[1]

On October 26, 1998, petitioners[2] Enrique C. Andreu ["Mr. Andreu"] and Sonia Andreu ["Mrs. Andreu"] timely filed a petition under the National Childhood Vaccine

[1] Because I have designated this decision to be published, petitioners have 14 days to request redaction of any material "that includes medical files, the disclosure of which would constitute a clearly unwarranted invasion of privacy." Vaccine Rule 18(b). Otherwise, the entire decision will be publicly available. 42 U.S.C. § 300aa–12(d)(4)(B).

[2] I will use the term "petitioners" to refer to Mr. and Mrs. Andreu collectively in this opinion.

Injury Act, 42 U.S.C. § 300aa–10, *et seq.*,[3] ["Program" or "Vaccine Act"] on behalf of their minor son, Enrique M. Andreu ["Enrique"].[4] The petition ["Pet."] alleged that Enrique suffered an encephalopathy and seizure disorder as a result of a diphtheria, tetanus, and whole-cell pertussis ["DPT"] vaccination he received on October 31, 1995. Pet. at pp. 2-3.

I. PROCEDURAL HISTORY

This case was initially assigned to Special Master Elizabeth Wright. Order, dated October 26, 1998. It was subsequently reassigned to Special Master Richard Abell. Order, dated April 12, 1999. Based on significant conflicts between the contemporaneous medical records and affidavits of petitioners and other family members regarding onset of Enrique's seizures, Special Master Abell conducted a hearing on August 27, 1999, to ascertain the facts surrounding onset of Enrique's seizures. He issued a bench ruling at the conclusion of the hearing, and supplemented it with an onset decision on October 20, 1999. The factual findings from that hearing are incorporated into this decision, and will be set forth in some detail, *infra*.

Thereafter, at the request of petitioners, the case was stayed from November 18, 1999 until August 9, 2000. Orders dated November 18, 1999; June 2, 2000; and July 21, 2000. Petitioners had difficulty locating an expert to opine on causation (*see* Order to Show Cause, dated January 30, 2001) and numerous delays ensued between August 2000 and April 2001, when Special Master Abell issued an order staying the case until August 13, 2001.[5] Order, dated April 18, 2001. A second order to show cause was issued on November 9, 2001. In response, petitioners filed a statement by Dr. Marcel Deray, one of Enrique's treating physicians. The statement stopped short of opining that the DPT vaccination caused Enrique's condition, but noted the absence of any other cause for Enrique's seizures. Petitioners simultaneously requested additional time to file an expert report, again citing potential legislative changes to the Vaccine Act that might have an impact on this case. Response to Order to Show Cause and Request for Extension of Time, dated December 10, 2001, and Exhibit A thereto (refiled as Petitioners' Exhibit ["Pet. Ex."] 22). No expert report ensued and on June 19, 2002, Special Master Abell granted one final extension of time, until July 20, 2002, to file the expert medical opinion. Order, dated June 19, 2002. On August 9, 2002, petitioners made an untimely request that the case be stayed, pending completion of the Autism Omnibus Proceeding. That request was granted and the case was once again stayed.

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[3] Hereinafter, for ease of citation, all "§" references to the Vaccine Injury Compensation Act will be to the pertinent subparagraph of 42 U.S.C. § 300aa (2000 ed.).

[4] To avoid confusion, I will refer to the child as "Enrique" and to his father as "Mr. Andreu."

[5] Both of these stays were issued at the request of petitioners in anticipation of legislative changes to the Vaccine Act. The anticipated changes did not occur.

Order, dated October 2, 2002.[6]

On November 14, 2005, petitioners requested that the case be removed from the Autism Omnibus Proceeding and reassigned to Special Master Abell. That request was granted (Order, dated November 15, 2005) and on November 28, 2005, petitioners filed the report of Dr. Carlo Tornatore. In a series of status conferences in February and March 2006, Special Master Abell began moving the parties toward an entitlement hearing date.

On April 5, 2006, the case was reassigned to me. I ordered petitioners to contact Dr. Tornatore and secure a statement from him that his expert opinion was based on the facts found by Special Master Abell, as set forth in his bench ruling and subsequent onset decision. Order, dated May 12, 2006. I issued this order because Dr. Tornatore's report appeared to rely upon the affidavits of Mr. and Mrs. Andreu and others for facts surrounding the onset of Enrique's seizures. Special Master Abell's bench ruling and onset decision made it clear that he rejected many assertions from Mr. and Mrs. Andreu's affidavits, as well as substantial portions of their hearing testimony.[7] Doctor Tornatore's statement was filed on June 9, 2006, after several delays. Pet. Ex. 26. Respondent's expert report by Dr. Joel Herskowitz (Respondent's Exhibit ["Res. Ex."] C) was filed on April 18, 2006. I then set the case for a hearing.

The causation hearing was conducted on November 3, 2006.[8] Testifying for petitioners was Dr. Tornatore; respondent's sole witness was Dr. Herskowitz.[9] Petitioners listened to the proceedings by telephone.

II. STATUTORY BASIS FOR THE PETITION

Under the Vaccine Act, there are two separate methods for establishing entitlement to compensation: by proving the existence of a "Table" injury, in which

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[6] This order also reassigned the case to Special Master George Hastings.

[7] The bench ruling indicated primary reliance on the testimony of Mr. Jesus Gutierrez, Enrique's great-grandfather, and secondary reliance on the testimony of Eric Andreu ["Eric"], Enrique's half-brother. To quote Special Master Abell's Onset Decision: "Petitioners' preponderance burden would not have been met were it not for the firm integrity and veracity reflected in Señor Guiterrez's [sic] testimony." Onset Decision, issued October 20, 1999. Special Master Abell's omission of the parents' testimony when discussing the basis for his decision regarding onset made it obvious that he rejected many assertions from Mr. and Mrs. Andreu that were not substantiated by contemporaneous records or the testimony of others. The likely reason for his rejection of their testimony is discussed later in this opinion.

[8] The hearing was postponed from the original date of August 18, 2006, at petitioners' request, because Dr. Tornatore developed a scheduling conflict.

[9] I accepted both witnesses as experts in the field of neurology. A more complete discussion of their credentials and testimony appears, *infra*.

causation is presumed, or by proving a causal link between the vaccine and the injury claimed. A "Table" injury is a condition listed on the Vaccine Injury Table, 42 C.F.R. § 100.3, corresponding to the vaccine received within the time frame specified. Actual causation claims are often referred to as "off-Table" injuries, and require that petitioners establish by preponderant evidence that a covered vaccine caused or significantly aggravated an illness, disability, injury or condition. § 300aa–11(c)(1)(c)(ii)(II). Under both mechanisms, petitioners must establish other statutory criteria, including that: the vaccine administered is one covered by the Vaccine Act; it was administered in the United States (or meets a narrow list of exceptions); and the claimed condition has persisted for at least six months. In this case, the only statutory requirement in dispute is that of causation.

Petitioners initially contended that Enrique's medical condition on November 1, 1995, constituted an encephalopathy within the meaning of the Vaccine Table, 42 C.F.R. .§ 100.3. They also asserted a causation in fact claim. Pet. at ¶ 11. During the course of the entitlement hearing, after considerable testimony by Dr. Tornatore about encephalopathy, petitioners' counsel conceded that petitioners were proceeding only on an actual causation, or "off-Table" injury, claim. *See* Transcript ["Tr."][10] at 58. Thus, petitioners must prove that the DPT vaccination administered to Enrique on October 31, 1995, actually caused the seizure activity Enrique first displayed on November 1, 1995, and the sequelae of those seizures.[11]

III. FACTS REGARDING ONSET

While it would be possible to set forth the facts as found by Special Master Abell in his bench ruling and in his onset decision separately from those additional facts detailed below, the sequence of events would be more difficult to understand. When the following facts are drawn from Special Master Abell's rulings, I have so indicated. When they are based on testimony at the onset hearing or information from the medical records, I have likewise indicated the source for the facts. I have independently concluded that all the facts set forth below are established by preponderant evidence, while fully adopting Special Master Abell's bench ruling and onset decision.

A. Enrique's Birth through DPT Vaccination

Enrique was born on September 5, 1995, at South Miami Hospital. The labor and delivery appear to have been entirely normal, with the exception of meconium staining of the amniotic fluid. Enrique weighed 6 pounds, 11.8 ounces, with Apgar

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[10] There are two transcripts in this case. The abbreviation "Tr." will refer to the transcript from the causation hearing. The abbreviation "On. Tr." will be used for the onset hearing transcript.

[11] The petition asserts that Enrique's first seizure occurred on November 3, 1995. Special Master Abell adopted the testimony of Enrique's great-grandfather, Mr. Gutierrez, in finding that onset of the seizure disorder occurred on November 1, 1995.

scores of nine and nine.[12] The delivering physician noted his condition as satisfactory, with vigorous movements, a lusty cry, and unlabored respiration. Pet. Ex. 2, p. 5. Enrique was discharged to home on September 9, 1995. *Id*., p. 3.

Enrique's pediatrician was Dr. Jose Azaret. On. Tr. at 15. Doctor Azaret's records, filed as Pet. Ex. 9, indicate that Enrique had his first well-baby checkup on September 12, 1995, when he was one week old. He had no problems and received his first hepatitis B vaccination on that date. Pet. Ex. 9, p. 4.

Enrique's next pediatric visit was on September 21, 1995, for an unidentified rash. He was seen again on September 29, 1995, for diaper rash. *Id.* He had an upper respiratory infection at his next visit on October 10, 1995, and an ear infection on October 16, 1995. *Id*., p. 3. He was prescribed an antibiotic and received his second hepatitis B vaccination at the October 16, 1995, visit. Checklists for both of these October visits indicate that Enrique was developing normally with no problems, other than the rashes and ear, nose, and throat problems noted. *Id.*

On October 31, 1995, Dr. Azaret[13] recorded continued problems with diaper rash and noted that Enrique had bilateral otitis media, but was otherwise normal.[14] Enrique received a prescription for another antibiotic and received his first vaccination against DPT that day. *Id*., p. 2. There is no indication in the records that Enrique had a fever on October 31, 1995, prior to this DPT vaccination.

B. Vaccination through Initial Diagnosis on November 11, 1995

At the time of Enrique's birth, Mr. Gutierrez resided with Mr. and Mrs. Andreu and assisted them in caring for Enrique. On. Tr. at 125-26. Prior to November 1, 1995, he had not noticed any problems with Enrique. On. Tr. at 126. On the evening of

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[12] The Apgar score is a numerical assessment of a newborn's condition, usually taken at one minute and five minutes after birth. The score is derived from the infant's heart rate, respiration, muscle tone, reflex irritability, and color, with zero to two points awarded in each of the five categories. *See* DORLAND'S ILLUSTRATED MEDICAL DICTIONARY ["DORLAND'S"] at 1670 (30th ed. 2003). Enrique received the maximum score in every category except color. His high Apgar scores and benign neonatal course indicate that he likely did not experience any ill effects from the meconium in his amniotic fluid.

[13] Mrs. Andreu testified that Dr. Azaret was Enrique's only doctor until November 11, 1995. On. Tr. at 15. The signatures on the medical records from September 12 through October 31,1995, are illegible. Pet. Ex. 9, pp. 2-4.

[14] Doctor Azaret's handwriting is difficult to read. The chart entry appears to say "Both TM's [tympanic membranes] are abnormal after cleaning for impacted wax." Pet Ex. 9, p. 2. A clearer indication of otitis media (an ear infection) would be an entry specifying what was abnormal about the eardrums, but the fact that Dr. Azaret prescribed an antibiotic indicated that he found some evidence of an ear infection. At Enrique's visit on October 16, 1995, Dr. Azaret removed a large amount of wax from Enrique's left ear and recorded findings consistent with an ear infection–that the left tympanic membrane was dull and bulging. *Id.*, p. 3.

November 1, 1995, he was alone with Enrique, who was playing in his carriage. Mr. Gutierrez saw Enrique move his left arm, as if he were nervous. *Id.* at 126-27. He also noticed that there was something wrong with the child's face at the time that he observed these things. *Id.* at 143-44 (bench ruling of Special Master Abell).

Mr. Gutierrez observed Enrique make the same movement about three to four days later, but he was unable to say exactly how long the movement lasted. On. Tr. at 127-28. When he observed the movements, he also noted that Enrique's face was "not too well, not the way it was before." *Id.* at 131.

In clarifying his testimony, Mr. Gutierrez stated that the first time he saw the tremors or shaking in Enrique, he was feeding Enrique his bottle. After the shaking began, Enrique stopped drinking the bottle. He first mentioned to his granddaughter (Mrs. Andreu) on November 3, 1995, that Enrique was "fighting his sleep" and mentioned it again on several subsequent occasions. Mr. Gutierrez did not describe any other symptoms in Enrique. He did not mention fever or altered interaction with others, although he noted that there was something not right about Enrique's facial expression during the shaking episodes.

By the time he first told his granddaughter and her husband specifically what he had seen in the way of tremors, other family members had noticed them, and Mr. Gutierrez was confirming that he had seen them earlier. On. Tr. at 136-37. Mr. Gutierrez also related his November 1, 1995 observations of Enrique to a doctor after Enrique was hospitalized, but he could not recall the name of the doctor. *Id*. at 129. Other evidence indicates that it was Dr. Reuben Montalon.[15] Mr. Andreu was present during this conversation. *Id.* at 97-98.

In his onset decision, Special Master Abell also indicated his reliance on the testimony of Eric Andreu, Enrique's half-brother, in reaching his factual conclusions. On. Tr. at 142-43. Eric testified that he moved in with his father, stepmother, and half-brother about two weeks before Halloween in 1995. On. Tr. at 116-17. On one occasion while he was watching Enrique, he observed that the baby's left fist was clenched and his arm was jittering. He placed the date of this event as November 2, 1995, by remembering it was two days after Halloween and two days before a planned party on Saturday, November 4, 1995. *Id.* at 118. The shaking lasted for about 30 seconds. *Id*. at 119. He saw Enrique shake his left hand in a similar manner again on November 6, 1995. At that point, he also observed Enrique looking to his right. *Id.* at 119, 121. Eric reported these earlier observations to Mr. and Mrs. Andreu some five months after Enrique's hospitalization in November 1995. Apparently Eric's recollection

[15] Mr. Gutierrez talked with Dr. Montalon, of Miami Children's Hospital ["MCH"] Genetics-Metabolic Service, on November 13, 1995, alerting him to the fact that Enrique's seizure activity had actually begun on November 1, 1995. Res. Ex. A, p. 18. Nearly all of Enrique's medical histories reflect dates other than November 1, 1995, for onset of the seizures, most of them using the November 8th date provided during the history taken in the MCH emergency room.

of Enrique's earlier behavior was triggered by his observations of Enrique having seizures in April 1996. *Id*. at 123.

In the bench ruling, Special Master Abell found that petitioners themselves did not notice any shaking or tremors of Enrique's left arm or that Enrique was holding his arm at a 90 degree angle prior to November 8, 1995. On. Tr. at 139. He concluded that Enrique's tremors on November 8, 1995, manifested behavior that was identical to that described by Mr. Gutierrez in his testimony as having occurred on November 1, 1995, and again three to four days later. *Id*. at 141-42.

Special Master Abell also found that there was no evidence, other than on the day the DPT vaccination was administered, of any alteration in Enrique's "sleeping patterns, or eating patterns, or apparently other patterns, other than what the grandfather specifically described." *Id.* at 143. He further found that on the date the vaccine was administered, Enrique cried and had a local reaction at the injection site, with swelling, hardness, and sensitivity to touch. *Id.* Special Master Abell omitted from these factual findings the testimony of Mr. and Mrs. Andreu regarding Enrique's unusual cry after the DPT vaccination and their testimony concerning the persistence of his crying during the 24 hours after vaccination. For reasons noted below, I conclude that Special Master Abell's omission was deliberate.

I adopt all of Special Master Abell's factual findings as my own, recognizing that he had the opportunity to see and hear the witnesses. I find the following additional facts:

(1) There is no evidence that Enrique was febrile at any point between the administration of the DPT vaccination on October 31, 1995, and his hospitalization on November 11, 1995.[16] I base this finding on the lack of any entry regarding fever in the medical records at the time of the vaccination (Pet. Ex. 9, p. 2) and also on Mrs. Andreu's testimony that Enrique did not have a fever when he was vaccinated. On. Tr. at 17, 22. I also relied on the relatively contemporaneous medical histories. At the December 27, 1995 follow up visit after Enrique's hospitalization, Dr. Resnick noted that there was no fever or irritability after the DPT shot. Pet. Ex. 7, pp. 31-32. In a 1996 history, Enrique was reported to be normal between his immunization and the first seizure.[17] *Id*., p. 7-8. In a medical history provided to Dr. Jimenz on November 11,

[16] It appears from Pet. Ex. 9 that Dr. Azaret's office did not routinely record Enrique's temperature during well-baby or other visits. Mrs. Andreu testified that the nurse at Dr. Azaret's office took Enrique's temperature prior to the vaccination on October 31, 1995. On. Tr. at 22.

[17] In this record, the first seizure was recorded as occurring on November 3, 1995, which is consistent with the testimony of Mr. and Mrs. Andreu at the onset hearing, but earlier than the date of onset provided in the contemporaneous medical records when Enrique was first hospitalized. This is circumstantial evidence that the information about Enrique's normal behavior between vaccination and seizure was provided by Enrique's parents and not simply a review of the earlier medical records.

1995, Mrs. Andreu reported that Enrique did not have a fever.[18] Res. Ex. A, p. 11.

(2) Although Mr. Andreu testified that they gave the baby Motrin over the 24 hour period after the vaccination, Enrique did not display any symptoms consistent with a fever over that period. No one described him as hot or sweating that evening or having any other symptoms of fever during the following ten or eleven days.

(3) Enrique cried at the time of the vaccination and throughout the evening of October 31. On. Tr. at 23, 73; Pet. Ex. 17, p. 1 (affidavit of Mr. Gutierrez).

(4) Over the next ten days, other than the brief seizure activity described by Mr. Gutierrez and Eric Andreu, Enrique's behavior was essentially normal. He breast-fed as he did before the vaccination. He had no difficulty swallowing, sleeping, or voiding. Other than during the seizures, his facial expressions were normal. He made the same type of eye contact with Mrs. Andreu after the vaccination as he had done before the vaccination. On. Tr. 51-52.

(5) On the evening of November 10, 1995, Mr. Andreu first observed Enrique making a fist with his left hand and shaking his left arm for more than two or three jerks for approximately 45 seconds. On. Tr. at 33-34, 71. He discussed this with his wife, who advised him that she had seen something similar three days earlier. Petitioners contacted Dr. Azaret's office during the early morning of November 11, 1995, after they observed Enrique display the same movements at about 4:00 AM. Doctor Montiel, another physician in Dr. Azaret's practice, returned their call at about 6:00 AM, and instructed them to bring Enrique into the office that morning.

(6) At the office visit, Dr. Montiel observed the left arm tremors, told petitioners that these movements were seizures, and arranged for Enrique to be seen at MCH that day. Pet. Ex. 14, p. 1.

C. Credibility Issues Surrounding Petitioners' Testimony at the Onset Hearing

Special Master Abell's factual findings reflect a lack of reliance upon the testimony of Mr. and Mrs. Andreu. In his bench ruling, Special Master Abell stated that if he had only the testimony of the parents and Eric, he could not say what conclusions he would have reached. On. Tr. 140. In the Onset Decision, he stated that petitioners' "preponderance burden would not have been met, were it not for the firm integrity and veracity" of Mr. Gutierrez's testimony.

The obvious reason for his lack of reliance on Mr. and Mrs. Andreu's testimony

[18] Mrs. Andreu testified that her husband did all the talking to the doctors after Enrique's hospitalization on November 11, 1995. On. Tr. at 35-36. Mr. Andreu provided similar testimony. On. Tr. at 79. The records reflect that Mrs. Andreu was the historian.

is Petitioners' Exhibit 21, a growth and development baby book first presented at the onset hearing on August 27, 1999, and actually filed with the court on November 8, 1999. This exhibit was not disclosed to respondent or the Special Master prior to the hearing, contrary to the prehearing order to identify all exhibits prior to the onset hearing. Onset Prehearing Order, p. 2, dated July 2, 1999. Mrs. Andreu testified that she and her husband provided the baby book to their attorney the evening prior to the hearing, although they had told him about it earlier. On. Tr. at 61. Mr. Andreu indicated that they found the book during a recent move. *Id.* at 91.

Although Mr. and Mrs. Andreu testified at the onset hearing that the entries in this exhibit were made contemporaneously with the events recorded, it was clear that Special Master Abell did not accept their testimony, largely based on the entries found on page 16 of the book.[19] The entries on page 16 purport to record that Enrique experienced "focal seizures" on November 3, a call to the doctor on this date, and "focal seizures" on November 11, 1995.[20] Special Master Abell questioned Mr. Andreu's use of the term "focal seizures" in an entry purportedly made on November 3, 1995, at a time before any medical professional had observed Enrique's twitching or jerking movements or diagnosed seizure activity.[21] On. Tr. at 92. He obviously considered it unlikely that, had the parents actually called Dr. Azaret's office on November 3, 1995, anyone would have diagnosed focal seizures or even mentioned the term "focal seizures" over the telephone. If Dr. Azaret or any other health care professional had concluded that Enrique's symptoms were indicative of focal seizures, it is equally unlikely that the health care provider would have advised the parents to wait, rather than bringing Enrique to the office or hospital immediately (as Dr. Montiel actually did on November 11, 1995). I find that the entry in Pet. Ex. 21 purportedly made on November 3, 1995 was actually made on some date after Enrique's seizures were first diagnosed, and therefore at some time on or after November 11, 1995.

Based on the testimony surrounding the baby book, I share Special Master Abell's apparent concern about the credibility of Enrique's parents' testimony. Thus, when I have found facts based on their testimony, I have done so only when their testimony was corroborated by contemporaneous records or the statements or

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[19] Mrs. Andreu testified that the entries on the sheet called "Record of Illness" were made by her husband on the dates indicated in the book. On. Tr. at 48, 61-62. Mr. Andreu's testimony is at On. Tr. at 90-92.

[20] A focal seizure (also called "partial seizure") is "any seizure due to a lesion in a specific, known area of the cerebral cortex; symptoms vary with different lesion locations." DORLAND'S at 1676. *See also,* Tr. at 122.

[21] On cross-examination by respondent's counsel, Mr. Andreu was asked when he first heard the words "focal seizure." He testified that he believed it was on the 3rd, and then indicated that he really couldn't remember exactly. On. Tr. at 102-03. As the cross-examination continued, Special Master Abell curtailed respondent's counsel's questions on this topic, saying that the court "comprehends your point and the explanation." *Id*. at 104.

testimony of others.

D. Hospitalization November 11-15, 1995

A triage message in the MCH records, dated November 11, 1995 at 1225, indicates that Enrique was having focal seizures. This note appears to be a telephone message from Dr. Montiel informing the hospital emergency room that Enrique and his parents were en route. Res. Ex. A, p. 2.[22] They arrived at the MCH emergency room at approximately 1315. *Id*., p. 3. Enrique's temperature was recorded as 99.4 degrees, which is about one half degree above normal.[23] *Id*. By 1700, his temperature was nearly normal at 98.7 degrees. *Id*., p. 4. His heart rate upon admission was 120, and his respirations were 30. *Id*, p. 3. At 1338, Enrique was observed to have jerking movements in his left arm with a staring episode that lasted about 45 seconds. This was assessed as a seizure. Enrique was moved to another room and the pediatric neurologist on call, Dr. Apolo, was notified. *Id*. The emergency services chart reflected that Enrique had been having "left jerky movements of his arm since Wednesday, three days ago." *Id*, p. 1. He was admitted with plans to perform a lumbar puncture[24] and a computed tomography ["CT"] scan. *Id*., p. 12. The pediatric history at Res. Ex. A, p. 11, indicated that, other than the jerky left arm movements, there were no other significant symptoms during the episodes: there was no color or activity change and Enrique maintained good eye contact and smiled. Enrique's physical exam was basically normal, with slight hypotonia in his lower extremities. His anterior fontanelle was open and soft. He was described as active, awake, and alert. *Id*., p. 12.

Enrique remained hospitalized at MCH through November 15, 1995. Neither fever nor excessive sleepiness were noted during the hospitalization. Respondent's Exhibit A includes the nursing notes, which record the child's condition at frequent

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[22] Ordinarily, medical records are filed as Petitioners' Exhibits. At the request of Special Master Abell, respondent obtained the medical records of Enrique's November 1995 hospitalization at MCH. The petition asserted that the medical records of the November 1995 hospitalization involved approximately 6,000 pages (Pet. ¶ 13); however, footnote 1 to respondent's Notice of Filing, dated February 8, 1999, indicates that the 90 pages simultaneously filed as Res. Ex. A constituted the entire record of this MCH hospitalization. *See also*, Res. Ex. B, p. 2 (stamp and notation indicating that Res. Ex. A was the entire record from MCH).

[23] None of the medical records of this hospitalization indicate the administration of Tylenol or any other fever-reducing drug. Res. Ex. A.

[24] A lumbar puncture involves placing a needle in the subarachnoid space of the spinal column to measure pressure and to obtain cerebrospinal fluid for laboratory examination. MOSBY'S MANUAL OF DIAGNOSTIC AND LABORATORY TESTS ["MOSBY'S LABS"] at 677-86. (3d ed. 2006). Enrique's cerebrospinal fluid was within normal limits, other than a finding of one red blood cell. Red blood cells may indicate cerebral hemorrhage or that the needle has inadvertently penetrated a blood vessel before entering the subarachnoid space. *Id*. at 680. A finding of increased white blood cells during the lumbar puncture could be indicative of an infectious process. *Id*., Table 5-2. The white blood cells found were within normal limits. Res. Ex. A, pp. 26-28.

intervals throughout the hospitalization, and with the exception of Enrique's seizure activity, those notes contain no evidence of encephalopathy, altered consciousness, or indifference to his environment. *Id*., pp. 4, 8, 49-81.

Although Enrique was observed to have focal seizures during the hospitalization period (Res. Ex. A., pp. 13, 15-16; 23-24), the lumbar puncture was essentially normal and the initial CT scans were negative. *Id*., pp. 14, 26. He remained afebrile during the seizure activity. A video electroencephalogram ["EEG"] conducted from November 12-14, 1995, demonstrated interictal spikes and slowing over the right centroparietal region. It recorded several focal seizures involving Enrique's left shoulder, elbow, and fist. The findings were consistent with localized partial seizures, with the seizure focus in the right side of his brain. *Id.* at 23-24.

On the evening of November 12, 1995, petitioners discussed with one of Enrique's treating physicians their belief that the DPT vaccination may have caused Enrique's seizures. The on-call physician's note indicated that petitioners had a Medline article stating that convulsions could be due to a DPT vaccination. The person who wrote the note was unable to reach Dr. Trevor Resnick, Enrique's treating physician.[25] Res. Ex. A, p. 14.

A brain SPECT scan,[26] performed during a seizure on November 14, 1995, was markedly abnormal. It demonstrated focal hyperperfusion[27] in the right precentral gyrus, a portion of the top front of Enrique's brain.[28] There was diminished perfusion in the left temporal lobe, which the radiologist interpreted as consistent with atrophy or underdevelopment. Res. Ex. A, p. 21. However, a brain magnetic resonance imaging ["MRI"] performed less than two hours later was normal. *Id.*, p. 22; Pet. Ex. 3, p. 2. There was no evidence of lesions and no sites where abnormal contrast enhancement appeared. The myelin pattern was immature, but unremarkable for Enrique's age. *Id*.

Some amino acid values were elevated, but they did not display any pattern consistent with a metabolic disorder. Pet. Ex. 3, p. 3.

In short, the staff at MCH were unable to find a cause for Enrique's seizures. In spite of Mr. Andreu's insistence that the DPT vaccination was causal, none of the

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[25] Nursing notes at Res. Ex. A, p. 60 also record Mr. Andreu's concern that the DPT shot may have caused Enrique's seizures.

[26] "SPECT" stands for single-photon emission computed tomography, a brain scan that uses a radioactive substance to visualize anatomic and biochemical changes within the brain. MOSBY'S LABS at 828-29.

[27] Hyperperfusion is increased blood flow. Hypoperfusion is decreased blood flow. Tr. at 84.

[28] Plate 11, DORLAND'S at 247, contains an illustration of the precentral gyrus.

physicians who examined and treated Enrique attributed his condition to the vaccine.

Enrique was placed on phenobarbital on November 12, 1995, and remained on this drug after his discharge. Pet. Ex. 7, p. 35; Res. Ex. A, p. 38.

E. Treatment Post-Discharge: November 1995 - November 1998

Enrique's first examination after his discharge from MCH was performed by Dr. Resnick on December 27, 1995. Doctor Resnick noted that Enrique had continued to demonstrate normal neurodevelopmental progress post-discharge. He commented that the imaging studies performed during the hospitalization could not correlate his seizures to any brain injury, although Enrique demonstrated some ipse lateral atrophy. He remarked: "The one consideration was the fact that the seizures did occur in temporal relationship to his DPT immunization, although no other symptomatology such as fever or irritability occurred." Enrique's physical examination was entirely normal. Doctor Resnick advised against any further pertussis immunizations, but stated that Enrique could receive all other immunizations. Pet. Ex. 7, pp. 31-32.

An EEG in February 1996 was read as normal (*id.*, p. 36), in spite of another seizure that month, apparently one associated with apnea. Although no records of the treatment for this seizure were filed, Dr. Resnick referenced the seizure during his examination of Enrique in May 1996 (Pet. Ex. 7, p. 27) and Dr. Israel Alfonso described it in July 1996. *Id*., p. 25. Doctor Alfonso first saw Enrique during this seizure and described it as lasting 45 minutes and requiring Ativan to stop the seizure. *Id*.

In May 1996, Dr. Resnick noted that Enrique had remained seizure-free since the February 1996 episode and that his neurological and neuro-developmental examinations were normal. He planned to see him again in four months. Pet. Ex. 7, p. 27.

An EEG in July 1996 was normal (Pet. Ex. 7, p. 37), as was his neurological examination by Dr. Alfonso on July 26, 1996. Doctor Alfonso commented that the etiology of Enrique's seizure disorder was not determined. Pet. Ex. 7, p. 25. A sleep study and EEG performed in August 1996 by Dr. Deray were both normal. *Id*., pp. 22-24 (additional copies appear at pp. 12-14, and 20-21).

Enrique remained seizure free from February 1996 until October 1996, when he was hospitalized for febrile seizures. According to the neurology consultation during this hospitalization, Enrique had five brief febrile seizures over a 12-hour period between October 15 and 16, 1996. Most of these seizures were associated with a temperature between 100.5 and 102 degrees. They lasted less than 45 seconds, with a brief post-ictal period. The history recorded Enrique's first seizures as afebrile and without encephalopathy, occurring a week after his DPT shot. Despite phenobarbital, he continued to have breakthrough focal seizures that later became generalized. Pet.

Ex. 4, p. 15. During the course of this hospitalization, mild cellulitis was noted. Pet. Ex. 4, p. 3. He had no seizures while hospitalized and both an MRI and an EEG were normal. *Id.*, pp. 3, 21-22. He was discharged on October 20, 1996. *Id*., p. 3.

On October 22, 1996, Enrique's pediatric neurologist, Dr. Resnick, assessed him as normal in development and age-appropriate in all spheres. He noted that Enrique's focal seizures had progressed to generalized seizure activity, but considered his seizures to be well-controlled on phenobarbital. Pet. Ex. 7, p. 10. Three days later, Enrique was seen at Baptist Hospital of Miami with a viral syndrome and seizures. Pet. Ex. 5, pp. 1, 5.

Over the next month, Enrique continued to have seizures that began with jerking of his arm and then became generalized. He was treated with phenobarbital, Tegretol, and Klonopin; his parents were given a prescription for Ativan suppositories to be used if the seizures progressed to status epilepticus. *See generally*, Pet. Ex. 7, pp. 7-8. An EEG done in November 1996 showed generalized epileptiform discharges, indicating diffuse bilateral cerebral dysfunction and a lowered seizure threshold. *Id.*, pp. 39, 42.

On May 22, 1998, Dr. Glen Morrison, a neurologist at MCH, assessed Enrique as somewhat developmentally delayed. While he walked at the age of one year, he was unbalanced. Doctor Morrison recorded a history of a cardiac arrest in the MCH Pediatric Intensive Care Unit, but did not state when this occurred. He noted that Enrique was frequently seen in the emergency room at MCH. He diagnosed Enrique with infractible epilepsy and recommended another MRI. Pet. Ex. 15, pp. 10. An MRI performed on June 5, 1998 was compared to the one performed during Enrique's first hospitalization in November 1995. Neither showed any evidence of brain abnormalities. *Id*., p. 3.

An interdisciplinary team assessment of Enrique in July 1998 noted an IQ of 63 and significant delays in development, receptive language, expressive language, and fine motor skills. Pet. Ex. 15, pp. 24-27.

The most recent medical records date from November 1998, and concern a slight improvement of Enrique's seizures on a ketogenic diet. As both experts who testified at the causation hearing were in agreement that whatever caused Enrique's initial seizures in November 1995 was responsible for the subsequent seizure activity, further medical records are unnecessary to the causation determination. Tr. at 148-49, 225.

IV. Expert Testimony and Scientific Evidence of Causation.

A. Dr. Carlo Tornatore, MD.

1. Qualifications

Doctor Tornatore testified in person at the causation hearing. His report was filed as Pet. Ex. 23, his curriculum vitae as Pet. Ex. 24, and a supplemental statement regarding his report was filed as Pet. Ex. 26. His references (six articles discussing aspects of neurotoxicity) were filed as Pet. Ex. 25, Tabs A-F. Additional medical journal articles were filed after submission of post-hearing briefs, but Dr. Tornatore did not file a supplemental report commenting on them. Those articles are discussed separately in Part IV C, below.

After medical school at Georgetown University, Dr. Tornatore completed a neurology residency there. Tr. at 6-7. He worked for the National Institutes of Health ["NIH"] for six years, where he did research involving children with HIV, how viruses affect the nervous system, and the toxic affects of bacterial and viral products on cells. *Id*. at 7. He returned to Georgetown after NIH, where he currently heads the multiple sclerosis and autoimmune disorders clinic at Georgetown Hospital. He deals with children and adolescents through the spasticity clinic, which accounts for about 1% of his total population. As the director of education in the neurology department, he trains medical students and neurology residents and fellows. *Id.* at 8-9. He is board certified in neurology. *Id.* at 9. I accepted him as an expert in neurology and the pathogenesis of brain injury. Tr. at 10-11.

2. Issues Concerning Dr. Tornatore's Testimony

Much of Dr. Tornatore's testimony in this case involved his opinion that Enrique suffered an acute encephalopathy after the administration of the DPT vaccination.[29] Tr. at 13. In spite of the clear language of Special Master Abell's factual findings on onset concerning Enrique's behavior in the 24 hours following his vaccination (which I read to Dr. Tornatore during the hearing (Tr. at 16-17)), Dr. Tornatore insisted in relying upon contrary statements from the parents' affidavits, perhaps because he was unaware of the issues regarding their credibility that arose at the onset hearing.[30] He also engaged in verbal sparring with respondent's counsel and the court during efforts to ascertain the factual and medical underpinnings of his opinions. *See, e.g.*, Tr. 20-21; 38-41; 43-44.

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[29] This testimony occurred before petitioners' counsel indicated that petitioners were no longer proceeding on a Vaccine Injury Table claim.

[30] On October 30, 1996, as part of the prehearing order, I "encouraged counsel for both parties to go over testimonial facts with their expert witnesses, noting that the bench ruling and onset decision relied primarily upon the testimony of Enrique's grandfather and half-brother." I further "noted that expert testimony appearing to rely on other facts might be problematic."

Doctor Tornatore testified that Enrique's crying on the evening of Halloween constituted an acute encephalopathy. Tr. at 46. When respondent's counsel referred him to the Vaccine Table definition of "acute encephalopathy" found in the Qualifications and Aids to Interpretation ["QAI"] portion of the Table,[31] the following exchange ensued:

> Q And are you aware that the petition in this case alleges that Enrique did suffer a table encephalopathy?
>
> A Well, what the table calls encephalopathy is fine.
>
> Q I just want an answer to the question. Are you aware that the petition in this case alleges that Enrique suffered a table encephalopathy?

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[31] The QAI provides in pertinent part:

> (2) Encephalopathy. For purposes of the Vaccine Injury Table, a vaccine recipient shall be considered to have suffered an encephalopathy only if such recipient manifests, within the applicable period, an injury meeting the description below of an acute encephalopathy.
>
> (I) An acute encephalopathy is one that is sufficiently severe so as to require hospitalization (whether or not hospitalization occurred).
>
> (A) For children less than 18 months of age who present without an associated seizure event, an acute encephalopathy is indicated by a "significantly decreased level of consciousness" (see "D" below) lasting for at least 24 hours. Those children less than 18 months of age who present following a seizure shall be viewed as having an acute encephalopathy if their significantly decreased level of consciousness persists beyond 24 hours and cannot be attributed to a postictal state (seizure) or medication.
>
> (D) 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 (*see* paragraphs (2)(I)(A) and (2)(I)(B) of this section for applicable timeframes):
>
> *(1)* Decreased or absent response to environment (responds, if at all, only to 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).
>
> (E) The following clinical features alone, or in combination, do not demonstrate an acute encephalopathy or a significant change in either mental status or level of consciousness as described above: Sleepiness, irritability (fussiness), high-pitched and unusual screaming, persistent inconsolable crying, and bulging fontanelle. Seizures in themselves are not sufficient to constitute a diagnosis of encephalopathy. 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.

The Vaccine Injury Table must be interpreted by reference to the QAI's definition of key terms. *Althen v. Sec'y, HHS*, 58 Fed. Cl. 270, 280 (2005), *aff'd*, 418 F.3d 1274 (Fed. Cir. 2005).

A Yes. Encephalopathy by its definition is any change in someone's behavior. Encephalopathic behavior is a change in behavior which can have–

Q Let's stay away from that, and you can get to that definition later. Let's first talk about the table definition. Are you familiar with the table's definition of an encephalopathy?

A Yes. Yes, I am.

Q Okay. And is it your opinion that Enrique meets the criteria for an encephalopathy as that term is defined in the Vaccine Injury Table?

A I do.

Q Okay. Let's explore that a little bit. Are you aware that to have an encephalopathy under the table, it must be first an acute encephalopathy, and to have an acute encephalopathy would require Enrique to exhibit within 72 hours of vaccination a significantly decreased level of consciousness persisting for at least 24 hours and not attributable to a postictal state? Are you aware that that is the definition?

A Yes.

Q And then let me ask you further are you aware that the table defines significantly decreased level of consciousness to require one of these three following manifestations? The first is a decreased or absent response to the environment. Responds, if at all, only to loud voice or painful stimuli. Did Enrique exhibit that?

A I'm sorry?

Q Did Enrique meet that sign? Did he exhibit a decreased or absent response to the environment?

A We don't have any evidence. We don't know that for a fact. We know he cried a lot.

Q Right.

A But we don't know that he was not responsive to the environment.

Q Right. Crying is not synonymous with decreased or absent response to the environment, is that correct?

A It's a sign of someone who is in distress, but I would say right, not unresponsive to their environment, but in a way, he responded to some internal problem. See, if you have someone who is encephalopathic or he is irritable, either they're going to respond to the external stimuli by being lethargic. We can get the opposite. You may have somebody who is overexcited who can't respond. Now here we had a baby who was apparently crying for an extended period of time. He's not even responding to the parents' comforting.

Q Is there any evidence in the record suggesting that Enrique was unresponsive to his environment lasting for 24 hours after vaccination?

A Well, was he unresponsive to his parents' trying to comfort him. Your answer there would be yes, he was not unresponsive. See, if you're going to take–

Q And did it last for 24 hours?

A May I finish? If we're going to take that a child has to be unconscious, then it's going to be that no parent would ignore a child, but if you look at what encephalopathy means, if somebody has a drink of alcohol and they're not responding to their environment properly, that's encephalopathy. You don't have to be unconscious, and I think this is very important. I know the table, and I think the important thing is that you have to look at what encephalopathy means. Encephalopathy means a disruption in the way the brain is working, an inability to interact with your environment. Did this baby have a difficult time interacting with their environment? The answer is yes, because the parents were not able to console the child. Something was happening to them that made them reach that point.

Tr. at 48-51.

Doctor Tornatore professed familiarity with the Table definitions[32] and then

[32] Perhaps Dr. Tornatore's testimony can be best understood in the historical context of the Vaccine Injury Table. An earlier version of the Vaccine Injury Table defined "encephalopathy" more broadly. The original version of § 300aa-14(b)(3)(A) provided in part: "Signs and symptoms such as high pitched and unusual screaming, persistent unconsolable crying, and bulging fontanel are compatible with an encephalopathy, but in and of themselves are not conclusive evidence of encephalopathy." The earlier definition of "encephalopathy" ("significant acquired abnormality of, or injury to, or impairment of function of the brain") was more consistent with Dr. Tornatore's use of the term (other than the "significant" qualifier). The Secretary of Health and Human Services amended the Vaccine Table and the QAIs in 1995 to include the current (and more restrictive) definition of an encephalopathy. This administrative amendment process and its constitutionality were discussed In *Terran v. Sec'y,, HHS*, 195 F.3d. 1302, 1307-08 (Fed. Cir. 1999). The court found the process to be constitutional. *Terran*, 195 F.3d at 1314-15.

offered opinions that ignored them. His efforts to contort the facts and the definitions to bring Enrique's symptoms within the Table were obvious. It was patently ridiculous for him to contend that protracted crying for less than 24 hours after vaccination constituted an encephalopathy in terms of the Vaccine Act, in light of its QAI definition of that term. Doctor Tornatore testimony was more evocative of the term "hired gun" than that of "expert witness."[33] His later testimony, taken after a short recess, was much less confrontational and more objective and cogent.[34] In short, he began testifying more as a medical expert and less as a partisan advocate. However, his contorted testimony on the later-abandoned claim of a Table injury adversely affected his credibility throughout the remainder of the case.

3. Testimony and Evidence Regarding Dr. Tornatore's Theory of Causation

a. *In general*.

Doctor Tornatore's testimony on the "off-Table" injury claim was, in essence: (1) seizures are caused by brain injury or brain cell death; (2) whole-cell pertussis vaccine contains neurotoxic components; (3) research indicates that these components can cause brain injury or brain cell death; (4) "wild-type" pertussis infections are known to cause central nervous system injuries; (5) Enrique's clinical picture and test results support a finding of brain cell injury or brain cell death consistent with a neurotoxic event; and (6) the seizures began in close temporal proximity to the vaccination. Therefore, it was more probable than not that the pertussis component of his DPT vaccine caused a brain injury or brain cell death, resulting in his initial seizures and subsequent seizure disorder.

Additionally, Dr. Tornatore stated that Enrique's treating physicians agreed that the vaccine caused his seizures. However, Dr. Tornatore "interpreted" these statements out of the context in which they were written. He asserted, without proper foundation, that these statements were reflective of vaccine causation. In fact, the treating physicians stopped well short of opining that the DPT vaccine was causal.

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[33] I note that I am not the only special master to find Dr. Tornatore more a partisan advocate than expert witness. *See, e.g., Hopkins v. Sec'y, HHS*, No. 00-745V and 00-746V, slip op. at 17 (Cl. Ct. Spec. Mstr. Aug. 10, 2007) ("Dr. Tornatore is...at times, a questionable expert. In supporting his opinion, he weaves together one questionable piece of evidence together with another to create a piece of medical tapestry that to the untrained eye–the undersigned–appears superficially enticing. But while the untrained eye detects flaws in the fabric, the trained eye...uncovers clear and critical defects." The Chief Special Master determined that Dr. Tornatore's testimony was "of dubious quality.")

[34] Immediately after the recess, I addressed Dr. Tornatore on the record, informing him that his responses to questions were less than helpful to the court and asked him to help the petitioners by helping me to understand the basis for his opinion, rather than treating questions with hostility. Tr. at 69-70. At the conclusion of my questions, I commented on the higher quality of his testimony post-recess. Tr. at 152.

b. *Postulated Mechanism of Brain Injury*.

Doctor Tornatore started from the unassailable position that the DPT vaccination Enrique received contained pertussis toxin and endotoxin.[35] Tr. at 29. He then testified that both pertussis toxin (sometimes referred to in the testimony as pertussigen) and endotoxin are poisonous chemicals that can transcend the blood-brain barrier very quickly and can adversely affect the brain and nervous system. Tr. at 29-30, 34. Although the blood-brain barrier acts to keep many toxins in the bloodstream from reaching the brain, transporter molecules permit the barrier to be breached. Tr. at 76-77.

These chemical components of the DPT vaccine, which he later described as proteins (Tr. at 73), have a toxic or irritating effect on nerves and supporting cells. In an extreme case, this irritation could cause a seizure, which could occur quickly after administration of the vaccine. Tr. at 30. He explained this theory by analogizing nerves to electrical wires; when the nerves become excited, they produce excess electricity, a manifestation of which is a seizure. Tr. at 73-74. He also analogized to anaphylactic reactions, testifying that after vaccination or injection of other drugs such as lidocaine or penicillin, anaphylactic reactions can occur very rapidly. These reactions may include seizures. Tr. at 75-76.

None of his six reference articles filed before the hearing directly addressed the issue of DPT-caused seizures. He explained the reference articles by asserting that they supported the biological basis for causation because they demonstrated that pertussis toxin can cause changes in the nervous system.[36] Tr. at 31-32, 97-100. One article, Pet. Ex. 25, Tab A,[37] involved a study to determine if a particular substance (12-HETE) could reduce glutamate toxicity by protecting cells from excitotoxic effects. Researchers subjected cell cultures from fetal rat brains to various chemicals and excitotoxicity was measured. Pertussis toxin was used to determine how 12-HETE exerted its effect. Doctor Tornatore interpreted this article as demonstrating that pertussis toxin can adversely affect the calcium balance in cells, causing injury and cell

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[35] *See* S. Plotkin and W. Orenstein, VACCINES ["VACCINES"] at pp. 295-97 and Table 14-1 (3d ed. 1999). Endotoxin's role in the disease process is not clear, but is suspected to contribute to immediate adverse reactions. *Id*. at 297.

[36] Doctor Tornatore acknowledged that the reference articles were highly technical. The hearing transcript inaccurately characterized my response to his statement that the articles were likely to induce sleep in the reader (Tr. at 31). My response was actually a statement that I found them "pretty hard slogging."

[37] A. Hampson and M. Grimaldi, "12-Hydroxyiecosatetrenoate (12-HETE) Attenuates AMPA Receptor-Mediated Neurotoxicity: Evidence for a G-Protein-Coupled HETE Receptor," The Journal of Neuroscience, Jan. 1, 2002 (pp. 2-9 of Pet. Ex. 25).

death in an excitotoxic effect.[38] The excessive activity that results from the pertussis-induced calcium imbalance would cause seizures or similar effects in brain tissue. Tr. at 32.

He testified that each of the other referenced articles (Pet. Ex. 25, Tabs B-F) discussed nerve injury by pertussis toxin as the result of an excitotoxic effect.[39] Tr. at 33-34, 98. He indicated that there is laboratory evidence that pertussis toxin and endotoxin cause nerves to "fire erratically." Tr. at 74. Whether the reference articles constituted the laboratory evidence or whether Dr. Tornatore was referring to some other research was not clear, but the cited articles did not involve direct research into pertussis toxin's effect on cells. For example, the article at Pet. Ex. 25, Tab F, reported the use of a substance called "NMDA"[40] to induce excitotoxicity in the cell cultures, as did the research at Tab D of the same exhibit.

When cross-examined on the articles, Dr. Tornatore acknowledged that each of them involved testing done on cultures of mouse brains and involved injecting pertussis toxin, among other substances, directly into the brain cultures (Tr. at 94), a mechanism different from an injection of a vaccine into an extremity. He could not confirm that the injected pertussis toxin came from the formulations or strength similar to those found in DPT vaccines, but the injected pertussis toxin was "probably" "pretty close" to the whole cell pertussis found in the DPT vaccine. Tr. at 95-96. He acknowledged that the researchers and the cited studies did not draw any specific conclusions about the role

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[38] At one point, Dr. Tornatore testified that these articles speak to the toxic effect of pertussis toxin and other toxins on the nervous system. Tr. at 12. These highly technical reference articles did not involve direct research on the excitotoxic effects of pertussis toxin. The research involved the use of cultured fetal or infant rat and mouse brain cells to measure the protective effects of various compounds on neuronal excitotoxicity. Pertussis toxin interfered with the protective effect of studied compounds or cell receptors. Pertussis toxin was not used to demonstrate excitotoxicity in any of the studies.

[39] Tab B involved a study of the toxic effects of an HIV-1 protein called Tat. Tat appears to directly activate pertussis-toxin sensitive proteins, triggering the release of calcium from the endoplasmic reticulum of cells. Pet. Ex. 25, pp. 10, 13, and 18. Tab C involved the study of anoxia-induced cell death in a type of neuronal cell; the presence of pertussis toxin eliminated the protective effect of a serotonin receptor (5-HT_{1A}-R). Pet. Ex. 25, pp. 21, 24-25. Tab D's research involved the role of glutamate receptors in NDMA-induced cell death. Once again, the presence of pertussis toxin reduced the protective effect of the studied agent. Pet. Ex. 25, pp. 30, 32. Tab E contained an article studying the cytotoxic effect of lindane (an insecticide) and the protective effects of baclofen. Pertussis toxin reversed the protective effects of baclofen only in the highest lindane concentrations. Pet. Ex. 25, p. 39. In the research located at Tab F, NDMA was used to trigger excitotoxicity to measure the protective effect of an agonist called DCG-IV. Preincubation of the neuronal cells in pertussis toxin blocked the protective effect. Pet. Ex. 25, pp. 48-49, 51.

[40] *N*-methyl-D-aspartate. N. Davis, MEDICAL ABBREVIATIONS, p. 250 (12th ed. 2005). *See also,* Pet. Ex. 25, Tab C, p. 21, T. Adayev, *et al.*, "Agonist Stimulation of the Serotonin$_{1A}$ Receptor Causes Suppression of Anoxia-Induced Apoptosis via Mitogen-Activated Protein Kinase in Neuronal HN2-5 Cells," Journal of Neurochemistry, Vol. 72, No. 4 (1999) (discussing NMDA receptors' role in protection of neurons against excitotoxicity).

of pertussis vaccine and seizures or the effects of pertussis toxin on humans Tr. at 98-99. He was not aware if any of the studies had been cited in other literature for the conclusion that DPT vaccine causes brain injury. Tr. at 102.

c. *Pertussis-Caused Central Nervous System Disorders.*

If the natural disease causes certain conditions, perhaps a vaccine against that disease can do so as well. Dr. Tornatore advanced this position during his testimony, referring to the central nervous system ["CNS"] effects of pertussis infections. Doctor Tornatore testified that in a wild-type pertussis infection, a constellation of symptoms may develop, including "an incredible encephalopathy" and seizures. Tr. at 74, 95. However, he overstated the risk of encephalopathy and seizures from pertussis infections, testifying that if someone is not vaccinated against pertussis and they contract a "wild-type infection," they "will have" encephalopathy and seizures. Tr. at 97. Studies cited by the Institutes of Medicine ["IOM"] report, ADVERSE EFFECTS OF PERTUSSIS AND RUBELLA VACCINES (1991), [hereinafter "IOM Report"] pp. 11-12, show CNS complications (which would include, but not be limited to, seizures) in 1.7 to 7 percent of pertussis infections and rates of encephalopathy at 0.7 percent. While the Centers for Disease Control note that these figures may not be entirely accurate because of under-reporting of pertussis infections (*id*. at 12), they most certainly do not approach Dr. Tornatore's assertions that "wild-type" pertussis infection leads inevitably to seizures and encephalopathy.

The IOM Report noted that the major complications of pertussis infections are respiratory, CNS, and nutritional. Respiratory effects are most common. *Id.*, at 11-12. In the CNS arena, pertussis infections may cause acute encephalitis that can progress to convulsions, stupor, coma, and death. Autopsies of pertussis encephalitis victims demonstrate cerebral hemorrhage and edema (swelling). Such encephalopathies may manifest suddenly with convulsions, unconsciousness, or coma, or insidiously, with body temperatures rising to high fevers and leading to somnolence, comas, or unconsciousness. *Id*.

Although the IOM Report supports Dr. Tornatore's testimony that "wild-type" pertussis infections can cause CNS disorders, the symptoms manifested in such disorders differ markedly from Enrique's clinical picture. There was no evidence of encephalitis, no progression to stupor or coma, no evidence of any fever (much less a high one), no somnolence, and no unconsciousness. Enrique's seizures were so subtle that various family members observed them for ten days without concern before his parents took him to the pediatrician. Testing did not reveal any evidence of cerebral hemorrhage or edema in Enrique's brain.

Further, the IOM Report notes that in the majority of whooping cough (the disease caused by pertussis) encephalopathies, no CNS inflammation was observed. IOM Report at 89. In the few cases of post-pertussis immunization deaths studied, no patterns of damage to the structure of the brain were identified. While the study

referenced in this portion of the IOM Report was not definitive (*id*. at 90), if a component of the pertussis vaccination were as toxic to the brain as Dr. Tornatore's testimony

indicated, it is likely that some brain injury would have been observed in the death cases.[41]

d. *Test Results and Clinical Picture in Enrique's Case*.

Enrique underwent several tests during his initial hospitalization and afterwards. Both experts addressed the significance of the tests. The 24-hour EEG performed during Enrique's first hospitalization correlated with the SPECT scan showing that the seizures originated on the right side of Enrique's brain. Tr. at 125-26. The brain MRI performed on November 14, 1995, was normal, with no evidence of lesions, structural abnormalities, or abnormal contrast enhancement, indicating no apparent structural abnormality in Enrique's brain.[42] Pet. Ex. 3, p. 2; Tr. at 23, 149-50. An MRI shows the structure or anatomy of the brain, but without great detail. Tr. at 150-51. However, the SPECT scan, performed during one of Enrique's seizures during his initial hospitalization, was abnormal.[43] Tr. at 25. What Dr. Tornatore found remarkable about the SPECT scan was that, while there was increased blood flow to the portion of Enrique's brain where the seizure originated, there was decreased blood flow to the other side of his brain. To Dr. Tornatore, this indicated that there was "something globally" happening in terms of brain impairment. Tr. at 25-26.

Doctor Tornatore testified that when nerves are sufficiently injured by chemical action, they may die or form scars. The scars are what cause ongoing seizure disorders. Tr. at 78. He theorized that in Enrique's case, a cytotoxic effect of the vaccination injured or killed some nerves, causing scarring in his brain. Tr. at 78-79. As support, he noted that the SPECT scan showed hypoperfusion in the left temporal area. This would be indicative of cell injury in that area. Cell injury or death cannot be seen directly through a SPECT scan, but the decreased perfusion in one lobe of Enrique's brain would indicate cell death. Tr. at 80-81; 86-87. This hypoperfused area was not the same area of the brain where Enrique's seizures originated, but the decreased perfusion demonstrated that something was not functioning properly in this area. The treating doctors were focused on the ictal side. Tr. at 81-82, 85. The decreased perfusion could have been chemically induced but could also be the result of an hypoxic event–the loss of oxygen to an area of the brain. Tr. at 82-83. Changes in brain perfusion can happen very quickly. Tr. at 86.

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[41] This point was emphasized in the testimony of Dr. Herskowitz (Tr. at 187), discussed, *infra*.

[42] Subsequent MRIs were also normal. *See, e.g.*, Pet Ex. 4, p. 21 (performed on October 17, 1996) and Pet. Ex. 15, p.3 (performed on June 5, 1998).

[43] A SPECT scan examines blood flow to the brain. A radioactive material injected into the bloodstream is taken up by the brain and shows areas of increased blood flow. Tr. at 151.

In explaining how pertussis toxin might have induced the decreased blood flow, Dr. Tornatore noted that when the brain is injured, there is decreased blood flow to the area of injury. He commented that in cases of brain death, the brain tissue itself would be hypoperfused. Although the heart is still beating and blood is circulating to the brain, the dead area does not take up blood. Tr. at 87-88. A dead area of the brain could be seen on an MRI, but a very small area of dead tissue might not be observable. Tr. at 88-89. An MRI could be normal, but upon autopsy, profound cellular changes may be observed, such as in Parkinson's or early Huntington's diseases. Tr. at 89-90. An excitotoxin might simply irritate the nerves without killing the brain cells.

When pressed to explain how an excitotoxic event could cause both increased perfusion in one area of Enrique's brain and decreased perfusion in another, Dr. Tornatore explained that the initial injury to the nerves could result in increased perfusion, but as the injury progressed to cell death or injury sufficient to cause the cells to "shut down," decreased perfusion would result. At one point, Dr, Tornatore seemed to indicate that there was decreased perfusion on both sides of Enrique's brain. Tr. at 91-92. Because the more profoundly injured areas, based on the decreased perfusion, were in the left temporal lobe, an areas of the brain that is "silent," he would not necessarily expect any clinical symptoms from this injury. Tr. at 93. Enrique's initial seizures were focal in nature; therefore a specific section of the brain was injured. Tr. at 106. The focal nature of the seizures would not rule out a toxic event.

e. *Absence of Other Causes*.

Doctor Tornatore agreed that neurologists are sometimes unable to pinpoint the cause of seizures; in infants, seizures may be caused by hereditary factors, metabolic issues, infections, and other unknown factors. In addition, vaccinations cause seizures. Tr. at 104-05. There is always a reason for a seizure, but in many cases doctors are unable to figure out that cause. Tr. at 106-07. He did not explicitly agree or disagree with a patient handout in Res. Ex. A, p. 89 that indicated that no cause is identified in over 50% of patients with seizures. Because Enrique seized a day after vaccination, he would attribute the seizures to the vaccination, just as he would attribute seizures to a preceding infection or head injury if either was reflected in the patient's history. Tr. at 108-10.

If Enrique displayed persistent high-pitched crying after the vaccination, Dr. Tornatore would find that consistent with the child experiencing a toxic event, with the vaccine causing "encephalopathically pictured seizures." Tr. at 118. He agreed that the absence of a high-pitched cry would make vaccine causation less likely. Tr. at 119-20. A marked change in sleeping or eating patterns associated with seizure activity would make vaccine causation more likely, but the absence of either would not make vaccine causation less likely. Tr. at 120. The length of time between the initial seizure event and any developmental delays would not affect Dr. Tornatore's opinion on vaccine causation because both the seizures themselves and the medications used to treat seizures can result in developmental delay.

f. *Febrile versus Afebrile Seizures and Causation.*

Initially, Dr. Tornatore asserted that a medical journal article filed as Pet. Ex. 27 supported his position that DPT vaccine was associated with afebrile seizures. Tr. at 111-15. The article actually compared the incidence of febrile seizures associated with DPT vaccine versus the rate of febrile seizures associated with the DTaP vaccine.[44] When questioned more closely on this assertion, he admitted that the article appeared to be comparing the incidence of febrile, rather than afebrile, seizures between the two vaccines. Tr. at 115. Doctor Tornatore was unable to cite to any other article that supported an association between DPT vaccine and afebrile seizures. I invited petitioners' counsel to file representative articles in support of the proposition that DPT vaccine causes afebrile seizures (Tr. at 116-17; 228-29).[45]

g. *Support for Vaccine Causation by Treating Physicians*.

Doctor Tornatore opined that two of Enrique's treating physicians felt that the DPT vaccination was "in fact behind the cause of the subsequent seizure disorder," stating that "we have two treating pediatric neurologists who both feel that the seizures were directly caused by immunizations." Tr. at 27-28. However, Dr. Tornatore overstated what the physicians actually wrote.

He referred first to Dr. Resnick's report (found at Pet. Ex. 7, p. 32) which included the comment that Enrique should not receive future pertussis immunizations. He interpreted this as Dr. Resnick's belief that the pertussis component was causal.[46] Doctor Tornatore took this statement out of both written context and medical context. On the page of the report prior to Dr. Resnick's recommendation about future immunizations, Dr. Resnick stated: "The one consideration was the fact that the

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[44] DTaP vaccine contains the same diphtheria and tetanus toxins as the DPT vaccine. The difference between the two vaccines is that the more recent DTaP vaccine contains acellular pertussis as opposed to whole-cell pertussis. VACCINES at 311.

[45] Petitioners' counsel asserted that the issue of DPT vaccine causing afebrile seizures had 'been debated for years" and was one of the reasons the Vaccine Act existed. Tr. at 116. I noted that I had not found any references supporting an association between DPT vaccine and afebrile seizures. Tr. at 117. I invited petitioners to file such references. The only arguably responsive filing was Pet. Ex. 34, an excerpt from a textbook on child neurology. The excerpted section is entitled "Encephalopathy after Pertussis Vaccination." It does not include the footnotes/endnotes containing the articles referenced. The exhibit refers to "afebrile seizures, which are generalized" within 72 hours of vaccination. Pet. Ex. 34, p. 3. As Enrique did not have either generalized seizures or an encephalopathy afer his DPT vaccination, I placed little weight on this excerpt.

[46] Later in his testimony, in response to my questions about this statement, Dr. Tornatore indicated that this comment reflected Dr. Resnick's concern that Enrique had experienced something other than "garden variety febrile seizures." Tr. at 134. Interestingly, this characterization tracks nicely with the IOM Report indicating that febrile seizures are relatively common and generally benign. IOM Report at 87-88.

seizures did occur in temporal relationship to his DPT immunization, although no other symptomatology such as fever or irritability occurred." Pet. Ex. 7, p. 31. As Dr. Herskowitz later pointed out, DPT vaccinations have been causally linked to febrile seizures (Tr. at 221-22) and physicians have commonly recommended against further pertussis immunizations for infants who have experienced seizures. Tr. at 178-80; *see also*, VACCINES, at 305 (indicating that pertussis vaccine was once considered contraindicated in infants who have experienced seizures within three days of a pertussis vaccination, with or without fever, but that such a seizure history is more properly characterized as precautionary, rather than a contraindication for vaccine administration).

Contrary to Dr. Tornatore's assertion, Dr. Resnick did not opine that the DPT vaccination caused Enrique's seizures. As a pediatric neurologist, Dr. Resnick would have been well aware of the medical literature linking DPT and febrile seizures. The juxtaposition of his two comments, one on the temporal connection between vaccine and seizures, and the other on the lack of any fever or irritability, indicates the lack of a relationship between the two factors, because the absence of fever trumped temporality. Also, as febrile seizures commonly have a benign outcome, the lack of fever might suggest that Enrique's seizures were more serious, without unduly alarming his parents.

The second physician whose statements Dr. Tornatore interpreted as supportive of pertussis causation was Dr. Marcel Deray. Tr. at 27-28. At a time when the assigned special master was contemplating dismissal of the petition for failure to file an expert report, Dr. Deray wrote a very short statement, addressed "To Whom It May Concern" (found at Pet. Ex. 22), noting that no other neurologic cause had been found for Enrique's encephalopathy and no explanation was offered other than the DPT vaccination. This statement stopped short of an opinion that the DPT vaccine was causal, notwithstanding Dr. Tornatore's testimony that Dr. Deray felt "that the seizures were caused directly by immunizations."[47]

Doctor Tornatore dismissed an October 17, 1996 evaluation of Enrique (Pet. Ex. 4, p. 15), written by Dr. K. Butler, which noted that Enrique had seizures without encephalopathy at two months of age with onset a week after his DPT vaccination, stating that the doctor got the timing of the seizures wrong, and that she therefore "didn't take an adequate history."[48] Tr. at 64, 68. When Dr. Butler evaluated Enrique, virtually all of Enrique's medical records referred to a seizure onset of one week post-

[47] Doctor Tornatore acknowledged that he had never spoken with either Dr. Resnick or Dr. Deray. Tr. at 41.

[48] Petitioners' Exhibit 4, p. 22 indicates that a Dr. Kenneth Butler evaluated Enrique's EEG. This October 17, 1996, neurology consultation (at Pet. Ex. 4, p. 15) was signed by a "K. Butler." Although Dr. Tornatore referred to Dr. Butler as "she," it is likely that the doctor who signed the neurology consult was the same Kenneth Butler who reviewed the EEG.

vaccination, consistent with the histories taken from his parents during his first hospitalization.[49] On November 22, 1996, Dr. Deray recorded a history of seizures beginning three days after Enrique's vaccination (Pet. Ex. 7, p 7), which was the position taken by Mr. and Mrs. Andreu at the onset hearing and in their affidavits. Based on all the evidence presented, I conclude that the "inaccuracy" in Dr. Butler's history about the timing of the first seizure is not to due to the adequacy of the history he took, but rather due to what the parents told Dr. Butler or previous health care providers. Doctor Tornatore's characterization of the evidence is disingenuous. His statement: "you'd have to go with the family members" (Tr. at 68) implies that the statements of the family members regarding onset or the nature of Enrique's post-vaccination symptoms were consistent. They were not.

h. *Relationship between Initial Seizures and Subsequent Seizure Disorder.*

About a year after his initial focal seizures, Enrique developed febrile seizures. Tr. at 139. Doctor Tornatore explained that the mechanism by which fevers trigger seizures is not known, but febrile seizures are very common, even in those without a pre-existing seizure disorder. Tr at 139-40. At this point, Enrique's seizures had become generalized; both sides of his brain were affected. Tr. at 141. Because there are connections between the sides of the brain, a seizure can travel between the two hemispheres. Tr. at 141. These October 1996 febrile seizures were likely generalized because of Enrique's fever. Tr. at 143. A child or an adult with a seizure disorder is even more predisposed to suffer from febrile seizures. Tr. 147.

B. Dr. Joel Herskowitz, MD.

1. Qualifications

Doctor Herskowitz also testified in person. His report was filed as Res. Ex. C and his curriculum vitae as Res. Ex. D. His references were filed as Res. Exs. E-F. After attending Chicago Medical School and Albert Einstein Medical School, he completed a pediatric residency at Boston City Hospital, trained in neurology and child neurology at Boston University School of Medicine, and has practiced pediatric neurology at Boston University and Tufts University School of Medicine since 1979. Tr. at 164-65; Res. Ex.

[49] The sole exception was Dr. Montalon's consultation report, which noted that the "grandfather" may have noted a focal seizure one week prior to the parents' onset history. Res. Ex. A, p. 18. All of the other medical histories from this initial hospitalization record November 8, 1996, as the date of onset, consistent with the history taken in the emergency room on November 11, 1996 (*id*., pp. 1, 3) and the pediatric history recorded on the same day. *Id*., p. 11. I note that the pediatric history contains greater detail than the initial history in the emergency room, and thus was not likely simply copied from earlier records. Given that Enrique's parents were apparently convinced at the time of Dr. Butler's evaluation that the onset of his seizures was one week after his vaccination, Dr. Butler can hardly be faulted for taking an "inadequate" history.

D. He holds a teaching position as assistant professor of pediatrics and neurology at Boston University School of Medicine. Tr. at 165. He is currently employed as a staff pediatric neurologist at New England Medical Center Hospital, Boston, MA. Res. Ex. D.

Doctor Herskowitz is board certified in pediatrics and pediatric neurology and is engaged in clinical practice three days a week, seeing approximately 1200-1500 patients annually. Tr. at 165-66. He sees only a few seizure patients a month currently, but has seen considerably more seizure patients in past decades. Tr. at 166, 191. I accepted him as an expert in pediatric neurology. Tr. at 166.

2. Testimony and Evidence Regarding Causation

a. *In General.*

Although there were several areas of agreement between the two medical experts, Dr. Herskowitz disagreed with Dr. Tornatore on the central question of vaccine causation. Doctor Herskowitz opined, "to a reasonable degree of medical certainty," that Enrique's DPT vaccination did not cause his seizure disorder. Tr. at 167-68. He based this opinion on the significant body of medical research that had failed to find any connection between DPT vaccination and afebrile seizures. He agreed with Dr. Tornatore that seizures can be caused by brain injury and that the injection of toxins, or even benign substances in toxic concentrations, can cause seizures, but disagreed that Enrique's clinical picture and test results evinced a global insult of that nature to his brain. Finally, he disagreed with Dr. Tornatore's assertion that a recommendation to withhold further pertussis vaccinations meant that Enrique's treating doctors believed the vaccine had caused his seizure disorder.

Explaining the factual underpinnings of his opinion, Dr. Herskowitz demonstrated familiarity with the medical records, the onset hearing testimony, and the factual findings of Special Master Abell. *See*, Tr. at 169-71.

b. *Research Fails to Show a Connection between DPT Vaccination and Afebrile Seizures.*

In essence, Dr. Herskowitz opined that Dr. Tornatore's theory of injury did not outweigh the numerous medical studies that failed to find a relationship between afebrile seizures and DPT vaccination. According to the medical literature, the fact that Enrique's seizures were afebrile was of tremendous importance. Tr. at 188. The New England Journal of Medicine article filed as Res. Ex. F[50] illustrated this point. The article described a study of over half a million children and found no increased risk of afebrile seizures after vaccination with DPT. It found an increased risk of febrile

[50] William E. Barlow, *et al.*, "The Risk of Seizures after Receipt of Whole-Cell Pertussis or Measles, Mumps, and Rubella Vaccine." N. ENGL. J MED., Vol. 345, No. 9 (Aug. 30, 2001).

seizures only on the day of vaccination. The article also referred to earlier studies that had likewise failed to find any increased risk of afebrile seizures. Tr. at 189; Res. Ex. F, pp. 656, 659.

A second article, filed as Res. Ex. E,[51] was a 1994 population-based case-control study.[52] The study matched confirmed cases of neurological illness during a 12-month period with two other children with similar birth dates, gender, and birth location. Immunization records were used to determine whether the illness occurred within one week of DPT vaccination. Febrile seizures, afebrile seizures, infantile spasms, and acute encephalopathies were all examined. While the study was not designed to provide a definitive answer regarding causality of the pertussis component of the DPT vaccination and neurological illness, its findings were consistent with other studies that had found no association between afebrile seizures and DPT vaccination. Res. Ex. E, pp. 37, 39, 41; Tr. at 190.

Although Dr. Herskowitz was unable to specify what body temperature would be used to define a seizure as "febrile" (Tr. 192-93), initially speculating that a degree of fever might be sufficient and then backing off from that position, DORLAND'S ILLUSTRATED MEDICAL DICTIONARY loosely defines febrile seizures or convulsions as "those associated with high fever." DORLAND'S at 1676 (directing the reader to "convulsion" for a definition of febrile seizures) and 415 (defining "febrile convulsion"). An article referenced by Dr. Herskowitz (Res. Ex. E, p. 38) defined "febrile seizures" as those where the child's temperature was at least 38 degrees Celsius [100.4 degrees Fahrenheit]. The article defined non-febrile seizures as "those not accompanied by fever." *Id.*

The difference in body temperature necessary to define a seizure as "febrile" is not particularly significant, given the facts of this case, because petitioners did not establish that Enrique had any fever during the relevant period of October 31 - November 15, 1995. No family member testified that he had a fever prior to his hospitalization. His temperature on admission was essentially normal; at its highest point in the two weeks after his vaccination, Enrique's temperature was less than a degree above normal. His treating physicians did not think his seizures were febrile, nor, apparently, did his parents when they provided his medical history upon admission to MCH on November 11, 1995. In the absence of any evidence linking either Enrique's initial seizure on November 1, 1995, or his seizures in the following two weeks to fever,

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[51] James L. Gale, *et al.*, "Risk of Serious Acute Neurological Illness after Immunization with Diphtheria-Tetanus-Pertussis Vaccine: A Population-Based Case-control Study," Vol. 271 Journal of the American Medical Association, No. 1, pp. 37-41, sometimes referred to as "SONIC" ["Study of Neurological Illness in Children"] (1994).

[52] A case control study compares a group of individuals with a particular disease or condition to another group of similar individuals without the disease or condition. Federal Judicial Center, REFERENCE MANUAL ON SCIENTIFIC EVIDENCE, (2d ed. 2000), p. 342.

these articles and Dr. Herskowitz's testimony interpreting them, significantly undercut petitioners' case for vaccine causation.

c. *Biologic Plausibility*.

Doctor Herskowitz acknowledged that in a laboratory setting, pertussis antigen can cause neurotoxicity, thus agreeing with Dr. Tornatore's basic premise regarding biologic plausibility, but he also opined that there was no evidence of such an effect from the vaccine as routinely administered to people. Tr. at 196-97. Petitioners' counsel attempted to impeach Dr. Herskowitz with his testimony in another vaccine case[53] regarding whether pertussis antigen can cause neurologic symptoms, but I did not find his attempt particularly persuasive. Doctor Herskowitz merely reiterated what Dr. Tornatore had already acknowledged–that none of the studies provided by Dr. Tornatore involved pertussis toxin-induced neurological symptoms in human brains. Tr. at 199-200, 94. The quoted prior testimony concerned the effects of the acellular pertussis vaccine; thus any opinion he expressed regarding that vaccine in another case would have little impeachment value in this one involving whole cell pertussis vaccine.

Doctor Herskowitz agreed that the polio virus was capable of causing symptoms ranging from mild gastrointestinal upset to devastating paralysis. Tr. at 203-04. He rejected, however, an analogy to the effects of pertussis toxin, noting that there was not a specific pathology related to the effects of pertussis on the neurological system. While some children with pertussis infections developed neurological symptoms, pertussis toxin is not commonly considered a neurotropic toxin. Tr. at 204-05, 218-19. Doctor Herskowitz drew a plausible distinction between polio virus, which is neurotropic in nature, and the pertussis toxin, which has been known to cause CNS complications when accompanied by fever. Tr. at 204-05.

d. *Enrique's Clinical Picture and Test Results*.

Doctor Herskowitz testified that Dr. Tornatore's theory did not account for Enrique's clinical presentation, particularly the lack of identifiable brain injury or atrophy. Doctor Tornatore's theory was predicated on a toxin or poison affecting Enrique's brain; however, such a poison would be highly unlikely to cause dysfunction in a small, localized area of the brain, rather than affecting the brain in general. Tr. at 217-18. A toxin affecting the brain would likely manifest with significant changes in mental status that would be inconsistent with Enrique's behavior during the time period of the first

[53] This line of questioning raises the issue of a possible violation of § 300aa–12(d)(4)(A), which provides that information submitted to a special master in a proceeding on a petition may not be disclosed to a person who is not a party to the proceedings without the express consent of the person who submitted the information. Petitioners' counsel improperly identified the name of the petitioner in the previous case when he attempted to impeach Dr. Herskowitz's testimony with a portion of the transcript of those proceedings.

seizures. Tr. at 185-87. A metabolic insult would normally present with multifocal seizures. Because Enrique was on an EEG for a day or two during this initial hospitalization, there is a record of how his brain was functioning and that record contains no evidence of a serious or severe toxin affecting his brain. Tr. at 187. There was no evidence of dying brain cells, such as brain atrophy, a falloff in head circumference, or a change in personality or behavior. Tr. at 184,187-88.

A child may have chronic seizures without a diminished head circumference or MRI evidence of injury. Tr. at 228. However, given the postulated mechanism of injury in this case, a global insult to the brain from a toxin, Dr. Herskowitz would expect to see atrophy, ventricular dilation, or a white matter injury. Tr. at 216-17. An MRI is very good at demonstrating brain atrophy, damage, or abnormal gray matter. Tr. at 215-16. None of these were found in Enrique's tests.

In interpreting the EEG, SPECT scan, and MRI performed during Enrique's November 1995 hospitalization, Dr. Herskowitz noted that the EEG demonstrated a localized seizure discharge that was not correlated to observable seizure activity, suggesting a very subtle brain dysfunction. Tr. at 170-71. As did Dr. Tornatore, he interpreted the radiologist's report of the ictal SPECT scan in light of the MRI findings.[54] While the SPECT scan suggested that the diminished perfusion in the left temporal lobe of Enrique's brain might be suggestive of atrophy or under development, Dr. Herskowitz testified that what was called diminished perfusion on the left should be read in comparison to the increased perfusion on the right side because the MRI two hours later did not show any injury. Tr. at 172, 174-75.

Subsequent MRIs cast additional doubt upon Dr. Tornatore's hypothesis of pertussis injury to brain cells or their supporting cells, according to Dr. Herskowitz. He explained that nerve cells are gray matter. Glia, which are among the supporting cells, make up the myelin that sheathes the nerves. The later MRIs demonstrate that the myelination of Enrique's brain was age-appropriate, indicating that the supporting cells had not been damaged.

Dead brain tissue results in fluid collection in the brain's ventricles. Because the MRIs never revealed any ventricular enlargement, there was no evidence for death of brain matter. Tr. at 181-82. Thus, there is no evidence for a serious multi-focal or global insult at the time of his first hospitalization for seizures.

e. *Opinions of Treating Physicians*.

Doctor Herskowitz disagreed with Dr. Tornatore on the significance of a recommendation against further pertussis vaccinations in Dr. Resnick's December 1995 (Pet. Ex. 7, pp. 31-32) evaluation of Enrique. As he explained, pediatricians are trained

[54] He disagreed, however, with Dr. Tornatore's characterization of SPECT scans as "fuzzy."

to recommend against further pertussis vaccinations for children displaying an intense localized reaction to a previous DPT vaccination, even in the absence of seizures. Thus, it is not true that a physician must feel very strongly about vaccine induction of seizures in order to recommend against future pertussis immunizations. Tr. at 178-79. As a pediatric neurologist, Dr. Resnick was simply recommending against further pertussis vaccinations in an abundance of caution, rather than opining on DPT causality of Enrique's seizures. Tr. at 178-79. The pertussis component of the vaccine was not singled out based on good medicine or objective studies, but simply based on common practice. On cross-examination, Dr. Herskowitz agreed that although other vaccines can cause fever and thus present the issue of triggering febrile seizures, it was common practice to recommend against further pertussis immunizations but not to withhold other vaccines. Tr. at 195-96.

C. Post-Hearing Evidence

1. References Filed by the Special Master

In a written order issued on March 29, 2007, I notified the parties of my intent to rely upon the 1991 IOM Report and on Chapter 14, VACCINES, which is a standard medical reference textbook. I provided the parties the opportunity to file additional "comments, reports, or argument, **based on the information in these resources**...." (emphasis original). As the order indicated, I was exercising my statutory authority under § 300aa-12(d)(3)(B)(I) to require evidence necessary for me "to understand the issues raised by the medical records, expert reports, testimony, and other filed references." Order, dated March 29, 2007.

As the discussion in Parts IV A and B, above, indicates, the two reference articles were used in a very limited manner: (1) to understand Dr. Tornatore's testimony about the components of the pertussis vaccine (referenced in footnote 44); (2) to consider the adverse effects of the disease (whooping cough) caused by pertussis and the frequency of various complications therefrom (discussed in Part IV A(3)c)); and (3) to better understand the basis for the treating doctors' recommendations against further pertussis vaccinations for Enrique, as there was a conflict between Dr. Tornatore's assertions that this was unusual and an important indicator of the treating doctors' belief in vaccine causation, and Dr. Herskowitz's assertions that this was a standard pediatric recommendation made in an abundance of caution. I might add that, even without recourse to the reference regarding further pertussis vaccinations post-seizure, I found Dr. Herskowitz's testimony on this factor more credible than Dr. Tornatore's, based on my overall assessment of witness credibility as well as on Dr. Herskowitz's greater experience in dealing with pediatric patients.

2. Petitioners' Response to the March 29, 2007 Order

a. *General.*

Petitioners' counsel responded ["Pet. Res."] to my order filing the two reference articles with a timely request that the hearing be reopened so that the experts could address any specific issues. In the alternative, he offered argument based on excerpts from and citations to a number of scientific and medical references not previously filed. Petitioners did not file any expert commentary on the two reference articles filed by the court.

b. *Request to Reopen the Hearing.*

I considered petitioners' request to reopen the hearing, but declined to do so. Order, dated May 8, 2007. The two reference matters I listed are standard and often-cited materials on vaccines and immunizations and any expert qualified to opine on vaccine causation would be familiar with these references. Neither is difficult reading or highly technical and I am quite capable of understanding them without the benefit of expert testimony. As I noted in my order, the Federal Circuit has found that Vaccine Rule 8(b) gives special masters the authority to rely upon an IOM report that neither party filed. *Stroud v. Sec'y, HHS*, 113 F.3d 1258 (Fed. Cir. 1997). The 1991 IOM report referenced has been cited in a number of Vaccine Act decisions, as well as by other federal courts. *See, e.g., O'Connell v. Shalala*, 79 F.3d 170, 172 (1st Cir. 1996); *Liable v. Sec'y, HHS,* No. 98-120V, 2000 U.S. Claims LEXIS 209, *15 (Fed. Cl. Spec. Mstr., Sept. 7, 2000)*; and Moberly v. Sec'y, HHS,* No. 98-0910V, 2005 U.S. Claims LEXIS 220 (Fed. Cl. Spec. Mstr. June 30, 2005).

c. *Additional Evidence*.

Petitioners' counsel belatedly filed a compact disk containing Pet. Ex. 28-49, an assortment of medical or scientific journal articles, editorials, and case reports, many of which had little relevance to the issues in this case or the two references to which they were responsively filed. Not wishing to penalize petitioners for their counsel's untimely response to my order establishing a deadline for filing any new matter, I have carefully read each of those articles. They do not alter my previous analysis of the evidence, assessments of witness qualifications and credibility, or the weight I have accorded the expert testimony. I have also carefully considered the arguments made in the timely response to my order; none alters my opinion that petitioners have failed to establish causation by preponderant evidence. Nevertheless, I address several of those arguments below:

(1) Post-pertussis encephalopathies.

Many of the new exhibits dealt with encephalopathies developing post-pertussis exposure. *See, e.g.,* Pet. Exs. 30 (evaluation of murine studies of encephalopathy), 36 (case report of encephalopathy after pertussis infection), 38 (murine study of pertussis encephalopathy with multiple injections); 45 (murine study of encephalomyelitis after pertussigen administration). As I found no evidence of an encephalopathy in Enrique

after his vaccination, these articles had little relevance to this case.

Petitioners also argued that the belatedly-filed reference materials support a finding that DPT vaccine can cause a vaccine-related encephalopathy. In view of counsel's concession that this is not a Table case, that conclusion is irrelevant. Even if the articles supported the existence of "pertussis encephalopathy," a seizure alone does not constitute a Table encephalopathy. Enrique's post-seizure behavior did not manifest a significantly decreased level of consciousness. QAI, ¶ (2)(I). Crying throughout the evening of the vaccination does not constitute an encephalopathy. I have factually concluded, based on the contemporaneous medical records and treating doctors' assessments, that Enrique did not have an encephalopathy, post-vaccine.

> (2) National Childhood Encephalopathy Study ["NCES"] References.

The response also referenced the NCES. There was no testimony proffered on the NCES at the hearing, likely because Enrique would not have met the criteria for inclusion in the study.

The NCES is a well-known study conducted in Great Britain to measure adverse events after DPT vaccination. In *Liable*, 2000 WL 1517672, Special Master Hastings engaged in a comprehensive review of the medical literature concerning whole cell pertussis vaccine and chronic neurologic damage, explaining the relationship among the NCES, the 1991 IOM study I referenced, a 10-year follow-up study to the NCES,[55] and a 1994 IOM report based on the NCES follow-up study. Special Master Hastings also analyzed the decisions of the other special masters after the 1994 IOM study and the 1995 changes to the Table. His exhaustive opinion is essential reading for any special master considering a claim of serious neurologic injury from a whole cell pertussis vaccination.

Special Master Hastings summarized the test for finding vaccine causation adopted by nearly every special master in cases related to whole cell pertussis and neurologic injuries: "[I]f a neurologically-intact vaccinee (1) suffers, within seven days after a pertussis vaccination, a neurologic episode that would have qualified as a 'serious acute neurologic illness' under the NCES; (2) goes on to experience chronic neurologic dysfunction of the type described in the NCES; and (3) no other cause for that dysfunction can be identified; then it is appropriate to causally attribute the chronic neurologic dysfunction to the vaccination." 2000 U.S. Claims LEXIS 209 at *41.

Special Master Edwards, in another comprehensive opinion, also summarized the medical literature on pertussis vaccination and serious neurologic damage. *See Moberly,* 2005 U.S. Claims LEXIS 220. Special Master Edwards slightly restated the

[55] An article concerning this follow-up study was filed as Pet. Ex. 37.

causation test as whether: "(1) a previously neurologically intact infant entered the hospital with a condition that would have prompted notification to the NCES; (2) the onset of the infant's condition requiring hospitalization occurred within seven days after a DPT vaccination; (3) the infant developed chronic neurological dysfunction; and (4) there is no other identifiable cause for the infant's dysfunction...." *Moberly* at *9.

What makes these tests (and the NCES) inapplicable to Enrique's case is the criteria of a "serious acute neurologic illness" or an illness that would have qualified for inclusion in the NCES as a "case child." In *Liable*, Special Master Hastings set forth the 1994 IOM definition of serious acute neurologic illness, which was based on the NCES criteria. It included encephalitis, encephalomyelitis, or encephalopathy; an unexplained loss of consciousness; Reye syndrome; convulsions [seizures] with a total duration of more than half an hour, or seizures followed by coma lasting two hours or more, or seizures followed by paralysis or other neurologic signs not previously present and lasting 24 hours or more; or infantile spasms (West syndrome). Since Enrique did not experience any of these symptoms–his seizures in the week following his vaccination lasted only seconds to minutes–he would not have qualified as a "case child" under the NCES criteria or as having a serious acute neurologic illness under the 1994 IOM criteria.

(3) Other Issues with Petitioners' Additional Arguments and References.

Some of the articles appear to have no relevance at all to the facts or issues in this case. *See, e.g.,* Pet. Ex. 29 (corticosteroid therapy for a condition with which Enrique has not been diagnosed). At least one argument advanced in Pet. Res. is premised on a highly selective reading of and misstatements concerning the referenced articles. Petitioners made the claim that "studies of large populations of vaccinated children actually found cases of non-febrile seizures after DPT vaccinations." That statement is literally true: most infants who develop seizures have had at least some prior vaccinations. However, the support for this statement, later filed as Pet. Ex. 47, included a table that petitioners argued showed an increased risk of afebrile seizures within the 30 days after DPT vaccination. The analysis in the article from which the table was drawn actually concludes that the DPT vaccine was not associated with an increased risk of nonfebrile seizures. Pet. Ex. 47, pp. 1, 5. The table showed a very small number of nonfebrile seizures in the week after vaccination (four events) and an extremely wide confidence interval[56] associated with the relative risk computed. These are both factors that would contribute to the conclusion of the study's authors that the

[56] See Federal Judicial Center, REFERENCE MANUAL ON SCIENTIFIC EVIDENCE, (2d ed. 2000), p. 389, defining "confidence interval" as: "A range of values calculated from the results of a study within which the true value is likely to fall; the width of the interval reflects random error....The width of the confidence interval provides an indication of the precision of the point estimate or relative risk found in the study; the narrower the confidence interval, the greater the confidence in the relative risk estimate found in the study."

DPT vaccination was not associated with any increased risk of afebrile seizures.[57]

The argument drawn from this table contains other factual flaws. Counsel attributed a relative risk of 1.94 to the total of 10 seizure events in the first 30 days after DPT vaccination. This was a misstatement of the data. That relative risk was actually only attributable to the first seven days after vaccination, not the full 30 days. In any event, it was not deemed to be statistically significant by the study's authors. Counsel's failure to point out this conclusion is inexplicable.

The cited relative risk is inadequate to establish vaccine causation. A relative risk must exceed two in order for epidemiological evidence to serve as preponderant evidence of causation. *Liable,* 2000 WL 1517672 at *15; *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 43 F.3d 1311, 1321 (9th Cir. 1995), *cert. denied,* 516 U.S. 869 (1995); *DeLuca v. Merrell Dow Pharmaceuticals, Inc.,* 911 F.2d 941, 959 (3d Cir. 1990). *See also*, Federal Judicial Center, REFERENCE MANUAL ON SCIENTIFIC EVIDENCE, (2d ed. 2000), p. 384 (discussing relative risk greater than 2.0 as permitting an inference that the condition was caused by the implicated agent).

3. Respondent's Response to the March 29, 2007, Order

Respondent filed a brief indicating that the two reference articles supported Dr. Herskowitz's testimony, outlining authority for the special master to consider additional matters *sua sponte*, and noting the high degree of deference given to IOM Reports by special masters. Respondent did not file any additional reference materials or expert commentary.

V. Conclusions of Law

A. Issues Presented

This case presents the two issues that appear most frequently in actual causation cases arising under the Vaccine Act: (1) the credibility of the experts testifying and the plausibility and reliability of their opinions and (2) what constitutes a *prima facie* case of vaccine causation. *Cf. Lampe v. Sec'y, HHS*, 219 F.3d. 1357, 1361 (Fed. Cir. 2000) (noting the importance of expert medical testimony in "off-Table"causation cases).

B. Legal Standards to be Applied

1. In General

[57] Had petitioners' counsel been citing a case, rather than a medical article, one might be less charitable in concluding that the references were not deliberately misleading. Given that this is a medical article and counsel is not a doctor, I choose to give him the benefit of the doubt.

In the case of an "off-Table" injury, a petitioner must "show by preponderant evidence that the vaccination brought about [the] 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. See also, *Hines v. Sec'y, HHS*, 940 F.2d 1518, 1525 (Fed. Cir. 1991). Circumstantial evidence and medical opinions may be sufficient to satisfy the second *Althen* factor. *Capizzano v. Sec'y, HHS*, 440 F.3d 1317, 1325 (Fed. Cir. 2006).

Petitioner need not show identification and proof of specific biological mechanisms, as "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." *Althen*, 418 F.3d at 1280. The petitioner need not show that the vaccination was the sole cause or even the predominant cause of the injury or condition; showing that the vaccination was a "substantial factor" in causing the condition and was a "but for" cause is sufficient for recovery. *Shyface v. Sec'y, HHS*, 165 F.3d 1344, 1352 (Fed. Cir. 1999). *See also, Pafford v. Sec'y, HHS,* 451 F.3d 1352, 1355 (Fed. Cir. 2006) (petitioner must establish that vaccinations were a substantial factor and that harm would not have occurred in the absence of vaccination). Petitioner may not be required to show "epidemiologic studies, rechallenge, the presence of pathologic markers or genetic disposition, or general acceptance in the scientific or medical communities to establish a logical sequence of cause and effect...." *Capizzano v. Sec'y, HHS*, 440 F.3d 1317, 1325 (Fed. Cir. 2006). Causation is determined on a case by case basis, with "no hard and fast *per se* scientific or medical rules." *Knudsen v. Sec'y*, *HHS,* 35 F.3d 543, 548 (Fed. Cir. 1994). Close calls regarding causation must be resolved in favor of the petitioner. *Althen*, 418 F.3d at 1280. *But see, Knudsen*, 35 F.3d at 550 (when evidence is in equipoise, the party with the burden of proof failed to meet that burden).

When a petitioner alleges an "off-Table" injury, eligibility for compensation is established when the petitioner demonstrates, by a preponderance of the evidence, that: (1) petitioner received a vaccine set forth on the Vaccine Injury Table; (2) he received the vaccine in the United States; (3) he sustained or had significantly aggravated an illness, disease, disability, or condition caused by the vaccine; and (4) the problem has persisted for more than six months.[58] Vaccine litigation rarely concerns whether the vaccine appears on the Table, the situs for administration, or whether the symptoms have persisted for the requisite time. Currently, vaccine litigation focuses most often on the issue of whether the injury alleged was caused by the vaccine.

[58] Section 300aa–13(a)(1)(A). This section provides that petitioner must demonstrate by a preponderance of the evidence the matters required in the petition by section 300aa–11(c)(1)..." Section 300aa–11(c)(1) contains the four factors listed above, along with others not relevant in this case.

2. Causation and the *Prima Facie* Case

Petitioner must present evidence of a reliable medical theory. Thus, the trier of fact must determine the reliability and plausibility of the expert medical opinions offered and the credibility of the experts offering them. When petitioner establishes entitlement to compensation, the burden shifts to respondent to establish, "also by a preponderance of the evidence, that the injury was in fact caused by factors unrelated to the vaccine." *Whitecotton v. Sec'y, HHS*, 17 F.3d 374, 376 (Fed Cir. 1994), *rev'd and remanded sub nom*. *Shalala v. Whitecotton*, 514 U.S. 268 (1995). Determining when the burden shifting occurs is complicated by the two meanings that have attached to the term "*prima facie* case" in Vaccine Act decisions.

In its classic sense, a *prima facie* case is a case that could withstand a motion for summary judgment. In the context of the Vaccine Act, this would mean that if the evidence filed established all the statutory requirements, including, in off-Table cases, some evidence that the vaccine was responsible for the injury, petitioner's case could not be dismissed on motion for summary judgment and the burden of production would shift to respondent.

The second meaning of "*prima facie* case" involves the point at which petitioner's evidence tips the balance in favor of vaccine causation. The difference between the two meanings of "*prima facie*" rests on the principle that, outside the summary judgment arena, not all evidence carries equal weight with a trier of fact. Medical opinions on causation may be based on medical histories that are factually incorrect or the opinion may be made by someone without the necessary training, education, or experience to offer a reliable opinion. An expert may offer an opinion that is unpersuasive for a variety of reasons. Courts, whether they deal with vaccine injuries, medical malpractice claims, toxic torts, or accident reconstruction, must base their decisions on reliable evidence. *Daubert v. Merrell Dow Pharmaceuticals, Inc*., 509 U.S. 579, 594 (1993). *Daubert* provides a useful framework for evaluating scientific evidence in Vaccine Act cases. *Terran v. Sec'y, HHS*, 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). *See also*, *Ryman v. Sec'y, HHS*, 65 Fed. Cl. 35, 40 (Fed. Cl. 2005) (special master performs gatekeeping function when he "determines whether expert testimony may be admitted or credited or otherwise relied upon").

Thus, in off-table Vaccine Act cases, the term *"prima facie* case" is frequently used to indicate the point at which the trier of fact is sufficiently satisfied that the vaccine is, more likely than not, the cause of the petitioner's injury. For special masters who are the fact-finders, this is a somewhat artificial distinction, because it implies that there is a precise point in a case, other than in a motion for summary judgment, when the burden of production becomes one of persuasion. *See Althen*, 418 F.3d at 1278 (burden shift occurs when there is adequate evidence of each of the three factors). Often, it is impossible to pinpoint when this occurs, which is in keeping with the Vaccine

Act's requirement that a special master consider all the evidence in determining whether to award compensation. Section 300aa-13(a)(1) provides that the special master shall award compensation when the record as a whole demonstrates entitlement.

The Vaccine Act clearly contemplates that the special masters will weigh the evidence presented in making entitlement decisions. Special masters are not bound by any particular "diagnosis, conclusion, judgment, test result, report, or summary" and in determining the weight to be afforded to these matters, "shall consider the entire record...." § 300aa–13(b)(1). Respondent may challenge the factual underpinnings of a causation opinion, the opinion itself, or both before the special master determines whether a *prima facie* case has been established. Special masters weigh the evidence found in the medical records (*see, e.g., Ryman*, 65 Fed. Cl. at 40-41); consider evidence of bias or prejudice on the part of a witness, affiant, or expert (*see, e.g., Baker v. Sec'y, HHS*, 2003 U.S. Claims LEXIS 290, No. 99-653V, 2003 WL 22416622 (Fed. Cl. Spec. Mstr. Sept. 26, 2003)); weigh opposing medical opinions and the relative qualifications of experts (*see, e.g., Epstein v. Sec'y, HHS*, 35 Fed. Cl. 467, 477 (1996) and *Lankford v. Sec'y, HHS*, 37 Fed. Cl. 723, 726-27 (1997)); examine medical literature, studies, reports, and tests submitted by both sides (*see, e.g., Sharpnack, v. Sec'y, HHS*, 27 Fed. Cl. 457 (1993), *aff'd*, 17 F.3d 1442 (Fed. Cir. 1994)); as well as consider a myriad of other factors in determining the facts of the case and the mixed questions of law and fact that arise in causation determinations. Special masters decide questions of credibility, plausibility, reliability, and ultimately determine to which side the balance of the evidence is tipped. *See, e.g., Burns v. Sec'y, HHS*, 3 F.3d 415, 417 (Fed. Cir. 1993) (credibility determinations uniquely within the special master's purview). *See also, Pafford*, 451 F.3d at 1359 ("Notably, this court accords great deference to a Special Master's determination on the probative value of evidence and the credibility of witnesses.").

In an off-Table case, if the special master concludes that petitioner's evidence of causation is lacking, then the burden never shifts to respondent to demonstrate the "factors unrelated" as an alternative cause for petitioner's injury. *Bradley* 991 F.2d at 1575 (when petitioner has failed to demonstrate causation by a preponderance, alternative theories of causation need not be addressed) and *Johnson v. Sec'y, HHS*, 33 Fed. Cl. 712, 722 (1995), *aff'd,* 99 F.3d 1160 (Fed. Cir. 1996) (even in idiopathic disease claims, the special master may conclude petitioner has failed to establish a *prima facie* case). If petitioner fails to establish one or more of the *Althen* factors, petitioner has failed to establish causation. By challenging any of *Althen's* three causation factors, through cross-examination, introduction of medical literature, contrary testimony of well-qualified experts, or some other method, respondent may stymie petitioner's efforts to establish a *prima facie* case.

3. Conclusions Regarding Causation

The temporal connection between the first seizure on November 1, 1995, and the vaccination less than 24 hours earlier was striking. Temporal connection alone, however, is not enough to establish causation. *Strother v. Sec'y, HHS*, 18 Cl. Ct. 816 (1989), *aff'd,* 950 F.2d 731 (Fed. Cir. 1991). *Althen* requires a "proximate temporal relationship"; here, I have a dearth of evidence of what precisely that temporal relationship would be. Although Dr. Tornatore testified that he would expect to see an excitotoxic effect in the brain "fairly quickly," (Tr. at 30) he never specified when, after vaccination, he would expect to see seizure activity, or why that seizure activity would persist in the absence of continuing doses of pertussis toxin or endotoxin. If the toxins caused brain cell damage, he could not explain the toxins' affinity for a specific (or focal) region of the brain, rather than causing global insult.

Although petitioners advanced an hypothesis regarding vaccine causation as the source of Enrique's injury that was theoretically possible, it was not persuasive. The postulated "excitotoxic" effect of pertussis vaccine on the brain did not square with the other evidence in this case. The clear failure in petitioners' case was their inability to draw the logical connection *Althen* requires between the postulated mechanism of injury and the clinical evidence in this case.

Whatever theoretical allure the excitotoxin theory regarding the cause of seizures may have, the weight of the scientific and clinical evidence adduced here does not support pertussis toxin as the cause of Enrique's afebrile seizures. Petitioners were not aided in the quest to establish a reliable medical theory by the obvious problems of credibility attached to Dr. Tornatore's testimony and the documentary evidence upon which it was based.

Although Dr. Tornatore's testimony on the "off-Table" injury causation issue was more probative than his Table encephalopathy testimony, the reliability of his opinions was undercut by hyperbole and leaps in logic, as well as his failure to address the significant body of medical research that has failed to find a connection between afebrile seizures and the DPT vaccine. I recognize that a minority medical opinion, supported by a reliable medical theory and demonstrating a logical sequence of cause and effect (*see Althen*, 58 Fed. Cl. at 284) may constitute sufficient evidence of causation under the Vaccine Act. However, Dr. Tornatore's testimony was troubling given his misreading of Pet. Ex. 27, the tenuous relevance of the other articles upon which he relied (Pet. Ex. 25, Tabs A-F), his failure to address the body of scientific opinion that DPT does not cause afebrile seizures, and his failure to refute the epidemiologic evidence filed by respondent or explain why such evidence would be inapplicable or irrelevant to Enrique's case. All of these factors contributed to my

finding that his testimony was unpersuasive.[59]

He relied on evidence from witnesses whose statements and testimony were not deemed reliable by Special Master Abell, after being advised in writing against doing so. He contorted facts and definitions in an attempt to bring Enrique's case within the ambit of the Vaccine Table. He took statements of treating physicians out of context, and attributed to those physicians opinions on causation that were not fully supported by the records. He cited studies in neurotoxicity of pertussis toxin as support for his medical theory, when the authors of those studies drew no conclusions regarding the role of pertussis toxin in causing seizures.

In contrast, Dr. Herskowitz' testimony was well-grounded in the objective medical records, was supported by medical literature, and was in accord with the weight of scientific opinion on the lack of connection between DPT vaccination and afebrile seizures. The general acceptance of a theory within the scientific community may affect an assessment of the theory's reliability. *Daubert,* 509 U.S. at 594.

In weighing and evaluating the opinions of the experts, I also considered their relative qualifications. Doctor Herskowitz is board-certified in both pediatrics and neurology; Dr. Tornatore is a neurologist, but not a pediatric neurologist. Neither expert currently cares for a significant number of patients for seizure disorders, although Dr. Herskowitz has cared for many pediatric seizure patients in the past. Doctor Tornatore has done so far less frequently. Doctor Tornatore has had a past research focus on the pathogenesis of brain disease, but is currently involved in treating patients with demyelinating diseases (multiple sclerosis). I also considered the basis for their opinions and the degree to which their opinions are supported by research and literature. While *Althen* teaches that petitioners may not be required to produce medical literature in support of their theories for causation, when the parties file such literature in support of their respective positions, the special master may consider the literature for its tendency, if any, to support or refute the positions advanced. In this case, the clear weight of medical authority is against petitioners.

In interpreting Enrique's clinical picture and test results, I found Dr. Herskowitz to be more persuasive. Even accepting Dr. Tornatore's premise that pertussis toxin is neurotoxic, the clinical presentation and test results were not consistent with a global insult to Enrique's brain. He advanced no persuasive medical theory that pertussis toxin has a special affinity for a particular area of the brain. Additionally, none of Enrique's treating physicians during his November 1995 hospitalization attributed his

[59] Doctor Tornatore testified that he would have to go back through the literature to determine if there were any studies supporting the proposition that DPT vaccination was associated with an increased risk of afebrile seizures. I twice offered petitioners' counsel the opportunity to file such studies into the record after the hearing. Tr. at 116-17; 229. Petitioners' counsel represented that there were "literally hundreds of articles" (Tr. at 116), but only Pet. Ex. 34, inapplicable for the reasons discussed above, was ever filed.

seizures to the DPT vaccine. They noted only a temporal, not causal, relationship. Petitioners, themselves, raised the issue of the vaccination's connection to Enrique's seizures to those health care providers, yet none of them identified DPT as causal.

VI. Conclusion

Petitioners must present adequate evidence of each of *Althen's* three causation factors. 418 F.3d at 1278. Evidence that a DPT vaccination occurred before an injury and could, theoretically, be neurotoxic is insufficient. Petitioners must demonstrate, either directly or through circumstantial evidence, that the vaccination more likely than not caused Enrique's seizures. In meeting their burden to demonstrate "but for" causation, petitioners must do more than show that the vaccination was "an insubstantial contributor in, or one among several possible causes of, the harm." *Pafford*, 451 F.3d at 1355. The absence of an alternative cause for Enrique's seizures is an insufficient basis for determining that the vaccine was causal. *Lampe*, 219 F.3d at 1361; *Grant,* 956 F.2d at 1149.

Petitioners have not demonstrated all of the three *Althen* factors by preponderant evidence. They have failed to show that Enrique's seizures were caused by his DPT vaccination on October 31, 1995. They have thus failed to establish a *prima facie* case for compensation and the petition for compensation is therefore DENIED. In the absence of a motion for review filed pursuant to RCFC, Appendix B, the clerk is directed to enter judgment accordingly.[60]

IT IS SO ORDERED.

s/Denise K. Vowell
Denise K. Vowell
Special Master

[60] Pursuant to Vaccine Rule 11(a), entry of judgment can be expedited by each party's filing a notice renouncing the right to seek review.