# In the United States Court of Federal Claims

## OFFICE OF SPECIAL MASTERS

No. 03-2820V
Filed: November 29, 2010

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| HARRY TEMBENIS and GINA TEMBENIS, administrators of the estate of ELIAS TEMBENIS, Petitioners, v. SECRETARY OF HEALTH AND HUMAN SERVICES, Respondent. | ) | Entitlement; Death; DTaP; Seizure disorder; epilepsy; Cause-in-fact; Complex febrile seizure; No alternative cause |

Ronald C. Homer, Conway, Homer & Chin-Caplan, P.C., Boston, MA for Petitioners.
Ryan D. Pyles, United States Department of Justice, Washington, D.C. for Respondent.

## DECISION ON ENTITLEMENT[1]

**LORD**, Chief Special Master.

## I. INTRODUCTION AND OVERVIEW

On December 16, 2003, Petitioner Harry Tembenis filed this case on behalf of his son, Elias Tembenis, under the National Childhood Vaccine Injury Act ("Vaccine Act" or "Act").[2] Petitioner filed a "Short-Form Autism Petition for Vaccine Compensation," and joined the Omnibus Autism Proceeding ("OAP"). On August 27, 2008, Petitioner filed a notice to proceed separately from the OAP, and he also filed an amended petition that alleged that a Diphtheria-Tetanus-acellular-Pertussis ("DTaP") vaccination administered on December 26, 2000, caused Elias to develop a seizure disorder that eventually led to his death. On November 13, 2008, the caption was amended to name Harry and Gina Tembenis, as administrators of Elias's estate, as

[1] The undersigned intends to post this decision on the United States Court of Federal Claims's website, in accordance with the E-Government Act of 2002, Pub. L. No. 107-347, 116 Stat. 2899, 2913 (Dec. 17, 2002). As provided by Vaccine Rule 18(b), each party has 14 days within which to request redaction "of any information furnished by that party (1) that is trade secret or commercial or financial information and is privileged or confidential, or (2) that are medical files and similar files the disclosure of which would constitute a clearly unwarranted invasion of privacy." Vaccine Rule 18(b). Otherwise, the entire ruling will be available to the public. Id.

[2] The National Vaccine Injury Compensation Program ("Vaccine Program") comprises Part 2 of the National Childhood Vaccine Injury Act of 1986, Pub L. No. 99-660, 100 Stat. 3755, codified as amended, 42 U.S.C. §§ 300aa-10 et seq. (2010). Hereinafter, individual section references will be to 42 U.S.C. § 300aa of the Vaccine Act.

Petitioners. An entitlement hearing was convened on October 23, 2009. The final post-hearing brief was filed on October 7, 2010. This case is now ripe for decision.

To receive compensation under the Vaccine Act, a petitioner must prove that either: 1) he suffered a "Table Injury"-- that is, an injury falling within the Vaccine Injury Table -- corresponding to one of his vaccinations, or 2) he suffered an "off-Table" injury that was actually caused by or "caused-in-fact" by a vaccine. See §§ 13(a)(1)(A), 11(c)(1); Shalala v. Whitecotton, 514 U.S. 268, 270 (1995); see also 42 C.F.R. § 100.3(a). In this case, Petitioners have alleged that Elias suffered an off-Table injury.

To prove an off-Table claim, a petitioner must provide evidence, in the form of medical records or reliable medical opinion, to establish "(1) a medical theory causally connecting the vaccination to the injury, (2) a logical sequence of cause and effect showing the vaccination was the reason for the injury, and (3) a proximate temporal relationship between the vaccination and the injury." Althen v. Sec'y of Dep't of Health & Human Servs., 418 F.3d 1274, 1278 (Fed. Cir. 2005). A petitioner must show that but for her vaccination she would not have been injured, and that the vaccination was a substantial factor in bringing about her injury. Shyface v. Sec'y of Dep't of Health & Human Servs., 165 F.3d 1344, 1352 (Fed. Cir. 1999). The vaccination only must be a substantial factor; it does not need to be the sole factor. Id.

The facts of this case can be summarized as follows. Elias received a DTaP vaccine. Within one day, he developed a fever, which led to a complex febrile seizure. Subsequently, Elias developed epilepsy. This fact pattern is commonly seen in the Vaccine Program. See Nance v. Sec'y of Dep't of Health & Human Servs., No. 06-730V, 2010 WL 3291896, *8 (Fed. Cl. Spec. Mstr. July 30, 2010) (citing cases); Simon v. Sec'y of Dep't of Health & Humans Servs., No. 05-941V, 2007 WL 1772062 (Fed. Cl. Spec. Mstr. June 1, 2007). Because special masters must base their decisions on both the particular facts and specific expert opinions in a case, a special master is not bound by other special masters' decisions in different cases; however, although those decisions are not binding, they may be persuasive authority. See Nance, 2010 WL 3291896, at *8.

At a post-hearing status conference, I discussed with the parties the applicability of the decision in Simon to this case. In Simon, the special master found that a DTaP vaccination caused a febrile seizure, which caused a child's epilepsy and subsequent death. The special master found that "on a probability scale, it is reasonable to conclude that where the vaccine is associated with fever and seizure and the seizure is of a complex nature, in the absence of proof of an alternative cause, it is the vaccine that is legally responsible for a subsequent epilepsy and residual sequela." Simon, 2010 WL 1772062, at *6. Because the record in this case was incomplete as to that theory, I requested additional briefing from the parties after the hearing. The parties agree that the DTaP vaccine can cause a fever, and that a fever sometimes can initiate a seizure. The issues here are whether a vaccine-induced febrile seizure can cause epilepsy, and if it can, whether Elias's initial febrile seizure caused his epilepsy.

Based on the medical literature and expert opinions submitted in this case, I find that Petitioners have established that, in circumstances like Elias's, a complex febrile seizure can lead to epilepsy. Further, Petitioners have established a logical sequence of cause and effect showing that Elias's vaccine-induced complex febrile seizure was a legal cause of his subsequent epilepsy. Although the record shows that Elias may have suffered from other conditions, unrelated to vaccination, that increased his risk of developing epilepsy, Respondent

has not shown that those conditions were at work here. In essence, Respondent's argument is that the vaccination did not cause the epilepsy because, based on the statistics, it is more likely that Elias's epilepsy was caused by a congenital condition than by a vaccine reaction. This fact, alone, is insufficient to negate causation. See Knudsen v. Sec'y of Dep't of Health & Human Servs., 35 F.3d 543, 550 (Fed. Cir. 1994) (discussing burden of proving an alternative factor in an on-Table case).

The medical literature shows that some uncertainty exists in the medical community as to the cause of the documented association between a complex febrile seizure and epilepsy. Although Petitioners have not proven that Elias's DTaP vaccination was a medically certain cause of his epilepsy and subsequent death, that is not the standard for causation under the Vaccine Act. In enacting the Vaccine Act, Congress made a deliberate choice not to impose on petitioners the burden of producing conclusive scientific proof that an unlikely event actually occurred. Instead a petitioner must only provide reliable scientific evidence to support vaccine causation. Moberly v. Sec'y of Dep't of Health & Human Servs., 592 F.3d 1315, 1325 (Fed. Cir. 2010). That policy choice guides my decision here.

After carefully evaluating and weighing all of the evidence, I find that Petitioners have satisfied their burden of making a prima facie case under Althen, and that Respondent has failed to prove that Elias's epilepsy and death were caused by an alternative factor. Accordingly, Petitioners are entitled to compensation under the Act.

## II. BACKGROUND

### A. Summary of the Relevant Medical Conditions

The parties' disagreement largely concerns what types of seizures have a causal relationship with epilepsy and whether Elias had that type of seizure. The parties also disagree over whether Elias suffered from a genetic condition that could have caused his epilepsy. The features and signs of the relevant medical conditions provide a context that is important to understanding the significance of Elias's medical history, which follows.

According to the literature filed by the parties, some types of seizures are associated with an increased risk of epilepsy, while others are not. The three types of seizures relevant to this case are benign febrile seizures, complex febrile seizures, and prolonged febrile seizures.

Febrile seizures are frequent in infancy, and most are termed "benign" because they are not associated with an increased risk of future seizures. Pet'r Ex. 42 at 1. Benign febrile seizures last only a few minutes, are followed by little or no postictal state (altered state of consciousness after a seizure), and involve bisymmetrical and tonic or tonic-clonic convulsions. Id.[3] The literature submitted by the parties did not discuss simple febrile seizures in detail. Nelson's Textbook of Pediatrics gives a general overview of seizures, which provides some more background. Nelson's Textbook of Pediatrics (Robert Kliegman, M.D., et al. eds., 18th ed. 2007). A simple febrile convulsion usually "is initially generalized and tonic-clonic in nature, lasts a few seconds and rarely up to 15 minutes, is followed by a brief postictal period of

[3] Tonic means characterized by continuous tension. Dorland's Illustrated Medical Dictionary (30th ed. 2002) at 1920. Tonic-clonic means both tonic and clonic, or exhibiting both continuous tension of the muscles and alternating muscular contraction and relaxation in rapid succession. Id. at 377, 1920.

drowsiness, and occurs only once in 24 [hours]." Id. at 2457. Additionally, febrile seizures are rare before nine months of age. Id. "Factors that are associated with a substantially greater risk of later epilepsy include the presence of complex features during the seizure . . ., an initial febrile seizure before 12 [months] of age, delayed developmental milestones, or a pre-existing neurologic disorder." Id. at 2458.

A complex febrile seizure, however, is not considered benign. The medical literature filed by the parties defined a complex seizure as a seizure with one or more of the following characteristics: more than 15 minutes' duration, more than one seizure in 24 hours, or focal features. Karin Nelson & Jonas Ellenberg, Prognosis in Children with Febrile Seizures, 61 Pediatrics 720-27, 721 (1978) (Pet'r Ex. 42-G); accord C. Huang & Y. Chang, The Long-Term Effects of Febrile Seizures on the Hippocampal Neuronal Plasticity – Clinical and Experimental Evidence, 31 Brain & Dev. 383-87, 383 (2009) (Resp't Ex. M). A complex initial seizure, along with a family history of afebrile seizures and a preexisting neurological abnormality, has been identified as a risk factor for developing epilepsy. Nelson & Ellenberg, supra, at 720. Petitioners argued that the medical literature supports a causal association between a complex initial febrile seizure and epilepsy.

The medical literature also discussed prolonged febrile seizures, which are a type of complex febrile seizure, and their association with epilepsy. The literature does not, however, provide a clear definition as to what qualifies as a "prolonged" seizure; some articles said the seizure must last more than 30 minutes, others said more than 20 minutes, and some, including one filed by Respondent, said more than 15 minutes. See, e.g., supra, Huang & Chang, at 383. One specific type of prolonged seizure is "status epilepticus," which is defined as "a continuous series of generalized tonic-clonic seizures without return to consciousness, a life-threatening emergency." Dorland's at 1756. Some studies have found that prolonged febrile seizures can cause brain damage, that such brain damage is visible on an MRI, and that this can lead to temporal lobe epilepsy. Respondent argued that, although complex seizures are associated with epilepsy, only prolonged febrile seizures that cause brain damage have a causal association with epilepsy.

Additionally, Respondent argued that Sotos syndrome could explain Elias's seizure disorder. According to literature submitted by both parties, Sotos syndrome is an overgrowth condition that can be identified by a few cardinal features: a characteristic dysmorphic facial appearance, learning disability, and overgrowth, especially in height and head-size. G. Baujat & V. Cormier-Daire, Sotos Syndrome, Orphanet J. Rare Diseases 2:36 (2007) (Resp't Ex. C); K. Tatton-Brown & N. Rahman, Sotos Syndrome, Eur. J. Hum. Genetics 15: 264-71, 264 (Pet'r Ex. 31-A). Some other features of Sotos syndrome are advanced bone age, seizures, hypotonia, macrocephaly, and recurrent episodes of otitis media. Baujat & Cormier-Daire, supra, at 2-3. [4] Testing can help identify whether a person has Sotos syndrome. An abnormality of the NSD1 gene occurs in at least 90% of Sotos syndrome cases. Tatton-Brown & Rahman, supra, at 268-69. Many persons with Sotos syndrome show specific abnormalities on an MRI. G. Bradley Schaefer et al., The Neuroimaging Findings in Sotos Syndrome, 68 Am. J. Med. Genet. 462-65, 463 (1997) (Pet'r Ex. 41) at 463; Baujat & Cormier-Daire, supra, at 4.

## B. Facts and Medical History

[4] Otitis media is the inflammation of the middle ear, often caused by a viral or bacterial upper respiratory tract infection. Nelson's at 2634. Hypotonia is a condition of diminished tone of the muscles. Dorland's at 900.

Elias was born on August 23, 2000. Pet'r Ex. 13 at 14. Until December 26, 2000, it appears that Elias was a healthy baby. Pet'r Ex. 2 at 12; Harry Tembenis Aff., Aug. 14, 2008, at 1 (Pet'r Ex. 25).

On December 26, 2000, Elias received his second dose of the DTaP vaccine. Pet'r Ex. 2 at 14. Elias's parents recall that there was some swelling around the injection site. Tembenis Aff. at 1-2; Pet'r Ex. 14 at 133 (doctor noted "imm[unization] site red RUE [right upper extremity]"). Early in the morning on December 27, 2000, Elias's parents found him seizing in his crib and took him to the emergency room ("ER"). Pet'r Ex. 14 at 132; Tembenis Aff. at 1-2. The seizure lasted about 15 minutes and was controlled with medication by the doctors in the ER. Pet'r Ex. 14 at 132. Five minutes later, Elias began seizing again with apnea, and according to the timeline in the medical records, the second seizure was stopped when Elias was given an Ativan IV and oxygen. Id. at 132-33. The medical records are unclear, but the second seizure lasted at least a few minutes, and it could have lasted as long as 15 minutes. Pet'r Ex. 14 at 132-33 (noting that the first seizure was stopped at 4:30 a.m., the second seizure started five minutes later, and the second seizure was stopped at 4:50 a.m.).

The medical records document Elias's condition on admission and his progression. On admission, Elias was cyanotic and actively seizing. Id. at 133.[5] His temperature was approximately 102 degrees. Id. at 132 (102 degrees); id. at 135 (102.3); id. at 139 (101.7). It was noted that Elias had no rash. Id. at 132. Elias's seizures involved bilateral arm twitching, with eyes rolled back with right side deviation. Id. at 139. He was in the postictal phase for about 30 minutes, with shallow breathing, posturing, and grunting. Id. Elias was admitted to the pediatric intensive care unit for monitoring. Id. at 133.

The neurology consult on December 27, 2000, noted that Elias had returned to baseline. Id. at 147. Dr. Paul Marshall was the consulting doctor. Id. at 121. The assessment was "[questionable] febrile seizure vs. seizure disorder vs. reaction to pertussis component of DTaP." Id. at 148. Dr. Marshall noted that, "The prolonged seizure [and] the young age (< 6 months) required additional circumspection re: question of chronic anticonvulsant." Id. at 138. Elias had a very high white blood cell count, which suggested that the seizure was related to fever from infection rather than fever from immunization. Id. Elias was administered ceftriaxone as a prophylactic, to be discontinued if bacterial cultures came back negative. Id. at 139.[6] Elias had no symptoms of an upper respiratory infection. Id. A CT scan of Elias's head and an EEG were normal. Id. at 139-40.

On December 28, 2000, the parents reported that Elias seemed to be completely himself. Id. at 143. Although the bacterial cultures came back negative, ceftriaxone was continued to rule out sepsis. Id. at 142. A handwritten note described Elias's condition as "s/p [status post] prolonged sz [seizure] assoc[iated] with fever [at] 4 [months of] age." Id. at 143. The note also stated that given the high "WBC [White Blood Cell count], this is more likely [secondary] to infection than simply a febrile rx [reaction] to his immunizations." Id. Later that day, it was found that Elias had otitis media, and he was to continue on ceftriaxone to treat it.

[5] Cyanotic means a bluish discoloration of the skin, usually indicating a lack of oxygen in the blood. Dorland's at 455.

[6] Ceftriaxone is an antibiotic that is effective against a wide range of bacteria. Dorland's at 315.

Id. at 144. Elias was discharged on December 29, 2000, with instructions to continue using phenobarbitol and to follow up with Dr. Marshall in one month. Id. at 121.

On January 29, 2000, Elias saw Dr. Marshall for a follow up visit. Dr. Marshall noted that the etiology of the seizure was uncertain, and he was concerned about a possible association with Elias's DTaP vaccination. Pet'r Ex. 2 at 62-63. Dr. Marshall recommended not giving the next DTaP dose until a follow up EEG was completed. Id. He noted that Elias's height was under the 75$^{th}$ percentile, weight was above the 95$^{th}$ percentile, and head circumference was above the 95$^{th}$ percentile. Id. Dr. Marshall also observed that Elias's father's head circumference was above the 95$^{th}$ percentile for adults. Id.

On February 6, 2001, Elias was admitted to the hospital again for seizures. The seizure lasted for approximately 20-25 minutes. Pet'r Ex. 14 at 327. When the seizure started, Elias's eyes rolled up and to the right and he had jerking of the right arm, but these focal aspects generalized to tonic-clonic movements of all four extremities. Id. at 327-28, 332. Elias's mother reported that he was afebrile when the seizure started, and the medical records noted that there was a question as to DTaP's role in causing the first seizure. Id. at 325. The diagnosis was status epilepticus. Id. at 328. Elias was discharged on February 7, 2001. Id. at 332. An undated, handwritten note in Dr. Marshall's records stated that, after Elias's February 6, 2001 seizure, his epilepsy was almost definitively established. Pet'r Ex. 2 at 63.

Elias again was admitted to the hospital for seizures on February 20, 2001. Pet'r Ex. 14 at 275. His temperature on admission was not noted, although he had a slight fever (99-100 degrees) the following day. Id. at 280. An EEG performed on February 21, 2001 was normal. Pet'r Ex. 14 at 289. An MRI taken on February 26, 2001 was mostly normal, but the report noted the MRI showed evidence of frontal lobe atrophy of uncertain etiology. Pet'r Ex. 2 at 64. Dr. Marshall was not certain if the atrophy was clinically significant. Id. at 65.

In March 2001, Elias did not receive his 6-month (third) DTaP vaccination. Id. at 67. Elias was noted to be "an alert, chubby, vigorous, handsome infant." Pet'r Ex. 20 at 143. His muscle bulk and tone were normal. Id.

Elias had seizures with some regularity over the next year. For example, on April 13, 2001, Elias had a febrile seizure. Pet'r Ex. 14 at 410. On August 28, 2001, Elias had a febrile seizure the day after he received pneumococcal and varicella vaccines. Id. at 388. In November 2001, Elias was seen because he had a series of afebrile seizures. Pet'r Ex. 2 at 73. In November 2001, Dr. Irina Anselm, Elias's treating neurologist, noted that Elias was a very attractive, non-dysmorphic child. Id.

In 2002, doctors observed that Elias displayed signs of other disorders. On January 31, 2002, Dr. Anselm noted that Elias had features of Pervasive Developmental Disorder ("PDD"), which is an autism spectrum disorder. Id. at 45-46. On March 13, 2002, it first was noted that Elias's condition was consistent with Sotos syndrome. Pet'r Ex. 4 at 9.

It appears that Elias may have had Sotos syndrome, but the medical records are not entirely clear on this point. Elias had some physical signs of Sotos syndrome, such as a large head and body. Elias had been diagnosed with PDD and developmental delay. Pet'r Ex. 2 at 22. On April 9, 2002, doctors observed that "he may have an advanced bone age;" Elias, who

was 20 months old, had a bone age of 28 months. Id. at 75.[7] Elias had recurring otitis media. Pet'r Ex. 6 at 14; Pet'r Ex. 2 at 24. On April 9, 2002, Elias had a genetics evaluation, which found that Elias's genetics were normal, but the evaluation did not test for the NSD1 abnormalities associated with Sotos syndrome. Pet'r Ex. 2 at 75; Pet'r Ex. 4 at 50.

On the other hand, Elias's condition was not entirely consistent with Sotos syndrome. Although Elias had a large head, Elias's father had a head size in the 95th percentile. And although Elias's head was big, it was not characteristically dysmorphic. Additionally, it appears Elias was a large but proportionally sized baby, rather than just tall as seen in Sotos syndrome. See Pet'r Ex. 2 at 36 (on October 21, 2002, height: 57th percentile, weight: 93rd percentile); id. at 62-63 (On January 29, 2000, height: under the 75th percentile, weight: above the 95th percentile, head circumference: above the 95th percentile).

Despite the uncertainty of the findings, over the next few years the medical records consistently mentioned diagnoses of Sotos syndrome. See, e.g., id. at 22, 40-41; Pet'r Ex. 15 at 176. However, two doctors appear not to have accepted entirely the Sotos syndrome diagnosis. On August 29, 2002, Dr. Anselm described Elias as having a history of "possible Sotos syndrome." Pet'r Ex. 2 at 40. On May 8, 2003, Dr. Anselm noted that the "issue with Sotos syndrome is still not settled." Id. at 28. The medical records show that Dr. Anselm never stated that she thought Elias had Sotos syndrome. In July 2003, Elias was taken to the Sotos Syndrome Support Association Annual Meeting. Dr. G. Bradley Schaefer, an expert on Sotos syndrome, evaluated Elias, and he diagnosed Elias as having a "Sotos-like" disorder, "possibly just macrocephaly." Pet'r Ex. 28 at 3.

On February 25, 2002, Elias started receiving his DTaP vaccinations again, but the record does not indicate the reason. Pet'r Ex. 2 at 7, 14. On September 1, 2002, Harry Tembenis wrote a letter to Elias's pediatrician, in which he noted that Elias had experienced almost 40 seizure bouts between his 4 month checkup and his 18 month checkup. Id. at 43. In the previous six months, Elias had experienced only two febrile seizure bouts, both caused by ear infections. Id.

On March 27, 2003, Elias had surgery to have tubes placed in his ears due to recurring otitis media that was unresponsive to therapy. Pet'r Ex. 6 at 14.

After December 2003, Elias had only occasional seizures. Pet'r Ex. 19 at 22 (note on May 24, 2005, stating that Elias had not had a seizure since December 2003); Pet'r Ex. 20 at 111 (one seizure in January 2006). Elias continued to be developmentally delayed.

On November 16, 2007, Elias went to the emergency room with a fever and a cough. Pet'r Ex. 16 at 12. While there, he had a seizure and went into status epilepticus, followed by bradycardiac arrest. Id. at 14. On November 17, 2007, due to the absence of any neurologic functioning on repeated exams and overwhelming organ failure, it was decided to withdraw aggressive life support. Id. at 36. Elias was pronounced dead six minutes later. Id. The immediate cause of death was multisystem organ failure, which was a consequence of cardiac arrest, which was a consequence of Elias's seizure disorder. Pet'r Ex. 15 at 393.

[7] The medical records state that the standard deviation for bone age is four months, and note that Elias's bone age was two standard deviations above average. Pet'r Ex. 2 at 75.

## C. Summary of the Parties' Arguments

Petitioners argued that they have satisfied their burden under the Vaccine Act. They argued that Elias showed no symptoms of a seizure disorder, had a DTaP vaccine that can cause a fever, had a fever that can cause seizures, had a seizure that can cause epilepsy, suffered epilepsy, and died as a result of his epilepsy. In the absence of an alternative cause, Petitioners asserted it was logical to conclude that the vaccine caused the epilepsy and death. Petitioners argued in the alternative that, if Elias were found to have a genetic disorder, the DTaP vaccine significantly aggravated that condition. See Pet'r Post-Hr'g Br., Aug. 27, 2010, at 47.[8]

Petitioners relied on the opinion of Dr. Marcel Kinsbourne. It was Dr. Kinsbourne's opinion that an initial complex febrile seizure can lead to epilepsy.[9] Dr. Kinsbourne described Elias's first seizure as a complex febrile seizure because of the focal nature of the seizure and the occurrence of a second seizure a few minutes after the first one. He asserted that an initial complex febrile seizure is associated with a greater risk of epilepsy, and that such a seizure can cause epilepsy. Based on the risk factors and the absence of an alternative cause, it was Dr. Kinsbourne's opinion that Elias's epilepsy was caused by his initial seizure, which was caused by Elias's DTaP vaccination. Dr. Kinsbourne supported this theory with literature submitted post-hearing.

Dr. Kinsbourne further opined that the record was unclear as to whether Elias suffered from Sotos syndrome. Although Elias was diagnosed with Sotos syndrome, the record shows that Elias did not show some of the cardinal characteristics of the disorder, and it seems that doctors may have backed away from this diagnosis. See Tr. at 46-50. In addition, Elias did not show the characteristic abnormalities of Sotos syndrome on an MRI. Pet'r Post-Hr'g Br. at 28. Even if Elias had Sotos syndrome, however, it would not have changed Dr. Kinsbourne's opinion.

In their post-hearing brief, Petitioners analogized this case to Sucher v. Secretary of Department of Health & Human Services, No. 07-58V, 2010 WL 1370627 (Fed. Cl. Spec. Mstr. Mar. 15, 2010). Petitioners argued that the facts of that case are similar to the facts here, and they noted that the same experts appeared in both cases. In Sucher, the special master found that the petitioner had established that a DTaP vaccination caused the vaccinee to develop a fever and a seizure, and that the seizure caused the vaccinee to develop epilepsy. The vaccinee had her first seizure within 24 hours of a DTaP vaccination, and had two five-minute seizures, followed by several staring and facial twitching episodes. Id. at *3. The diagnosis of those seizures was status epilepticus. Id. The special master found that the DTaP vaccine caused a fever; the fever caused a seizure; a complex febrile seizure can lead to epilepsy; the vaccinee's seizure was severe, complex, and prolonged and not short, simple, and benign; the

[8] Because I do not find that Elias had a genetic condition that could explain his seizure disorder, this decision does not further address Petitioners' significant aggravation argument.

[9] Dr. Kinsbourne also presented a theory about the pertussis toxin in DTaP having the same effects as in DTP. Dr. Kinsbourne and Petitioners claimed that the National Childhood Encephalopathy Study ("NCES") on DTP is applicable to DTaP because both vaccines contain a pertussis toxin. I find that application of the NCES DTP studies to DTaP is not warranted by any scientific evidence, and that such application is speculation. Like other special masters who have considered this theory, I do not find it to be reliable. See Simon, 2007 WL 1772062, at *7.

vaccinee had a genetic predisposition to having seizures; and the vaccination was a but for cause and a substantial factor in causing the vaccinee's seizure and subsequent epilepsy. Id. at *38-*40.

Respondent contested that Petitioners have satisfied their burden under the Vaccine Act. Respondent argued that Dr. Kinsbourne's opinion was unreliable and ill-adapted to the facts of this case. Under prong 1, Respondent maintained that an association between an initial complex febrile seizure and subsequent epilepsy is observed because many children who have complex febrile seizures also have a pre-existing, underlying brain abnormality. Therefore, a complex seizure does not cause subsequent epilepsy; it is just the first sign of an existing disorder. Respondent's position was that Petitioners cannot prove this is not true. Nonetheless, Respondent has conceded that DTaP can cause a fever, and a fever can cause a seizure.

Even if a complex seizure could cause epilepsy, Respondent argued that it did not do so in Elias's case. Respondent argued that Elias's first seizure was caused by otitis media because it was suspected that Elias's fever may have been due to an infection, and Elias received a diagnosis of otitis media two days after his initial seizure. Additionally, Respondent claimed that Elias did not have the type of seizure that can lead to epilepsy. Respondent argued that this case is different from cases like Simon and Sucher, because the initial seizure in those cases was diagnosed as status epilepticus and Elias's initial seizure was not. According to Respondent, Elias's epilepsy was more consistent with Sotos syndrome, and thus, there was an alternative explanation for Elias's epilepsy.

Respondent relied on the opinion of Dr. Max Wiznitzer. Dr. Wiznitzer contested that Elias had the type of seizure that can lead to epilepsy. He characterized Elias's seizure as too short to cause permanent brain damage. Dr. Wiznitzer also asserted that Elias's seizure was the result of an underlying brain disease, and the underlying brain disease caused the epilepsy. Dr. Wiznitzer opined that Sotos syndrome was clearly the cause of Elias's epilepsy.

## III. DISCUSSION

### A. Petitioner's Burden of Proof

A petitioner seeking to establish causation-in-fact must show, by a preponderance of the evidence, that but for her vaccination she would not have been injured, and that the vaccination was a substantial factor in bringing about her injury. Shyface, 165 F.3d at 1352. Mere temporal association is not sufficient to prove causation in fact; a petitioner must present a medical theory that is supported either by medical records or by the opinion of a competent physician. Grant v. Sec'y of Dep't of Health & Human Servs., 956 F.2d 1144, 1148 (Fed. Cir. 1992). Proof of actual causation must be supported by a sound and reliable "medical or scientific explanation that pertains specifically to the petitioner's case, although the explanation need only be 'legally probable, not medically or scientifically certain.'" Moberly, 592 F.3d at 1322 (Fed. Cir. 2010) (quoting Knudsen, 35 F.3d at 548-49); see also Grant, 956 F.2d at 1148 (medical theory must support actual cause).

The preponderance of evidence standard under the Vaccine Act requires proof that a vaccine more likely than not caused the vaccinee's injury. Althen, 418 F.3d at 1279. Causation is determined on a case-by-case basis, with "no hard and fast per se scientific or medical rules." Knudsen, 35 F.3d at 548. A petitioner may use circumstantial evidence to prove her case, and

"close calls" regarding causation must be resolved in favor of the petitioner. Althen, 418 F.3d at 1280.

Respondent may offer evidence of an alternative theory of causation to show that a petitioner has not satisfied an element of her case. Doe 11 v. Sec'y of Dep't of Health & Human Servs., 601 F.3d 1349, 1358 (Fed. Cir. 2010). When a petitioner bases her case in part on the absence of alternative causes, it is proper for the special master to consider evidence of alternative causes that is presented by Respondent in evaluating whether the petitioner has met her burden of proof. Id.

Once the petitioner has met the initial burden of proof, "the burden shifts to the government to prove '[by] a preponderance of the evidence that the petitioner's injury is due to a factor unrelated to the . . . vaccine.'" de Bazan v. Sec'y of Dep't of Health & Human Servs., 539 F.3d 1347, 1352 (Fed. Cir. 2008) (citations omitted). If the petitioner fails to establish a prima facie case of causation, however, the burden does not shift. Doe 11, 601 F.3d at 1357-58.

In evaluating whether a petitioner has presented a legally probable medical theory, "the special master is entitled to require some indicia of reliability to support the assertion of the expert witness." Moberly, 592 F.3d at 1324. Assessing the reliability of an expert's opinion in Vaccine Act cases can be challenging, because often there is little supporting evidence for the expert's opinion. See Althen, 418 F.3d at 1280 (noting that the "field [is] bereft of complete and direct proof of how vaccines affect the human body"). Consequently, most expert opinion will be an extrapolation from existing data and knowledge. The weight to be given to an expert's opinion is based in part on the size of the gap between the science and the opinion proffered. Cedillo v. Sec'y of Dep't of Health & Human Servs., 617 F.3d 1328, 1339 (Fed. Cir. 2010). A special master is not required to rely on a speculative opinion that "'is connected to existing data only by the ipse dixit of the expert.'" Synder v. Sec'y of Dep't of Health & Human Servs., 88 Fed. Cl. 706, 745, n.66 (2009) (quoting Gen. Elec. Co. v. Joiner, 522 U.S. 136, 146 (1997)).

## B. Prong 1

Under Althen prong 1, a petitioner must set forth a biologically plausible theory explaining how the vaccine received by the petitioner could cause the injury complained of. See, e.g., Andreu v. Sec'y of Dep't of Health & Human Servs., 569 F.3d 1367, 1375 (Fed. Cir. 2009). This requirement has been interpreted as "can the vaccine(s) at issue cause the type of injury alleged?" Pafford v. Sec'y of Dep't of Health & Human Servs., 451 F.3d 1352, 1355-56 (Fed. Cir. 2006). Evidence should be viewed by the preponderance of the evidence standard and "not through the lens of the laboratorian." Andreu, 569 F.3d at 1380. Although the theory of causation need not be corroborated by medical literature or epidemiological evidence, the theory must be sound, reliable, and reputable -- in other words, the theory need not be scientifically certain, but it must have a scientific basis. See id. at 1379-80.

In this case, the parties agree that DTaP can cause a fever, and a fever can sometimes lead to a seizure. Resp't Post-Hr'g Br. at 18. The main point of contention is whether a complex febrile seizure can lead to a seizure disorder or if only a prolonged febrile seizure can. This issue was briefed post-hearing, and Petitioners have submitted a supplemental report from Dr. Kinsbourne and some supporting medical literature. Respondent has submitted the rebuttal report of Dr. Wiznitzer and some additional literature, which challenged whether the submitted literature supports Dr. Kinsbourne's opinion.

The submitted literature shows that the medical profession recognizes that some classes of febrile seizures are not benign and instead are associated with a greater risk of epilepsy.[10] Although the association with greater risk has been documented, based on the literature in this record, it appears that the source of this risk is not entirely understood. Dubé 2004, supra, at 709; Huang & Chang, supra, at 383 ("the impact of early-life febrile seizures on the developing brain has not been fully resolved"); Nelson & Ellenberg, supra, at 720 (there is "uncertainty concerning the magnitude of risks facing children with febrile seizures"). One article stated: "The association between complex febrile convulsions and partial seizures . . . may reflect either a causal association or the presence of preexisting brain disease that is responsible for both the complex febrile seizures and later partial seizures." Annegers, supra, at 493. Another stated: "However, in studies in vivo one cannot directly test the hypothesis [that seizures beget seizures] and unravel its underlying mechanism because of the multiple sites at which the event may occur or the agent may act." Ben-Ari 2006, supra, at 140.

The discussion in the literature of the hypothesis that a complex febrile seizure can cause epilepsy shows that the theory is accepted by the medical community as one plausible explanation for the increased risk associated with a complex febrile seizure. The articles made clear that the increased risk is associated with a first seizure that is complex, which is a seizure with a long duration, focal features, and/or repeated episodes. See Nelson & Ellenberg, supra, at 721. Although some studies specifically explored the connection between a prolonged seizure and epilepsy, the articles did not limit causal association to the cases where the initial seizure is prolonged and results in status epilepticus.

Dr. Wiznitzer's opinion is that the submitted literature does not provide statistically significant experimental data showing that a complex febrile seizure can cause epilepsy. Although Dr. Wiznitzer is correct on this point, the literature nonetheless documents that complex febrile seizures are associated with a greater risk of epilepsy, and the medical community considers Petitioners' theory to be plausible. Petitioners' theory does not need to be directly proven by scientific studies. Rotoli v. Sec'y of Dep't of Health & Human Servs., 89 Fed. Cl. 71, 87 (2009), appeal docketed, 2010-5163 (Fed. Cir. Sept. 24, 2010) (finding that petitioner's theory was legally probable, despite lack of direct proof by scientific studies). Many of the articles Dr. Kinsbourne submitted show that scientists are still studying the association, and that scientists consider a causal relationship to be plausible. See Irma Holopainen, Seizures in the Developing Brain, 52 Neurochem. Int'l 935-47, 943 (2008) (Pet'r Ex. 42-F) at 943; Céline Dubé et al., Febrile Seizures: Mechanisms and Relationship to Epilepsy, 31 Brain & Dev. 366-71, 366, 368 (2009) (Pet'r Ex. 42-E) [hereinafter "Dubé 2009"].

Dr. Wiznitzer also opined that the increased risk of epilepsy following a seizure is caused by the presence of an underlying brain disease. The submitted literature confirms that Dr. Wiznitzer's theory is also one considered plausible by the medical community. Thus, the literature shows that both Petitioners' and Respondent's theories are plausible, but this does not

[10] This was observed in many of the articles filed. See Nelson & Ellenberg, supra (Pet'r Ex. 42-G); John Annegers et al., Factors Prognostic of Unprovoked Seizures after Febrile Convulsions, New Eng. J. Med., 316(9):493, 493 (1987) (Pet'r Ex. 42-A); Y. Ben-Ari, Seizures Beget Seizures: the quest for GABA as a Key Player, Crit. Rev. Neurobiol., 2006;18(1-2):135-44, 140 (Pet'r Ex. 42-B) [hereinafter Ben-Ari 2006"]; Céline Dubé et al., Serial MRI after Experimental Febrile Seizures, 56 Annals Neurol. 709-14, 709 (2004) (Resp't Ex. K) [hereinafter "Dubé 2004"].

cast doubt on the reliability or plausibility of Petitioners' theory. Dr. Wiznitzer's testimony shows only that Petitioners' theory of causation is not medically certain.

Dr. Wiznitzer appears to have interpreted the medical literature as limiting a causal association between a complex seizure and epilepsy to cases where the initial seizure is prolonged. Dr. Wiznitzer noted that some articles, including the Annegers article, discussed how a prolonged seizure can lead to brain cell death and temporal lobe epilepsy. See Annegers, supra, at 497; Resp't Ex. J at 1-2 (Dr. Wiznitzer's Supplemental Expert Report). One study found that prolonged febrile seizures can sometimes cause brain damage, and typically, that damage could be seen on an MRI. Dubé 2004, supra, at 709. Another study examined whether prolonged febrile seizures, the most common type of early-life febrile seizure, could cause temporal lobe epilepsy. See Céline Dubé et al., Temporal Lobe Epilepsy after Experimental Prolonged Febrile Seizures, 129 Brain 911-22, 911-12, 920 (2006) (Resp't Ex. L) [hereinafter "Dubé 2006"].

The Annegers article, while it discussed how a prolonged seizure can cause epilepsy, did not find that the only way a febrile seizure can lead to epilepsy is through cell death; it only mentioned that cell death/temporal lobe epilepsy is one mechanism that has been explored, and that limited data supported that mechanism. See Annegers, supra, at 497. The other studies reached much the same conclusion; they merely presented data from murine models showing that prolonged febrile seizures can sometimes cause brain damage and epilepsy, and they did not rule out other mechanisms of causation.

While Dr. Wiznitzer conceded that a seizure that was prolonged and sufficiently severe to cause brain damage could cause epilepsy, he challenged that a seizure of less than 30 minutes could do so.[11] Resp't Ex. J. Dr. Wiznitzer did not contest that a seizure of more than 15 minutes was a risk factor, but he noted that the medical literature showed no statistically significant increased risk of epilepsy for febrile seizures of less than 30 minutes. For example, for a seizure lasting 30 minutes or more, he stated that Nelson & Ellenberg showed no statistically significant increase in risk of epilepsy, and he opined that, "Obviously a seizure lasting 16-29 minutes would also not be associated with a statistically significant increased risk of subsequent epilepsy." Id. at 1.

Dr. Wiznitzer's opinion overlooked some important aspects of the literature. The Nelson & Ellenberg article stated that, "prolonged duration of febrile seizures was not a major determinant of subsequent epilepsy[;] [m]ore than 90% of children who developed epilepsy after febrile seizures had never had a febrile seizure which lasted as long as 30 minutes." Nelson & Ellenberg, supra, at 725-26. Nelson & Ellenberg found, however, that a complex first seizure was associated with an increased risk of epilepsy, and the age of onset was associated with an increased risk of subsequent febrile seizures. Id. at 725; see Annegers, supra, at 497 (reaching same conclusion). Additionally, the literature neither provided a clear definition as to what qualifies a "prolonged" seizure nor limited a causal association with epilepsy to only seizures that are prolonged.

After considering the opinions of Drs. Kinsbourne and Wiznitzer, along with the filed medical literature, I find that Petitioners have presented a biologically plausible theory of

[11] Elias's first seizure lasted for about fifteen minutes, and he had a second seizure a few minutes after the first one stopped. His second seizure lasted between five and fifteen minutes. Pet'r Ex. 14 at 132-33.

causation showing that DTaP can cause a febrile seizure, and that a complex febrile seizure can then cause epilepsy. In doing so, I reach the same conclusion as other special masters who have considered this same question. See Simon, 2010 WL 1772062, at *6. I recognize that the record shows the existence of some uncertainty as to the precise relationship between a complex febrile seizure and subsequent epilepsy. However, a petitioner is not held to the standard of medical certainty. In this case, Petitioners have satisfied by a preponderance of the evidence prong 1 of Althen.

## C. Prong 2

The second prong of Althen requires a petitioner to prove "'a logical sequence of cause and effect show[ing] that the vaccination was the reason for the injury.'" Andreu, 569 F.3d at 1374 (quoting Althen). The sequence of cause and effect must be "'logical' and legally probable, not medically or scientifically certain." Knudsen, 35 F.3d at 548-49. Under prong 2 of Althen, petitioners are not 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 of Dep't of Health & Human Servs., 440 F.3d 1317, 1325 (Fed. Cir. 2006). Instead, circumstantial evidence and reliable medical opinions may be sufficient to satisfy the second Althen factor. Capizzano, 440 F.3d at 1325-26; Andreu, 569 F.3d at 1375-77 (treating physician testimony).

### 1. The Expert Opinions

Dr. Kinsbourne opined that seizures beget seizures. He opined that the medical community accepts that an initial complex febrile seizure can cause epilepsy, although the precise mechanism of causation is still being studied. He described Elias's first seizure as complex because of the focal nature of the seizure and the occurrence of two seizures back-to-back. Pet'r Ex. 42 (Dr. Kinsbourne's Second Supplemental Report). When epilepsy follows a complex febrile seizure, subsequent seizures are likely to be complex partial seizures. Dr. Kinsbourne opined that Elias "has this type of seizure disorder." Id. It was Dr. Kinsbourne's opinion that Elias's complex febrile seizure caused his epilepsy.

To support his position, Dr. Kinsbourne relied on the Nelson & Ellenberg article to show that Elias's initial seizure was of a type that is associated with a greater risk of epilepsy. The authors discussed risk factors for developing epilepsy (afebrile seizures) when the initial seizure is febrile, and also risk factors for having recurring febrile seizures. Nelson & Ellenberg, supra, at 720 (identifying family history of afebrile seizures, preexisting neurological abnormality, and complicated initial seizure as risk factors for epilepsy). The article defined a complex seizure as a seizure with one or more of the following characteristics: more than 15 minutes' duration, more than one seizure in 24 hours, or focal features. Id. at 721; accord Huang & Chang, supra, at 383 (Resp't Ex. M). Although a duration of more than 15 minutes was a risk factor, the article noted that, "Ninety-one percent of children who developed epilepsy following febrile seizures (31 of 34 children) had never had a febrile seizure which lasted 30 minutes or more." Nelson & Ellenberg, supra, at 724.

The Annegers article documented the risk factors in developing epilepsy. In addition, Annegers found that age of onset has some influence on the development of subsequent epilepsy. The occurrence of a first febrile seizure before one year of age is weakly associated

with an increased risk of epilepsy. Annegers, supra, at 497. Dr. Kinsbourne testified similarly at hearing. Tr. at 101.

In response, Respondent argued that otitis media caused Elias's first seizure. Further, Dr. Wiznitzer contested Elias had the type of seizure that can lead to epilepsy. Dr. Wiznitzer characterized Elias's seizure as short, or at least not prolonged, and more characteristic of a benign febrile seizure than a prolonged seizure that can cause temporal lobe epilepsy. Dr. Wiznitzer asserted that the literature provided experimental evidence only for the proposition that a prolonged febrile seizure can lead to temporal lobe epilepsy. He also asserted that Elias's seizure was the result of an underlying brain disease, and the underlying brain disease caused the epilepsy. He contended that the underlying brain disease theory was proposed and established in the Annegers article.

Dr. Wiznitzer contended that the only way the seizure could have caused epilepsy was if the seizure was prolonged and damaged the brain. Based on the medical literature, Dr. Wiznitzer stated that had the seizure caused brain damage and epilepsy, the brain damage would be visible on Elias's MRI. Dr. Wiznitzer stated that Elias does not have any brain damage on his MRI, and therefore, the seizure did not cause brain damage and could not have caused Elias's epilepsy.

### 2. The Cause of Elias's Initial Seizure

Petitioners argued that the DTaP vaccination caused Elias to develop a fever, and the fever caused Elias to have a seizure. Petitioners argued that no other cause for Elias's fever and seizure appears in the record. Respondent claimed Elias's fever and seizure likely were caused by otitis media, which was one of Elias's diagnoses following his initial seizure. Respondent claimed Elias was given cefriaxone for his otitis media. Respondent also stated that the medical records note that Elias had a high white blood cell count, supporting a finding that infection caused the fever.

The record is not clear on whether otitis media preceded the seizures, as it was not until a few days after the seizure that Elias was diagnosed with otitis media. Elias received his DTaP vaccination at his four month well child visit. That record does not document an ear infection, Pet'r Ex. 2 at 12, although the presence of an infection is not always noticed by doctors, see Tr. at 85-88 (Dr. Kinsbourne stated that vaccines usually are not given in the presence of an infection, but infections are not always noticed). Further, when Elias was admitted to the hospital for his first seizure, otitis media was not noted in the records, and the records stated that Elias showed no signs of upper respiratory infection.[12] In addition, all of Elias's bacterial cultures taken upon admission to the hospital came back negative. The ER admission record does document, however, that the site of the DTaP injection was red. Pet'r Ex. 14 at 133.

One month after the seizure, Dr. Marshall evaluated Elias's condition. Dr. Marshall noted his concern that the DTaP vaccine might have caused the seizure, but made no mention of the otitis media as a potential cause. Pet'r Ex. 2 at 62-63. Dr. Marshall, who treated Elias in the hospital, knew about the elevated white blood cell count and the otitis media, see Pet'r Ex. 14 at 138 (Dr. Marshall noted the elevated white blood cell count suggested seizure was related

[12] An upper respiratory infection frequently accompanies otitis media. See Nelson's at 2634.

to infection), but he apparently felt that those facts were not sufficient to rule out DTaP as a causal factor.

Given the uncertainty in the timing of otitis media, and Dr. Marshall's apparent discounting of the significance of the otitis media, I find that otitis media most likely was not the cause of Elias's initial fever. Instead, I find it more likely that Elias's fever and subsequent seizure were caused by his DTaP vaccination.

### 3. Type of Initial Seizure: Elias's Initial Seizure Was a Complex Febrile Seizure

Elias, at four months of age, received his second DTaP vaccination on December 26, 2000. Within 12 hours, he developed a fever, and then started to have a seizure. He was taken to the hospital where doctors stopped his seizure. A few minutes later, he had a second seizure, which was controlled. The seizures had complex features: they lasted for approximately 15 to 20 minutes, they had focal components, and he had two seizures within 24 hours. The December 27, 2000 medical records confirm that the seizure's features were a cause of concern. Pet'r Ex. 14 at 138 (a note by Dr. Marshall stated "The prolonged seizure [and] the young age (< 6 months) required additional circumspection re: question of chronic anticonvulsant"); id. at 143 (Elias's condition described as "[status post] prolonged [seizure] assoc[iated] with fever"); id. at 133 (attending physician noted concern because Elias was not using his right side and he had right eye deviation); but see id. at 139 (progress note stated seizure activity "with bilateral arm twitching, eyes rolled back with [question about] right sided eye deviation").

The features of Elias's two seizures were more like a prolonged complex febrile seizure than a simple febrile convulsion. His seizures satisfied the criteria for a complex seizure specified in the medical literature, and his initial seizure was not like the brief, generalized tonic-clonic seizures that are typically associated with benign febrile seizures. See Pet'r Ex. 42 at 1; see generally Nelson's at 2457. In addition, Elias showed other risk factors identified in the submitted medical literature. For example, Elias had his first febrile seizure at four months of age, and if an initial seizure occurs before one year of age, that is a risk factor for epilepsy. See Annegers, supra, at 497.[13] Accordingly, I find that Elias's initial seizure was a complex febrile seizure.

The sequelae following Elias's initial seizure also appear to be related to the seizure. Elias developed both recurring febrile seizures and afebrile seizures. Id. ("Febrile seizures with focal features, repeated episodes, and long duration were strongly associated with partial unprovoked seizures"); Nelson & Ellenberg, supra, at 724 ("The most frequent sequela of an

[13] At hearing, Dr. Kinsbourne testified that seizures that begin in infancy tend to be more severe than ones that do not begin until later. Tr. at 101. The medical literature recognizes the occurrence of a febrile seizure before one year of age as a potential indicator of future problems. See Nelson & Ellenberg, supra (febrile seizure before one year of age associated with increased risk of future febrile seizures); Huang & Chang, supra, at 386 (the authors note that most febrile seizures do not impair global intelligence and memory function, but concerns remain "regarding those children who experience febrile seizures during the first postnatal year, having prior developmental delay, and pre- or peri-natal events").

initial febrile seizure was the recurrence of febrile seizures").[14] Some of Elias's subsequent seizures had focal components, although he also had recurring seizures that were generalized tonic-clonic seizures. Dr. Kinsbourne described this as a common sequela to an initial complex febrile seizure, and opined that Elias's epilepsy was caused by his initial seizure. I agree that this constitutes a logical sequence of cause and effect.

Respondent's counterarguments are unpersuasive. Respondent argued that because Elias's seizure was less than 30 minutes, there was no statistically significant risk of developing epilepsy. Although some articles recognize an association between prolonged febrile seizures and temporal lobe epilepsy, prolonged febrile seizures are not the only type of complex febrile seizure to lead to epilepsy. See Nelson & Ellenberg, supra, at 725-26 (stating that over 90% of children who developed epilepsy after febrile seizures had never had a febrile seizure that lasted 30 minutes or more).

Dr. Wiznitzer maintained that the only way a seizure could cause epilepsy was if it caused visible damage to the hippocampus. Dr. Wiznitzer opined that Elias's MRIs showed no signs of deterioration in the temporal lobe, and Dr. Kinsbourne agreed. See Tr. at 81-82, 117-19. Nonetheless, because the medical literature does not limit the causal association between a seizure and epilepsy to cases where an MRI shows damage to the hippocampus, the lack of damage does not negate the logical sequence of cause and effect in this case.

### 4. Sotos Syndrome

To cast doubt on whether a petitioner has satisfied her burden of proof, Respondent may offer evidence showing that a petitioner has not satisfied an element of her case. Doe 11, 601 F.3d at 1358. Here, Respondent maintained that Sotos syndrome was "a clinically manifest genetic syndrome" that fully explained Elias's seizure disorder. Resp't Post-Hr'g Br. at 22-23.

According to literature submitted by both parties, the cardinal features of Sotos syndrome are: a characteristic dysmorphic facial appearance, learning disability, and overgrowth, especially in height and head-size; other features include: advanced bone age, seizures, hypotonia, and recurrent episodes of otitis media. Baujat & Cormier-Daire, supra, at 2-3; Tatton-Brown & Rahman, supra, at 264. Although seizures are listed as a feature, the term "seizures" is not further defined, i.e., a single febrile seizure or epilepsy, and neither expert was sure of the incidence of seizures in individuals with Sotos syndrome. See Tr. at 50-51, 178.

Dr. Wiznitzer relied on the diagnosis in the medical records. He also pointed to the signs of Sotos syndrome in Elias: large head, developmental delay, hypotonia, a high forehead, and advanced bone age. Tr. at 173. Under cross examination, Dr. Wiznitzer agreed that Elias did not exhibit the common signs of Sotos syndrome in the neonatal period. Tr. at 160-164. He also conceded that the first mention of hypotonia was when Elias was six years old, but he claimed that "actual assessment of hypotonia is fraught with error," and the lack of mention of hypotonia in the medical records before age six "does not preclude the fact that he might not have had some hypotonia that was missed on exam." Tr. at 174-75. Dr. Wiznitzer also asserted that Elias's February 26, 2001 MRI showed signs of Sotos syndrome, although he

[14] The Nelson and Ellenberg article documents an increased risk of recurring febrile seizures and an increased risk of epilepsy in children who experience complex febrile seizures. Nelson & Ellenberg, supra, at 725.

appeared to concede that Elias's MRI did not show many of the neuroimaging anomalies that are frequently found in Sotos syndrome. Tr. at 177-78; see Baujat & Cormier-Daire, supra, at 4; Schaefer et al., supra, at 463.

Although Elias exhibited some of the signs of Sotos syndrome, his condition was not entirely congruent with it. Elias was described on numerous occasions as attractive and non-dysmorphic. Elias's overgrowth did not fit the Sotos syndrome pattern; he was big but proportionally so, and he was not abnormally tall at birth. His large head could be explained by ordinary genetics (his father's head was big) or by his autism spectrum disorder. Tr. at 40, 49. Elias had PDD, which resulted in developmental delay, but it does not appear that this necessarily was related to his other conditions. At one time, Elias had advanced bone age, but the literature stated this is a non-specific finding and not limited to persons with Sotos syndrome.

Some medical records stated that Elias had a diagnosis of Sotos syndrome, while others stated that he did not. One of Elias's treating neurologists, Dr. Anselm, did not view the Sotos syndrome diagnosis as definitive. Pet'r Ex. 24 at 14, 16. And, most pertinently, Dr. Scheaffer, an expert on Sotos syndrome, did not accept Elias's diagnosis of Sotos syndrome, and instead suggested that it was a "Sotos-like" disorder, "possibly just macrocephaly." Pet'r Ex. 28 at 3.

Although a DNA test became available for Sotos syndrome, Elias did not have it performed because insurance would not cover it. Pet'r Ex. 24 at 14. Prior genetic testing revealed no abnormalities. Pet'r Ex. 2 at 75; Pet'r Ex. 4 at 50.

Based on this record, I do not find it more likely than not that Elias had Sotos syndrome. Although he had features of Sotos syndrome and a diagnosis, it appears that doctors eventually decided against the diagnosis. Although it is a close call, I find that a preponderance of the evidence weighs against it.

Even if Elias did have Sotos syndrome, nothing in the record indicates that the seizures associated with it are particularly severe. Respondent argued that Elias's seizures were more consistent with Sotos syndrome, and that Elias did not have the type of seizure that can lead to epilepsy. However, Respondent did not present any evidence regarding the type of seizures typically experienced by someone with Sotos syndrome. Therefore, I am not persuaded that the seizures Elias experienced are of the type that ordinarily occur in persons with Sotos syndrome.

Based on the record as a whole, Petitioners have established a logical sequence of cause and effect. Although Elias suffered from a variety of problems, Petitioners have presented evidence from which I can conclude that, more likely than not, it was the DTaP vaccine that caused Elias's first seizure, and that that seizure led to Elias's epilepsy.

## D. Prong 3

To show causation, a petitioner must establish that the injury occurred within a time frame that is consistent with the theory of causation set forth. Pafford, 451 F.3d at 1358. A temporal relationship between receipt of a vaccine and the alleged onset of symptoms, without more, however, is insufficient to establish a causal relationship in a cause-in-fact case. Grant, 956 F.2d at 1148. What constitutes an appropriate temporal association is a question of fact and will vary with the particular theory of causation advanced. Id.; de Bazan, 539 F.3d at 1352.

Dr. Kinsbourne opined that the fever and seizures occurred within a medically appropriate time frame. Respondent has not contested that 12 hours between vaccination and the onset of seizures is medically reasonable. Additionally, this time frame is consistent with other cases that have considered the same question. See Simon, 2010 WL 1772062. Based on the medical literature and expert opinions, I find that Petitioner has satisfied prong 3.

## E. Evidence of an Alternative Cause

Once the petitioner has met the initial burden of proof, "the burden shifts to the government to prove '[by] a preponderance of the evidence that the petitioner's injury is due to a factor unrelated to the . . . vaccine.'" de Bazan, 539 F.3d at 1352 (citations omitted).

Respondent has not established, by a preponderance of the evidence, that Elias's initial seizure or his subsequent epilepsy was caused by an alternative factor. Although the record shows that Elias had PDD and that he had some symptoms of Sotos syndrome, Respondent has not established that either condition caused Elias's initial seizure or subsequent epilepsy. The reasons for my finding are clearly set forth in the previous sections, and need not be repeated here.

## IV. CONCLUSION

Petitioners have satisfied the legal requirements for proving that Elias's December 26, 2000 DTaP vaccination was a legal cause of his epilepsy and death. Respondent has not overcome Petitioners' evidence by proving an alternative cause. Therefore, I find that Petitioners have established entitlement to compensation under the Vaccine Act.

**IT IS SO ORDERED.**

s/ Dee Lord
Dee Lord
Chief Special Master