In the United States Court of Federal Claims

No. 05-1133V

(Filed Under Seal: January 30, 2013)
(Reissued for Publication: February 15, 2013)[1]

WILLIAM TAYLOR, parent of JOSEPH TAYLOR, a minor,	*	
Petitioner,	*	Vaccine Act; Motion for Review of Special Master's Decision; DTaP Vaccination; Infantile Spasms; Lack of Evidence of Causation; Althen Test.
v.	*	
SECRETARY OF HEALTH & HUMAN SERVICES,	*	
Respondent.	*	

Ronald Craig Homer, with whom was *Sylvia Chin-Caplan*, Conway, Homer & Chin-Caplan, P.C., Boston, Massachusetts, for Petitioner.

Ryan D. Pyles, with whom were *Stuart F. Delery*, Principal Deputy Assistant Attorney General, *Rupa Bhattacheryya*, Director, *Vincent J. Matanoski*, Deputy Director, and *Catherine E. Reeves*, Assistant Director, Torts Branch, Civil Division, United States Department of Justice, Washington, D.C., for Respondent.

OPINION AND ORDER

WHEELER, Judge.

[1] This opinion originally was issued under seal on January 30, 2013. Pursuant to Rule 18(b) of the Vaccine Rules of the United States Court of Federal Claims ("Vaccine Rules"), the parties had 14 days within which to propose redactions to the opinion prior to publication, but no such redactions were proposed. Accordingly, the opinion is herein reissued for publication, unsealed.

This case comes before the Court on review of Special Master Dee Lord's September 20, 2012 decision denying compensation to Petitioner, Joseph Taylor, through his father, William Taylor, under the National Childhood Vaccine Injury Act ("Vaccine Act"), 42 U.S.C. §§ 300aa-1 et seq. Petitioner alleges that the Diphtheria-Tetanus-acellular-Pertussis ("DTaP")[2] vaccine Joseph received on December 5, 2003 "caused him to suffer an off-Table encephalopathy, a seizure disorder, and subsequent developmental delays." Pet'r Br. 1. According to Respondent and the Special Master, Petitioner has failed to establish by a preponderance of the evidence that the DTaP vaccine caused his injury. The Court expresses its sympathy for the injuries that Joseph has endured, but for the reasons explained below, the Court affirms the Special Master's decision.

Factual Background[3]

Joseph Taylor was born to William and Audrey Taylor on June 10, 2003, and appeared healthy for the first six months of his life. On December 5, 2003, Joseph received the DTaP vaccine, the Inactivated Polio vaccine ("IPV"), the Haemophilus Influenzae type b ("Hib") vaccine, and the Hepatitus B ("hep B") vaccine. Later that day, Mrs. Taylor observed that Joseph seemed to be experiencing seizures, and took him to the Palomar Medical Center Emergency Room ("ER") in Escondido, California. The record from this visit reflects that Joseph had a temperature of 100.1 degrees, and notes that Joseph received vaccinations earlier in the day. He had no episodes during the ER visit and had normal chest x-rays, urinalysis, and cultures, and a complete blood count. Joseph was discharged, and his parents were instructed to follow up with his pediatrician in 24 hours.

The following day, the Taylors noticed Joseph experiencing similar episodes, and took him to the Children's Hospital in San Diego, as advised by the on-call doctor at their pediatrician's office. Joseph experienced seizure episodes while at the hospital, and was admitted for a full evaluation. During the course of his hospital stay, Joseph underwent a series of tests: he had a normal MRI and echocardiogram, negative urine, blood, and CSF cultures, but a "markedly abnormal electroencephalogram ["EEG"] due to a pattern

[2] As the name indicates, the DTaP vaccine is the acellular version of the pertussis vaccine. It has replaced the previously used whole cell pertussis vaccine, DTP. Ct. Ex. 2 at 1 n.2.

[3] The facts contained in the first three paragraphs of this section are uncontested. See Joint Post-Hr'g Mem., Jan. 26, 2012.

of electrical activity consistent with hypsarrhythmia.[4] Such findings may be associated with infantile spasms." Pet'r Ex. 6 at 252. Joseph continued to experience seizures and was started on adrenocorticotropic hormone ("ACTH"). His seizures decreased, and Joseph was discharged on December 12, 2003.

Joseph's treating physicians diagnosed him with infantile spasms, also known as West Syndrome, a particular type of seizure disorder. Pet'r Ex. 6 at 294. In later years, Joseph continued to be treated by a child neurologist and receive ACTH therapy. He underwent physical, speech, and language therapy for developmental and gross motor delays, expressive language disorder, and hearing loss. Joseph was hospitalized for his seizures twice in 2006. The most recent medical records indicate that Joseph has been clinically seizure free since February 2007, though he still has an abnormal EEG and a diagnosis of pervasive developmental delays.

Infantile spasms are a recognized epileptic condition. Resp't Ex. C at 1; Tr. II 169.[5] The disorder of infantile spasms typically commences in infancy, with an average age of onset at six months. Resp't Ex. C at 2. The disorder is characterized by a triad of a particular type of seizures, developmental retardation, and EEG abnormalities known as hypsarrhythmia. Pet'r Ex. 21 at 4. Infantile spasms are considered an epileptic encephalopathy,[6] which indicates that over a period of time, the seizing process results in subsequent mental deficits. Tr. II 46. Infantile spasms are frequently treated with

[4] Hypsarrhythmia is "an electro-encephalographic abnormality sometimes observed in infants, with random, high-voltage slow waves and spikes that arise from multiple foci and spread to all cortical areas." Dorland's Illustrated Medical Dictionary 908 (32d ed. 2012).

[5] There were two hearings before Special Masters in this case. "Tr. I" refers to the transcript of the March 16, 2007 hearing, and "Tr. II" refers to the transcript of the October 25, 2011 hearing.

[6] Encephalopathy is defined as "any degenerative disease of the brain." Dorland's Illustrated Medical Dictionary 614 (32d ed. 2012). The Vaccine Act gives the following, more detailed description:

> The term "encephalopathy" means any significant acquired abnormality of, or injury to, or impairment of function of the brain. Among the frequent manifestations of encephalopathy are focal and diffuse neurologic signs, increased intracranial pressure, or changes lasting at least 6 hours in level of consciousness, with or without convulsions . . . 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.

42 U.S.C. § 300aa-14(b)(3)(A).

ACTH, and although initial response to ACTH may be positive, relapses can, and often do, occur. Resp't Ex. C at 11-13; Pet'r Ex. 22 at 4.

Much of the literature regarding infantile spasms includes classification systems, and during this case, the parties devoted significant effort to addressing the various characterizations of infantile spasms. An earlier classification system categorized infantile spasms as idiopathic, cryptogenic, or symptomatic. Pet'r Ex. 31 at 2. Generally speaking, idiopathic and cryptogenic spasms are those of unknown origin or cause, and symptomatic spasms are those with identified causes of an abnormal brain condition. See id.; Resp't Ex. I at 3. A more recent classification system categorizes infantile spasms as genetic, structural/metabolic, or unknown. Pet'r Ex. 31 at 2 n.1. Under this system, all symptomatic spasms would fall under "structural/metabolic," and idiopathic and cryptogenic spasms would fall under either "unknown" or "genetic." Id.

Both Petitioner's and Respondent's experts conceded, however, that at bottom, the classification systems are of little assistance in determining the cause of infantile spasms. When asked on cross-examination whether Joseph Taylor's infantile spasms should be categorized under the older, or symptomatic/cryptogenic classification system, Petitioner's expert, Dr. David Griesemer, responded:

> Well, from my perspective that's an irrelevant question because these are arbitrary, poorly defined boundaries to begin with. And when I'm meeting with a family, I don't say, this is cryptogenic infantile spasms or this is symptomatic infantile spasms. I mean, it's infantile spasms and either we do or don't know what the cause of the problem is. This was a system that was identified a few decades ago in order to gather research data, I believe.

Tr. II 35. This testimony is consistent with Dr. Griesemer's statement at an earlier hearing that "[t]here is no question that Joseph Taylor could be placed in either group, cryptogenic or symptomatic." Tr. I 87. Similarly, Respondent's expert, Dr. Mary Anne Guggenheim, noted that it is the underlying cause of infantile spasms, and not the classification of the disorder, that determines a child's eventual outcome. Resp't Ex. O at 3.

History of Proceedings

Petitioner filed this Vaccine Act petition on October 19, 2005, alleging that the December 5, 2003 DTaP vaccine caused Joseph Taylor's seizure disorder. The Office of Special Masters ("OSM") assigned the case to Special Master John Edwards, who held an entitlement hearing on March 16, 2007. Special Master Lord held a second entitlement hearing on October 25, 2011, and afforded the parties an opportunity to supplement the record with additional evidence. Petitioner's and Respondent's experts each provided four written expert reports. See Pet'r Exs. 13, 19, 31, 37; Resp't Exs. A, I, O, U. Doctors Griesemer and Guggenheim testified at both of the entitlement hearings.

a. Petitioner's Expert, Dr. Griesemer

Petitioner submitted the expert reports and testimony Dr. David Griesemer. Dr. Griesemer is the chief of pediatric neurology at The Floating Hospital of Tufts University and director of the Child Neurology Fellowship Program. Tr. II 7. Dr. Griesemer is board-certified in neurology with special competence in child neurology and in clinical neurophysiology. Pet'r Ex. 14 at 1. In his review of Joseph's medical records, Dr. Griesemer noted that "[t]he development of infantile spasms in a child at 6 months of age is not diagnostically specific for a vaccine injury[,]" Pet'r Ex. 13 at 3, but he nonetheless concluded that Joseph "developed seizures and other neurologic impairment as a consequence of receiving vaccinations on December 5, 2003 . . . ," id. at 1. Dr. Griesemer asserted that there was a direct causal relationship between the immunizations and Joseph's seizures, pointing to various factors as the basis for this conclusion:

> [C]areful inspection of the records reveals no indication of gradual or insidious onset of infantile spasms, which is typically the case. Also, Joseph's seizures have proven refractory to control, which is not the case in most children with infantile spasms. This suggests that Joseph's seizures are not the result of an age-specific developmental abnormality but the result of an insult to the brain. Further, the presence of mild spasticity or "high tone" offers additional evidence, in addition to the residual seizure disorder, of brain dysfunction . . . . Finally, the very clear temporal correlation of seizure onset – within about 6 hours –

> of immunization suggests at the least that the seizures were triggered by his response to vaccination.

Id. at 3.

In a later report, Dr. Griesemer further explained the significance of the recurrent nature of Joseph's seizures, arguing that this factor classified Joseph's disorder as symptomatic, with the identified cause being vaccination. Dr. Griesemer cited medical literature indicating that "up to 38% of patients with cryptogenic spasms may display normal development" as support for his characterization that Joseph's "poor long-term outcome more closely resembles that of *symptomatic* infantile spasms[.]" Pet'r Ex. 19 at 2. Because Joseph did not display normal development, Dr. Griesemer concluded that Joseph's "response to vaccination [w]as the only neurologically abnormal event in his medical history," id., thereby establishing a causal relationship and rendering the infantile spasms symptomatic, Pet'r Ex. 31 at 2.

As additional support for the symptomatic classification, Dr. Griesemer pointed to an article by Sara Kivity, et al. (the "Kivity article"). Pet'r Ex. 28. The study concluded that "[e]arly treatment of cryptogenic infantile spasms with a high-dose ACTH protocol is associated with favorable long-term cognitive outcomes." Id. at 2. Based on this data, and the fact that Joseph received "immediate" treatment but nonetheless experienced "persistent seizures, persistent EEG abnormalities, and poor cognitive outcome," Dr. Griesemer surmised that the Kivity study "suggests the implausibility of Joseph having cryptogenic infantile spasms." Pet'r Ex. 31 at 4-5.

In his final expert report and throughout the 2011 hearing, Dr. Griesemer promoted a slightly different theory of causation, based on "additional scientific evidence of the relationship between pertussis toxin and its role in disrupting the balance between excitatory and inhibitory neurotransmitters in the brain." Pet'r Ex. 37 at 2; Tr. II 15-19. Dr. Griesemer explained that gamma-amniobutyric acid ("GABA") "is the predominant inhibitory neurotransmitter in the brain. It exerts inhibitory control of neuronal networks via the activation of $GABA_A$ and $GABA_B$ receptors." Pet'r Ex. 37 at 2 (citations omitted). He noted animal studies showing that the pertussis toxin has the ability to bind with subunits of $GABA_B$, thereby "disrupt[ing] $GABA_B$ receptor function [which] provides a mechanism for disturbing the balance between the excitatory and inhibitory neurotransmission in the brain." Id. at 2-3. Dr. Griesemer explained that this disturbance

of the $GABA_B$ receptor function causes[7] seizures and "may also compromise brain development." Id. at 3.

Dr. Griesemer stated that this theory of causation required the pertussis toxin to enter the brain through a breach of the blood brain barrier. Tr. II 40-42.[8] The pertussis toxin would then cause a direct toxic insult to Joseph's brain, he postulated, causing the development of infantile spasms. Pet'r Mot. 28-30. Dr. Griesemer conceded, however, that there was no clinical evidence of a breach of Joseph's blood brain barrier, such as signs of encephalopathy ("somnolence, irritability, inconsolability"). Tr. II 40, 77-78.

Dr. Griesemer was careful to highlight the differences between the whole cell pertussis vaccine (DTP) and the acellular version (DTaP). Pet'r Ex. 37 at 3. He explained that the acellular pertussis vaccine Joseph received was designed to "minimize some of the endotoxin effects and to reduce the amount of pertussis toxin that the brain is exposed to," Tr. II 43, and the "adoption of acellular pertussis vaccine (in DTaP) reduces or mitigates the available pertussis toxin, but the toxin remains central to producing the immunizing effect," Pet'r Ex. 37 at 3 (citation omitted). In discussing the toxicity of the vaccine, Dr. Griesemer admitted that he was not an expert in this area, and that he was "just saying we don't know with certainty that there is no endotoxin effect." Tr. II 43-44.

Despite the lack of evidence regarding a breach of Joseph's blood brain barrier as well as the toxicity of the DTaP vaccine, Dr. Griesemer maintained his conclusion that Joseph's infantile spasms and developmental delays were caused or substantially contributed to by the vaccine. In support, Dr. Griesemer referenced the following factors: (1) pertussis toxin disrupts intracellular function which can lead to increased seizures; (2) Joseph's treating physicians looked for alternative causes of infantile spasms and found none; (3) the "dramatic and acute onset of seizures," instead of the typically insidious development of infantile spasms; (4) the temporal proximity of his spasms to the administration of the vaccine; and (5) Joseph's slightly increased muscle tone, which is atypical in cases of infantile spasms. Tr. II 30-31. Petitioner argues that Dr. Griesemer's

[7] Dr. Griesemer's testimony at the 2011 hearing was slightly inconsistent with his previous statement regarding the reported causative role of disrupted receptor function: "When we encounter clinical settings in which the $GABA_B$ receptor is compromised or the G proteins are compromised, the effect is *increased* seizure activity." Tr. II 18 (emphasis added).

[8] During the 2007 hearing, Dr. Griesemer stated "I don't know that I have the experience to offer a very qualified answer about [the toxic effect of the vaccine on a child's brain]." Tr. I 100. As this theory of a direct toxic effect is precisely the theory now relied upon by the Petitioner, the Court presumes that Dr. Griesemer had acquired the requisite knowledge and experience in the intervening years.

medical opinion and the relevant medical literature on which it is based are sufficient to establish causation by a preponderance of the evidence.

b. Respondent's Expert, Dr. Guggenheim

Respondent offered Dr. Mary Anne Guggenheim as its expert. Resp't Exs. A-B. Although currently retired, Dr. Guggenheim is an expert in child neurology and practiced clinical pediatric neurology for many years. Tr. II 98-100. She is board-certified in pediatrics as well as psychiatry and neurology, with special competence in child neurology. Tr. II 98-101. From the outset of these proceedings, Dr. Guggenheim expressed her opinion that, despite the misfortune of Petitioner's disorder, there was no causal relationship between the vaccine and infantile spasms. Resp't Ex. A at 3. Dr. Guggenheim unequivocally stated that "there is no data to support Dr. Griesemer's allegation that the immunizations caused the [infantile spasms]." Resp't Ex. O at 5. She noted that "[b]ecause of concern that childhood immunizations might cause [infantile spasms], this particular hypothetical etiology has been carefully studied." Resp't Ex. I at 3. Thus, in forming her opinion, Dr. Guggenheim was able to draw upon numerous reports, studies, and texts in medical literature which have concluded that there is "no causative relationship between childhood immunization and infantile spasms." Resp't Ex. A at 3; accord, e.g., Resp't Exs. I, K, N, P, Q; Pet'r Ex. 21; Ct. Ex. 1. Through her reports and testimony, Dr. Guggenheim addressed each of the factors cited by Dr. Griesemer as bases for his assertion that the DTaP vaccine caused Joseph's injury, ultimately concluding that his theory is not biologically plausible and there is no causal link between the vaccine and Joseph's injury.

Dr. Guggenheim noted that the recurring nature of Joseph's seizures offered little probative value in determining causation. Joseph's treating physician, Dr. William Lewis, diagnosed him with cryptogenic infantile spasms, a diagnosis espoused by Dr. Guggenheim as well. Resp't Ex. A at 1. Dr. Guggenheim also addressed the Kivity article that Dr. Griesemer used to support his diagnosis of Joseph's infantile spasms being symptomatic:

> Dr. Griesemer uses the Kivity article and [another article] to support his allegation that if a child has cryptogenic (or unknown) [infantile spasms] they have a uniformly good outcome, if treated early, and thus Joseph cannot be classified as such. However, he does not refer to other publications

> (Glaze 1988, Riikonen, 2001) in which some cases of "cryptogenic" as well as "early treated" [infantile spasms] did not respond and had a poor outcome. These authors emphasize that it is the underlying cause, not just a classification of cryptogenic or early treatment that appears to determine outcome.

Resp't Ex. O at 3 (also explaining the concurrence of Drs. Frost and Hrachovy, "acknowledged leaders in the medical community regarding infantile spasms." Taylor v. Sec'y of Health & Human Servs., No. 05-1133V, 2012 WL 4829293, at *18 n.25 (Fed. Cl. Spec. Mastr. Sept. 20, 2012) ("Taylor")).

Addressing Petitioner's medical theory of causation, Dr. Guggenheim agreed that pertussis is indeed a neurotoxin which has the potential to interfere with the $GABA_B$ receptor function. Tr. II 138. As Dr. Griesemer indicated, however, the DTaP, or detoxified pertussis antigen, vaccine that Joseph received was designed "to reduce the amount of pertussis toxin that the brain is exposed to," relative to the former whole cell vaccine. Tr. II 43. Dr. Guggenheim expressed doubt on whether this small amount of pertussis toxin arguably present in DTaP would in any way cause seizures generally, much less Joseph's specific disorder of infantile spasms. Tr. II 109-15. In support of this position, Dr. Guggenheim pointed to the fact that there was no evidence of an aberration of Joseph's blood brain barrier, a necessary condition of Dr. Griesemer's theory of a direct toxic insult to Joseph's brain. Tr. II 121 (explaining that there was no indication of an edema on MRI scans and no elevation of spinal cord protein, "a general hallmark"). Additionally, there was no clinical evidence of a direct toxic insult to Joseph's brain. Dr. Guggenheim explained that if a child suffered a toxic insult to the brain severe enough to cause infantile spasms, he would present as acutely encephalopathic. See Tr. I 125-26; see also Tr. II 170 (explaining that an acute encephalopathy is one that manifests at the time the injury has occurred). She described a child as encephalopathic as one "who had obtundation, altered mental status, [and was] excessively irritable in the sense of not being able to be calmed."[9] Tr. II 120. In contrast, Joseph's medical records reflected that "[h]is neurologic examination was normal and he was alert and responsive without any evidence of acute encephalopathy." Resp't Ex. A at 1. Therefore, Dr. Guggenheim concluded that Joseph did not suffer a direct toxic injury to his brain.

[9] This clinical description is consistent with the Vaccine Act's definition of an encephalopathy. See *supra*, note 5.

According to Dr. Guggenheim, the mere fact that Joseph's treating physicians identified no other cause for his disorder is wholly unremarkable. Etiologically speaking, there is an excess of 200 putative causes of infantile spasms, but of these, only seventeen brain conditions are currently established as causing infantile spasms. Resp't Ex. I at 2. Joseph does not suffer from one of the seventeen brain conditions, and as such, the underlying cause for Joseph's infantile spasms and his associated developmental abnormalities is "presently unknown." Resp't Ex. O at 5.

Regarding Dr. Griesemer's reference to the "dramatic and acute onset" of Joseph's seizures, Dr. Guggenheim noted that such an event is not altogether inconsistent with the development and eventual diagnosis of infantile spasms. Although she agreed that the onset on infantile spasms is typically insidious, Dr. Guggenheim also explained that the early signs of infantile spasms and seizing often go unnoticed:

> Q: [Mr. Pyles] Is it a common habit of onset for infantile spasms to first present when a child is in transition between being asleep and being awake?
>
> A: [Dr. Guggenheim] Yes. That's the primary time when they will occur – either drowsiness or on awakening.

Tr. II 124-25; see also Tr. II 180 (Dr. Guggenheim) (noting that parents often do not recognize the first seizures because they are very subtle or brief); Resp't Ex. N at 5 ("The earliest manifestations of infantile spasms are subtle and may be easily missed, making it difficult to identify the precise age of onset."). This explanation was confirmed by Dr. Griesemer, who stated that "most times infantile spasms develop very insidiously and the onset is very difficult to recognize." Tr. II 31.

Dr. Guggenheim also pointed out that the temporal proximity of Joseph's spasms to the administration of the vaccine, a factor relied upon by Dr. Griesemer, belies his theory of causation. As a result of information gathered through her own clinical experience and a study conducted in collaboration with Drs. James D. Frost, Jr. and Richard A. Hrachovy, Dr. Guggenheim explained that infantile spasms do not develop within hours or days following a post-natal injury, but instead, there is a latency period of some months. See Resp't Ex. O at 4. In their 2008 study, these doctors observed that "[t]he interval between brain injury and the onset of infantile spasms ranged from 6 weeks to 11 months (mean = 5.1 months)," findings which "refute claims that a close

temporal association between an immunization and the onset of infantile spasms establishes causation." Resp't Ex. Q at 3. Therefore, Dr. Guggenheim concluded, "[t]he temporal proximity of a few hours between the DTaP vaccination and the onset of Joseph Taylor's infantile spasms is contrary to these findings" and cannot be used as a basis for causation. Resp't Ex. U at 4.

Regarding Dr. Griesemer's factor of "hypertonia," Dr. Guggenheim remarked that not only was there minimal evidence of increased muscle tone in Joseph's medical records, but such a symptom would be insignificant to a determination of causation. Tr. I 121. Dr. Guggenheim pointed out that Joseph's examining neurologist described him as having "normal tone," and stated that even the presence of such increased muscle tone would be a "red herring," id. at 121-122, as she "know[s] of no supporting data for the statement that increased muscle tone is atypical in infantile spasms," Resp't Ex. A at 3.

c. The Special Master's Decision

On September 20, 2012, Special Master Lord issued her decision denying compensation. The Special Master found that although it is unfortunate that Joseph suffers from West Syndrome, "Petitioner has not shown by preponderant evidence a reliable theory of vaccine causation or a logical cause and effect between Joseph's vaccination and his epilepsy." Taylor, at *1. Her conclusion was based, in part, on the following observations: "Boiled down to the essentials, the only evidence favoring [Petitioner's] theory is the *ipse dixit* of Petitioner's expert. Against th[is] theory, among other factors, are the medical literature finding no causal association, the significant gaps in Petitioner's expert testimony, and the countervailing testimony of Respondent's expert." Id. at *25.

On October 19, 2012, Petitioner filed a motion for review of the Special Master's decision. Respondent filed a response on November 19, 2012, asking this Court to affirm the decision. The Court heard oral argument on January 4, 2013.

Standard of Review

In Vaccine Act cases, the Court reviews the decision of the special master to determine if it is "arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law." Masias v. Sec'y of Health & Human Servs., 634 F.3d 1283, 1287 (Fed. Cir. 2011) (quoting 42 U.S.C. § 300aa-12(e)(2)(B)). The Court is highly

deferential to a special master's factual findings. Id. Thus, "[i]f the special master has considered relevant evidence of record, drawn plausible inferences and articulated a rational basis for the decision, reversible error will be extremely difficult to demonstrate." Id. at 1287-88 (quoting Hines v. Sec'y of Health & Human Servs., 940 F.2d 1518, 1528 (Fed. Cir. 1991)). On questions of law, however, the Court "owe[s] no deference to [] the special master." Althen v. Sec'y of Health & Human Servs., 418 F.3d 1274, 1278 (Fed. Cir. 2005). Accordingly, the Court reviews applications of law *de novo*. Masias, 634 F.3d at 1288.

Causation Standard

Under the Vaccine Act, a petitioner may prove causation in two different ways, depending on the alleged injury. Pafford v. Sec'y of Health & Human Servs., 451 F.3d 1352, 1355 (Fed. Cir. 2006). The first occurs when a petitioner proves that he received a vaccine appearing on the Vaccine Injury Table ("Table") and, within a prescribed time period, suffered a corresponding injury listed on the Table for that vaccine. See § 300aa-14. In such instances, causation is presumed, and the respondent bears the burden of proving that the actual cause of injury was a factor unrelated to the vaccine. Pafford, 451 F.3d at 1355 (citing § 300aa-13(a)(1)).

The second situation occurs when a petitioner proves that he has received a vaccine appearing on the Table, but sustained an injury not appearing on the Table or not occurring within the prescribed time period ("off-Table injury"). Id. Here, Petitioner seeks redress for his illness under the Vaccine Act's compensatory provision for an off-Table injury. As such, Petitioner must prove causation by satisfying the Althen test:

> [Petitioner's] burden is to show by preponderant evidence that the vaccination brought about [his] 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. If a petitioner satisfies all three prongs of the Althen test by a preponderance of the evidence, a *prima facie* case is established, which shifts the burden to the respondent to prove that a factor unrelated to the vaccine was the "sole substantial

factor in bringing about the injury." de Bazan v. Sec'y of Health & Human Servs., 539 F.3d 1347, 1354 (Fed. Cir. 2008) (citing Knudsen v. Sec'y of Health & Human Servs., 35 F.3d 543, 548 (Fed. Cir. 1994)).

Discussion

Petitioner challenges Special Master Lord's decision to deny compensation on four grounds: (1) for requiring direct proof of Petitioner's "mechanism of injury"; (2) for relying on epidemiological studies as support for finding no association between the DTaP vaccine and infantile spasms; (3) for failing to consider evidence that the DTaP vaccine can "trigger" infantile spasms; and (4) for determining that Petitioner had not met its burden of establishing a logical sequence of cause and effect. The Court addresses each of these grounds in turn and ultimately concludes that the Special Master's rulings were in accordance with the law and her factual findings were not arbitrary and capricious.

I. The Special Master Applied the Proper Standard in Finding That Petitioner Failed to Prove a Reliable Theory of Causation.

On review, Petitioner argues that the Special Master imposed a heightened burden of proof by requiring a showing of causation to the level of "scientific certainty" rather than by a preponderance of the evidence. Specifically, Petitioner alleges that "the special master required *direct proof* of a mechanism of injury, and in doing so, committed clear legal error." Pet'r Mot. 24-25.

Under the first prong of the Althen test, a petitioner must demonstrate a "persuasive medical theory" by "proof of a logical sequence of cause and effect showing that the vaccination was the reason for the injury." Althen, 418 F.3d at 1278 (internal quotations omitted). This "logical sequence" should be supported by "reputable medical or scientific information," such as scientific studies or expert medical testimony. Id. When evaluating a proffered theory of causation, a court must view the evidence under the more lenient preponderant evidence standard, and "not through the lens of the laboratorian." Andreu v. Sec'y of Health & Human Servs., 569 F.3d 1367, 1380 (Fed. Cir. 2009). This standard does not require "scientific certainty," id., but rather a showing of "more likely than not," Moberly v. Sec'y of Health & Human Servs., 592 F.3d 1315, 1322 (Fed. Cir. 2010). Moreover, a petitioner must demonstrate that this "reputable medical or scientific explanation . . . pertains *specifically to the petitioner's case* . . . ."

Id. (emphasis added). "Although probative, neither a mere showing of a proximate temporal relationship between vaccination and injury, nor a simplistic elimination of other potential causes of the injury suffices, without more, to meet the burden of showing actual causation." Althen, 418 F.3d at 1278 (citing Grant v. Sec'y of Health & Human Servs., 956 F.2d 1144, 1149 (Fed. Cir. 1992)).

Petitioner contends that he satisfied the first prong of the Althen test by offering "a reasonable, plausible biological mechanism as to how [Joseph's] DTaP vaccination may have caused functional damage to his brain," resulting in his seizure disorder. Pet'r Mot. 25. However, as the Federal Circuit clarified in Moberly, "proof of a 'plausible' or 'possible' causal link between vaccine and the injury . . . is not the statutory standard." 592 F.3d at 1322. Although Petitioner is correct in pointing out that a medical theory may be supported by expert medical testimony, the mere existence of such testimony is insufficient to satisfy the burden of showing a "persuasive" medical theory – this theory must also preponderate.

Through the expert reports and testimony of Dr. Griesemer, Petitioner established the general hypothesis that pertussis toxin can cause seizures through interference with neuronal signaling. See, e.g., Pet'r Ex. 37 at 3; Tr. II 20. Starting from this broad premise, Dr. Griesemer then concluded that the reduced amount of pertussis toxin present in the DTaP vaccine (as opposed to the DTP vaccine) caused Joseph's infantile spasms via a "direct toxic insult" to Joseph's brain. Pet'r Mot. 27-29. It bears repeating that Dr. Griesemer is unaware of the amount of pertussis toxin in the acellular vaccine, Tr. II 43-44, but notes that the DTaP "reduces or mitigates the available pertussis toxin," Pet'r Ex. 37 at 3. See also Tr. II 87 ("[W]e are dealing with a neurotoxin that has in the past caused enough problems that there have been intense efforts to reformulate it so it's less toxic.").

Although pertussis has been demonstrated to be a neurotoxin in medical literature, there was no evidence other than Dr. Griesemer's reports and testimony indicating that pertussis toxin could cause infantile spasms generally, much less indicating that the small amount of pertussis in the DTaP vaccine caused Joseph's infantile spasms specifically. Taylor, at *26. At the 2007 hearing, Dr. Griesemer cast further doubt on his pertussis causation theory when he stated "I don't know what component of the [acellular] vaccine exists that would trigger this mechanism that I've hypothesized." Tr. I 112. The Special Master was correct to require additional evidence showing that interference with GABA receptors at the hands of the DTaP vaccine can cause infantile spasms, as "a petitioner

must provide a reputable medical or scientific explanation that pertains specifically to the petitioner's case." Broekelschen v. Sec'y of Health & Human Servs., 618 F.3d 1339, 1345 (Fed. Cir. 2010). Therefore, Petitioner's argument that the Special Master erroneously applied a heightened burden of proof in violation of the law necessarily fails, as she merely required Petitioner to show precisely what the law requires. See W.C. v. Sec'y of Health & Human Servs., 2013 WL 151714, *8-9 (Fed. Cir. Jan. 15, 2013) (finding the special master was correct to require additional evidence showing that molecular mimicry can cause the influenza vaccine to significantly aggravate multiple sclerosis).

Moreover, even supposing that Petitioner had been able to establish a causal link between pertussis toxin and infantile spasms, the record is devoid of any evidence that this proposed mechanism was at work in Joseph's case. In his testimony, Dr. Griesemer explained that a necessary condition of a direct toxic insult is a breach of the blood brain barrier. Tr. II 40-42.[10] Dr. Griesemer conceded, however, that there was no clinical evidence demonstrating a breach of the blood brain barrier in Joseph's case, Tr. II 40, 77-78, an observation confirmed by Dr. Guggenheim, Tr. II 121, 172. This was precisely the situation in Moberly, where the expert also put forth the blood brain barrier theory as causative of the petitioner's seizure disorder following DPT vaccination. 592 F.3d at 1320-21. There, the Federal Circuit held that the special master did not err in rejecting the expert's theory of causation when the expert "conceded that there was no evidence in the record suggesting that the proposed mechanism was at work in [petitioner's] case." Id. at 1324.

Finally, Dr. Griesemer himself conceded that the evidence does not tilt in one direction or the other on whether Joseph's injury was "caused solely by an interaction in the brain with pertussis or pertussis interacting with a preexisting brain abnormality." Tr. II 36. Despite his extensive review of the records, Dr. Griesemer admitted that he could not discern why "in this particular case, the vaccine . . . caused [Joseph's] infantile spasms." Tr. II 77. These statements significantly undermine the reliability of Petitioner's causation theory.

[10] In the Motion for Review, Petitioner now attempts to argue that certain areas of the brain have no blood brain barrier, and therefore, no breach of said barrier would be necessary to Dr. Griesemer's theory of a direct toxic insult to the brain. Pet'r Mot. 29. As counsel for Respondent correctly pointed out at oral argument, this approach was not presented at the evidentiary stage and cannot now be countenanced by the Court. Moreover, even supposing this argument had been properly presented at an earlier stage, the onset of Joseph's seizures is inconsistent with a direct toxic insult to the brain, as discussed below.

The task of the Special Master is to determine, "based on the record evidence as a whole and the totality of the case, whether it has been shown by a preponderance of the evidence that a vaccine caused the [petitioner's] injury." Hibbard v. Sec'y of Health & Human Servs., 698 F.3d 1355, 1366 (Fed. Cir. 2012) (quoting Porter v. Sec'y of Health & Human Servs., 663 F.3d 1242, 1249-50 (Fed. Cir. 2011)). Upon evaluating the clinical record, the theories and testimony of both experts, as well as the corresponding medical literature, the Special Master determined that "the size of the gap between the scientific evidence presented by Dr. Griesemer and the theory of possible vaccine causation he expounded in [Joseph's] case is too large." Taylor, at *27 (citations omitted). The Court agrees. Accordingly, the Special Master did not err in concluding that the blood brain barrier theory did not support Petitioner's claim of causation, and necessarily, the first prong of the Althen test was not met.

II. The Special Master Did Not Err in Considering Epidemiological Evidence.

Next, Petitioner contends that the Special Master erred in relying on epidemiological studies "as support for her finding that there is not an association between DTaP vaccination and infantile spasms." Pet'r Mot. 31. "[T]he 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, and therefore, "a paucity of medical literature supporting a particular theory of causation cannot serve as a bar to recovery," Andreu, 569 F.3d at 1379. Accordingly, a claimant may, but need not, produce medical literature or epidemiological evidence to establish causation. Id. at 1379-80. However, as a claimant's theory of causation must be supported by a "reputable medical or scientific explanation," a Special Master may assess epidemiological evidence in "reaching an informed judgment as to whether a particular vaccination likely caused a particular injury." Id. at 1379 (citing Daubert v. Merrell Dow Pharm., Inc., 509 U.S. 579, 593-97 (1993)).

The essence of Petitioner's theory is that pertussis toxin caused Joseph's infantile spasms. Vaccines containing pertussis toxin have been administered in the United States for decades. Through its evolution, manufacturers have endeavored to minimize the amount of toxin in the vaccine, resulting in the low level of toxicity in the modern DTaP vaccine. The effects of the toxin on persons receiving this vaccine have been intensely studied over the years. Childhood immunizations are often administered within the medically established time frame for the onset of infantile spasms, and therefore, the hypothetical relationship between pertussis and the disease has been carefully examined.

Resp't Exs. I at 3-6; G at 3. The bevy of medical literature and epidemiological evidence submitted by the parties reinforces this state of affairs[11] and demonstrates that "a paucity of medical literature" is not an issue in this case. Given the wealth of information regarding a possible relationship between infantile spasms and pertussis vaccination, it would indeed be, as the Special Master noted, "irresponsible to ignore the result of the[] investigations." Taylor, at *28. Therefore, the Special Master did not err in considering epidemiological evidence, along with the clinical record, expert testimony and other medical literature, to reach her informed judgment that Petitioner's theory of causation was more unlikely than not.

Within the same section of his brief, Petitioner makes the paradoxical argument that the Special Master "abused her discretion in failing to consider the evidence in the epidemiologic studies that was supportive of an increased risk of infantile spasms following a pertussis vaccination." Pet'r Mot. 35.[12] In particular, Petitioner highlights two studies in the record as supportive of his theory that the DTaP vaccine caused Joseph's infantile spasms, Infantile Spasms and Pertussis Immunisation, ("Bellman article") and Temporal relationship modeling: DTP or DT immunizations and infantile spasms ("Goodman article"). Pet'r Mot. 33-34 (citing Resp't Exs. G, N). Petitioner seizes on non-statistically significant data mentioned within these articles as "probative," arguing that it "indicate[s] an increased risk of infantile spasms following a pertussis vaccination." Pet'r Mot. 34. Although the studies do show more reports of infantile spasms in the seven days following vaccination than in the next three weeks, the authors quickly disclaimed any hypothetical causal association with the following two explanations: (1) spasms would have occurred anyway because of the underlying disorder and were merely accelerated by the vaccine; and (2) heightened vigilance of parents following immunizations procedures. Taylor, at *28 (citing Resp't Exs. N at 4-6; K at 132); Resp't Ex. G at 3. The Special Master considered the so-called "probative" value of this data along with the other extensive evidence against a causal relationship between the vaccine and infantile spasms, and concluded that Petitioner's theory of causation was extremely unlikely. Id. at *28-29. This Court cannot say that the Special Master's weighing of the expert testimony was arbitrary and capricious. See W. C., 2013 WL

[11] Between the two parties, an excess of twenty different articles and studies were submitted into evidence, a count which does not include the extensive references to other sources within the expert reports.

[12] Remarkably, in the immediately preceding sentence, Petitioner states: "The special master made an error by relying on conclusions of the epidemiologic studies as support that a pertussis vaccination cannot cause infantile spasms." Pet'r Mot. 35.

151714, at *8-9 (finding that special master did not err in giving minimal weight to non-statistically significant data within studies when the bulk of the evidence weighed against petitioner's theory).

Moreover, as the Special Master observed, both the Bellman and Goodman articles concluded that pertussis, as received through DTP, or the whole cell version of the vaccine, has no causal relationship to infantile spasms. Resp't Exs. G at 3; N at 5-6. Joseph Taylor received the DTaP, or acellular, vaccine, which Dr. Griesemer himself noted was formulated "to reduce that amount of pertussis toxin that the brain is exposed to," in comparison to the DTP vaccine. Tr. II 43.[13] Thus, the "probative" value of (1) non-statistically significant data (2) within a study of a vaccine that Joseph did not receive, is minimal to non-existent.

III. The Special Master Carefully Considered All Relevant Evidence.

As a third objection to the Special Master's decision, Petitioner argues that the Special Master failed to consider "evidence relating to medical literature that supports a finding that the pertussis toxin is known to trigger infantile spasms." Pet'r Mot. 35. Specifically, Petitioner contends that the Special Master failed to consider a 1994 Institute of Medicine ("IOM") report which was referenced within the Goodman article, Respondent's Exhibit N. The IOM report was one of seventeen references within the Goodman article, all of which were consulted in arriving at the conclusion that there was "a no-effect relationship" between the DTP vaccine and infantile spasms. Resp't Ex. N at 4-7.

As Petitioner rightly points out, a Special Master "must consider all relevant and reliable evidence governed by principles of fundamental fairness to both parties." Vaccine Rule 8(b)(1), RCFC App. B. Here, the Special Master did just that, and thoroughly documented her review of the parties' positions and submitted evidence, demonstrated through her thoughtful and comprehensive 41-page opinion. As discussed in the preceding section, the Special Master carefully weighed the evidence in the record, including the Goodman article and its conclusion that no causal relationship exists between the DTP vaccine and infantile spasms. Taylor, at *28 (citing Resp't Ex. N). Respondent aptly states in its reply belief that "[t]his argument belies credulity, as the Decision is replete with citation of, and consideration of, the Goodman article." Resp't

[13] As the Federal Circuit has noted, "[t]he general consensus is that the older [DPT] vaccine is more dangerous than the newer [DTaP] version." Andreu, 569 F.3d at 1375 n.1.

Reply 15 (citing Taylor, at *5 n.10, *6 n.11, *22, *28, *29). Accordingly, Petitioner's third objection is wholly without merit, and the Court need not address it further.

IV. The Special Master Properly Concluded That Petitioner Failed to Establish a Logical Sequence of Cause and Effect.

Finally, Petitioner alleges that the Special Master erred in finding no logical sequence of cause and effect between the DTaP vaccine and Joseph Taylor's injury. Although she concluded that Petitioner failed to meet the first prong of the Althen test, in the interest of judicial efficiency, the Special Master also evaluated whether Petitioner's theory met the second prong of the Althen test. Under this prong, a petitioner must establish, by a preponderance of the evidence, "a logical sequence of cause and effect showing that the vaccination was the reason for the injury." Althen, 418 F.3d at 1278; Capizzano v. Sec'y of Health & Human Servs., 440 F.3d 1317, 1326 (Fed. Cir. 2006) ("'A logical sequence of cause and effect' means what it sounds like – the claimant's theory of cause and effect must be logical."). Although "definitive confirmation" of each aspect within this sequence is not required, the evidence must establish that the links in the causal chain are logical. See Hibbard, 698 F.3d at 1370-74 (O'Malley, J., dissenting) (noting a tendency in Vaccine Act cases to "increase the hurdles . . . [c]laimants must overcome"). Circumstantial evidence may be sufficient to meet this burden, but "[t]here may well be a circumstance where it is found that a vaccine *can* cause the injury at issue and where the injury was temporally proximate to the vaccination, but it is illogical to conclude that the injury was actually caused by the vaccine." Capizzano, 440 F.3d at 1327 (noting that evidence used to satisfy one prong of the Althen test may overlap to satisfy another prong). Accordingly, "neither a mere showing of a proximate temporal relationship between vaccination and injury, nor a simplistic elimination of other potential causes of the injury suffices, without more, to meet the burden of showing actual causation." Althen, 418 F.3d at 1278 (citing Grant, 956 F.2d at 1149).

Here, Petitioner argues that he has established a logical sequence of cause and effect through circumstantial evidence. Specifically, Petitioner submits that (1) Dr. Griesemer's testimony and reports that pertussis can cause infantile spasms, (2) the onset of Joseph's infantile spasms within hours of the vaccine, and (3) the lack of an alternative cause of Joseph's disorder makes it "illogical to conclude otherwise." Pet'r Mot. 37-38. As detailed above, Petitioner has failed to establish that the DTaP vaccine can cause the specific seizure disorder of infantile spasms. Thus, this first link in Petitioner's chain of cause and effect is missing. Additionally, as demonstrated by the evidence in the record,

the "circumstantial evidence" surrounding Joseph's injury contradicts the very conclusion of causation that Petitioner advocates.

Upon receiving the DTaP vaccination, Joseph did not manifest any symptoms indicative of a toxic insult to the brain, the theory advanced by Petitioner. There was no evidence of the "necessary" condition of a breach of the blood brain barrier, Tr. II 40, nor were there any signs of a generalized toxic insult to the brain, Tr. II 77-78, 120-21. Moreover, as Petitioner highlights, Joseph "developed symptoms of [infantile spasms] *within hours* of his pertussis vaccine." Pet'r Mot. 38. Dr. Guggenheim demonstrated through her testimony and peer–reviewed study that the onset of infantile spasms after an insult to the brain does not occur for a period of some weeks. Therefore, the temporal relationship between vaccine and alleged injury is wholly illogical when applied to Dr. Griesemer's theory of a direct toxic injury.

Additionally, the record evidence established that the peak onset age of infantile spasms is six months, see, e.g., Tr. II 89, 177, consistent with the age at which Joseph's infantile spasms became clinically recognizable.[14] Although the development of infantile spasms is typically insidious, both experts indicated that early signs of the disorder are subtle and often overlooked by parents. Thus, the temporal proximity of Joseph's vaccination and his injury is more suggestive of coincidence rather than causation.

As demonstrated by expert testimony and exhibits, infantile spasms are a unique seizure disorder with a broad range of potential causes, some established, some as of yet undiscovered. Resp't Exs. I at 2; J at 1. Here, the mere fact that no other cause has been identified for this unfortunate disorder is insufficient to show that the DTaP vaccine was more likely than not the cause of Joseph's suffering from infantile spasms. See Althen, 418 F.3d at 1278.

Finally, the Court notes that Petitioner dedicates substantial portions of his motion for review to reproducing excerpts from Joseph's medical records in an effort to bolster his causation theory. In particular, Petitioner relies on Andreu for the proposition that the testimony of treating physicians can be "quite probative" in establishing the second prong of the test. Andreu, 569 F.3d at 1375 (citing Capizzano, 440 F.3d at 1326); Moberly, 592 F.3d at 1323 (noting that causation may be established by a treating physician's reliable, persuasive opinion that a vaccine caused the petitioner's injury); cf. Cedillo v. Sec'y of

[14] Joseph received his vaccinations when he was five months and three weeks. See Joint Post-Hr'g Mem. at 4.

Health & Human Servs., 617 F.3d 1328, 1348 (Fed. Cir. 2010) (affirming that treating physicians' notations in medical records "simply indicat[ed] an awareness of a *temporal*, not causal, relationship").

Petitioner's reliance on Andreu is inapposite, however, as the evidentiary record in that case was significantly different from the case at bar. In Andreu, the Federal Circuit found that the testimony of a claimant's treating pediatric neurologist that he "unequivocally . . . believed that the DPT inoculation caused [the claimant's] seizures" was sufficient to establish a logical sequence of cause and effect. Id. at 1375-76. Additionally, in Andreu, the testimony of the admitting neurologist at the time of the claimant's initial hospitalization also supported a causal connection between the vaccine and the child's seizures. Id. 1376. Here, in stark contrast to the role of the physicians in Andreu, it was Dr. Griesemer alone who drew a causal link between Joseph's seizures and the DTaP vaccination, and not any of his treating physicians. As the Special Master pointed out, although there are multiple references to Joseph's immunization history in his medical records, the physicians merely note the temporal relationship between the vaccination and the onset of the seizures.[15] Therefore, these notations of a temporal relationship are not probative of causation.

In sum, Petitioner's theory of causation is speculative at best, and inconsistent with decades of medical research regarding pertussis vaccinations and infantile spasms. The Court agrees with the Special Master that "there is no logical reason to assume, and no evidence in the record to support, the idea that the remote possibility of coincidence was more remote than the remote possibility of vaccine causation." Taylor, at *30. Accordingly, the Court affirms the Special Master's ruling that Petitioner failed to establish a *prima facie* case entitling him to compensation.

Conclusion

For the foregoing reasons, the Special Master's September 20, 2012 decision denying compensation is AFFIRMED. This Court finds that the Special Master did not err in denying Joseph Taylor's claim. Accordingly, Petitioner's motion for review is DENIED.

[15] Discharge diagnosis from Joseph's initial hospital stay: "[i]nfantile spasms of idiopathic [unknown] origin," Pet'r Ex. 6 at 138; treating neurologist's assessment: "new onset of seizure disorder of unknown etiology. [Joseph] will be evaluated for infantile spasms[,]" id. at 256; emergency department report: "[c]oncern was *initially* for either an atypical febrile seizure or an immunization reaction to the vaccines that he received yesterday," id. at 267.

Pursuant to Rule 18(b) of the Court's Vaccine Rules, the parties may submit any proposed redactions of confidential or other protected information within fourteen days from the date of this opinion before it is released for publication.

IT IS SO ORDERED.

s/Thomas C. Wheeler
THOMAS C. WHEELER
Judge