In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

Filed: May 15, 2018

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MADISON ASTLE,	*	
	*	No. 14-369V
Petitioner,	*	
	*	
v.	*	Chief Special Master Dorsey
	*	
SECRETARY OF HEALTH AND HUMAN SERVICES,	*	Intracranial Hypertension; Chronic Headaches; Pseudotumor Cerebri; Varicella Vaccine.
	*	
	*	
Respondent.	*	
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Clifford J. Shoemaker, Shoemaker, Gentry & Knickelbein, Vienna, VA, for petitioner.
Glenn Alexander MacLeod, U.S. Department of Justice, Washington, D.C., for respondent.

RULING ON ENTITLEMENT[1]

I. Introduction

On April 30, 2014, Stephanie Astle filed a petition for compensation under the National Vaccine Injury Compensation Program ("the Program"),[2] on behalf of her then minor daughter, Madison Astle ("petitioner"), in which she alleged that the human papillomavirus ("HPV") and varicella vaccinations that Madison received on January 16, 2012, caused her to develop severe

[1] This decision will be posted on the website of the United States Court of Federal Claims' website, in accordance with the E-Government Act of 2002, 44 U.S.C. § 3501 (2012). **This means the Decision will be available to anyone with access to the internet.** As provided by 42 U.S.C. § 300aa-12(d)(4)B), however, the parties may object to the published Decision's inclusion of certain kinds of confidential information. Specifically, Under Vaccine Rule 18(b), each party has 14 days within which to request redaction "of any information furnished by that party: (1) that is a trade secret or commercial or financial in substance and is privileged or confidential; or (2) that includes medical files or similar files, the disclosure of which would constitute a clearly unwarranted invasion of privacy." Vaccine Rule 18(b). Otherwise, the whole decision will be available to the public in its current form. Id.

[2] The National Vaccine Injury Compensation Program is set forth in Part 2 of the National Childhood Vaccine Injury Act of 1986, Pub. L. No. 99-660, 100 Stat. 3755, codified as amended, 42 U.S.C. §§ 300aa-1 to -34 (2012) ("Vaccine Act" or "the Act"). All citations in this decision to individual sections of the Vaccine Act are to 42 U.S.C. § 300aa.

headaches and increased spinal fluid pressure.[3] Petitioner stated that since her vaccinations, she has "continued to experience headaches, and [] cannot handle noise, crowds or stress." Petition ("Pet.") at ¶2. Subsequently, petitioner filed an amended petition specifying that one or both of the vaccines cased "a cerebral venous thromboembolic event, which resulted in increased cerebrospinal fluid pressures resulting in a pseudotumor cerebri-like condition that has led to Madison's continued headaches and other problems." Amended Pet. at ¶ 2.

Respondent recommended against compensation, stating that petitioner failed to present adequate evidence to show that Madison's vaccinations caused any injury. See Respondent's Rule 4(c) Report ("Resp. Rept.") at 2, 11.

The parties filed expert reports in support of their respective positions. Petitioner filed two expert reports from neurologist Carlo Tornatore, M.D. Petitioner's Exhibits ("Pet. Exs.") 27 and 36. Respondent filed two expert reports from neurologist Peter M. Bingham, M.D. Resp. Exs. A, C. An entitlement hearing was held on November 7, 2017, in Washington, D.C., during which petitioner and the parties' respective experts testified.

After carefully analyzing and weighing all of the evidence and testimony presented in this case in accordance with the applicable legal standards, I find that petitioner has provided preponderant evidence that her varicella vaccination more likely than not caused her injuries, which satisfies her burden under Althen v. Sec'y of Health & Human Servs., 418 F.3d 1274, 1280 (Fed. Cir. 2005). Accordingly, I find that petitioner is entitled to compensation.

II. Issues to be Decided

The parties set forth the following facts in dispute: Whether petitioner's post-vaccine chronic headache syndrome is caused by intracranial hypertension; and, whether petitioner suffered a "cerebral venous thromboembolic event," following her January 16, 2012 vaccinations. Amended Joint Prehearing Submissions ("Am. Prehrg Sub.") dated Nov. 3, 2017 (ECF No. 96) at 1.

Further, the parties asked the undersigned to resolve whether petitioner has shown by preponderant evidence that her January 16, 2012 vaccinations caused her chronic headache syndrome. First, as required under Althen Prong 1, whether petitioner presented a medical theory showing that the HPV and/or varicella vaccine(s) can result in chronic headache syndrome due to persistent intracranial hypertension. Am. Prehrg Sub. at 1-2. Second, whether there is a logical sequence of cause and effect under Althen Prong 2 showing the HPV and/or varicella vaccination(s) caused Madison to suffer "a cerebral venous thromboembolic event" that resulted in persistent intracranial hypertension and subsequent chronic headache syndrome. Id. at 2. Third, whether petitioner has shown a proximate temporal relationship between her HPV and varicella vaccinations and her chronic headache syndrome under Althen Prong 3. Id.

[3] Since the filing of the petition, Madison has reached the age of majority, and the case is now captioned in her name.

III. Procedural History

Petitioner filed this case on April 30, 2014, alleging that Madison suffered, and continues to suffer from headaches, and has a decreased tolerance to noise, crowds, and stress, as a result of receiving the HPV vaccination on January 16, 2012. Petition at 1-2, ¶¶ 2-3. Petitioner filed the first set of medical records on May 16, 2014, and made subsequent filings of medical records on June 24, June 26, June 27, and July 31, 2014. Petitioner also filed a statement of completion on July 31, 2014. Petitioner then filed an Amended Petition on August 28, 2014, alleging that Madison continues to suffer from headaches and other issues as a result of a vertebral venous thromboembolic event, which increased cerebrospinal fluid pressures resulting in a pseudotumor cerebri-like condition. Am. Petition at 1-2, ¶¶ 3, 4. Respondent addressed petitioner's claims in a report filed pursuant to Vaccine Rule 4(c), wherein respondent argued that petitioner was not entitled to compensation under the Program. Resp. Report at 2.

The parties also filed expert reports in support of their respective positions. On March 27, 2015, petitioner filed an expert report from neurologist Dr. Carlo Tornatore along with his *curriculum vitae*. Dr. Tornatore concluded that "the vaccinations that Madison received on January 16, 2012, resulted in intracranial hypertension with subsequent chronic headaches." Pet. Ex. 27 at 18. Thereafter, on September 9, 2015, respondent filed an expert report from neurologist Dr. Peter M. Bingham along with his *curriculum vitae*. Supplemental expert reports were also filed by petitioner on February 8, 2016, and by respondent on July 12, 2016. Thereafter, petitioner filed additional medical records on September 2, and September 8, 2016, the latter accompanied by an amended statement of completion.

Petitioner filed her prehearing submission on September 11, 2017, and respondent filed his prehearing submission on October 6, 2017. The parties also filed a joint prehearing submission outlining the facts and issues that were and were not in dispute on October 16, 2017. As stipulated by the parties, there are no disputed facts in this case, and the parties adopt the facts as set forth in the respondent's Rule 4(c) Report. Joint Prehearing Submission at 1. The parties agree that Madison's alleged injury is not set forth on the Vaccine Injury Table, nor do they dispute whether she received these vaccines in the United States. Additionally, the parties do not contest that Madison has suffered from the residual complications of the vertebral venous thromboembolic event for more than six months since the administration of the HPV vaccination.

IV. Summary of Medical Records[4]

[4] Although the undersigned considered the record as a whole in reaching this decision, this section provides only a brief summary of relevant facts. A more detailed recitation of the facts may be found in respondent's Rule 4(c) Report and the parties' expert reports. Also, petitioner submitted several affidavits, including Pet. Ex. 48 (affidavit of Stephanie Astle) and Pet. Ex. 49 (affidavit of Madison Astle). The undersigned reviewed the affidavits, but in forming her opinions, she generally relied on the facts set forth in the contemporaneous medical records, as she finds these records to be reliable. See Reusser v. Sec'y of Health & Human Servs., 28 Fed. Cl. 516, 523 (Fed. Cl. 1993) (holding that "[W]ritten documentation recorded by a disinterested person at or soon after the event at issue is generally more reliable than the recollection of a party

In their amended joint prehearing submissions filed on November 3, 2017, the parties stipulated to the medical summary and facts set forth in the Respondent's Rule 4(c) Report, however, the parties did not limit the relevant facts to those solely set forth in the report. The undersigned also find the following facts to be relevant to her decision.

Madison and her twin sister were born on December 26, 1998, at 30 weeks gestation. Their APGAR Scores were 7 and 9, respectively. Madison's weight at birth was 2.75 pounds, but by February 1, 1999, she weighed 4.2 pounds. Pet. Ex. 22 at 85. During her early childhood, she was diagnosed with asthma, sinusitis, and gastroesophageal reflux disease, but otherwise Madison had no significant health problems. Id. at 69-85. By age 12, Madison's only health issue was asthma, which was treated with medications. Id. at 64-67.

On January 16, 2012, at age 13, Madison received her second HPV vaccine and a varicella vaccine. Pet. Ex. 22 at 3. Two days later, on January 18, 2012, she presented to her pediatrician with complaints of a painful, red and swollen right arm at the site of vaccination. Madison had a "quarter size erythema" at the vaccination site. At that visit, Madison's diet was ok, and she was sleepy. There was no mention of headache. Treatment with Tylenol and Motrin was recommended. Id. at 11. Madison returned to her pediatrician for a follow-up visit on January 24, 2012. At this visit, Madison's arm remained red and swollen, and the area of redness extended below her elbow. For the first time since vaccination, Madison also complained of headaches, decreased appetite, and sleep disruption. Id. at 9. She was diagnosed with cellulitis of the arm post-vaccination and was treated with antibiotics. Id. On January 25, 2012, a telephone call from Madison's family indicated that the area of redness on her arm was getting larger, and prednisone was ordered. Id. at 98.

Madison was next seen by her pediatrician on January 30, 2012. She was "taking ibuprofen around the clock, unable to concentrate, had intermittent neck pain, was not eating well, and sleeping more than usual." Pet. Ex. 22 at 9. The area of redness at the vaccine site was improved, but she still had discoloration and bruising at the site. Id. Diagnostic tests were ordered, including magnetic resonance imaging ("MRI") and magnetic resonance venography ("MRV"). Id. MRI performed on February 3, 2012, was normal except for "left sphenoid sinusitis." Pet. Ex. 10 at 26. MRV[5] performed the same day, however, showed "question of upper left jugular vein thrombosis or occlusion. Clinical correlation suggested." Id. at 63.

Two days later, on February 5, 2012, Madison was seen in the emergency room ("ER") at Sinai Hospital of Baltimore, and she was admitted to the hospital by pediatric neurologist Dr. Edward Gratz. His report provided a thorough history, and is set forth below, as follows:

History of Present Illness:

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to a lawsuit many years later.").

[5] A MRV is an "imaging modality for the evaluation of the venous system," similar to a MRI but used to look at blood vessels, specifically venous blood vessels. IMAGING OF THE CARDIOVASCULAR SYSTEM, THORAX, AND ABDOMEN 115 (Luca Saba ed., 2017).

> This is the [first] Sinai Hospital of Baltimore admission for this 13-year-old, right-handed girl who was in her usual state of excellent health until [January 17, 2012], one day after receiving each [HPV] [v]aricella injection, right deltoid. She developed a local reaction with erythema, warmth and local tenderness. She experienced the onset of headache at that time described as a bilateral frontal pressure-like discomfort, throbbing and pounding, intermittent. The headache was worsened with routine activity, and she preferred to lie down and rest, but denied significant sensitivity to light or noise. There was no associated dizziness or nausea. She, however, was unable to participate in her usual activities and has not attended school since [January 18, 2012]. There are no preceding or accompanying visual, motor, or sensory symptoms. The headache has remained continuous, but fluctuating in severity, but has always remained moderate to severe. Local reaction was initially treated with Benadryl and hydrocortisone cream for several days, without improvement. She initially was treated with a [five] day course of Bactrim and subsequently a ten day course of clindamycin which was discontinued on [February 2, 2012]. Because of the persistent headache, she was seen in the emergency room at Sinai Hospital on [February 3, 2012]. Her headache initially did not respond to IV Toradol 30mg, two doses at approximately [six] hours apart. Because of concerns regarding thrombophilia associated with [HPV] vaccine, an MRI of brain and MR venogram were obtained and normal by report.[6] She was also seen by ophthalmology consultant who noted healthy ophthalmological examination without evidence of papilledema. Returning from MR imaging studies, she was given metoclopramide 10 mg IV, followed by DHE 0.25mg, with decrease in the severity of her headache from [seven] to [eight out of ten] to approximately [one out of ten]. She went home from the emergency room at approximately 05:00 a.m., on [February 4, 2012]. She slept; however, by approximately 2:00 p.m., the headache recurred and has remained [eight out of ten] since that time. She returned to the emergency room and [was] subsequently admitted for treatment of headache. There had been no history of previous significant headache or migraine. No reported family history of migraine.
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> Pet. Ex. 10 at 93.

Madison was discharged from Sinai Hospital on February 9, 2012. Several weeks later, on February 22, 2012, Madison returned to the ER at Sinai Hospital and was again seen by Dr. Gratz. He noted that about one week after her prior hospital discharge, Madison's headache became more severe and over the past 48 hours, her headache caused pain described as 8/10, with intermittent throbbing, some nausea, and was worse with activity. She also had sensitivity to light and noise. Her physical exam was normal. Dr. Gratz ordered IV Toradol and valproic acid, as well as metoclopramide and dihydroergotamine ("DHE"). A small dose of morphine was also administered. After treatment, Madison's headache improved, and she was discharged

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[6] In fact, the report by Dr. Frachtman states: "Question of upper left jugular vein thrombosis or occlusion." Pet. Ex. 10 at 68.

to outpatient management to continue on preventative therapy with topiramate and Depakote, as well as tapering doses of prednisone, and analgesics. Pet. Ex. 6 at 8-11.

Madison was seen by Dr. Gratz for follow-up care on March 16, 2012. Despite medication, she continued to have chronic daily headaches which worsened with routine activity and which prohibited her from attending school.[7] Several times weekly, her headaches were more severe, usually in the evenings. Madison's severe headaches were bifrontal in location and characterized by throbbing pain, with sensitivity to sound. Dr. Gratz adjusted Madison's medication. Pet. Ex. 10 at 60-62.

Due to persistent headache, Dr. Gatz readmitted Madison to Sinai Hospital on March 27, 2012, for a lumbar puncture, in order to evaluate the possibility of pseudotumor cerebri without papilledema. The lumbar puncture was performed and noted to be "mildly traumatic." Opening pressure was 30 [cmH2O]. CSF revealed approximately 4000 red blood cells, 5 white blood cells, and elevated protein of 50. Lyme antibody studies and Epstein-Barr titers were all negative. Pet. Ex. 10 at 77-80. Madison did not experience relief of her headaches after the lumbar puncture procedure. Dr. Grazt diagnosed her with chronic persistent headache, and he initiated treatment with 250 mg of Diamox twice daily for "presumptive therapy of pseudotumor cerebri without papilledema." Pet. Ex. 10 at 77-80. Dr. Grazt also requested consultation by pediatric infectious diseases. Infectious disease consultant, Dr. Susan Lipton, evaluated Madison and reported that she had "subjective, debilitating, severe headaches since vaccinations with human papillomavirus and Varicella on 01/16/2012." Like Dr. Gratz, Dr. Lipton noted, "There is evidence of pseudotumor with the increased intracranial pressure even though there is no funduscopic evidence of this." Id. at 90.

A repeat MRV performed March 28, 2012, showed, "minimal peripheral irregularities in the left sigmoid sinus, similar to the prior examination on February 3, 2012, which can denote chronic changes versus anatomic variant. There is now interval recanalization of the left distal internal jugular vein. The left distal jugular internal vein is smaller in caliber in comparison to the right." Pet. Ex. 10 at 66.

Subsequently, Madison was evaluated by a pediatric endocrinologist, Dr. Judith McLachlan, due to a decreased calcium level reported from her prior laboratory results (calcium decreased at 7.9 on February 28, 2010). Repeat labs drawn April 23, 2012, confirmed that Madison had a low calcium level of 8.7, as well as decreased parathyroid hormone level less than 3, which was very low. Pet. Ex. 10 at 52-53. These findings suggested that Madison had hypoparathyroidism and Hashimoto's thyroiditis. Id. at 52; Tr. 197. An ophthalmology consult was also obtained, and Madison had a normal exam with no evidence of papilledema.[8]

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[7] Madison has never returned to school and instead received home schooling. Tr. 16.

[8] Papilledema is optic disc swelling caused by increased intracranial pressure. It is the "hallmark of PTCS"." Resp. Ex. D6 at 2. Dr. Bingham also referred to it more simply as a "swollen optic nerve." Tr. 182. However, pseudotumor cerebri can occur in the absence of papilledema, although generally patients without papilledema may have lower lumbar puncture opening pressures. Pet. Ex. 56 at 2.

Madison next followed-up with Dr. Grazt on May 3, 2012, where it was noted that she continued to have "intractable chronic daily headaches." She had not been able to return to school since January 18, 2012, but did have a home school teacher. Madison reported exacerbation of her headaches with activity such as homework, meeting with her teacher, or walking. She also reported increasing insomnia. Dr. Grazt concluded that Madison had "chronic persistent headaches with associated elevated increased intracranial pressure suggesting the possibility of pseudotumor cerebri without papilledema. Pseudotumor cerebri has been reported to occur secondary to hypoparathyroidism, although the pathophysiology was not well understood." Pet. Ex. 10 at 56-59.

Madison was evaluated by Dr. Howard Jacobs at the University of Maryland Pediatric Headache Clinic on December 13, 2012. Pet. Ex. 22 at 158. At this time, Madison was 14 years old and continued to experience daily headaches, with her pain rated as 7/10 up to 9/10. She had been out of school since January 2012 due to headache. She had taken a number of medications, including tramadol, Aleve, amitriptyline, Lexapro, Depakote, acetazolamide, Topamax, Migranal, Treximet, and Maxalt. She was diagnosed with chronic migraine, and Dr. Jacobs noted that she "may also have a high-pressure component to her headache although she does not have pseudotumor cerebri." Pet. Ex. 22 at 159. Dr. Jacobs initiated treatment with propranolol, Amerge, and prednisone.

At her primary care visit on January 18, 2013, Madison was noted to have lost 20 pounds over the last year. In February 2014, she was again seen by her primary care physician with a complaint of headaches. At that time, she was taking tramadol for her headaches.

In May 2014, now age 15, Madison was seen at Johns Hopkins Bayview Clinic by neurologist Dr. Abhay Rajeshwar Mogheker. After reviewing her history, Dr. Mogheker questioned whether Madison might have intracranial hypertension without papilledema, given her opening pressures reported at her initial lumbar puncture. Dr. Mogheker wanted to confirm if sedation was used during the lumbar puncture procedure since sedation "can artificially elevate intracranial pressure…and opening pressure of 30 cm under sedation …would not be considered elevated." Dr. Mogheker diagnosed Madison with "possible intracranial hypertension without papilledema and chronic daily headache." Pet. Ex. 11 at 4-6, 8.

Madison first saw Dr. Carlo Tornatore, her expert neurologist, on October 6, 2014, who noted that she continued to suffer debilitating headaches. Pet. Ex. 41 at 2. He recorded that she had daily headaches with diffuse pain which ranged from a four out of ten to a ten out of ten on the pain scale. Id. At that visit, he diagnosed her with "benign intracranial hypertension" and prescribed Diamox 225 mg per day. Id. at 3. At a follow up with Dr. Tornatore on November 13, 2014, he noted that Madison experienced paresthesia in her arms and legs after taking Diamox, and thus he adjusted her medications. Id. at 5. At a visit on April 16, 2015, Dr. Tornatore noted that Madison's headache was better after taking pain medications and that she took Diamox twice per day on Monday, Wednesday, and Fridays, and that she took up to four tabs of Tramadol at a time, up to four times per day. Id. at 12. He indicated that he wanted to taper her off Tramadol, as this could cause secondary headaches. Id. at 13. Madison continues to follow up with Dr. Torantore every few months. See Pet. Exs. 41, 44.

Significant to the undersigned's decision are the results of Madison's four MRVs, which were performed between February 3, 2012, and August 29, 2012. The first study performed on February 3, 2012, was interpreted by Dr. Richard Frachtman. Dr. Thelma D. Lopes interpreted the other three studies, and she also reviewed the first study, as a basis for comparison. The dates and pertinent findings of the studies are as follows:

February 3, 2012 MRV: Dr. Frachtman writes, "Severe [headache] [two] weeks after varicella and HPV immunizations[.] [Rule out] pseudotumor cerebri[.] [Rule out] sinus thrombosis …. Comparison: None …. The right internal jugular vein is visualized, but the left internal jugular is not well seen, particularly in the upper portion. This could be technical, but I cannot exclude thrombosis in this area …. Impression: …. Question of upper left jugular vein thrombosis or occlusion. A preliminary report was called to Dr. Schuester." Pet. Ex. 10 at 68.

March 28, 2012 MRV: Dr. Lopes observed, "13 year old female presented with headache. Comparison is made to prior examination dated 2/3/2012. There is minimal peripheral irregularities in the left sigmoid sinus, similar to the prior examination which can denote chronic changes vs. anatomic variant. There is now recanalization of the left distal internal jugular vein." Pet. Ex. 10 at 66.

July 24, 2012 MRV: Dr. Lopes noted, "Since prior examination dated [March 28, 2012], there is worsening [of] the irregularity involving the left sigmoid sinus. There is minimal irregularity of the right sigmoid sinus that it new since prior examination …. Impression: There is interval progression of irregularities involving the left sigmoid sinus as well as development of minor irregularities involving the right sigmoid sinus …. I discussed this case with Dr. Gratz on [July 24, 2012]." Pet. Ex. 10 at 24.

August 29, 2012 MRV: Dr. Lopes stated, "Since prior examination [on July 24, 2012], there is improved appearance of the left sigmoid sinus now with normal flow. There are no signs of sinus thrombosis." Pet. Ex. 10 at 28.

V. Intracranial Hypertension

Intracranial hypertension, also referred to as pseudotumor cerebri ("PTC") and idiopathic intracranial hypertension ("IIH"), is a clinical syndrome ("PTCS") characterized by signs and symptoms of increased intracranial pressure. Pet. Ex. 31 at 1. The condition was first used to describe patients who had increased intracranial pressure in the absence of a brain tumor, thus the word "pseudotumor" was coined. Id. at 5. PTC may be used interchangeably with idiopathic intracranial hypertension ("IIH"), although IIH is not the technically appropriate name for patients who have an "identifiable secondary cause" of intracranial hypertension. Resp. Ex. D6 at 1. Thus, Friedman[9] and others recommend the umbrella term of PTCS over IIH. Id. They also recommend that patients be subdivided into "primary vs. secondary PTC… [and that the]

[9] Friedman, Deborah et al., "Revised Diagnostic Criteria for the Pseudotumor Cerebri Syndrome in Adults and Children," 81 NEUROLOGY 1159-65 (2013) [Resp. Ex. D6].

secondary group would include causes such as venous sinus thrombosis, medications, and medical conditions." Id.

Signs and symptoms of intracranial hypertension may include headache, papilledema, elevated cerebrospinal fluid ("CSF") pressure, normal MRI/CT scans, normal neurological exam, and normal composition of CSF. Resp. Ex. D6 at 1. In adults, the cause is usually unknown and is often referred to as idiopathic. Intracranial hypertension is rare in children, and its clinical profile is different than that seen in adults. Id. at 5. Unlike adults, in children the majority of cases are secondary to endocrine abnormalities, trauma, medications or drugs, and infections. Id. at 1, 7. In fact, Per et al.[10] report that 53-78 percent of pediatric cases have been associated with identifiable conditions, including infections. Pet. Ex. 31 at 1. Infections associated with intracranial hypertension include acute sinus infection, varicella (chickenpox), urinary tract infection, and measles. Id. It has also been associated with venous sinus thrombosis. Pet. Ex. 56 at 6.

While headache is the most common symptom, other symptoms include blurred vision, diplopia, visual loss, nausea, vomiting, dizziness, and tinnitus. Pet. Ex. 31 at 2-3. Photophobia, anorexia, myalgias and lightheadedness may also be present. Id. at 5. Up to 31% of children may be asymptomatic. Id. at 6. A child may give a history of a worsening headache, as compared to past headaches. Pet. Ex. 55 at 2. In at least one report, up to 41% of patients have a history of pre-illness headaches or migraines. Id.

The articles filed by the experts suggest that there is a lack of consensus regarding diagnostic criteria for pediatric patients. Pet. Ex. 50 at 3. The modified Dandy criteria, the Friedman 2013 revised diagnostic criteria, and criteria adapted from Rangwala[11] were referenced in the literature here. Madison did not have papilledema. The applicable Friedman revised criteria for PTCS without papilledema is set forth below:

Table 2 Diagnostic criteria for pseudotumor cerebri syndrome

1. Required for diagnosis of pseudotumor cerebri syndrome[a]
A. Papilledema
B. Normal neurolog c examination except for cranial nerve abnormal ties
C. Neuroimaging: Normal brain parenchyma without evidence of hydrocephalus, mass, or structural les on and no abnormal meningeal enhancement on MRI, with and without gadolinium, for typical patients (female and obese), and MRI, w th and without gadolinium, and magnetic resonance venography for others; if MRI is unavailable or contraind cated, contrast-enhanced CT may be used
D. Normal CSF composit on
E. Elevated lumbar puncture opening pressure ($250 mm CSF in adults and $280 mm CSF in children [250 mm CSF if the child is not sedated and not obese]) in a properly performed lumbar puncture
2. Diagnosis of pseudotumor cerebri syndrome w thout papilledema

[10] Per, Huseyin et al., "Clinical Spectrum of the Pseudotumo Cerebri in Children: Etiological, Clinical Features, Treatment and Prognosis," 35 Brain & Development 561-68 (2013) [Pet. Ex. 31].

[11] Rangwala LM, Liu GT, "Pediatric Idiopathic Intracranial Hypertension," 52 Survey of Ophthalmology 597-617 (2007).

In the absence of papilledema, a diagnosis of pseudotumor cerebri syndrome can be made if B–E from above are satisfied, and in addition the patient has a unilateral or bilateral abducens nerve palsy
In the absence of papilledema or sixth nerve palsy, a diagnosis of pseudotumor cerebri syndrome can be suggested but not made if B–E from above are satisfied, and in addition at least 3 of the following neuroimaging criteria are satisfied:
i. Empty sella
ii. Flattening of the posterior aspect of the globe
iii. Distention of the perioptic subarachnoid space with or without a tortuous optic nerve
iv. Transverse venous sinus stenosis

[a] A diagnosis of pseudotumor cerebri syndrome is definite if the patient fulfills criteria A–E. The diagnosis is considered probable if criteria A–D are met but the measured CSF pressure is lower than specified for a definite diagnosis.

Table 2, Resp. Ex. D6 at 3.

In a 2017 study published by Gerstl et al.,[12] the authors concluded that the revised criteria cited above were too strict and could lead to "missed diagnosis," especially in children who did not have papilledema. Pet. Ex. 51 at 5, 9. Gerstl recommends that that the "threshold value" for lumbar puncture opening pressure be changed from 28 cmH2O to a range of ≥20 to 30 cmH2O." Id. at 9.

Perhaps more important to the facts of this case, the diagnostic criteria above may or may not be relevant if MRV shows cerebral venous narrowing. Resp. Ex. D6 at 3. "MRV may show venous narrowing supportive of a diagnosis of PTCS in any patient …. [V]enous sinus occlusion … may produce PTCS." Id. Moreover, "Cerebral venous thrombosis[13] has been found in 11.4% of patients who were presumed to have IIH." Pet. Ex. 56 at 6. Dural sinus thrombosis[14] can cause a clinical presentation similar if not identical to IIH and thus MRV has become routine to exclude underlying venous sinus pathology. Pet. Ex. 30 at 4. Due to these studies and findings, it has been suggested that the pathophysiological mechanism underlying intracranial hypertension may be related to abnormalities of the venous outflow system of the brain. Pet. Ex. 56.

The goal of treatment is to reduce intracranial pressure to prevent vision loss and relieve symptoms. Ex. 31 at 7. Lumbar puncture to drain spinal fluid may be effective to reduce intracranial pressure. Medications such as acetazolamide may also be used to reduce pressures.

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[12] Gerstl, Lucia et al., "Pediatric Idiopathic Intracranial Hypertension – Is the Fixed Threshold Value of Elevated LP Opening Pressure Set Too High?" 21 EUR. PAED. NEUROL. SOC. 833 (2017) [Pet. Ex. 51].

[13] A cerebral thrombosis is "a thrombosis of a cerebral vessel, which may result in a cerebral infarction or thrombotic stroke." Dorland's at 1923. A thrombosis is "the formation, development, or presence of a thrombus." Id. A thrombus is "a stationary blood clot along the wall of a blood vessel, frequently causing vascular obstruction." Id.

[14] Dural sinus thrombosis is the "thrombosis of a sinus of the dura mater, usually secondary to head injury or to infection of a nearby structure," and also known as "intracranial thrombosis" and "intracranial sinus thrombosis." Dorland's at 1923.

Id. The mean duration of treatment described by Per et al., was 9 months. Id. Visual loss has been reported in up to 38% of patients. Id. Patients may relapse or continue to experience headaches, even after normalization of intracranial pressure. Ex. 56 at 2.

VI. Expert Testimony

A. Standards of Adjudication for a Causation Claim

To receive compensation under the Vaccine Act, petitioner must prove either (1) that she suffered a "Table Injury" – i.e., an injury falling within the Vaccine Injury Table – corresponding to one of the vaccinations in question, or (2) that her injury was actually caused by a vaccine (a "non-Table injury"). See §§ 300aa-13(a)(1)(A), 11(c)(1); § 300aa-14(a) as amended by 42 C.F.R. § 100.3; 300aa-11(c)(1)(C)(ii)(I); see also Moberly v. Sec'y of Health & Human Servs., 592 F.3d 1315, 1321 (Fed. Cir. 2010); Cappizzano v. Sec'y of Health & Human Servs., 440 F.3d 1317, 1320 (Fed. Cir. 2006). Since no Table Injury is alleged in this case, petitioner must prove causation in fact.

Petitioner bears the burden of demonstrating actual causation by a preponderance of the evidence. See Cedillo v. Sec'y of Health & Human Servs., 592 F.3d 1315, 1321 (Fed. Cir. 2010); § 300aa-13(a)(1). To do so, petitioner must provide: "(1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of a proximate temporal relationship between the vaccination and injury." Althen, 418 F.3d at 178. The preponderance of the evidence standard requires a petitioner to demonstrate that it is "more likely than not" that the vaccine caused her injury. Moberly, 592 F.3d at 1322 n.2. Proof of medical certainty is not required. Bunting v. Sec'y of Health & Human Servs., 931 F.2d 867, 873 (Fed. Cir. 1991). In particular, petitioner must demonstrate that the vaccine was "not only [a] but for cause of the injury but also a substantial factor in bringing about the injury." Moberly, 592 F.3d at 1321 (quoting Shyface v. Sec'y of Health & Human Servs., 165 F.3d 1344, 1352-53 (Fed. Cir. 1999)); Pafford v. Sec'y of Health & Human Servs., 451 F.3d 1352, 1355 (Fed. Cir. 2006). The undersigned must consider the record "as a whole" and may not rule in petitioner's favor solely based on petitioner's own claims "unsubstantiated by medical records or medical opinion." § 13(a)(1).

Causation is determined on a case by case basis, with "no hard and fast per se scientific or medical rules." Knudsen v. Sec'y of Health & Human Servs., 35 F.3d 543, 548 (Fed. Cir. 1994). The Althen court noted that a petitioner need not necessarily supply evidence from medical literature supporting petitioner's causation contention, so long as the petitioner supplies the medical opinion of an expert. Id. at 1279–80. The court also indicated that, in finding causation, the fact-finder may rely upon "circumstantial evidence," which the court found to be consistent with the "system created by Congress, in which close calls regarding causation are resolved in favor of injured claimants." Id. at 1280. In other words, any close calls regarding causation must be resolved in favor of the petitioner. Althen, 418 F.3d at 1280.

B. Expert Reports and Testimony

In Vaccine Act cases, expert testimony is usually evaluated according to the factors for analyzing scientific reliability set forth in Daubert v. Merrell Dow Pharm., Inc., 509 U.S. 579, 594-96 (1993); see also Cedillo, 617 F.3d at 1339 (citing Terran v. Sec'y of Health & Human Servs., 195 F.3d 1302, 1316 (Fed. Cir. 1999). "The Daubert factors for analyzing the reliability of testimony are: (1) whether a theory or technique can be (and has been) tested; (2) whether the theory or technique has been subjected to peer review and publication; (3) whether there is a known or potential rate of error and whether there are standards for controlling the error; and (4) whether the theory or technique enjoys general acceptance within a relevant scientific community." Terran, 195 F.3d at 1316 n.2 (citing Daubert, 509 U.S. at 592-95). In Vaccine Program cases, these factors are used in the weighing of the scientific evidence actually proffered and heard. Davis v. Sec'y of Health & Human Servs., 94 Fed. Cl. 53, 66–67 (Fed. Cl. 2010) ("uniquely in this Circuit, the Daubert factors have been employed also as an acceptable evidentiary-gauging tool with respect to persuasiveness of expert testimony already admitted"), aff'd,420 F. App'x 923 (Fed. Cir. 2011). The flexible use of the Daubert factors to determine the persuasiveness and/or reliability of expert testimony in Vaccine Program cases has routinely been upheld. See, e.g., Snyder v. Sec'y of Health & Human Servs., 88 Fed. Cl. 706, 742–45 (2009).

Where both sides offer expert testimony, a special master's decision may be "based on the credibility of the experts and the relative persuasiveness of their competing theories." Broekelschen v. Sec'y of Health & Human Servs., 618 F.3d 1339, 1347 (Fed. Cir. 2010) (citing Lampe v. Sec'y of Health & Human Servs., 219 F.3d 1357, 1362 (Fed. Cir. 2000)). However, nothing requires the acceptance of an expert's conclusion "connected to existing data only by the ipse dixit of the expert," especially if "there is simply too great an analytical gap between the data and the opinion proffered." Snyder, 88 Fed. Cl. at 743 (quoting Gen. Elec. Co. v. Joiner, 522 U.S. 146 (1997)). Weighing the relative persuasiveness of competing expert testimony, based on a particular expert's credibility, is part of the overall reliability analysis to which special masters must subject expert testimony in Vaccine Program cases. Moberly, 592 F.3d at 1325–26 ("[a]ssessments as to the reliability of expert testimony often turn on credibility determinations"); see also Porter v. Sec'y of Health & Human Servs., 663 F.3d 1242, 1250 (Fed. Cir. 2011) ("this court has unambiguously explained that special masters are expected to consider the credibility of expert witnesses in evaluating petitions for compensation under the Vaccine Act").

In the present case, two experts testified at the hearing, Dr. Tornatore for petitioner and Dr. Bingham for respondent. The experts' respective qualifications and opinions are summarized below.

i. Petitioner's Expert, Dr. Carlo Tornatore

Dr. Carlo Tornatore received a Bachelor of Arts in neurobiology from Cornell University, and he completed a Master's of Science at Georgetown University in the Department of Physiology. Pet. Ex. 28 at 2. He attended Georgetown University School of Medicine in Washington, D.C., and completed his residency in neurology at Georgetown University Hospital. Id. After his residency, Dr. Tornatore worked as a Senior Staff Fellow at the National Institutes of Health in the Section on Molecular Virology and Genetics in the Laboratory of Viral and

Molecular Pathogenesis. Id. He is board certified in neurology by the National Board of Psychiatry and Neurology, and he is licensed to practice medicine in the District of Columbia. Id. at 1. Dr. Tornatore currently serves as an associate professor of neurology at Georgetown University Medical Center, and he is a member of the American Academy of Neurology, the American Association for the Advancement of Science, and the American Society for Neural Transplantation. Id. at 5. He also serves as an ad hoc reviewer for five medical journals and has published numerous articles on neurology over the course of his career. Id. at 5-16.

1. Diagnosis of Intracranial Hypertension

Dr. Tornatore opined that Madison had intracranial hypertension based on her elevated spinal fluid pressure, abnormal MRV studies, and the fact that her treating physicians considered this diagnosis. Tr. 33-34. He opined that this condition triggered Madison's chronic headaches. Id. at 35. The medications she began taking for her chronic headaches may also have contributed to her chronic headaches. Id. at 35-36.

Prior to receiving the vaccines at issue here, Madison was healthy. Her growth chart shows that she was approximately 75% for weight, based upon her age and height. After her vaccinations, her weight dropped off dramatically. Tr. 11-12. Pre-vaccination, Madison's scholastic record was very good, and she had no prolonged school absences. She had a variety of interests, and was a "very engaged and vibrant" adolescent. Id. at 15. She did experience occasional headaches prior to her vaccinations, but these were associated with sinus infections or chronic sinus problems. Id. 19-20. Before the vaccines, Madison had facial pain under her eyes, or in the back of her head. Id. 20-21. After she underwent sinus dilation, she improved. Id. at 21. After the vaccines, her pain was in the back of her head and neck, and her headaches became significantly worse. Id. at 22.

On March 28, 2012, Madison had a lumbar puncture, and her opening pressure was 30 cmH20, which Dr. Tornatore opined was elevated. Tr. 33; Pet. Ex. 23 at 209-210. A significant question raised by Madison's treating physicians, and the experts, was whether her opening pressure of 30 cm was diagnostic for increased intracranial pressure. Dr. Tornatore cited several articles in support of his position that an opening pressure of 30 cm did indicate increased intracranial pressure.

In the Gerstl paper,[15] twelve patients between the ages of five and seventeen were studied. The diagnosis of intracranial hypertension was based on papilledema, visual symptoms, dizziness, headache and nausea, and a lumbar puncture opening pressure of greater than 25 cm. Ten of the patients were sedated. Lumbar puncture opening pressures ranged from 21 to 50 cm. Eight of the children had an opening pressure of 28 cm or greater. The authors discussed their concern about the strict revised criteria published by Friedman, in which the threshold elevation for an opening pressure was ≥ 28 cm. They believed that the Friedman threshold of ≥28 cm could lead to missed diagnoses of PTC in children, especially in the absence of papilledema.

[15] Gerstl et al., 21 EUR. PAED. NEUROL. SOC. 833 [Pet. Ex. 51].

Pet. Ex. 51 at 5. Gerstl advocated an opening pressure "range of ≥20 to 30 cm" should be adopted instead. Id. at 9.

In another 2017 study, by Inger et al.,[16] of 50 children, the authors defined an elevated opening pressure of ≥ 28, or ≥ 25, if the child was not sedated and not obese. By this measure, ten of the children did not have an elevated opening pressure, although they had a clinical course consistent with intracranial hypertension. And in the Digre[17] article, 353 patients were studied. The mean opening pressure was 309 mm (30.9 cm) in those patients who did not have papilledema.[18] Pet. Ex. 38 at 1.

In addition to the abnormal opening pressure, Dr. Tornatore testified that Madison also had abnormalities of her CSF fluid. Specifically, she had an elevated protein of 50, elevated red blood cells of 4000, and five white blood cells. Tr. 105-06. Dr. Tornatore attributed the red and white blood cell abnormalities to the fact that the procedure was "a little traumatic," resulting in bleeding. Dr. Tornatore explained that for every 1,000 red blood cells, there is usually one "tagalong" white blood cell, which explains Madison's count of five white blood cells. As for the elevated protein, Dr. Tornatore explained that some increase in the CSF protein would be attributable to the red blood cells caused by the traumatic nature of the procedure. However, he did not think that this explained all of the increase. He opined that at least part of the abnormally-elevated protein was a "bona fide elevation" consistent with his mechanistic theory. Tr. 202-03.

Madison did not have papilledema, and she had spontaneous venous pulsations ("SVP"). Both experts testified about whether there can be a diagnosis of PTC in the absence of papilledema and the presence of SVP. Tr. 204. Papilledema is a swollen optic nerve, a classic finding in intracranial hypertension. SPV is the presence of pulsing in the veins overlying the front of the optic nerve. If the pressure in the brain is very elevated, it will impinge on these blood vessels to prevent them from pulsing. Tr. 136. Thus, the lack of pulsing is a diagnostic sign of intracranial pressure. Id.

Dr. Tornatore emphasized that the absence of papilledema and the presence of SVP does not preclude the diagnosis of intracranial hypertension. Tr. 204-05. He cited a study by Digre et al., in support of his opinion. In Digre, the authors studied 353 patients with intracranial hypertension and found that 5.7% did not have papilledema, and of those, 75% had SVP. Pet. Ex. 38 at 1. The authors concluded that while less common, intracranial hypertension can occur in the absence of papilledema and the presence of SVP. Id. at 6. Another study published in

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[16] Inger, Hilliary E. et al., "Diagnostic Criteria in Pediatric Intracranial Hypertension," J. AAPOS (2017). [Pet. Ex. 50].

[17] Digre, Kathleen B. et al., "A Comparison of Idiopathic Intracranial Hypertension With and Without Papilledema," 49 HEADACHE 185 (2009) [Pet. Ex. 38; Resp. Ex. D4].

[18] Papilledema is "an edema of the optic disk (papilla), most commonly due to increased intracranial pressure, malignant hypertension, or thrombosis of the central retinal vein." Dorland's at 1372.

2017 by Gerstl also supports the proposition that intracranial hypertension can occur in the absence of papilledema. In Gerstl, six of the 12 children studied did not have papilledema. Pet. Ex. 51 at 3.

Dr. Tornatore explained that the changes on Madison's MRVs show changes in the veins that can be associated with cranial hypertension. Tr. 33. Serial MRVs performed in February, March, May, July, and August 2012 were abnormal and showed abnormalities in the venous anatomy of the brain. The first MRV, February 3, 2012, raised a question of "upper left jugular vein thrombosis." Tr. 55. The right internal jugular vein was visualized but the left jugular was not well seen, and thrombosis could not be excluded. Pet. Ex. 10 at 63. Dr. Tornatore explained that on MRV, if a vessel is not seen, it is because there is no blood flow through the vessel or there is a technical problem. Tr. 56-57. On March 28, 2012, Madison's MRV showed minimal peripheral irregularities of the left sigmoid sinus similar to the prior study. It also showed "interval recanalization of the left internal vein." Id. at 26. Dr. Tornatore explained that the suggestion of recanalization indicates that the left internal vein may have previously been occluded by an embolus or clot. Id.

In addition to the elevated opening pressure at the time of initial lumbar puncture and the abnormal MRV studies, Dr. Tornatore was also influenced by the opinions of Madison's treating physicians. On March 27, 2012, Madison was admitted to Sinai Hospital where Dr. Gratz diagnosed her with "chronic persistent headache, possibly secondary to intracranial hypertension without papilledema." Pet. Ex. 10 at 77-80. Dr. Gratz again questioned the diagnosis of intracranial hypertension when he saw Madison at her follow-up appointment on May 3, 2012. At that visit, he concluded that she had "chronic persistent headaches with associated elevated increased intracranial pressure suggesting the possibility of pseudotumor cerebri without papilledema. Pseudotumor cerebri has been reported to occur secondary to hypoparathyroidism, although the underlying pathophysiology is not understood." Pet. Ex. 10 at 56-59.

Dr. Gratz made the same diagnosis when he saw Madison again on July 18, 2012. Pediatric infectious disease specialist, Dr. Susan Lipton, who saw Madison in March 2012, noted that "There is evidence of pseudotumor even though there is no funduscopic evidence of this." Pet. Ex. 10 at 88-91. These physicians did not attribute Madison's condition to her varicella vaccination, but they consistently raised the diagnosis of intracranial hypertension as the cause of Madison's headaches.

In the literature cited by Dr. Tornatore, patients with headaches due to intracranial hypertension usually have resolution of their headaches following treatment (i.e. administration of diuretic or lumbar puncture to drain cerebrospinal fluid) to reduce intracranial pressure. Madison's headaches, however, did not resolve after treatment. Dr. Tornatore testified that once her intracranial pressure normalized, her headaches continued and became chronic due to a number of factors. Tr. 76. After her first lumbar puncture, her intracranial pressure decreased so quickly that she had what is known as a "spinal tap headache." Id. at 95. Dr. Tornatore also opined that Madison's medications, and analgesic overuse, especially long term use of Tramadol, contributed to her ongoing headaches. Id. Lastly, in some patients, chronic headaches are very difficult to treat. The electrical system of the brain is "so dysregulated" that it will not return to normal. Id. at 96-97. Given her history, Dr. Tornatore explained that Madison's headaches will

probably not go away. Id. at 104. He opined that some of Madison's headaches are caused by her use of Tramadol, and if she would wean off that medication, her headaches may not be as debilitating. Tr. 104. However, he testified that 30 to 35% of patients still have chronic daily headaches when weaned off medication like Tramadol. Id. at 105.

2. Causation and Althen Prongs

Dr. Tornatore explained that the varicella vaccine contains a live attenuated virus[19], and for reasons that are not clear, Madison had a "profound" reaction to the virus. Tr. 36-37. The varicella virus is "neurotropic" – that is, it is known to infect nerves and the nervous system. Dr. Tornatore proposed two alternative causal mechanisms. The first mechanism is that the virus infected nerves in the brain, causing them to become inflamed and swollen, which increased intracranial pressure. Tr. 38. His second proposed mechanism is that the varicella virus infected the blood vessels and the walls of blood vessels in the back of the brain so that the vessels became inflamed and irritated. Id. Varicella can infect the walls of blood vessels and inflame and irritate them, causing clots to form, or blood vessels to narrow. Id. at 38, 58. CSF drains into these veins, and when the veins are irritated, or occluded, the spinal fluid fails to properly drain into them, which increases intracranial pressure. Id. at 90.

Spinal fluid is constantly produced in the brain, at the rate of approximately 30 ml of fluid per hour, and this fluid is constantly draining out of the brain and into the venous sinuses (veins) of the brain. If there is an obstruction in the venous system, then the spinal fluid is unable to properly drain, which creates a backup of spinal fluid in the brain. This increase of spinal fluid pushes on the brain and blood vessels, causing headache. Tr. 90-91. The skull is a confined space – if the amount of spinal fluid increases, something else has to give. The brain does not have pain receptors but blood vessels in the brain do - blood vessels have nerves which sense pressure, and the increased pressure caused by the brain pushing on the blood vessels creates pain. Tr. 91. The spinal fluid pressure is elevated like it would be if there were a tumor, but because there is no actual tumor, the condition is referred to as "pseudotumor". Tr. 28.

Referencing the Farb article,[20] Dr. Tornatore provided demonstrative evidence of the normal venous anatomy of the sagittal, transverse, and sigmoid sinuses, as illustrated in the diagram below:

[19] The Physicians' Desk Reference entry for the VARIVAX varicella vaccine states that it is "a live, attenuated varicella-zoster vaccine . . . ." Pet. Ex. 58 at 3.

[20] Farb, R.I. et al., "Idiopathic Intracranial Hypertension: The Prevalence and Morphology of Sniovenous Stenosis," 60 NEUROLOGY 1418 (2003) [Pet. Ex. 30].

Figure 2A, Pet. Ex. 30 at 2.

The sagittal sinus vein comes across the top of the brain, down to the back of the skull and drains into the transverse veins, which then drain into the sigmoid sinuses, which then drain into the (internal) jugular veins. Tr. 81. The sigmoid and internal jugular veins were not well visualized in Madison's MRV studies. Id. Dr. Tornatore opined that in Madison's first MRV study, the left internal jugular vein was occluded. Subsequent MRVs also showed irregularities in the sigmoid sinus, and in her last study, these abnormalities were gone. Id. at 81-82. The irregularities seen in the veins on MRV may occur when the lumen of the veins are narrowed.[21] Blood flow through a vein is more turbulent due to narrowing, and clotting can occur in the narrowed areas. Narrowing may also be referred to as stenosis. Id. at 83. Stenosis can be profound, in which case an occlusion may occur, resulting in no blood flow. Id. at 83-84. When a virus infects a blood vessel, an inflammatory response occurs, causing stenosis and clotting, or results in irregularities of the veins, as described above. Id. at 86. Dr. Tornatore testified that he had seen this mechanism in his clinical practice, particularly in patients with otitis media, or infection of the middle ear, who developed focal inflammation of the sigmoid sinus as a result of their infection. Tr. 94.

The factual background also includes Madison's unrecognized pre-existing hypoparathyroidism and hypocalcemia, known risk factors for intracranial hypertension. Pet. Ex. 27 at 17. Dr. Tornatore opined that Madison's hypoparathyroidism may have put her at risk of developing pseudotumor. Id. at 18; Tr. 41.

In support of his opinions as to causal mechanisms, Dr. Tornatore referenced a number of articles. First, he cited articles to support his opinion that varicella infection can lead to intracranial hypertension, and thus this aspect of his proposed mechanism is a "well recognized phenomenon." Pet. Ex. 27 at 17. In an article published in 2014, Gilad[22] and his colleagues describe a case report of a 13 year-old girl who had headaches for two weeks associated with increased intracranial pressure. Pet. Ex. 32. Lumbar puncture opening pressure was 42 cmH2O, the patient had papilledema, and CSF showed mildly-elevated protein (57 mg/dL). Polymerase

[21] The lumen is "the cavity or channel within a tube or tubular organ." Dorland's at 1077.

[22] Gilad, Oded et al., "Primary Varicella Infection Presenting with Headache and Elevated Intracranial Pressure," J. CHILD NEUROL. 1 (2014) [Pet. Ex. 32]

chain reaction ("PCR") of CSF was positive for varicella zoster virus although the child did not have any rash or vesicles characteristic of varicella infection.[23]

The Gilad authors reported seven other cases of varicella infection associated with increased intracranial pressure in children ranging in age from ages six to 15, as described in the literature. All seven children had headache, papilledema, and lumbar puncture opening pressures ranging from 26cm to 42cm. Four of the children had a recent history of varicella infection and three did not. All had "high titers of IgG antibodies to varicella zoster virus." Pet. Ex. 32 at 3. The authors concluded that "primary varicella zoster infection may present solely with headache and elevated intracranial pressure." Id. A summary of the seven cases described in the medical literature is set forth below:

Abbreviati
prev., prev
[a]+, presen

Table 1, Pet. Ex. 32 at 2.

These case reports described by Gilad, Ravid, and others validate Dr. Tornatore's opinion that varicella infection can lead to increased intracranial pressure and that this is a recognized complication reported in the medical literature.

As to the mechanism at play, Gilad recognizes that the exact pathogenesis is not known, but research suggests that increased intracranial pressure may be caused by "venous outflow abnormalities…low-grade inflammation, [or] vascular clotting." Pet. Ex. 32 at 2. Similarly, Ravid et al.[24] state that while the "precise pathogenesis of intracranial hypertension remains

[23] Madison did not undergo PCR testing.

[24] Ravid, Sarit et al., "Reactivation of Varicella Presenting as Pseudotumor Cerebri: Three Cases and a Review of the Literature," 46 PED. NEUROL. 124 (2012) [Pet. Ex. 33].

unknown, [ ] proposed theories include venous outflow abnormalities." Pet. Ex. 33 at 2. Ravid also suggests that the mechanism may be "direct [infection] or immune-mediated vasculopathy." Id.

Lahat et al.[25] also describe the example given by Dr. Tornatore of ear infections causing intracranial hypertension. Before the wide-spread use of antibiotics, increased intracranial hypertension secondary to middle ear infections was commonplace. The mechanism was probably "thrombosis of one or more of the dural sinuses, specifically the lateral one." Ex. 34 at 2. Lahat suggests that intracranial hypertension associated with varicella infection "may have a vasculitic or immune-mediated pathogenesis." Id. Similarly, Konrad et al.,[26] concur in their case report of "deep venous thrombosis and [PTC] after chickenpox in an 8 year old," who also had a protein S deficiency. Pet. Ex. 35 at 1. Konrad states that there "have been repeated reports about thrombotic complications during recovery from chickenpox." Id. at 2. While Konrad discusses the interplay of contributing conditions, such as protein S auto-antibodies, anticardiolipin antibodies, and streptococcal co-infection, the case studies in the more recent articles by Gilad and Ravid do not suggest that contributing conditions or coagulation abnormalities are necessary for a varicella infection to be causally associated with intracranial hypertension.

Dr. Tornatore also cited the package insert for VARIVAX[27], which warns against contact with high risk individuals who may be susceptible to varicella because of possible transmission of the virus after vaccination. Ex. 27 at 17. Pet. Ex. 58 at 3. This adds support for Dr. Tornatore's opinion that the varicella vaccine can cause infection, a cornerstone to his causal theory.

To summarize Dr. Tornatore's explanation of a logical sequence of cause and effect, Madison had pre-existing low calcium levels due to her hypoparathyroidism. She was vaccinated with varicella, a live virus known to cause increased intracranial pressure via the mechanism described above. She then developed abnormalities in the dural sinus veins, the veins in the back of her brain, causing clots to form, or the vessels to narrow, with a resulting elevation of intracranial pressure. Madison's elevated intracranial pressure caused the onset of severe and chronic headaches. Tr. 38-41.

With regard to onset, Madison received her vaccines on January 16, 2012. The first documented reference in the medical records to headaches was January 24, 2012. See Pet. Ex. 22 at 11. Dr. Tornatore testified that the onset, or temporal relationship of her headaches, was

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[25] Lahat, E. et al., "Pseudotumor Cerebri Complicating Varicella in a Child," 87 ACTA PAEDIATR. 1310 (1998) [Pet. Ex. 34].

[26] Konrad, D. et al., "Psuedotumor Cerebri After Varicella," 157 EUR. J. PEDIATR. 904 (1998) [Pet. Ex. 35].

[27] VARIVAX is "a preparation of the Oka/Merck strain of live, attenuated varicella virus." Pet. Ex. 58 at 6.

about 10 days[28] after vaccination, which is "perfect" given his proposed mechanism of infection. Tr. 48. Based on the serial MRV studies, Dr. Tornatore opined that Madison's intracranial pressure probably normalized by the time of her August 29, 2012 MRV. That study no longer showed that her blood vessels were occluded or narrowed, and thus, it is probably "the most objective point where [one] can say that there is changes that would fit." Tr. 75, citing Ex. 10 at 28.

ii. Respondent's Expert, Dr. Peter Bingham

Dr. Bingham graduated with a Bachelor of Arts in Biology from Harvard College, and he received his M.D. from the Columbia College of Physicians and Surgeons in New York City. Resp. Ex. B at 1. He completed his residencies in pediatrics and neurology at the Children's Hospital of Philadelphia. Id. Dr. Bingham is licensed in neurology and child neurology and currently serves as a Professor of Neurology and Pediatrics at the University of Vermont. Id. He serves on a number of healthcare committees, and he is also a member of the American Academy of Neurology. Id. at 1-2. Dr. Bingham has also authored numerous publications and has contributed to a number of neurology symposia. Id. at 4-10.

1. Diagnosis of Petitioner's Condition

Dr. Bingham agreed that Madison developed an acute reaction to vaccinations, in that she had cellulitis at the site of the vaccine, and he also opined that she developed a headache within eight to 24 hours of vaccination.[29] Tr. 128. He agreed that Madison's headache was debilitating and kept her from attending school. Id. at 128-29. Madison described her headache as pressure that was intermittent, bilateral and throbbing. Id. at 129; see also Resp. Ex. A at 3. However, Dr. Bingham opined that Madison had migraine headaches, not intracranial hypertension. See Pet. Ex. 36 at 4.

Dr. Bingham gave several reasons for his opinion that Madison suffered from migraines and opined that they can be distinguished from PTC based on a patient's history. First, he believed that the characterization of Madison's pain fit the diagnostic criteria of a migraine. See Resp. Ex. A at 8. Often migraines involve nausea, gastrointestinal upset, and light and/or sound sensitivity. Tr. 130. Second, he testified that migraines often have an acute presentation, within minutes to an hour, which is different from PTC, where a throbbing headache is not expected at

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[28] Dr. Tornatore appears to be off by two days. Madison's headaches were first documented January 24, 2012, eight days after vaccination. Dr. Tornatore also testified as to mechanisms that could explain Madison's headaches, assuming an earlier onset (one to two days after vaccination). The undersigned finds, however, that onset occurred on or before January 24, 2012, approximately one week after vaccination, based on initial entries in the contemporaneous medical records.

[29] Dr. Bingham testified that Madison developed a headache 8 to 24 hours post vaccination. The medical records created at the time of these events by the pediatrician, however, do not reference a headache until January 24, 2012. See Pet. Ex. 22 at 9-13. Dr. Bingham may be relying on later records, which are less clear as to onset of headaches. See Pet. Ex. 10 at 93.

the initial presentation. Id. at 147. Dr. Bingham agreed, however, that there was an overlap of symptoms shared by both conditions. Id. at 130.

Dr. Bingham also testified that Madison suffered from migraines prior to her vaccinations. Tr. 147. Prior to her vaccines, Madison had a headache associated with nausea, which Dr. Bingham did not necessarily attribute to a migraine. Tr. 148; see Pet. Ex. 22 at 235. She also had headaches associated with sinusitis, which were not attributable to migraines. Tr. 148. But in 2011, Madison had a headache described as a tension headache, and Dr. Bingham thought this might have been a migraine. Id. at 150-51. Pain fibers that contribute to migraine pain are not in the brain, but throughout the sinuses, and caused by a local inflammatory response. Id.

Secondly, in disagreement with Dr. Tornatore, Dr. Bingham was impressed by the presence of SVP. He stated that Madison had venous pulsations documented by an ophthalmology examination on February 3, 2012, which he described as "compelling evidence of normal intracranial pressure." Tr. 135-136. Dr. Bingham agreed that the presence or absence of SVP is not an "infallible sign" of increased intracranial pressure, but he finds it to be a useful marker. Tr. 182. [30]

Third, and also in disagreement with Dr. Tornatore, Dr. Bingham opined that Madison's opening lumbar puncture pressure of 30 cmH2O was within the accepted range of normal in children and not a definitive sign of increased intracranial pressure. Tr. 134. To the extent that 30 cmH2O may have been on the higher range of normal, or even considered to be elevated, Dr. Bingham attributed any such elevation to the sedative given for the procedure. Dr. Bingham also noted that one of Madison's treating physician, Dr. Abhay Moghekar, also questioned whether the elevation was due to sedation.[31] Id. at 134-35. Dr. Bingham cited an article by Avery[32] for the position that opening pressures can be higher in children. Id. at 166-67. While the authors of Avery state that an opening pressure of ≥28 cm is normal for most children (Madison had an opening pressure of 30 cm), they recommend that the number be interpreted in concert with other clinical information. Resp. Ex. D2 at 284. Avery specifically looked at the factors of age and influence of sedation, especially ketamine, which was not used in Madison's procedure. They did not study other factors, such as the abnormal MRV findings here. Avery did advocate looking at the full concert of information, and seemed to guard against reliance on the opening pressure alone to make a diagnosis.

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[30] Dr. Tornatore disagreed with Dr. Bingham on this point, citing Digre et al. In Digre, out of 20 patients who met the criteria for PTC without papilledema, 12 (75%) had SVP. Resp. Ex. D4 at 3.

[31] Dr. Moghekar noted that the diagnosis of PTC "depends on an accurate measurement of opening pressure[,] and it maybe [sic] worthwhile repeating the lumbar puncture without sedation to exclude this diagnosis." Pet. Ex. 11 at 6.

[32] Avery, R. A., "Interpretation of Lumbar Puncture Opening Pressure Measurements in Children," 34 J. NEURO-OPTHALMOLOGY 284-87 (2014) [Resp. Ex. D2].

As for Madison's MRV studies, Dr. Bingham testified that the results were "not compelling." Tr. 141. He opined that in order for the reported abnormalities to be significant, the abnormalities in the veins or sinuses should have been bilateral, not just unilateral. Instead, Dr. Bingham believed that Madison's studies showed unilateral abnormalities of unknown significance. Id. at 137.

Citing the Farb study,[33] Dr. Bingham testified that 27 of the 29 patients had substantial bilateral stenosis, not just unilateral stenosis seen in Madison's studies. Dr. Bingham also cited an article by Alper[34] which reported that 24% of the normal population has anatomical asymmetry of their transverse sinuses. Tr. 166. He conceded, however, that the Farb and Alper findings only applied to the transverse sinus, not the (internal) jugular or sagittal sinuses. Id. at 184. As such, he agreed that the findings are not directly applicable to Madison's studies, which showed abnormalities in the sagittal sinuses and internal jugular, and not the transverse sinus, which were not studied by Farb or Alper.

Dr. Bingham also cited the Farb study for the point that technical artifacts on MRVs can appear as areas of stenosis, and he suggested that the abnormalities seen on Madison's studies were technical artifacts. Tr. 168. Dr. Bingham emphasized that the important point of Alper and Farb is that there can be technical issues which call into question the consistency of MRV interpretations. Id. at 185.

Dr. Tornatore testified there would be less reader variability, and thus greater consistency in Madison's MRV interpretations since the same person reviewed all of the studies. Tr. 201. Dr. Bingham agreed, and he testified that it was reasonable to give more emphasis to Dr. Lopes' interpretation of the MRV studies, since she reviewed all of them. Id. at 196. Notably, when interpreting the studies, Dr. Lopes questioned whether the abnormalities were signs of thrombosis or simply anatomic variations. Over the course of her review, from February to August 2012, Dr. Lopes reported on the progression of irregularities that suggested occlusion or thrombosis involving the left internal jugular vein and left sigmoid sinus, which improved by August 2012.

Also relevant to Dr. Bingham's opinion is the response that Madison had to dihydroergotamine ("DHE"). He testified that it is unusual for a patient with increased intracranial pressure to respond to this medication, and thus, this fact weighs against a diagnosis of pseudotumor. Tr. 142. However, this did not seem to be a strong point, and there was no compelling evidence introduced to support it.

Additionally, Dr. Bingham disagreed with the import given by Dr. Tornatore to the fact that Madison's treating physicians diagnosed her with PTC without papilledema. Dr. Bingham

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[33] Farb et al., 60 NEUROLOGY 1418 [Pet. Ex. 30; Resp. Ex. D5].

[34] Alper, Fatih et al., "Importance of Anatomical Asymmetries of Transverse Sinuses: An MR Venographic Study," 18 CEREBROVASC. DIS. 236-39 (2004) [Resp. Ex. D1].

believed that Madison's treating physicians were tentative in their diagnosis of pseudotumor, and thus he opined that there was never a firm diagnosis of pseudotumor. Tr. 145.

Lastly, Dr. Bingham cited Friedman diagnostic criteria for PTC without papilledema, and testified that Madison did not meet these diagnostic criteria. Tr. 169. He acknowledged, however, that Friedman's criteria were "stringent" and that others had contested that "stringency of [the] diagnostic criteria." Tr. 168-69.

Dr. Bingham testified that for all of the above reasons, especially the presence of SVP, and the fact that Madison's opening pressure was borderline, it more likely than not that Madison did not have intracranial hypertension following her vaccinations. Tr. 170.

2. Response to Petitioner's Theory of Causation and Althen Prongs

Dr. Bingham opined that there was "no substantial evidence" that the vaccinations Madison received either could cause, or did cause, her intracranial hypertension. Resp. Ex. A at 11. Citing a number of medical articles, Dr. Bingham emphasized several points. He cited a CDC publication[35] about the significant pathological differences between the wild varicella virus, and the attenuated vaccine virus. Tr. 157. The article, however, confirms that attenuated viruses, like those in vaccines, can cause disease, although usually in a milder form. R's. Ex. E-3 at 5. It also notes that "severe reactions are possible" with live attenuated vaccines. Id. at 4.

Dr. Bingham also cited Gilden,[36] for the proposition that because the author, a known varicella expert, did not mention or discuss varicella infection and pseudotumor, that a causal relationship may not exist. Tr. 158. However, Dr. Bingham's reliance on the article and the point he makes are misplaced. The stated purpose of Gilden's article is to review neurological complications caused by reactivation of the varicella zoster virus as a sequela after primary infection. It is not a discussion of the neurological complications caused by primary varicella infection. The article is noteworthy in that varicella zoster virus reactivation can cause so many diverse and significant illnesses, including but not limited to shingles, post-herpetic neuralgia, meningo-encephalitis, cerebellitis, and ocular disorders. After primary infection, the virus "becomes latent in ganglionic neurons along the entire neuraxis." Resp. Ex. E5 at 1. Thus, "zoster can develop anywhere in the body." Id.

Gilden also discusses vasculopathies which may occur due to reactivation, although the discussion related to arterial vasculopathies which cause strokes, not venous vasculopathies. Dr. Bingham agreed that in its wild form, varicella zoster virus can cause vasculopathy in arteries but

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[35] Centers for Disease Control and Prevention, "Principles of Vaccination," available at http://www.cdc.gov/vaccines/pubs/pinkbook/downloads/prinvac.pdf, last visited Sept. 8, 2015 [Resp. Ex. E3].

[36] Gilden, Don, "The Variegate Neurological Manifestations of Varicella Zoster Virus Infection," 13 CURR. NEUROL. NEUROSCI. REP. 374 (2013) [Resp. Ex. E5].

he did not believe that the same applied to veins. Tr. 185. He conceded, however, that he did not know whether the immunopathology that occurs in arteries due to varicella could also occur in veins. Id. at 187.[37]

Citing the DeSimone[38] article, Dr. Bingham testified that he sees and treats patients who have pseudotumor and then develop chronic migraines. Dr. Bingham testified that "it's understood that this sequence can occur." Tr. 167; Resp. Ex. D3. In DeSimone, patients with chronic headache had MRV studies to look for flow gaps or aplasia[39] or evidence of sinus stenosis. Out of a total of 56 patients, 52 had unilateral or bilateral segmental flow gaps or aplasia seen on MRV. The authors posit that intracranial hypertension is caused by increased resistance to CSF outflow in the cerebral venous blood system. Resp. Ex. D3 at 2. They suggest that sinus stenosis plays a causal role in PTC mechanisms. Id. at 3. The main finding of the study is that the large majority of patients with chronic migraine may actually suffer from a chronic headache due to PTC without papilledema. Id. at 4. While Dr. Bingham agreed that this mechanism may occur, he did not believe that the HPV or varicella vaccines could trigger intracranial hypertension. Resp. Ex. A at 7-8.

Lastly, Dr. Bingham disagreed with the temporal association aspect of Dr. Tornatore's theory. Unlike Dr. Tornatore, Dr. Bingham opined that Madison had a rapid onset of headache, within eight to twenty-four hours after vaccination.[40] Dr. Bingham testified that while it might be possible, it was very unlikely that rapid growth of a virus could cause an increase in intracranial pressure within 24 hours, as posited by Dr. Tornatore. Tr. 154. Instead, Dr. Bingham believed the process would take at least a week. Id. at 155. However, Dr. Bingham conceded that the immunopathogenesis of how viral infection can cause an inflammatory response is outside the scope of his expertise. Tr. 154.

VII. Analysis of Factual Disputes

a. Legal Framework

The Vaccine Act established the Program to compensate vaccine-related injuries and deaths. 42 U.S.C. § 300aa-10(a). "Congress designed the Vaccine Program to supplement the state law civil tort system as a simple, fair and expeditious means for compensating vaccine-

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[37] For articles discussing vasculitis in the context of the dural sinuses due to varicella, see Lahat, 87 ACTA PAEDIATR. 1310 [Pet. Ex. 34 at 2]; and Konrad, D. et al., "Pseudotumour Cerebri After Varicella," 157 EUR. J. PEDIATR. 904-06 (1998) [Pet. Ex. 35].

[38] DeSimone, R. et al., "Intracranial Pressure in Unresponsive Chronic Migraine," 261 J. NEUROL. 1365-73 (2014) (Resp. Ex. D3].

[39] Aplasia is "lack of development of an organ or tissue." Dorland's at 116.

[40] For reasons previous stated, the undersigned finds onset of headache was not within eight to twenty-four hours, but instead was approximately one week post vaccination, consistent with Madison's visit to her pediatrician on January 24, 2012.

related injured persons. The Program was established to award 'vaccine-injured persons quickly, easily, and with certainty and generosity.'" Rooks v. Sec' y of Health & Human Servs., 35 Fed. Cl. 1, 7 (1996) (quoting H.R. Rep. No. 908 at 3, reprinted in 1986 U.S.C.C.A.N. at 6287, 6344).

Petitioners' burden of proof is a preponderance of the evidence. 42 U.S.C. § 300aa-13(a)(1). The preponderance of the evidence standard, in turn, has been interpreted to mean that a fact is more likely than not. Moberly, 592 F.3d at 1322 n. 2. Proof of medical certainty is not required. Bunting, 931 F.2d at 873. A petitioner who satisfies this burden is entitled to compensation unless the government can prove, by a preponderance of the evidence that the vaccinee's injury is "due to factors unrelated to the administration of the vaccine." §300aa-13(a)(1)(B).

b. Elements of Petitioner's Claim

When a petitioner alleges that an injury listed on the Vaccine Injury Table ("the Table") occurs within the time frame set forth in the Table, then petitioner's vaccine claim is deemed a Table claim, and a presumption of vaccine causation attaches. See § 300aa-14; see also 42 C.F.R. § 100.3. If, however, a petitioner alleges an injury that is not listed on the Table (such as the injury alleged in this case), the vaccine claim is deemed a non-Table case, and there is no presumption of causation. Rather, petitioner must satisfy his burden of proof. See § 300aa-13(a)(1)(A).

To receive compensation under the Program, petitioner must prove either: (1) that Madison suffered a "Table Injury"—i.e., an injury listed on the Vaccine Injury Table—corresponding to a vaccine that she received, or (2) that she suffered an injury that was actually caused by the varicella vaccine. See 42 U.S.C. §§ 300aa-13(a)(1)(A) and 11(c)(1); Capizzano, 440 F.3d at 1319-20. Petitioners must show that the vaccine was "not only a but-for cause of the injury but also a substantial factor in bringing about the injury." Moberly, 592 F.3d at 1321 (quoting Shyface, 165 F.3d at 1352-53).

Because petitioners do not allege that Madison suffered a Table injury, they must prove that the varicella vaccine Madison received caused his injury. To do so, they must establish, by preponderant evidence: (1) a medical theory causally connecting the vaccine and Madison's injury ("Althen Prong One"); (2) a logical sequence of cause and effect showing that the vaccine was the reason for her injury ("Althen Prong Two"); and (3) a showing of a proximate temporal relationship between the vaccine and her injury ("Althen Prong Three"). Althen, 418 F.3d at 1278; 42 U.S.C. § 300aa–13(a)(1) (requiring proof by a preponderance of the evidence).

Because the causation theory must relate to the injury alleged, a petitioner must provide a reputable medical or scientific explanation that pertains specifically to the vaccinee's case, although the explanation need only be "legally probable, not medically or scientifically certain." Knudsen, 35 F.3d at 548-49. Petitioners cannot establish entitlement to compensation based solely on their assertions. Rather, a vaccine claim award must be supported either by medical records or by the opinion of a competent physician. § 300aa-13(a)(1). In determining whether petitioners are entitled to compensation, the special master shall consider all material contained in the record, § 300aa-13(b)(1), including "any . . . conclusion, [or] medical judgment . . . which

is contained in the record regarding . . . causation . . . of the petitioner's illness." §300aa-13(b)(1)(A). Thus, the undersigned must weigh the submitted evidence and the testimony of the parties' offered experts and rule in petitioners' favor when the evidence weighs in their favor. Moberly, 592 F.3d at 1325-26 ("Finders of fact are entitled—indeed, expected—to make determinations as to the reliability of the evidence presented to them and, if appropriate, as to the credibility of the persons presenting that evidence"); Althen, 418 F.3d at 1280-81.

c. Factual Disputes

There are two factual disputes: whether petitioner's post-vaccine headache syndrome is caused by intracranial hypertension and whether she suffered a "cerebral venous thromboembolic event" following her January 16, 2012 vaccinations.

The Federal Circuit has made clear that "identifying [the petitioner's] injury is a prerequisite" to the Althen analysis. Broekelschen, 618 F.3d at 1346. However, it is not necessary to diagnose an exact condition. In Lombardi, the Federal Circuit explained: "[t]he function of a special master is not to 'diagnose' vaccine-related injuries, but instead 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." Lombardi v. Sec'y of Health & Human Servs., 656 F.3d 1343, 1351 (Fed. Cir. 2011) (citing Andreu v. Sec'y of Health & Human Servs., 569 F.3d 1367, 1382 (Fed. Cir. 2009)). Furthermore, neither the Vaccine Act nor Althen burdens petitioner with establishing a specific diagnosis. See Kelley v. Sec'y of Health & Human Servs., 68 Fed. Cl. 84, 100 (2005) ("The Vaccine Act does not require petitioners coming under the non-Table injury provision to categorize their injury; they are merely required to show that the vaccine in question caused them injury – regardless of the ultimate diagnosis.")

In determining the petitioner's injury, the undersigned considered the record as a whole. § 13(a)(1). She reviewed and relied on statements in the medical records, as medical records are generally viewed as trustworthy evidence, since they are created contemporaneously with the treatment of the vaccinee. Cucuras v. Sec'y of Health & Human Servs., 993 F.2d 1525, 1528 (Fed. Cir. 1993). In addition, the treating physicians' opinions are "quite probative," as treating physicians are in the "best position" to evaluate the vaccinee's condition. Capizzano, 440 F.3d at 1326 (Fed. Cir. 2006). However, no treating physician's views bind the special master, per se; rather, their views should be carefully considered and evaluated. § 300aa-13(b)(1); Snyder, 88 Fed. Cl. at 745 n. 67. Each opinion from a treating physician should be weighed against other, contrary evidence present in the record – including conflicting opinions from other treating physicians. Hibbard v. Sec'y of Health & Human Servs., 100 Fed. Cl. 742, 749 (Fed. Cl. 2011), aff'd, 698 F.3d 1355 (Fed. Cir. 2012); Caves v. Sec'y of Health & Human Servs., 100 Fed. Cl. 119, 136 (Fed. Cl. 2011), aff'd, 463 Fed. Appx. 932 (Fed. Cir. 2012); Veryzer v. Sec'y of Health & Human Servs., No. 06-522V, 2011 WL 1935813 at *17 (Fed. Cl. Spec. Mstr. Apr. 29, 2011), aff'd, 100 Fed. Cl. 344 (2011).

After careful review of petitioner's medical records, the undersigned finds preponderant evidence that Madison's post-vaccine headache syndrome was caused by intracranial hypertension. This finding is based on the entire clinical presentation, including the initial

opening pressure at lumbar puncture of 30 cmH2O, abnormal MRV studies, medical literature, and most significantly, the fact that Madison's treating physicians diagnosed her with increased intracranial pressure. It is important to note that intracranial hypertension is rare in children, and that the majority of cases are not idiopathic but are caused by trauma, endocrine abnormalities, infection, or medications. Infections associated with the condition include those caused by the varicella virus.

A significant question raised by Madison's treating physicians and the experts was whether her opening pressure of 30 cmH2O at her initial lumbar puncture was diagnostic for increased intracranial pressure. The studies by Gerstl and Inger persuasively illustrate the point raised by Dr. Tornatore that previously recommended diagnostic criteria may be too restrictive. Further, the value must be read in context with other relevant evidence.

The most compelling evidence that Madison's headaches were caused by intracranial hypertension are the opinions documented in her medical records by Dr. Gratz. Dr. Gratz treated Madison beginning in February 2012, early in the course of her illness. He was her treating physician when she had her lumbar puncture, MRVs, and other diagnostic procedures. His work-up was comprehensive and his documentation was very thorough. In March 2012, Dr. Gratz initiated treatment with Diamox for "presumptive therapy of pseudotumor cerebri without papilledema." Pet. Ex. 10 at 77-80. In May 2012, Dr. Gratz documented that Madison had "chronic persistent headaches with associated increased intracranial pressure. . . ." Id. at 56-59. For these reasons, I find that Madison's post-vaccine headache syndrome was caused by intracranial hypertension.

The second fact in dispute is whether Madison suffered a "cerebral venous thrombotic event" following her January 16, 2012 vaccinations. Dr. Frachtman reviewed the first MRV on February 3, 2012, and reported that he was unable to see the left internal jugular vein and thus questioned whether there was a thrombosis or occlusion of the vein. In the next study, on March 28, 2012, Dr. Lopes reviewed both the February and March studies and concluded that the March study showed "recanalization of the left distal internal jugular vein." Pet. Ex. 10 at 66. This suggests that the vein had been previously occluded by a thrombus but there was now blood flow through the vessel. The reasonable interpretation is that the occlusion was caused by a clot or thrombus.

In addition to the occlusion of the left internal jugular vein, Dr. Lopes describes a progression of irregularities involving the left sigmoid sinus. In March, Dr. Lopes describes these changes as minimal, and in July, the abnormality in the left sigmoid sinus has "worsened," and now there is also an abnormality in the right sigmoid sinus. In August, Dr. Lopes describes improvement, with normal flow in these vessels. In August, Dr. Lopes concludes for the first time, "There is no sign of sinus thrombosis." She does not document such a conclusion in her reports in the earlier studies. Thus, there may have been narrowing and abnormality of the right and left sigmoid sinuses, but unlike the internal jugular, they were not occluded by a thrombus.

The medical literature filed by respondent's expert, Dr. Bingham, points out a number of valid concerns when interpreting the MRV studies, especially the problems caused by misinterpreting artifact as pathology. However, given that Madison had serial MRV studies and

given the progression of pathology described by Dr. Lopez, this weighs against the likelihood that the abnormalities were artefactual. Dr. Bingham agreed that the fact that the serial MRVs were reviewed by the same physician was significant, and that there would be less concern about inconsistency in interpretation. Tr. 196.

In summary, the undersigned finds preponderant evidence of an occlusion involving the left distal internal jugular vein and evidence of irregularity or abnormal flow of the left sigmoid sinus, and some minor irregularity of the right sigmoid sinus. Thus, the undersigned finds that Madison suffered a cerebral venous thromboembolic event following her January 16, 2012 vaccinations.

d. Althen Analysis

i. Althen Prong One: Petitioners' Medical Theory

Under Althen Prong One, petitioner must set forth a medical theory explaining how the received vaccine could have caused the sustained injury. Andreu, 569 F.3d at 1375. Under this prong, petitioner must make a showing that the received vaccine "can" cause the alleged injury. Pafford, 451 F.3d at 1355-56.

Petitioner's theory of causation need not be medically or scientifically certain, but it must be informed by "sound and reliable medical or scientific explanation." Knudsen, 35 F.3d at 548-495; see also Veryzer v. Sec 'y of Health & Human Servs., 98 Fed. Cl. 214, 223 (2011) (noting that special masters are bound by both § 300aa-13(b)(1) and Vaccine Rule 8(b)(1) to consider only evidence that is both "relevant" and "reliable"). If petitioner relies upon a medical opinion to support her theory, the basis for the opinion and the reliability of that basis must be considered in the determination of how much weight to afford the offered opinion. See Broekelschen v. Sec'y of Health & Human Servs., 618 F. 3d 1339, 1347 (Fed. Cir. 2010) ("The special master's decision often times is based on the credibility of the experts and the relative persuasiveness of their competing theories."); Perreira v. Sec'y of Health & Human Servs., 33 F.3d 1375, 1377 n.6 (Fed. Cir. 1994) ("An expert opinion is no better than the soundness of the reasons supporting it") (citing Fehrs v. United States, 620 F.2d 255, 265 (Ct. Cl. 1980)).

As framed by the parties, the relevant question as to Althen Prong One is whether petitioner has established preponderant evidence of a medical theory showing that HPV and/or varicella vaccination can result in chronic headache syndrome due to persistent intracranial hypertension.

As explained by Dr. Tornatore, the varicella vaccine contains a live attenuated virus known to infect nerves and blood vessels in the brain. Once infected, blood vessels become inflamed and irritated, causing clots to form or blood vessels to narrow. CSF drains into these blood vessels, and when there is obstruction of venous blood flow, there is a corresponding effect on the drainage of CSF fluid, creating a backup of fluid in the brain. The increase of spinal fluid in a confined space creates an increase in intracranial pressure.

Varicella infection is known to cause this phenomenon, as illustrated by the case reports described by Gilad,[41] Ravid,[42] Lahat[43] and Konrad.[44] While the exact mechanism is not known, Gilad posits that varicella infection may cause venous outflow abnormalities, low grade inflammation, or clotting. Pet. Ex. 32 at 2. Ravid also suggests that venous outflow abnormalities may cause intracranial hypertension. Pet. Ex. 33 at 2. Lahat describes PTC seen due to middle ear infections, prior to the use of antibiotics. Pet. Ex. 34 at 2.

The DeSimone article, cited by both experts, discusses venous stenosis and resulting intracranial hypertension due to increased resistance of CSF outflow. Resp. Ex. D3 at 1; Tr. 167. DeSimone explains that "[i]ntracranial hypertension results from an increased resistance to the CSF outflow into the cerebral venous blood collectors." Resp. Ex. D3 at 2. Moreover, DeSimone states that PTC without papilledema "should be considered in all patients with almost daily migraine pain, with evidence of sinus stenosis and unresponsive to medical treatment. Id. at 4.

For all of these reasons, the undersigned finds that petitioner has provided preponderant evidence that the varicella vaccine[45] can cause chronic headache syndrome due to persistent intracranial hypertension.

ii. Althen Prong Two: Logical Sequence of Cause and Effect

Althen Prong Two requires proof of a logical sequence of cause and effect, usually supported by facts derived from the vaccinee's medical records. Althen, 418 F.3d at 1278; Andreu, 569 F.3d at 1375-77; Capizzano, 440 F.3d at 1326; Grant, 956 F.2d at 1148. In evaluating whether this prong is satisfied, the opinions and views of the vaccinee's treating physicians are entitled to some weight. Andreu, 569 F.3d at 1367; Capizzano, 440 F.3d at 1326 ("medical records and medical opinion testimony are favored in vaccine cases, as treating physicians are likely to be in the best position to determine whether a 'logical sequence of cause and effect show[s] that the vaccination was the reason for the injury'") (quoting Althen, 418 F.3d at 1280). Medical records are generally viewed as trustworthy evidence, since they are created contemporaneously with the treatment of the vaccinee. Cucuras, 993 F.2d at 1528. The petitioner need not make a specific type of evidentiary showing, i.e., "epidemiologic studies, rechallenge, the presence of pathological markers or genetic predisposition, or general acceptance in the scientific or medical communities to establish a logical sequence of cause and

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[41] Gilad, J., CHILD NEUROL. 1 [Pet. Ex. 32]

[42] Ravid et al., 46 PED. NEUROL. 124 [Pet. Ex. 33].

[43] Lahat et al., 87 ACTA PAEDIATR. 1310 [Pet. Ex. 34].

[44] Konrad et al., 157 EUR. J. PEDIATR. 904 [Pet. Ex. 35].

[45] Petitioner failed to show by preponderant evidence that HPV vaccination can cause intracranial hypertension. Thus, the undersigned's decision is based solely on Madison's receipt of the varicella vaccine.

effect." Capizzano, 440 F.3d at 1325. Instead, petitioner may satisfy her burden by presenting circumstantial evidence and reliable medical opinions. Id. at 1325-26.

The second question relevant to the analysis of causation is whether petitioner has shown by preponderant evidence a logical sequence of cause and effect that the varicella vaccination caused petitioner to suffer a cerebral venous thromboembolic event that resulted in persistent intracranial hypertension and subsequent chronic headache syndrome. The undersigned finds that petitioner's clinical course, the elevated opening pressure for her initial lumbar puncture, her serial MRV results, and the opinions of her treating physicians, expert, and the medical literature provide preponderant evidence of a logical sequence of cause and effect. Dr. Tornatore's opinions, coupled with the opinions of the treating physicians and the medical case reports cited were persuasive. Dr. Gratz concluded that Madison's opening pressure of 30 was elevated. Dr. Lopes' interpretations of the MRV studies suggested thrombosis, occlusion, and irregularities of Madison's venous outflow system. Dr. Gratz, Dr. Lipton, and Dr. Tornatore all agreed there was evidence of PTC without papilledema. Madison's clinical course was also consistent with the facts set forth in the medical literature and case reports.

The undersigned thus finds that the facts of the case, when viewed in concert with petitioner's mechanism of causation, demonstrate a logical sequence of cause and effect sufficient to satisfy petitioner's burden under Althen Prong Two.

iii. Althen Prong Three: Is There a Proximate Temporal Relationship?

Althen Prong Three requires petitioner to establish a "proximate temporal relationship" between the vaccination and the injury alleged. Althen, 418 F.3d at 1281. That term has been equated to mean a "medically acceptable temporal relationship." Id. The petitioner must offer "preponderant proof that the onset of symptoms occurred within a timeframe which, given the medical understanding of the disease's etiology, it is medically acceptable to infer causation-in-fact." De Bazan v. Sec'y of Health & Human Servs., 539 F.3d 1347, 1352 (Fed. Cir. 2008). The explanation for what is a medically acceptable time frame must also coincide with the theory of how the relevant vaccine can cause the injury alleged (under Althen Prong One). Id.; Koehn v. Sec'y of Health & Human Servs. 773 F.3d 1239, 1243 (Fed. Cir. 2014); Shapiro v. Sec'y of Health & Human Servs., 101 Fed. Cl. 532, 542 (2011), recons. den'd after remand, 105 Fed. Cl. 353 (2012), aff'd mem., 2013 WL 1896173 (Fed. Cir. 2013).

Madison received her varicella vaccine on January 16, 2012, and the first reference in the contemporaneous medical records to headaches was approximately one week later, January 24, 2012. Dr. Tornatore testified that this was a "perfect" onset for his proposed mechanism. Tr. 47. In the case reports of patients with intracranial hypertension associated with varicella infection described by Gilad, three patients had a recent history of primary varicella infection, ranging from 5 days prior to three weeks prior to the presentation of intracranial hypertension. Pet. Ex. 32 at 2-3; See also Pet. Ex. 33 at 2. Ravid notes that "high levels of immunoglobulin G can be detected within a few days (usually 10-14 days) of the acute infection." Pet. Ex. 33 at 3.

Although Dr. Bingham conceded that immune-pathogenesis was outside his area of expertise, he opined that based on petitioner's proposed mechanism of infection, onset would be

approximately a week. Tr. 154-55. Thus, both experts opined that a temporal association of a week to 10 days would be appropriate. Medical literature supports onset of five days or more. The undersigned finds onset to be approximately one week based on the records and thus finds preponderant evidence of a medically acceptable temporal association in satisfaction of petitioner's burden under Althen Prong Three.

e. Alternative causation

Because the undersigned concludes that petitioners have established a prima facie case, they are entitled to compensation unless respondent can put forth preponderant evidence "that [Madison's] injury was in fact caused by factors unrelated to the vaccine." Whitecotton v. Sec'y of Health & Human Servs., 17 F.3d 374 (Fed. Cir. 1994), rev'd on other grounds sub nom., Shalala v. Whitecotton, 514 U.S. 268 (1995); see also Walther v. Sec'y of Health & Human Servs., 485 F.3d 1146, 1151 (Fed. Cir. 2007). While Dr. Bingham discussed alternate causes for chronic headache in Madison, the undersigned did not find the testimony persuasive given the facts and circumstances of this case.

VIII. Conclusion

For the reasons discussed above, the undersigned finds petitioner is entitled to compensation. A separate damages order will issue.

IT IS SO ORDERED.

s/ Nora Beth Dorsey
Nora Beth Dorsey
Chief Special Master