In the United States Court of Federal Claims
OFFICE OF SPECIAL MASTERS
(E-Filed: July 23, 2013)

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TESSIE DINGLE,	
Petitioner,	No. 08-579V
v.	Chief Special Master Campbell-Smith
SECRETARY OF HEALTH AND HUMAN SERVICES,	Hepatitis B vaccine; Postural Orthostatic Tachycardia Syndrome (POTS); Joint Hypermobility Syndrome (JHS); Insufficient Proof of Causation.
Respondent.	
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Richard Gage, Cheyenne, WY, for Petitioner.
Alexis B. Babcock, Washington, DC, for Respondent.

DECISION[1]

Tessie Dingle (petitioner) filed a petition on August 14, 2008 and an amended petition on April 27, 2009. She alleges that as a result of receiving a hepatitis B vaccination[2] on August 15, 2005–when she was 15 years old–she developed Postural Orthostatic Tachycardia Syndrome (POTS). See Am. Pet. p. 1. POTS is

[1] Because this decision contains a reasoned explanation for the undersigned's action in this case, the undersigned intends to post this decision on the United States Court of Federal Claims' website, in accordance with the E-Government Act of 2002, Pub. L. No. 107-347, § 205, 116 Stat. 2899, 2913 (codified as amended at 44 U.S.C. § 3501 note (2006)). As provided by Vaccine Rule 18(b), each party has 14 days within which to request redaction "of any information furnished by that party: (1) that is 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 entire" decision will be available to the public. Id.

[2] While the Amended Petition states that both the hepatitis B and tetanus/diphtheria (TD) vaccines Tessie received caused her POTS, petitioner's expert, Dr. Vera Byers, identified only the hepatitis B vaccine as the causal factor in the development of Tessie's injury. See July 20, 2012 Hr'g Tr. 44. ("Tr.")

> one of a group of disorders that have orthostatic intolerance (OI) as their primary symptom. OI describes a condition in which an excessively reduced volume of blood returns to the heart after an individual stands up from a lying down position. The primary symptom of OI is lightheadedness or fainting. In POTS, the lightheadedness or fainting is also accompanied by a rapid increase in heartbeat of more than 30 beats per minute, or a heart rate that exceeds 120 beats per minute, within 10 minutes of rising. The faintness or lightheadedness of POTS [is] relieved by lying down again. Anyone at any age can develop POTS, but the majority of individuals affected (between 75 and 80 percent) are women between the ages of 15 to 50 years of age. Some women report an increase in episodes of POTS right before their menstrual periods. POTS often begins after a pregnancy, major surgery, trauma, or a viral illness. It may make individuals unable to exercise because the activity brings on fainting spells or dizziness.
>
> Doctors [remain uncertain regarding] what causes the reduced return of blood to the heart that occurs in OI, or why the heart begins to beat so rapidly in POTS. Current thinking is that there are a number of mechanisms. Some patients have peripheral denervation (neuropathic POTS); some have symptoms that are due to sustained or parosyxmal overactivity of the sympathetic nervous system (hyperadrenergic POTS); and some individuals have POTS dominated by features of deconditioning.

National Institute of Neurological Disorders and Stroke (NINDS) Postural Tachycardia Syndrome Information Page, http://www.ninds.nih.gov/disorders/postural_tachycardia_syndrome/postural_tachycardia_syndrome.htm (last updated Oct. 4, 2011) (emphasis added).

In furtherance of her vaccine claim, petitioner has filed medical records, supporting literature, an affidavit from her mother, Lonnie Fay, and expert opinions from Vera Byers, M.D., Ph.D., an immunologist, and Marcel Kinsbourne, M.D., a neurologist. Respondent has filed a Rule 4(c) report recommending against Program compensation, an expert opinion from Peter Bingham, M.D., a pediatric neurologist, and supporting literature.

The undersigned held an entitlement hearing in Washington, D.C. in July 2012. The parties' experts testified, but Tessie and her treating cardiologist–who initially was expected to testify–did not. Following the hearing, the parties filed post-hearing briefs. The matter is now ripe for decision.

For the reasons set forth below, the undersigned finds that petitioner has failed to satisfy her burden of proving that the August 15, 2005 hepatitis B vaccine she received

was–more likely than not–both the but-for cause of and a substantial factor in causing her POTS injury. Accordingly, petitioner's claim must be dismissed.

I. FACTUAL BACKGROUND

Petitioner filed numerous records of medical treatment she received before and after her August 15, 2005 vaccination. The parties agree that Tessie was properly diagnosed with POTS. See Byers Expert Rpt. [3] 1; Bingham Expert Rpt. [4] 7. The parties disagree regarding the cause of her POTS, with the disagreement primarily focused on the timing of Tessie's symptom onset. See, e.g.,Pet'r's Post-Hr'g Br.[5]10-12 (arguing symptom onset occurred on August 25, 2005); Resp't's Post-Hr'g Br.[6] 15-19 (arguing symptom onset preceded the August 2005 hepatitis B vaccine). If onset occurred prior to the subject vaccination, the parties agree that the vaccination could not have caused Tessie's POTS. If onset occurred after the subject vaccination, the parties disagree as to whether the more likely cause of Tessie's POTS was the received hepatitis B vaccine, her probable viral illness as documented in August 2005, or her congenital joint hypermobility syndrome (JHS).

On August 25, 2005, ten days after receiving the vaccine at issue, Tessie left school feeling sick, and she did not return thereafter. Fay aff.[7] ¶¶ 4, 12. As documented by many of Tessie's treating physicians, the impact of Tessie's illness on her life has been quite serious. See, e.g., Pet'r's Ex. 7 at 4-5 (Dr. Wong opining after his October 2005 examination of Tessie, that POTS is difficult to treat and could be very debilitating); Pet'r's Ex. 44 pt. 2 at 21 (Dr. Canby observing in October 2008, nearly three years after Tessie's vaccination, that since being diagnosed with POTS, Tessie has not been able to complete school or move forward with her life).

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[3] Expert Report of Vera S. Byers, M.D., Ph.D., Feb. 3, 2012 (filed Feb. 9, 2012), ECF No. 59-1 (Pet'r's Ex. 42).

[4] Expert Report of Peter Bingham, M.D., Oct. 17, 2011 (filed Oct. 21, 2011), ECF No. 52-1 (Resp't's Ex. A).

[5] Petitioner's Post-Hearing Memorandum, Nov. 17, 2012, ECF No. 87 (Pet'r's Post-Hr'g Br.).

[6] Respondent's Post-Hearing Memorandum, Dec. 20, 2012, ECF No. 88 (Resp't's Post-Hr'g Br.).

[7] Affidavit of Lonnie Fay, Apr. 24, 2009 (filed Apr. 27, 2009), ECF No. 17-1 (Pet'r's Ex. 21).

Tessie's medical records and her mother's affidavit make clear that Tessie's illness has been disabling, and has presented a major disruption in the lives of Tessie and her family since August 2005. Because the nature and severity of Tessie's condition are undisputed, the undersigned focuses on those aspects of the record that speak to the pathogenesis of Tessie's POTS in this ruling.

Before reviewing the pertinent details of petitioner's medical history, the undersigned discusses the two relevant illnesses with which Tessie has been diagnosed.

A. Petitioner's Diagnosed Illnesses

After receiving the subject vaccination in August 2005, Tessie was diagnosed in October 2005 with POTS, Pet'r's Ex. 7 at 4-5, and one month later, in November 2005, she was diagnosed with hypermobility, a condition also known as joint hypermobility syndrome (JHS), Pet'r's Ex. 6 at 7. Because the two illnesses are relevant to the evaluation of petitioner's claim, a brief description of each disorder and its clinical symptoms follows.

1. POTS

POTS is a heterogeneous group of disorders that presents with similar clinical manifestations. Pet'r's Ex. 29 (2006 Grubb article)[8] at 108. There are two subtypes of the primary form of the disorder, partial dysautonomic and hyperadrenergic. Id. at 108-09. The partial dysautonomic form tends to appear abruptly after a febrile viral illness, pregnancy, trauma, surgery or immunization and is believed to be immune-mediated. Id. at 108. A variant of the partial dysautonomic subtype is the developmental form, which seems to affect adolescents (usually around 14 years of age) after a period of rapid growth. The symptoms seem to peak at 16 years of age, and then abate over the ensuing years. Id. at 108-09.

The hyperadrenergic form of the disorder is marked by a gradual and progressive onset. Id. at 109. It is believed to be genetic. Id.

POTS also may occur as a secondary disorder. The condition is recognized currently as a secondary condition in two circumstances. In the first circumstance, POTS may appear in association with various autoimmune diseases such as diabetes or lupus. Id. In the second circumstance, POTS may occur in association with joint hypermobility syndrome, a connective tissue disorder. Id.

[8] Blair P. Grubb et al., The Postural Tachycardia Syndrome: A Concise Guide to Diagnosis and Management, 17 J. Cardiovascular Electrophysiology 108 (2006) (Pet'r's Ex. 29).

A POTS diagnosis can be determined by objective measures. As Dr. Kinsbourne testified, a POTS diagnosis requires a heart rate on standing that is 30 beats per minute–or in a teenager perhaps 40 beats per minute–higher than the measured heart rate when sitting or lying down. Tr. 85. Such an abnormal heart rate may be determined by a tilt table test. See American Heart Association, http://www.heart.org/HEARTORG/Encyclopedia/Heart-Encyclopedia_UCM_445084_Encyclopedia.jsp (search on tilt- table test) (last visited July 18, 2013). According to the authors of the 2006 Grubb article, knowledge of this condition has grown "tremendous[ly]" between 1986 and 2006. See Pet'r's Ex. 29 at 108.

Although Tessie's medical records establish that she suffers from POTS, she has not been diagnosed with a particular subtype.

Of the various forms of POTS, petitioner has focused on the primary subtype of POTS known as partial dysautonomic form. Petitioner's expert, Dr. Kinsbourne, pointed to the 2006 Grubb article to describe this form of POTS. As the authors of the 2006 Grubb article observed:

> [Afflicted] patients seem to suffer from a mild type of peripheral autonomic neuropathy characterized by an inability of the peripheral vasculature to constrict in the face of orthostatic stress. This cause[s] a much larger than normal degree of blood pooling in the dependent areas of the body when upright, which in turn cause[s] a compensatory increase in heart rate and contractility that attempts to maintain cerebral perfusion [or the blood flow to the brain] at constant levels.

Kinsbourne Expert Rpt.[9] 5 (quoting Pet'r's Ex. 29 at 108). Nearly two months after Tessie received the vaccine at issue, she was diagnosed with POTS.

2. Joint Hypermobility Syndrome (JHS)

The second condition with which Tessie has been diagnosed is joint hypermobility syndrome. It is "one of the most common heritable disorders of connective tissue."

[9] Amended Expert Report of Marcel Kinsbourne, M.D., July 24, 2011 (filed June 8, 2012), ECF No. 75-2 (Pet'r's Ex. 61). Petitioner filed Dr. Kinsbourne's original expert report on July 25, 2011 as Pet'r's Ex. 24; upon the filing of Dr. Kinsbourne's amended report, the undersigned struck Pet'r's Ex. 24 from the record. See Order, July 10, 2012, ECF No. 78.

Resp't's Ex. A-3[10] (2003 Gazit article) at 33. The syndrome is characterized by joint laxity that can cause articular (or joint) dislocations, subluxations (which are partial dislocations or sprains), and arthralgia. Id. Patients with joint hypermobility syndrome frequently report symptoms that may be related to the autonomic nervous system, such as palpitations, lightheadedness/dizziness, and presyncope or syncope (fainting). In these patients, the complaints have not been connected to any autonomic nervous system dysfunction. Id.

In the 2003 Gazit article, researchers studied 48 patients with JHS. The subject patients showed certain symptoms typically associated with autonomic nervous system dysfunction. Such symptoms included those that are indicative of cerebral hypoperfusion (or diminished brain blood flow), specifically, dizziness/lightheadedness (88%), presyncope (83%), headache (75%), impaired concentration (71%), irritability (60%), blurred vision (56%), forgetfulness (50%), and confusion (29%). Resp't's Ex. A-3 at 35 tbl. 2. Other reported symptoms included palpitations (90%), chest discomfort (65%), flushing (63%), tremulousness (56%), nausea (54%), shortness of breath (52%), abdominal discomfort (46%), hyperventilation (40%), weight changes (35%), diarrhea (31%), constipation (31%), fatigue (physical) (71%), fatigue (central) (67%), nocturia (67%), ankle edema (12.5%), standing intolerance (56%), alcohol intolerance (69%), and heat intolerance (76%). Id. at 35 tbl. 2. The study's authors speculated that blood vessel abnormalities as well as connective tissue abnormalities were contributing to the subjects' symptomatic discomfort.

Tessie was born in July 1990 with bilateral dislocatable hips, a congenital disorder. See Pet'r's Ex. 18 at 1. The condition was treated by outfitting Tessie with a harness for the first two months of her life. Pet'r's Ex. 18 at 1; Pet'r's Ex. 19 at 161. About fifteen years later, on November 1, 2005, Tessie was diagnosed with hypermobility by her pediatric rheumatologist, Dr. Ruy Carrasco. Pet'r's Ex. 18 at 67.

On examination, Dr. Carrusco found that Tessie was "positive for hypermobility of the elbows and knees greater than 10 degrees of hyperextension. [Her] thumbs easily abducted to the forearms without any difficulty. She could hyperextend her fingertips to touch the dorsum of her hand well beyond even 90 degrees. She had hypermobility of the ankles as well." Id. at 69. Dr. Carrusco did not prescribe any treatment for this syndrome. See id. at 69-70.

Tessie was diagnosed with JHS nearly three months after she received the hepatitis B vaccine of concern.

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[10] Yael Gazit et al., Dysautonomia in the Joint Hypermobility Syndrome, 113 Am. J. of Med. 33 (2003) (Resp't's Ex. A-3).

B. Petitioner's Medical History Prior to the August 15, 2005 Vaccination

Before petitioner received the vaccination at issue in this case, she was noted to have symptoms of shortness of breath; but she was not diagnosed with asthma. She suffered a head injury, and she had episodes of weakness, fatigue, dizziness, headaches and problems concentrating. The undersigned reviews the records addressing these issues first.

1. Petitioner's Evaluation for Asthma

On December 3, 2002, three years before the vaccination of concern, Tessie visited her primary care physician, Dr. Sandra Thomas, for nasal congestion, vomiting and a sore throat. Pet'r's Ex. 4 at 3. There is a mention in the notes of that office visit that Tessie had a history of shortness of breath, but Dr. Thomas indicated that an evaluative work-up for asthma was negative. Id.

Eight months later, in August 2004, either Tessie or her mother completed a school health form reporting that Tessie did not have asthma. Pet'r's Ex. 8 at 11.

Consistent with the earlier reports in Tessie's medical records, the history section of a hospital emergency room record dated November 28, 2005, expressly stated that Tessie did not have asthma. Pet'r's Ex. 20 at 24.

Although the records were clear that Tessie did not have asthma, petitioner's expert, Dr. Kinsbourne, testified at hearing that she did, in an apparent effort to explain her documented shortness of breath prior to vaccination. See Tr. 136. But, as petitioner confirmed after the hearing, she has never been diagnosed with asthma. Response 2, Sept. 4, 2012, ECF No. 83.

2. Petitioner's Head Injury and Post-Concussive Syndrome

On September 2, 2003, nearly two years before petitioner received the vaccine at issue, she accidentally hit her head on a moving ceiling fan while on the top of a bunk bed. Pet'r's Ex. 5 at 34. She did not immediately tell her mother of this incident and thus, did not go to the emergency room until three days later. Id. at 34-37.

Upon presentation to the emergency room, Tessie reported symptoms of nausea and headache, Pet'r's Ex. 5 at 34, and difficulty concentrating, Id. at 36. A computed tomography (CT) scan suggested a small, non-displaced fracture. Id. at 20.

In March 2004, Tessie's pediatric neurologist, Dr. Dilip Karnik, diagnosed her with post-concussive syndrome and started her on medication. Pet'r's Ex. 6 at 23.

3. Petitioner's Weakness, Dizziness, Fatigue, Nausea, Headaches and Concentration

Petitioner's early medical history contains a number of notations concerning her symptoms of weakness, dizziness, fatigue, nausea, headaches and concentration issues. In March 1996, Tessie visited her pediatrician, Dr. Thomas Zavaleta, with complaints of being tired, having a stomachache, and feeling "faint." Pet'r's Ex. 19 at 30. Dr. Zavaleta suspected a viral illness. Id.

More than two years later, in December 1998, Tessie's mother reported symptoms of fatigue, malaise, and dizziness that had caused Tessie to miss school. The examining physician was of the view that Tessie had allergic rhinitis. Id. at 6.

Three years later, in May 2002, Tessie visited her family doctor, Dr. Thomas, complaining of abdominal pain, as well as weakness, dizziness, tiredness and nausea. Pet'r's Ex. 4 at 5. She tested positive for mononucleosis. Pet'r's Ex. 4 at 5; see Pet'r's Ex. 18 at 34.

Almost two years later, in January 2004, Tessie's primary care physician, Dr. Sidney Shinkawa, recorded that Tessie continued to have headaches and dizziness. He added that her short-term memory was not impaired. Pet'r's Ex. 5 at 4. It was Dr. Shinkawa's understanding from Tessie's mother that Tessie had a scheduled appointment with a neurologist; he offered to try to arrange an earlier neurologic appointment for Tessie if her mother would provide him with the doctor's name. Id. He also started Tessie on Fiorinal for her headaches. Id.

A couple of months later, in March 2004, Tessie saw Dr. Karnik, a pediatric neurologist. He recorded that Tessie intermittently had headaches that primarily affected her on the left side of her head. Pet'r's Ex. 6 at 23. She also felt dizzy, and suffered from nausea (without vomiting). Id. She had difficulty concentrating and maintaining focus at school which caused a drop in her grades. She reported problems with making decisions. Id. Based on her described symptoms, Dr. Karnik diagnosed Tessie with post-concussive syndrome. Id.

Three months later, in June 2004, Dr. Karnik saw Tessie again. Tessie complained of mild, daily headaches and was assessed as having chronic headaches of a neuromuscular type. Pet'r's Ex. 18 at 134.

In September 2004, Tessie's primary care doctor, Dr. Shinkawa, conducted a routine school physical. Tessie no longer was suffering from headaches or dizziness, and she was no longer taking medication for her headaches. Pet'r's Ex. 5 at 5. Dr. Shinkawa recorded that Tessie was doing well. Id.

About eight months later, in May 2005, Tessie returned to Dr. Karnik, complaining that she suffered from a headache every other day. Pet'r's Ex. 18 at 120. Tessie also complained of an episode during which objects had begun to move or oscillate from side to side; the referenced episode had lasted for about one minute or so. Id. It was Dr. Karnik's clinical impression that petitioner was suffering from a migraine. Id. Dr. Karnik ordered several tests to check for structural abnormalities and vascular problems. Among the ordered tests were an electroencephalogram (EEG), a magnetic resonance image (MRI) and a magnetic resonance arteriogram (MRA). Id. All of the tests came back normal. Id. at 117, 147.

In June 2006, Tessie's pediatric cardiologist, Dr. Richard Friedman, described the evolution of Tessie's various symptoms, writing:

> Tessie . . . was healthy until 2004, and over the last few years [she] has had multiple episodes of "blacking out" and several witnessed episodes of syncope. She states that ~ 2 years ago [about one year prior to the subject vaccination] she began having "blacking out" episodes when she first stood up from a seated position [, then] she would become dizzy, hear roaring noises in her ears, and sometimes need[ed] to sit back down.

Pet'r's Ex. 9 at 3.

4. Petitioner's August 1, 2005 Illness

On August 1, 2005, Tessie went to the emergency room with complaints of nausea and vomiting, after becoming ill during the preceding night. See Pet'r's Ex. 20 at 27. The records reflect that Tessie awakened in the middle of the night with nausea and vomited about six times. Id. The next morning she felt weak and still slightly nauseated. Id. Tessie collapsed, suffering mild trauma to the left side of her scalp–in the same location as her earlier head injury. Id.

Testing was performed at the hospital. Tessie's complete blood count (CBC) showed a slightly elevated white blood cell count of 11.4[11] (the stated reference range for the test was a reference range of 4.0 – 10.5), id. at 31, but the emergency room report stated that the "CBC [was] within normal limit," id. at 28. The examining physician also noted that Tessie's blood pressure showed some mild orthostatic change. Id.

[11] An increased white blood cell count (WBC) usually indicates infection, inflammation, tissue necrosis, or leukemic neoplasia. Trauma or stress–either emotional or physical–also may increase the WBC count. Mosby's Manual of Diagnostic & Laboratory Tests 549 (4th ed. 2010) ("Mosby's").

The emergency room physician opined that dehydration had led to Tessie's vasovagal episode. Pet'r's Ex. 20 at 28. He diagnosed her with a syncopal episode, nausea, and bruising of her scalp, right ribs, and left neck. Id. He also prescribed medication for her "probable viral syndrome." Id.

C. The Vaccination at Issue

On August 15, 2005, two weeks after her emergency room visit, Tessie received booster vaccinations of hepatitis B and tetanus/diphtheria (TD). Pet'r's Ex. 5 at 3. The vaccinations were administered during a routine physical by Dr. Shinkawa. Pet'r's Ex. 5 at 3; Pet'r's Ex. 12 at 1. Dr. Shinkawa's notes from this office visit contained no mention of any current problems. Pet'r's Ex. 5 at 3. He did remark that Tessie no longer had dizzy spells or seizures, and he described Tessie's condition as a "post headache; post-concussion syndrome." Id.

Petitioner has implicated the hepatitis B vaccine she received at Dr. Shinkawa's office on August 15, 2005 in her Program claim. Of note, she previously had received–without reported incident–three hepatitis B vaccinations. Those vaccinations were administered respectively on December 12, 2001,[12] Pet'r's Ex. 4 at 11, March 19, 2002, Id. at 12, and October 16, 2002, Id.

D. Petitioner's Post-Vaccination Records

As the record reflects, Tessie received a number of evaluations for various health complaints over the course of the year following the vaccination at issue. According to her mother, Tessie came home from school exhausted–ten days after her vaccination–on Thursday, August 25, 2005. Fay aff. at ¶ 4. She slept through the day until the next morning. Id.

Four days later, on Monday, August 29, 2005, Tessie saw her primary care physician, Dr. Shinkawa. He recorded a four-day history of chills, sore throat, and slight nausea. Pet'r's Ex. 5 at 3. Tessie's symptoms had resolved almost completely by the time she saw Dr. Shinkawa. Id. She continued, however, to feel tired and weak. Id. Dr. Shinkawa noted that the blood work completed during Tessie's August 15, 2005 physical was "normal,"[13] and he concluded that Tessie likely had a viral syndrome. Id.

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[12] Petitioner's counsel reported that Tessie's first hepatitis B vaccine was in August 1991, Tr. 25, however, the record counsel cited indicates it was in December 2001.

[13] The laboratory results for this blood work were not included in the medical records filed by petitioner.

On Wednesday, August 31, 2005, Tessie visited her pediatrician, Dr. Zavaleta, complaining of fatigue, excessive sleep since the preceding Thursday (that is August 25, 2005), nausea with vomiting, and presyncope followed by syncope. Pet'r's Ex. 14 at 1-2. Dr. Zavaleta recorded petitioner's various symptoms to include weakness, tiredness, lightheadedness, and decreased ability to focus. Id. at 1. He assessed her with idiopathic fatigue. Id. at 2.

On September 9, 2005, Tessie returned to Dr. Zavaleta. Id. She reported symptoms of blurred vision without fever, cold sweats, muscle aches, shortness of breath, and a rash. Id.

Three days later, on September 12, 2005, Tessie presented to the emergency room with complaints of fatigue, headache, weakness, blurred vision and skin burning sensations. Pet'r's Ex. 3 at 44. Laboratory test results showed a high ANA[14] and titers elevated for Epstein-Barr virus (EBV).[15] Id. at 54-55 (referring to Pet'r's Ex. 1 at 69, 79).

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[14] Antinuclear antibody (ANAs) are used to diagnose systemic lupus erythematosus (SLE) and other autoimmune diseases. Mosby's 90.

ANA results are reported as a titer with a particular type of immunofluorescence pattern (when positive), as revealed under a ultraviolet microscope. Id. 91-92. A speckled pattern is associated with autoimmune disorders such as SLE, scleroderma, rheumatoid arthritis, mixed connective tissue disease, Sjögren syndrome, and polymyositis. Id. 92 fig. 2-5 (emphasis added).

A titer is the quantity of substance required to produce a reaction given the volume of another substance, or the amount of one substance required to correspond with a given amount of another substance. Dorland's Illustrated Medical Dictionary 1932 (32nd ed. 2012). In general, the higher the titer of a certain ANA antibody known to be associated with a certain autoimmune disease, the more likely that disease exists and the more active the disease is. Mosby's 92. Many abnormal antibodies are present in patients with autoimmune (also called rheumatic or connective tissue) diseases. Id. 90 (emphasis added).

[15] An EBV titer is used to diagnose a suspected EBV infection (infectious mononucleosis). Id. 230. After recovery from a primary EBV infection, patients are life-long, latent EBV carriers. Id. In the last several years, specific immunologic tests to identify EBV activity indicate that latent EBV can reactivate and become associated with a constellation of chronic signs and symptoms resembling infectious mononucleosis. Id. Clinical manifestations of chronic EBV are variable and may include nonspecific symptoms, such as profound fatigue (chronic fatigue syndrome), pharyngitis, myalgia, arthralgia, low-grade fever, headache, paresthesia, and loss of abstract thinking. Id.

Later that month, on September 22, 2005, Tessie saw Dr. Carrasco, a pediatric rheumatologist. See Pet'r's Ex. 6 at 16-18. He noted that Tessie's previously reported symptoms of fatigue, headache and chills were ongoing. Id. Tessie had been referred to Dr. Carrasco to investigate further her chronic fatigue and her positive ANA finding. Id. at 16. While Dr. Carrasco did not address–in his detailed report–Tessie's joint hypermobility, he did note that his review of petitioner's systems and her clinical history offered no indication that Tessie had either lupus or any other autoimmune condition. See id. at 18.

A week thereafter, on September 29, 2005, Tessie saw a pediatric infectious disease specialist, Dr. Sarmistha Hauger. Dr. Hauger documented a six-week history of fatigue, headache, intermittent oral blisters, and a diminished ability to concentrate. Id. at 13. Tessie stated that she had periodic breathlessness (dyspnea)–unrelated to exercise–cold sweats, occasional blurry vision, and a burning sensation in her skin that was not accompanied by fever. Id. at 13-14. Tessie's fatigue was intense, but she did not suffer from insomnia. Id. She also complained of joint stiffness, ongoing nausea, and daily headaches with light sensitivity (photophobia). Id. at 14. On review of the results of Tessie's blood work (taken on September 2, 2005), Dr. Hauger found a "low positive" ANA and Epstein-Barr virus titers that showed antibodies with convalescence (an indication of a prior EBV infection). Id. (referring to Pet'r's Ex. 1 at 69, 79). In Dr. Hauger's view, Tessie most likely was suffering from chronic fatigue syndrome, a condition that can present in subjects with latent EBV infections as well as in POTS patients and those afflicted with joint hypermobility syndrome. Pet'r's Ex. 6 at 14; see also Mosby's 230.

On October 4, 2005, Tessie consulted with a pediatric cardiologist, Dr. Frank Wong. Pet'r's Ex. 7 at 4-5. Dr. Wong recorded a six-week history of chronic fatigue and tiredness, complaints of shortness of breath at rest, tingling and numbness in petitioner's extremities, cold feet, and significant dizziness when Tessie attempted any postural changes. Id. at 4. Tessie had not been in school since the onset of her symptoms nearly six weeks earlier (on August 25, 2005). See id.

Dr. Wong opined that Tessie's symptoms were highly suggestive of POTS because she satisfied the clinical criteria of a heart rate increase of 30 beats per minute (bpm) or more when she transitioned from a supine position to standing, in 10 minutes or less. Id. at 5. Dr. Wong noted that her symptoms of shortness of breath, tingling, cold extremities, and lightheadedness with postural changes were all characteristic for POTS. Id.

That same day, October 4, 2005, Tessie also was examined by a pediatric pulmonologist, Dr. Jason Fullmer. He too noted Tessie's six-week history of chronic

fatigue and intermittent headaches, with short episodes of breathlessness that resolved rapidly. Pet'r's Ex. 16 at 1-2.

Nine days later, on October 13, 2005, Dr. Hauger, an infectious disease specialist whom Tessie had seen previously, assessed Tessie with POTS that he believed to be related to her chronic fatigue syndrome. Pet'r's Ex. 3 at 72. Dr. Hauger was not persuaded that Tessie's symptoms had been caused by infection. See id.

On October 25, 2005, Tessie returned to Dr. Zavaleta, who documented Tessie's complaints of odd rashes, canker sores, blisters, joint pains, (particularly in the hips and knees), fatigue, cold hands and feet, burning sensations in the hands and skin, and some loss of hair. Pet'r's Ex. 1 at 6. In Dr. Zavaleta's assessment, petitioner had chronic idiopathic fatigue syndrome, vasodepressor syncope, and vocal cord dysfunction. Id.

On November 1, 2005, Dr. Carrasco detected café au lait spots and diagnosed Tessie with fatigue, POTS, and hypermobility. Pet'r's Ex. 6 at 7. He noted Tessie's ongoing complaint of severe headaches, a skin burning sensation, and a skin rash. Id. Tessie's feet felt cold and particularly so, at night. See id. at 9. Dr. Carrasco discussed Tessie's lab work which revealed an ANA that was both positive and negative on consecutive days, as well as a positive anticentromere titer that may have been indicative of an autoimmune disorder.[16] See id.

At the end of the month, on November 28, 2005, Tessie went to the Seton Hospital emergency room with symptoms that included a recent hallucination. Pet'r's Ex. 3 at 111-13. She was admitted and transferred, the next day, to the Children's Hospital of Austin. See Pet'r's Ex. 3 at 113; Pet'r's Ex. 9 at 26. She remained hospitalized there for 22 days until December 9, 2005. See Pet'r's Ex. 9 at 49-51. The admission records for Children's Hospital describe a history of fatigue, headaches, joint pain, nausea, and hallucinations that began in late August, presenting initially as severe fatigue. See Pet'r's Ex. 3 at 130-31. Tessie's complaints increased to include intermittent nausea, headaches, and joint pain in her wrists, ankles, and knees. She reported increased fatigue after a recent hallucination that she had seen a mouse. Id. at 130. On examination, the following conditions were ruled out: infection, an endocrine disorder, arrhythmia, anemia, and depression. See Pet'r's Ex. 20 at 25. Tessie's diagnosis on discharge was the same as she had received on admission–she was deemed to have chronic fatigue and POTS. Pet'r's Ex. 3 at 118.

[16] Dr. Carrasco's review indicates that laboratory studies were done on October 26, 2005, in which the ANA was not reactive, and labs also had been performed on October 25, 2005, in which the ANA was positive speckled pattern, and a positive anticentromere. Pet'r's Ex. 6 at 9. The October 25, 2005 lab results are located at Pet'r's Ex. 1 at 52. The undersigned does not know to what other laboratory result Dr. Carrasco was referring.

Four months after receiving the vaccine at issue, in December 2005, Tessie underwent a genetics evaluation by Dr. Ladonna Immken. Dr. Immken remarked that Tessie appeared to be heterozygous for an MTHFR mutation. Pet'r's Ex. 6 at 5. This particular mutation, which is present in about 10% of the normal population, conferred a slightly elevated risk for cardiovascular events. Pet'r's Ex. 6 at 5. Dr. Immken did not recommend any intervention, but she did observe that POTS can be caused by a deficiency in the gene that encodes for the norepinephrine transporter (SLC6A2), id., which is suspected to regulate the distribution of sympathetic activity between the heart, vasculature, and kidney in humans, see Antje F. Mayer et al., Influences of Norepinephrine Transporter Function on the Distribution of Sympathetic Activity in Humans, 48 Hypertension 120 (2006), available at http://hyper.ahajournals.org/content/48/1/120.long.

In January 2006, Tessie returned to Dr. Wong, her treating cardiologist. Pet'r's Ex. 7 at 2-3. He noted that Tessie had not responded to the beta-blocker, Atenolol, he had prescribed to modulate her heart rate. Id. at 2. He prescribed Mestinon, a therapy intended to regulate her nerve impulse transmissions across her neuromuscular junctions. Id. at 3. Dr. Wong observed that Tessie continued to be significantly symptomatic despite the earlier attempted beta-blocker therapy. Id. at 2.

In March 2006, Tessie returned to her pediatric neurologist, Dr. Karnik, for further evaluation. He noted Tessie's inability to perform activities over a period of months. Pet'r's Ex. 6 at 1-2. Dr. Karnik found Tessie's history to be consistent with chronic fatigue syndrome. Id. at 2.

In June 2006, Tessie was seen by a second pediatric cardiologist, Dr. Richard Friedman. Pet'r's Ex. 9 at 3. He wrote that Tessie complained of severe fatigue whenever she performed tasks beyond her usual routine. Id. Her dizziness, syncope, and severe headaches tended to be exacerbated by overstimulation. Id. On observation, Tessie had tachycardia (a rapid heartbeat) without an appreciable decline in her blood pressure, and her nails became cyanotic when she stood up. Id. at 5. In Dr. Friedman's view, Tessie exhibited an autonomic instability that was consistent with POTS. Id. at 4-5.

Efforts to treat Tessie were varied. Among her prescribed therapies were: (1) use of the antihyperkinetic clonidine in July 2006, Pet'r's Ex. 13 at 19; (2) chiropractic treatments in February 2007, Pet'r's Ex. 15 at 4; (3) physical therapy in June 2007, Pet'r's Ex. 2 at 345; and (4) intravenous hydration treatment in October 2007, Id. at 177.

As Dr. Wong observed in January 2008, Tessie remained significantly symptomatic, notwithstanding her various treatments and prescriptions. Pet'r's Ex. 7 at 1. Her physicians viewed her treatments as largely unsuccessful.

In October 2008, Tessie saw another cardiologist, Dr. Robert Canby, for an electrophysiology consultation. See Pet'r's Ex. 44 pt. 2 at 21-22. Dr. Canby noted that Tessie had been evaluated by Dr. Ben Levine at the University of Texas Southwestern Medical School, but this had not assisted her with any symptom relief.[17] Pet'r's Ex. 44 pt. 2 at 21. Dr. Canby agreed with the earlier assigned diagnosis of POTS, and he urged Tessie to seek care at a medical center where comprehensive care could be obtained.[18] Id. at 22.

In April 2009, Dr. Wong reevaluated Tessie. Pet'r's Ex. 44 pt. 1 at 11-12. He observed that while Tessie had been very symptomatic in 2007 and 2008, she had been "pretty good for the past 6 weeks." Id. at 11.

Nearly two years later, in February 2011, Dr. Wong again saw Tessie. Id. at 9-10. He found that Tessie was doing better overall, but he recommended that Tessie consult with Dr. David Robertson, a specialist in autonomic disorders at Vanderbilt University.[19] Id. at 10.

No further relevant records regarding Tessie's condition were filed prior to the July 2012 hearing.

II. APPLICABLE LEGAL STANDARDS

A. Causation

The Vaccine Act provides two separate methods by which a petitioner may obtain Program compensation. The first is as a Vaccine Injury Table (Table) claim; the second is as a causation in fact (off-Table) claim. Andreu v. Sec'y of Health & Human Servs., 569 F.3d 1367, 1374 (Fed. Cir. 2009).

If asserting a Table claim, a claimant is afforded a presumption of causation if she can show that she received a vaccine listed on the Table, 42 C.F.R §100.3(a), and that she suffered an injury listed on the Table within the prescribed time period. 42 U.S.C. § 300aa-11(c)(1)(C)(i); see Pafford v. Sec'y of Health & Human Servs., 451 F.3d 1352, 1355 (Fed. Cir. 2006). But, if unable to establish a Table claim, a claimant must show that her injury was "caus[ed] in fact" by the vaccine she received. See Capizzano v.

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[17] No records from Dr. Levine are contained in the record.

[18] There is no information in the record to indicate whether Tessie ever received an evaluation at either of the recommended clinics.

[19] There is no information in the record to indicate whether Tessie ever contacted Dr. Robertson.

Sec'y of Health & Human Servs., 440 F.3d 1317, 1320 (Fed. Cir. 2006).

In such circumstances, the petitioner must prove by preponderant evidence that her vaccination was a substantial factor in causing the illness, and that the suffered harm would not have occurred but-for the vaccination. Shyface v. Sec'y of Health & Human Servs., 165 F.3d 1344, 1352 (Fed. Cir. 1999).

The Federal Circuit has set forth a three-part test. For establishing causation in fact. To satisfy this test, petitioner must present:

> (1) a medical theory causally connecting the vaccination and the injury;
> (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and
> (3) a showing of a proximate temporal relationship between vaccination and injury.

Althen v. Sec'y of Health & Human Servs., 418 F.3d 1274, 1278 (Fed. Cir. 2005).

If petitioner proves a prima facie case, the burden then shifts to respondent to show, by preponderant evidence, that the asserted injury is due to factors unrelated to the administration of the vaccine. See 42 U.S.C. § 300aa–13(a)(1)(B). Respondent bears the burden of showing that a specific unrelated factor "was the sole substantial factor in bringing about the injury." de Bazan v. Sec'y of Health & Human Servs., 539 F.3d 1347, 1354 (Fed. Cir. 2008).

B. Consideration of Other Possible Causes

In making a determination as to whether petitioner has met her evidentiary burden, a special master must consider the record as a whole. See 42 U.S.C. § 300aa–13(a)(1) (requiring that a special master's findings be based "on the record as a whole"); de Bazan, 539 F.3d at 1353 (stating that proof of alternate causation may be considered during the petitioner's case-in-chief). As the Federal Circuit has observed,

> Our decisions support the commonsense proposition that evidence of other possible sources of injury can be relevant not only to the "factors unrelated" defense, but also to whether a prima facie showing has been made that the vaccine was a substantial factor in causing the injury in question. See, e.g., de Bazan v. Sec'y of Health & Human Servs., 539 F.3d 1347, 1353 (Fed. Cir. 2008) ("The government, like any defendant, is permitted to offer evidence to demonstrate the inadequacy of the petitioner's evidence on a requisite element of the petitioner's case-in-chief."); Pafford v. Sec'y of Health & Human Servs., 451 F.3d 1352, 1358-59 (Fed. Cir. 2006) ("[T]he

> presence of multiple potential causative agents makes it difficult to attribute 'but for' causation to the vaccination .... [A] Special Master properly [may] introduce[] the presence of the other unrelated contemporaneous events as just as likely to have been the triggering event as the vaccinations.").

Stone v. Sec'y of Health & Human Servs., 676 F.3d 1373, 1379-80 (Fed. Cir. 2012).

A petitioner is not required, however, to eliminate all possible alternate causes to establish causation. See Stone, 676 F.3d at 1380 (citation omitted); Walther v. Sec'y of Health & Human Servs., 485 F.3d 1146, 1150 (Fed. Cir. 2007) (concluding that "the Vaccine Act does not require the petitioner to bear the burden of eliminating alternative causes where the other evidence on causation is sufficient to establish a prima facie case"). Nonetheless, a petitioner may seek to eliminate potential non-vaccine causes of her injury in an effort to buttress her claim that the vaccine was the cause of her injury.

> [I]f the record indicates the existence of other possibilities as a reasonable culprit for the cause of the disease, it is very possible that the petitioner has not met either the "but for" or "substantial factor" requirement because those other possible culprits may well remain as viable alternatives that undercut the vaccine's causative role. In other words, as a practical matter, in such a circumstance, petitioners [who] eliminate other reasonably possible causes that exist in the record . . . [increase the likelihood of meeting their] burden of establishing a prima facie case for causation-in-fact.

Pafford v. Sec'y of Health & Human Servs., 64 Fed. Cl. 19, 30 (2005), aff'd 451 F.3d 1352 (2006).

The undersigned applies these guiding principles in considering the case at hand.

III. THE PARTIES' EXPERT TESTIMONY

A. The Law Pertaining to Expert Opinions in Vaccine Program Cases

The Court of Federal Claims recently provided the following instructive guidance:

> In cases in which a petitioner relies upon expert testimony to prove causation, the expert testimony must rest upon an objective and reliable scientific basis and must prove causation to a degree of legal certainty, but not to a medical or scientific certainty. See Moberly ex rel. Moberly v. Sec'y of Health & Human Servs., 592 F.3d at 1322 ("A petitioner must provide a reputable medical or scientific explanation that pertains specifically to the petitioner's case, although the explanation need only be

> 'legally probable, not medically or scientifically certain.'" (quoting Knudsen ex rel. Knudsen v. Sec'y of Health & Human Servs., 35 F.3d at 548–49)); see also Cedillo v. Sec'y of Health & Human Servs., 617 F.3d at 1339; Terran ex rel. Terran v. Sec'y of Health & Human Servs., 195 F.3d at 1316. Although a petitioner may rely solely on expert testimony, "[a]n expert opinion is no better than the soundness of the reasons supporting it." Perreira v. Sec'y of Health & Human Servs., 33 F.3d 1375, 1377 n.6 (Fed.Cir.1994). Therefore, a Special Master does not need to credit "expert opinion testimony that is connected to the existing data or methodology 'only by the ipse dixit of the expert,' or where 'there is simply too great an analytical gap between the data and the opinion proffered.' " Jarvis v. Sec'y of Health & Human Servs., 99 Fed. Cl. at 61 (quoting Cedillo v. Sec'y of Health & Human Servs., 617 F.3d at 1339).

Isaac v. Sec'y of Health & Human Servs., 108 Fed. Cl. 743, 768 (Fed. Cl. 2013) (footnote omitted).

When the opinion of a medical expert is offered in support of a claim, it must be evaluated; the reliability of an expert's opinion is not presumed. See Ultimo v. Sec'y of Health & Human Servs., 28 Fed. Cl. 148, 152 (1993) ("Simply because a witness is found qualified to testify as an expert does not mean that the trier of fact must accept his testimony."). Before reviewing the experts' positions, the undersigned considers the experts offered by the parties and their respective credentials.

B. Petitioner's Treating Cardiologists

Petitioner's expert immunologist, Dr. Byers, observed at hearing that her review of the medical literature concerning POTS indicated that "most of the interest in th[e] disease [POTS] has . . . not been from . . . neurologists, and it has not filtered over to . . . immunologists yet[.] [I]t's mostly been in the province of the cardiologists." Tr. 16.

Here, however, petitioner provided no written opinion or testimony from a cardiologist–although her medical records indicate that she conferred with a number of cardiologists. Petitioner did list her primary treating cardiologist, Dr. Frank Wong, as a possible witness for the July 2012 entitlement hearing. Pet'r's Witness List, June 8, 2012, ECF No. 69. Petitioner subsequently asked to accommodate Dr. Wong's participation by telephone. See Status Report, July 9, 2012, ECF No. 77. Dr. Wong, however, did not testify. Tr. 4-5. Nor would Dr. Wong make himself available to answer questions about this matter. In an effort to explain Dr. Wong's resistance to testifying, petitioner's counsel offered that "there has historically been a great deal of animosity between the legal and medical communities in Texas," where Dr. Wong lives. Response 2, Sept. 4, 2012, ECF No. 83.

In addition to consulting with Dr. Wong, Tessie consulted with at least two other pediatric cardiologists, Dr. Richard Friedman of Texas Children's Hospital on June 9, 2006, Pet'r's Ex. 9 at 3-5, and Dr. Robert Canby of Austin Heart on October 24, 2008, Pet'r's Ex. 44 pt. 2 at 20-22.

The cardiologists who evaluated Tessie repeatedly recommended that she seek treatment from a cardiologist or clinic able to provide more specialized care. In January 2006, Dr. Wong wrote he had contacted Dr. Blair Grubb, "a leading authority on POTS," on Tessie's behalf to arrange for an evaluation of Tessie in July 2006. Pet'r's Ex. 7 at 2-3. The parties describe Dr. Grubb as an indisputable expert on the condition of POTS, and he is the lead author on two articles discussed at the hearing. See Pet'r's Exs. 28/59[20] and 29. Whether Tessie ever sought treatment from Dr. Grubb, however, is unknown because no records of a visit to Dr. Grubb are contained in the record.

Nearly two years after Tessie's referral to Dr. Grubb, Dr. Canby recommended, in October 2008, that Tessie seek an evaluation "at a center that has the ability to approach autonomic disabilities in a comprehensive fashion, such as that which is available at Vanderbilt University or at the Mayo Clinic." Pet'r's Ex. 44 pt. 2 at 22. Again, whether Tessie ever sought treatment from the identified clinics is unknown from the record.

In February 2011, Dr. Wong made an additional recommendation that Tessie seek treatment from a specialist in autonomic disorders; he suggested Dr. David Robertson at Vanderbilt University. Pet'r's Ex. 44 pt. 1 at 10. Of note, the record is devoid of any indication that Tessie ever sought treatment from Dr. Robertson.

There is a suggestion in the record that Tessie conferred with Dr. Ben Levine, a cardiologist at the University of Texas Southwestern Medical School. As documented in Dr. Canby's notes, Tessie regarded Dr. Levine's approach to be unsuccessful in the treatment of her symptoms. See Pet'r's Ex. 44 pt. 2 at 21. But, petitioner filed no records from Dr. Levine.

Petitioner's own treating doctors and her expert immunologist recognized the importance of a cardiologist's role in the diagnosis and treatment of POTS. The record reflects that Tessie was evaluated by a number of cardiologists and was referred to several others. The undersigned expressed an interest in hearing from Tessie's treating cardiologist. Nonetheless, petitioner declined to produce any of her treating cardiologists for testimony.

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[20] Blair P. Grubb et al., The Postural Tachycardia Syndrome: A Brief Review of Etiology, Diagnosis and Treatment, 43 Hellenic J. of Cardiology 47 (2002) (Pet'r's Ex. 28/59) (2002 Grubb article). These are two filings of the same article, with different portions of the article highlighted.

C. Testifying Experts

In support of her vaccine claim, petitioner has offered the expert opinions of two medical doctors, Marcel Kinsbourne, M.D. and Vera S. Byers, M.D., Ph.D.

Dr. Kinsbourne received his medical degree, as well as additional degrees specializing in the fields of neurology and pediatrics, from Oxford University. Pet'r's Ex. 63 at 1; Tr. 77. Dr. Kinsbourne is licensed to practice in North Carolina, Massachusetts and Virginia, Pet'r's Ex. 63 at 1, and has served as an associate professor of neurology and pediatrics at Duke University Medical Center from 1967 to 1974, and in pediatric neurology at the University of Toronto from 1974 to 1980, Id. at 2; Tr. 78.

Since 1981, the focus of Dr. Kinsbourne's work has been on pediatric behavioral disorders, and he has not seen a pediatric patient on an acute basis for the treatment of anything other than behavioral illnesses since that time. Tr. 114. From 1981 to 1991, Dr. Kinsbourne served as the Director of the Behavioral Neurology Department at the Eunice Kennedy Shriver Center, focusing on both clinical and research in the field of mental development and its abnormalities, such as attention deficit and autism. Pet'r's Ex. 63 at 2; Tr. 79.

Since 1995, Dr. Kinsbourne has served as a professor of psychology at the New School in New York City, where he teaches neuroscience to both undergraduate and graduate students, but not to medical students. Pet'r's Ex. 63 at 2; Tr. 79, 114. Dr. Kinsbourne has published over 400 articles. Pet'r's Ex. 63 at 5-36; Tr. 81.

The undersigned accepted Dr. Kinsbourne as an expert in neurology. Tr. 83. Dr. Kinsbourne focused his opinion on describing the condition of POTS and its clinical manifestations. He discussed the symptoms exhibited by petitioner, and defined the onset date of her injury–after vaccination. He also provided testimony about the timeframe within which the appearance of vaccine-precipitated symptoms would be expected based on the proposed immunologic mechanism of harm. Tr. 109.

Petitioner's second expert, Dr. Byers, received her medical degree from the University of California at San Francisco, and completed a three-year residency in internal medicine in 1984, and is board certified in internal medicine. Pet'r's Ex. 62 at 1; Tr. 6. Although she is not board certified in immunology, Dr. Byers does hold a doctorate in immunology, and in 1973, she completed a two-year post-doctoral fellowship in clinical immunology. Pet'r's Ex. 62 at 1; Tr. 6.

Dr. Byers' curriculum vitae[21] (CV) shows that since 1990, she has served as a consulting medical director for various pharmaceutical companies. In this capacity, she has designed clinical trials for drugs treating autoimmune diseases and cancer, has selected clinical sites and principal investigators, has run the trials, has authored the clinical reports, has filed Product Licensing Applications (PLAs) and has defended the filings. Pet'r's Ex. 62 at 2.

Dr. Byers has held positions as an adjunct professor of microbiology and immunology at Texas Tech University, an adjunct assistant professor of immunodermatology at University of California, San Francisco, and as a special lecturer in tumor immunology at Nottingham University School of Medicine in England. Pet'r's Ex. 62 at 4-5; Tr. 7, 11-13. She has served on the National Institutes of Health review board for the National Cancer Institute, Pet'r's Ex. 62 at 1; Tr. 10, and has published extensively on issues pertaining to the immune system, autoimmune diseases, rheumatologic diseases, and oncology. Pet'r's Ex. 62 at 6-14; Tr. 13-14.

A named inventor on eight patents that were issued between 1988 and 2000, Pet'r's Ex. 62 at 5-6, Dr. Byers serves as an expert witness in environmental toxicology cases–focusing on cancer and autoimmune diseases–and in Vaccine Act cases, Pet'r's Ex. 62 at 3.

Dr. Byers acknowledged that she has "never seen a patient with POTS." Tr. 44. She did recall seeing one patient about the year 2000 who had lupus as well as POTS, "but at the time [she] did not realize it." Id. A review of her CV confirms her lack of experience treating POTS patients.

The undersigned accepted Dr. Byers as an expert in immunology. Tr. 14. Dr. Byers focused her testimony on the alleged autoimmune nature of Tessie's condition and how the hepatitis B vaccine she received triggered her POTS. Tr. 16. She also testified regarding the medical appropriateness of the temporal relationship between Tessie's vaccination and the onset of her symptoms of POTS.

Petitioner relied primarily on Dr. Byers' testimony to establish vaccine-related causation. The undersigned found several matters about Dr. Byers' testimony to be of concern. First, testimony about her clinical experience differed significantly from what was reflected in her CV.[22] Second, as Dr. Byers acknowledged, her opinion was based

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[21] Curriculum vitae of Vera S. Byers, M.D., Ph.D., filed July 2, 2012, ECF No. 76-1 (Pet'rs' Ex. 62).

[22] Simply put, Dr. Byers testimony suggested she had a 25-year clinical career (Cont'd on next page).

primarily on her review of Tessie's medical records and the medical literature filed in this case, Tr. 44, but she curiously was unable to support her assertions–even when afforded an opportunity to do so after the hearing–with either record citations or pinpoint cites to the literature.[23] Third, when Dr. Byers did discuss the literature, she appeared to have misread the relevant portions of the articles.[24]

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treating patients with autoimmune disorders–work directly relevant to the issues in this matter–that ended in about 2003, see Tr. 9, 43, but her CV indicated that this clinical work spanned only 3 years, from 1984 to 1987, see Pet'r's Ex. 62 at 3.

[23] Where review of the record shows medical records or the filed literature supports Dr. Byers' assertions, the undersigned credits such assertions. But, where petitioner provided no record citation and no support is disclosed in the medical records or literature, the undersigned regards these assertions as merely the ipse dixit of the expert. The Federal Circuit does not require that a court scour the record to find support for a petitioner's allegations or arguments. See Hubbard v. Dep't of Veterans Affairs, 51 Fed. Appx. 8, 9 (Fed. Cir. 2002), and the undersigned has not done so here.

[24] In her written report, Dr. Byers stated that "[m]ore than half of [POTS] cases are preceded by viral infections." Byers Expert Rpt. 2 (citing the 2002 Grubb article & Phillip A. Low et al., Postural Tachycardia Syndrome (POTS), 20 J. of Cardiovascular Electrophysiology 352 (2009) (Pet'r's Ex. 33) (2009 Low article). At the hearing, Dr. Byers referenced Table 2 of Mark J. Theieben et al., Postural Orthostatic Tachycardia Syndrome: The Mayo Clinic Experience, 82 Mayo Clinic Proceedings 308 (2007) (Pet'r's Ex. 40) (2007 Thieben article) (a review of 152 POTS patients treated at the Mayo Clinic in Rochester, Minnesota over an 11-year period, from 1993 to 2003), to support her earlier assertion about the number of POTS cases following viral infections. Tr. 49 (citing Pet'r's Ex. 40 at 310 tbl. 2).

Based on her review of the 2007 Theiben article, Dr. Byers testified that nearly 88% of POTS cases are preceded by some type of viral illness–not the 50% as she previously offered in her written opinion. Tr. 49. Notably, Dr. Kinsbourne similarly cited the same articles in his expert report for the proposition that nearly half of POTS cases are preceded by a form of viral illness. See Kinsbourne Expert Rpt. 6.

A review of the filed articles, however, indicates that neither Dr. Byers' nor Dr. Kinsbourne's representations obtained clear support from the filed literature. The 2007 Thieben article indicated that fewer than half (specifically, 27.6%) of all POTS cases were preceded by an illness; the article clarified that most were viral illnesses, but a few postoperative illnesses also were reported. See Pet'r's Ex. 40 at 310 tbl. 2.

The authors of the 2002 Grubb article to which Dr. Byers also cited did state that (Cont'd on next page).

The undersigned has some concern regarding whether Dr. Byers was able to concentrate properly during the hearing. Although she did not appear distracted or impaired in any manner, she did seem to have trouble with the details of her testimony. This difficulty did not assist the persuasiveness of her testimony.

Respondent offered the testimony of Peter Bingham, M.D. Dr. Bingham received his medical degree from Columbia College of Physicians and Surgeons. Resp't's Ex. B at 1; Tr. 143. He completed his postgraduate training at the University of Pennsylvania and received his board certification in neurology, with a special qualification in child neurology. Resp't's Ex. B at 1; Tr. 143.

Dr. Bingham currently serves as a pediatric neurologist and Associate Professor of Pediatrics and Neurology at the University of Vermont. Resp't's Ex. B at 1; Tr. 142. He spends the majority of his time with clinical projects and the remaining portion with research projects. Tr. 143. He teaches medical students, as well as neurology residents, pediatric residents, and child psychiatry fellows. Tr. 144. Dr. Bingham participates in continuing education programs and reviews for a pediatric journal. Resp't's Ex. B at 2; Tr. 144-45. He has diagnosed two adolescents with POTS and he has treated at least two other POTS patients. Tr. 145.

The undersigned accepted Dr. Bingham as an expert in pediatric neurology. Tr. 146.

The undersigned closely considered the opinions offered by these experts.

"a large number" of patients reported the appearance of symptoms after a severe viral infection, but the authors failed to provide specific numbers that would support an inference about any particular percentage of such cases. See Pet'r's Ex. 59 at 49. The authors of the 2009 Low article that Dr. Byers cited had noted that "[e]arly studies [had] suggested that approximately one-half of patients have an antecedent presumed viral illness, . . . [but] recent experience suggests that this is less common." Pet'r's Ex. 33 at 3 (emphasis added).

The misread articles, when considered in the context of Dr. Byers' other misstatements at hearing, call into question the quality of Dr. Byers' focus during the hearing. This may have been simply an off day for petitioner's expert, but it did attract the undersigned's notice.

IV. DISCUSSION

The injury for which petitioner seeks Program compensation is POTS. As referenced earlier in this decision, the 2006 Grubb article submitted by petitioner instructs that there are two primary and two secondary subtypes of POTS. See Pet'r's Ex. 29 at 108-10. Although Tessie's POTS diagnosis is undisputed, there is no indication in the record that any of Tessie's treating cardiologists ever diagnosed her with a particular subtype of POTS.

Dr. Kinsbourne, petitioner's expert neurologist, points to the sole immune-mediated form of POTS described in the 2006 Grubb article, the partial dysautonomic form of POTS, as the most representative of Tessie's illness. See Kinsbourne Expert Rpt. 5. Petitioner's expert immunologist, Dr. Byers, testified that Tessie "definitely" suffers from the primary, rather than secondary, form of POTS. Tr. 44. She theorized that the hepatitis B vaccine Tessie received in August 2005 triggered the immune-mediated form of the condition. See Byers Expert Rpt. 2-3; Tr. 17-18.

Critical to petitioner's case is a finding that Tessie suffered from an immune-mediated subtype of POTS. But, as informed by the 2006 Grubb article on which petitioner's experts rely, Tessie's documented symptoms fail to support the claims put forward by her experts. Before considering Tessie's symptoms, the undersigned first addresses the various subtypes of the condition POTS, turning initially to the two primary forms.

A. POTS Subtypes: The Two Primary Forms

1. The Partial Dysautonomic Form

This subtype usually presents abruptly after a febrile illness (presumed viral), as well as after pregnancy, immunizations, sepsis, surgery, or trauma. Pet'r's Ex. 29 at 108. According to the 2006 Grubb authors, a notable feature of this subtype of POTS is the "mild" nature of its presentation. Id. The authors observed that such patients "seem to suffer from a mild type of peripheral autonomic neuropathy characterized by an inability of the peripheral vasculature . . . constrict[ion] in the face of orthostatic stress." Id. (emphasis added). None of Tessie's treating cardiologists, however, ever described any of her symptoms as mild. Instead, her evaluating physicians consistently described her symptoms as significant.

After becoming ill in August 2005, Tessie never returned to school. In April 2009, almost four years after her August 2005 illness, Tessie's mother recalled that Tessie was unable to leave bed on most days, Fay Aff. at ¶ 11, and that Tessie required home schooling, id. at ¶ 12. In February 2011, more than five years after Tessie's August

2005 illness, Dr. Wong wrote that Tessie "continues to have significantly decreased exercise tolerance with frequent dizziness and palpitations." Pet'r's Ex. 44 pt. 1 at 9.

The 2006 Grubb authors further state that patients with postviral autonomic neuropathy (another type of immune-mediated POTS distinct from the vaccine-mediated form alleged by petitioner) show evidence of a certain autoantibody, specifically $alpha_3$ acetylcholine receptors of the peripheral autonomic ganglia. See Pet'r's Ex. 29 at 108. Dr. Bingham acknowledged that his review of the record had shown no evidence that Tessie was ever tested for this antibody. Tr. 166. Likewise, a review of the record by the undersigned revealed no such test.

The authors of the 2006 Grubb article described a variant of this partial dysautonomic form of POTS as generally affecting adolescents. This form of the condition is known as the partial dysautonomic form – developmental. Pet'r's Ex. 29 at 108. It usually begins around the age of 14 years, "often following a period of very rapid growth." Id. The "etiology [of the developmental form of POTS] is unclear, but appears to reflect a transient period of autonomic imbalance that occurs in rapidly growing adolescents." Id. at 108-09.

The patients may suffer from severe headaches, but the symptoms slowly fade over the years. Typically, by young adulthood (that is, between 19 and 24 years old) roughly 80% of the patients are asymptomatic. Id. at 109.

Several of Tessie's doctors documented both her height and weight in the two and one-half years prior to August 2005. A review of her treaters' notes does not reveal a period of rapid growth prior to the onset of her August 2005 symptoms.

On February 3, 2003, Dr. Thomas examined Tessie and recorded that she was the metric equivalent of 5' 3" tall (161 cm) and 128 pounds. See Pet'r's Ex. 4 at 1.

On September 8, 2004, Dr. Shinkawa examined Tessie for a sports physical, during which he recorded that she was 5' 4.5" tall and weighed 130 pounds. Pet'r's Ex. 5 at 5.

On May 18, 2005, Dr. Karnik recorded her height as the metric equivalent of 5' 4.9" inches (165 cm) and 128 pounds. See Pet'r's Ex. 18 at 121.

On August 15, 2005, the date on which Tessie received her hepatitis B vaccine, Dr. Shinkawa examined Tessie for a physical. See Pet'r's Ex. 5 at 3. He recorded that Tessie was 5' 4" tall, and weighed 126 pounds. Id. at 28.

On September 22, 2005, Dr. Carrasco examined Tessie. He recorded that she was the metric equivalent of 5' 4.4" tall (163.5 cm) and weighed 127 pounds. See Pet'r's Ex. 6 at 17.

In the two and one-half years prior to her receipt of the subject vaccine, Tessie grew approximately one and one-half inches, and she gained no weight. From this record, the undersigned does not discern a rapid growth period prior to Tessie's receipt of her August 15, 2005 vaccination.

Tessie did have severe headaches. See Pet'r's Ex. 9 at 3 (Tessie reporting to her cardiologist, Dr. Friedman, that in June 2006, she had severe headaches exacerbated by overstimulation). In February 2011 (when Tessie was 20 ½ years old), Dr. Wong noted that Tessie's symptoms had improved when compared to her condition over the previous three to four years, but he did not describe her as "asymptomatic." See Pet'r's Ex. 44 pt. 1 at 9-10. At that particular appointment, Dr. Wong recommended that Tessie seek an evaluation from a specialist in autonomic disorders at Vanderbilt University. Id. at 10.

There are no further records from Tessie's treating cardiologists in the record beyond February 2011. Thus, what Tessie's current symptoms are is unknown.

In the view of the undersigned, two factors militate against a finding that Tessie suffered from this developmental variant form of POTS. First, she did not experience the period of rapid growth that typically precedes the onset of this type of POTS. Second, while her symptoms showed some measure of improvement, Tessie was still significantly affected and referred for further evaluation several years after her documented diagnosis.

2. The Hyperadrenergic Form

Of the subtypes of POTS addressed in the 2006 Grubb article, only one was characterized by what Dr. Bingham termed as an indolent onset. All three experts discussed the 2006 Grubb article, in part, during the hearing. See Tr. 18 (Byers); Tr. 128 (Kinsbourne); Tr. 164 (Bingham). But, none of the experts discussed the portion of the article that described this subtype of POTS, nor did any of the experts address whether Tessie exhibited the clinical and laboratory symptoms associated with this primary form of the condition. See Pet'r's Ex. 29 at 109.

Identified in the 2006 Grubb article as a gradual onset subtype of POTS, the Grubb authors observed:

> The second (and less common) form of primary POTS is referred to as the "hyperadrenergic" form. These patients tend to report a gradual and progressive onset of symptoms as opposed to an abrupt onset. Hyperadrenergic POTS patients report significant tremor, anxiety, and cold

> sweaty extremities when upright. Many will report a significant increase in urinary output after being upright for even a short period of time, and over half suffer from true migraine headaches. The hallmark of this form of POTS is that in addition to orthostatic tachycardia they will often display orthostatic hypertension, as well as exaggerated response to isoproterenol infusions. As opposed to the [partial dysautonomic] POTS patients, the hyperadrenergic patients have significantly elevated serum catecholamine levels with serum norepinephrine levels > 600 ng/mL.

Id. (emphasis added).

Respondent's expert, Dr. Bingham, asserted that the symptoms of which Tessie complained on six different occasions prior to her receipt of the subject vaccine included: weakness, faintness, malaise, dizziness, fatigue, headache, and syncope. Resp't's Post-Hr'g Br. 17 (citations omitted). But Tessie did not complain of the symptoms listed in the 2006 Grubb article as characteristic in subjects with this gradual onset subtype of POTS; such symptoms included significant tremor, anxiety, cold sweaty extremities when upright, or significant increase in urinary output after being upright for even a short period of time.

Not only does the record indicate that Tessie did not manifest the symptoms associated with the gradual onset subtype of POTS described in the 2006 Grubb article, the relevant medical records provide no evidence that Tessie had either the clinical or laboratory markers that are indicative of the hyperadrenergic form of POTS. A review of the most prominent symptoms of this condition–and the absence of such symptoms in Tessie's case–follows.

a. Orthostatic Hypertension

Among the most prominent symptoms of the hyperadrenergic form POTS is orthostatic hypertension, which is a sudden rise in blood pressure upon standing. This sudden change in blood pressure that accompanies a positional change also may be referred to as orthostasis.

In September 2005, one of Tessie's treating physicians wrote: "Her resting pulse is slightly high at 100. Her blood pressures show very minimal orthostasis. Her supine blood pressure was 107/66, sitting 99/62, and standing 110/65." Pet'r's Ex. 18 at 34.

In October 2005, Dr. Frank Wong, a pediatric cardiologist, examined Tessie for the first time. Id. at 29-30. Dr. Wong recorded "[o]rthostatic blood pressures are: 94/61 with a heart rate of 90 bpm while supine. 83/60 with a heart rate of 131 bpm while standing." Id. at 29. In Dr. Wong's view, Tessie fit the clinical criteria for POTS, with a

heart rate increase of 30 bpm or more from supine to standing within 10 minutes or less. Id. at 30. He did not note, however, any orthostatic hypertension.

Tessie was evaluated about three months later, in December 2005, at Children's Hospital of Austin by another cardiologist, Dr. Richard Friedman. Pet'r's Ex. 9 at 40-41. The handwritten progress notes from this evaluation detailed both Tessie's blood pressure and her heart rate while she was lying down, then sitting and on standing. Tessie's heart rate continued to show the expected orthostatic increase, from 66 to 98 to 137 bpm. Id. at 41. Again, her blood pressure showed no evidence of orthostatic hypertension; instead it dropped slightly from 102/43 to 94/54 to 90/51. See id.

In June 2006, Tessie's exam continued to show an orthostatic heart rate, but not orthostatic blood pressure. See id. at 4. Her blood pressure when supine was 105/65, while after standing for three minutes it was 95/60. Id. Her heart rate increased from 83 to 113 bpm in the same period of time. Id.

A careful review of the record discloses no evidence that any of Tessie's treating physicians diagnosed her with orthostatic hypertension.

b. Urinary

Another prominent feature of hyperadrenergic POTS is a change in urinary habits.

During an evaluation Tessie received in September 2005, she showed "[n]o GU[25] symptomology." Pet'r's Ex. 18 at 33. A later physical evaluation in June 2006 disclosed, "[n]o history of hematuria or hysuria. No change in frequency or nature." Id. As the record dictates, Tessie did not develop any urinary symptoms.

c. Catecholamines

According to the authors of the 2006 Grubb article, hyperadrenergic patients have significantly elevated serum catecholamine levels with serum norepinephrine levels greater than 600 ng/mL. Pet'r's Ex. 29 at 109. Catecholamines are naturally occurring, nitrogen-containing compounds that are secreted by the adrenal glands. See The Free Dictionary, http://www.thefreedictionary.com/catecholamine (last visited July 18, 2013). They function as neurotransmitters and hormones. Id. Epinephrine, norepinephrine, and dopamine are types of catecholamines. Id.

In December 2005, Tessie was tested for "catecholamines plasma" including both epinephrine and norepinephrine. Pet'r's Ex. 18 at 19-20. The test results were "normal."

[25] Genitourinary system or urogenital system.

Id. The record does not yield any evidence that Tessie had the requisite catecholamine levels to support a finding of hyperadrenergic POTS.

Because Tessie lacked most of the indicators for this subtype of POTS, the undersigned cannot conclude on this record that Tessie's illnesses was consistent with the hyperadrenergic subtype of POTS.

In addition to the two primary subtypes of POTS, the Grubb authors describe two forms of POTS that occur in conjunction with other recognized conditions. See Pet'r's Ex. 29 at 109-10. The authors use the term secondary POTS to describe these subtypes of POTS. See id. at 109.

B. POTS Subtypes: The Two Secondary Forms

1. Autoimmune Diseases Accompanied by POTS

POTS may appear in association with various autoimmune diseases. Included among the disorders that may be accompanied by POTS are: chronic diabetes, lupus, and Sjogren's Syndrome. Id. POTS also may accompany heavy metal intoxication and may occur following chemotherapy. Id.

A heavy metals analysis was performed on Tessie in November 2005; the results were normal. See Pet'r's Ex. 1 at 41. And there is no mention in the extensive medical record before the undersigned that Tessie ever had cancer or received chemotherapy.

In September 2005, Dr. Carrasco, a pediatric rheumatologist, noted that Tessie did not have lupus or any other autoimmune condition. See Pet'r's Ex. 6 at 16-18. Petitioner makes no allegation that she suffers from any autoimmune disease other than POTS. Tr. 40 (Dr. Byers reporting that Tessie's rheumatologist found no evidence of an autoimmune disease); Tr. 68-69 (Dr. Byers opining that Tessie's sole autoimmune disease was POTS).

Because there is no evidence that Tessie suffered from other autoimmune disorders, the undersigned finds it unlikely that she suffered from this subtype of POTS.

2. Joint Hypermobility Syndrome Accompanied by POTS

Dr. Byers acknowledged that the literature she cited in support of her opinion suggests there are a variety of causes of POTS, including genetic ones, Tr. 45, and articles filed by both petitioner and respondent indicate that Joint Hypermobility Syndrome can be associated with the development of POTS. According to the authors of the 2006 Grubb article filed by petitioner,

> [a] recently recognized and important cause of secondary POTS is due to the connective tissue disorder known as the joint hypermobility syndrome (JHS). An inherited condition, it is characterized by joint hypermobility, [which is a type of] connective tissue fragility, . . . Orthostatic intolerance develops in these patients due to the presence of abnormally elastic connective tissue in the vasculature, which results in an increase in vessel distensibility in response to the augmented hydrostatic pressure that occurs during orthostatic stress. This leads to excessive peripheral venous pooling with a resultant compensatory tachycardia. Recent studies have suggested that up to 70% of patients with hypermobility syndrome may suffer from some form of orthostatic intolerance. Adolescents with the developmental form of POTS frequently have been noted to have features of JHS.

Pet'r's Ex. 29 at 109.

Respondent's expert, Dr. Bingham referred to another article–the 2003 Gazit article–in support of his claim that POTS has been associated with joint laxity, a condition with which Tessie has been diagnosed. Bingham Expert Rpt. 7 (referring to Resp't's Ex. A-3 at 1). None of the experts discussed the 2003 Gazit article at the hearing, but Dr. Bingham noted in his expert report that Tessie had been diagnosed with both the conditions described in the article. Id. 3, 7. Based on Tessie's history of joint laxity, Dr. Bingham posited that Tessie had a biological susceptibility to POTS that existed prior to her August 15, 2005 vaccination. Id. 7.

According to the authors of the 2003 Gazit article, "orthostatic hypotension, [POTS], and uncategorized orthostatic intolerance" were found in 78% of patients with JHS. Resp't's Ex. A-3 at 33. In comparison, only 10% of a non-JHS control group suffered from the noted orthostatic ailments. See id. The authors' evaluation of 48 patients with JHS indicated that substantial proportions of the studied patients experienced autonomic nervous system-related symptoms, including: palpitations (90%), lightheadedness/dizziness (88%), presyncope (83%), syncope (56%), headache (75%), impaired concentration (71%), shortness of breath (52%), nausea (54%), and physical fatigue (71%). See id. at 33, 35. The findings detailed by the 2003 Gazit authors suggested that "dysautonomia is an extraarticular manifestation in the joint hypermobility syndrome." Id. at 33.

Many of the symptoms outlined in the 2003 Gazit article were reported in Tessie's medical records over the years, and match the symptoms identified by Dr. Kinsbourne as characteristic of orthostasis–specifically weakness, nausea, lightheadedness, dizziness and fatigue.

Dr. Byers did not address Tessie's JHS in either her written opinion or her testimony. But, Dr. Kinsbourne acknowledged that Tessie's JHS created a "genetic

predisposition." Tr. 90. Because Tessie had managed with her genetic condition for 15 years before she became ill in August 2005, Dr. Kinsbourne postulated that "a second event" was necessary to trigger the expression of her POTS. Tr. 129. Dr. Kinsbourne seemed to suggest that the received vaccine and Tessie's JHS acted in concert to bring forth the symptoms of POTS. But nothing in either the 2006 Grubb or 2003 Gazit articles, suggests that an external trigger is necessary for those with JHS to develop POTS. This hypothesis appears to be solely Dr. Kinsbourne's, and contrary to his position, the medical literature indicates that a congenital JHS condition alone is sufficient to prompt the appearance of POTS symptoms.

Considering the record as a whole, it is difficult to find that Tessie suffered from the immune-mediated subtype of POTS, as petitioner and her experts have urged. Rather, Tessie's symptoms as vividly described by her treating physicians, are more likely than not consistent with the subtype of POTS that is related to JHS. That Tessie's symptoms so closely match the description of symptoms in those suffering from the secondary form of POTS related to JHS significantly undercuts petitioner's theory that she suffered from the immune-mediated form of POTS.

The undersigned turns now to evaluate Tessie's claims under the Althen prongs.

C. Althen Prong One

To satisfy her burden on Althen prong one, petitioner must present a theory of causation supported by a "reputable medical or scientific explanation." Althen, 418 F.3d at 1278 (citations omitted); see also Knudsen, 35 F.3d at 548 (requiring a "sound and reliable medical or scientific explanation"). Here, petitioner relies on (1) medical literature that speaks to the possibility that an immune-mediated mechanism can cause POTS and (2) the opinion of Dr. Byers regarding how such a mechanism could occur.

Petitioner asserts that the medical community accepts the fact that "immunological challenges generally, and vaccines in particular, can trigger the onset of POTS." Pet'r's Post-Hr'g Br. 8. In support of her claim, petitioner cited to the 2006 Grubb article, in which the authors discuss the partial dysautonomic subtype of POTS that is characterized by an "abrupt onset" of symptoms after, among other events, an immunization or a presumed viral illness. Id. (citing Pet'r's Ex. 29 at 108). This form of POTS is believed to have an immune-mediated pathogenesis. Id. Petitioner also relied on a 2002 article authored by Dr. Grubb, in which he observed that "[a] large number of patients report that symptoms of POTS appear after a severe viral infection, [which] suggest[ed] that an immune-mediated mechanism may be involved." Id. 9 (citing Pet'r's Ex. 28 at 49.)

Petitioner's expert, Dr. Byers, posited that "[a]s with most autoimmune diseases that follow infection or vaccination, [the immunologic processes of] molecular mimicry, bystander activation, and epitope spreading (in which invading antigens accelerate an

ongoing autoimmune process by local activation of antigen presenting cells and overprocessing of antigens) are usually included in the etiologies of these diseases." Byers Expert Rpt. 2; Pet'r's Post-Hr'g Br. 9.

Petitioner also pointed to an earlier Vaccine Program case, Dunbar v. Sec'y of Health & Human Servs., No 98-627V, 2007 WL 2844826 (Fed. Cl. Spec. Mstr. Sept. 14, 2007), in which–according to petitioner–"this Court held that a hepatitis B vaccination triggered the onset of POTS." Pet'r's Post-Hr'g Br. 9. As addressed in greater detail under Althen prong three, however, the Dunbar case provides petitioner with no support for her theory here.

Petitioner's theory depends on a finding that Tessie's POTS was immune-mediated. As previously discussed in the section of this decision reviewing the various subtypes of POTS, the undersigned is not persuaded that Tessie's POTS is immune-mediated. Thus, the undersigned does not decide the question of whether the hepatitis B vaccine can cause POTS through an immunologic mechanism because the facts of this case do not support a finding that Tessie's POTS condition was immune-mediated.

D. Althen Prong Two

To satisfy Althen prong two, petitioner must show a logical sequence of cause and effect between the received vaccine and the alleged injury.

Respondent challenged petitioner's claim alleging that her symptoms predated her receipt of the vaccine at issue. In response, petitioner asserted that if the "government wishes to sponsor a 'factors unrelated' defense, then it is the government's burden to prove, by preponderant evidence, that the vaccine was not a substantial factor in bringing about the injury." Pet'r's Post-Hr'g Br. 4.

Petitioner described respondent's burden of proof accurately, should the burden shift to respondent. But the burden does not shift to respondent, under § 300aa-13(a)(1)(B), until petitioner has established her case-in-chief. If petitioner fails to do so, the burden does not shift. Prior to any burden shifting, however, respondent may point to what she believes are weak points in petitioner's claim without triggering a shift in the burden of proof from petitioner to respondent, and the Federal Circuit has instructed that a special master may consider such evidence when evaluating petitioner's case-in-chief. See de Bazan,539 F.3d at 1353.

In determining whether petitioner has shown that it is more likely than not that the August 15, 2005 hepatitis B vaccine caused her POTS, the undersigned also considers a number of factors, including: (1) when petitioner's POTS symptoms first emerged, (2) whether Tessie's immune system was "upregulated" at her vaccinations and thus primed to trigger an adverse immunologic reaction, (3) what was the impact of her probable viral

illness documented on August 1, 2005, and (4) what was the impact of her joint hypermobility syndrome.

1. The Onset of Tessie's Symptoms

Petitioner asserts that Tessie's symptoms appeared abruptly ten days after the vaccine at issue. See Fay aff. ¶ 4; Byers Expert Rpt. 1. Tessie came home from school exhausted, Fay aff. at ¶ 4, and over the next four days experienced chills, sore throat, and slight nausea, see Pet'r's Ex. 5 at 3.

Respondent, however, points to several medical records dating back to 1996, describing symptoms that Dr. Bingham asserts were early indications of Tessie's later-diagnosed POTS. See Resp't's Post-Hr'g Br. 17. Dr. Bingham pointed to six different reports of symptoms that, in retrospect, were likely due to the emergence of her POTS condition prior to her August 15, 2005 vaccinations. Resp't's Ex. A at 7; Tr. 154-60. These were reports of weakness, faintness, dizziness, fatigue, headache, and syncope. Tr. 154-60; see also Pet'r's Ex. 19 at 30 (reporting faintness on March 20, 1996); Pet'r's Ex. 19 at 5-10 (reporting fatigue, malaise, dizziness, and missed school in December 1998); Pet'r's Ex. 6 at 23 (reporting headache and dizziness on March 9, 2004); Pet'r's Ex. 20 at 27 (reporting an episode of syncope on August 1, 2005); Pet'r's Ex. 9 at 3-5 (reporting a two-year history of blacking out on June 9, 2006).

Petitioner contends that these medical records document symptoms of other ailments, including viral illnesses and the post-concussive syndrome that followed her September 2003 head injury on a ceiling fan. See Pet'r's Post-Hr'g Reply Br.[26] 5-6.

But, Dr. Bingham asserted that the progression of Tessie's POTS-related symptoms over several years was consistent with the course of the disease. Resp't's Post-Hr'g Br. 17 (citing Tr. 147-51). In an apparent effort to discount petitioner's claim that she suffered the abrupt onset of an immune-mediated form of POTS, Dr. Bingham testified that only a minority of POTS cases have an acute onset and in his experience, the condition "is indolent in its onset." Tr. 149-50. Dr. Bingham defined indolent as waxing and waning over a period of months or years, as opposed to starting on a single day. Tr. 150. In support of his assertion that few POTS cases have an acute onset, Dr. Bingham cited the 2007 Thieben article. Tr. 149.

The 2007 Thieben article, however, did not offer the support Dr. Bingham suggested. In a study of 152 POTS patients, the Thieben authors defined symptom onset as either acute (if less than one month), subacute (if within one to three months), or

[26] Petitioner's Post-Hearing Reply Memorandum, Jan. 15, 2013, ECF No. 89 (Pet'r's Post-Hr'g Reply Br.).

insidious (if greater than three months). Pet'r's Ex. 40 at 310 tbl. 2. After reviewing the patients' histories, the authors were able to determine onset for only 49 of the 152 studied patients. The authors found that 12.5% of the studied patients had an acute onset, 13.8% had a subacute onset, 5.9% had an insidious onset and 67.8% had onset within an unknown time period. Id. Contrary to Dr. Bingham's claim, the authors of the 2007 Thieben article found that the percentage of patients with a known onset of three months or longer (insidious) was less than half the percentage of patients with an acute onset, that is 5.9% compared with 12.5%. The findings of the 2007 Thieben article indicate that onset is unknown in most cases, but acute onset seems to exceed insidious onset in cases where onset can be determined.

Even were the undersigned to credit Dr. Bingham's testimony regarding symptom onset–based on his limited experience with POTS patients–the statistical evidence on which respondent relied to address symptom onset does not dispose of the causation question in this case. See Knudsen v. Sec'y of Health & Human Servs., 35 F.3d 543, 550 (Fed. Cir. 1994) (discouraging use of a "bare statistical fact" as evidence of causation in a particular case). What does inform the issue of symptom onset is the record before the undersigned. This record contains mention of symptoms that are consistent with a POTS diagnosis well before Tessie received either the subject vaccination or her POTS diagnosis. The undersigned does not decide the specific question of precisely when Tessie's POTS symptoms first manifested–which would be important to bolster petitioner's claim of an immune-mediated injury–because such a determination is unnecessary on the facts of this case which strongly indicate that Tessie's POTS injury was secondary to a congenital condition.

As compelled by Althen prong two, the undersigned considers further whether the theory petitioner put forth in this case is at all consistent with the facts of this case.

2. Dr. Byers' Theory that Tessie's POTS was an Immune-Mediated Form of POTS

The crux of petitioner's theory is that she suffered from an immune-mediated form of POTS. Important to petitioner's claim is evidence that Tessie had a dysregulated immune system prior to receipt of the subject vaccine. The evidence of immunologic dysregulation on which petitioner relies are her laboratory test results. Finally, petitioner strongly discounts her "probable" viral illness–documented on August 1, 2005–as having no causal impact on the appearance of her symptoms.

a. The Claim that Tessie had a Dysregulated Immune System

As expressed in her expert report, Dr. Byers asserts that Tessie had "a dysregulated[27] immune system prior to vaccination which produced no clinical effect, and that she now suffers from . . . POTS" which condition was caused by the August 15, 2005 hepatitis B vaccine she received. Byers Expert Rpt. 3. Dr. Byers explained:

> Tessie was positive [for] both anti-nuclear antibodies (ANA) and anticentromere antibodies (ACA). The ANA test is almost routine for physicians to order if there is a suspicion of an autoimmune disease. It is probably measuring inflammatory activity. Tessie Dingle has repeatedly been found to have laboratory markers indicative of an autoimmune inflammatory disease, including increased ESR, high ANA and positive anticentromere B antibodies. . . . These lab findings prior to the onset of her POTS on August 25, 2005, show a dysregulated immune system.

Id. 2 (emphasis added). Although Dr. Byers makes the observation that Tessie had a dysregulated immune system prior to her August 15, 2005 vaccination, Tr. 27, she did not address the significance of this immunologic impairment as it pertains to her theory that the hepatitis B vaccination triggered Tessie's POTS.

Nor did she point to any literature that furnished support for her claim that a dysregulated immune system was a pertinent factor in the causal sequence between the receipt of a hepatitis B vaccine and the development of Tessie's POTS. Her testimony at hearing provided no further illumination on the subject. Tr. 27-30.

It is also unclear what Dr. Byers intended when she claimed that Tessie's laboratory markers were suggestive of an "autoimmune inflammatory disease" prior to the onset of her POTS symptoms. Byers Expert Rpt. 2. Petitioner's only allegation with regard to autoimmune disease is her POTS diagnosis. She has not asserted that she suffers from any other autoimmune disease. See Tr. 40 (Dr. Byers noted that Tessie's rheumatologist found no evidence of an autoimmune rheumatologic disease); Tr. 68-69 (Dr. Byers indicated that Tessie had no autoimmune disease other than her POTS condition).

Dr. Byers described the clinical signs that would be expected in a subject "with . . . low grade inflammation or an upregulated immune system." Tr. 30. Simply put, the subject would feel like she "had the flu. [And] feel a little bit under the weather." Id. After describing the expected symptoms, Dr. Byers acknowledged that nothing in the medical records indicated that Tessie had any "clinical symptoms . . . normally

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[27] Dr. Byers alternately used the term "upregulated," which she equated with a low grade inflammation. Tr. 30.

associate[d] with [a chronic] low grade inflammation or [an] upregulated immune system . . . prior to the onset of her POTS." Tr. 30-31.

Dr. Byers places great emphasis on the status of Tessie's immune system prior to the onset of her POTS, both in her written opinion and her testimony. But, Dr. Byers does not explain how the absence in Tessie's case of the prodromal flu-like symptoms "normally see[n]" in a subject with a dysregulated immune system is consistent with the expected clinical presentation under the theory she described. See id.

Ironically, the undersigned observes, the logical import of Dr. Byers' testimony that Tessie showed signs of an autoimmune disease–prior to the subject vaccination–when considered with the fact that the only autoimmune disease from which Tessie suffers is POTS (notwithstanding Dr. Byers assertions to the contrary) strongly suggests that Tessie suffered with POTS before she received the hepatitis B vaccine of interest here.

b. Tessie's Laboratory Test Results

Yet, persistent in her effort to support the claim that Tessie had a dysregulated immune system before receiving the vaccination at issue and that she suffered an immune-mediated subtype of POTS as a result of the vaccination, Dr. Byers pointed to the results of Tessie's laboratory tests. Of particular relevance were the measure of Tessie's erythrocyte sedimentation rate (ESR or SED rate), the measure of her antinuclear antibodies and the measure of her anti-centromere antibodies. Dr. Byers testified that Tessie's "SED rate on 6/1/05 [more than two months before the vaccination,] was 32 and her ANA was very quite elevated at 1:160." Tr. 28. Dr. Byers explained that the "hallmark of autoimmune disease is inflammation, and one of the ways that you measure inflammation is by measuring the SED rate, which is abbreviated ESR for erythrocyte sedimentation rate. Another [means of evaluating inflammation] is to measure the [level of] antinuclear antibody." Id. Dr. Byers provided no citation to the record for the laboratory results to which she pointed for Tessie.[28]

The ESR is a measurement of the rate at which the red blood cells settle in a solution over a period of time. Mosby's 234. It is a nonspecific test used to detect illnesses associated with acute and chronic infection, inflammation (collagen-vascular diseases), advanced neoplasm, and tissue necrosis or infarction. Id. It is not diagnostic for any particular organ disease or injury. Id. A close review of this record discloses that

[28] The only citations petitioner provided were to Tessie's lab results after her August 15, 2005 vaccine. See Response 2, Sept. 4, 2012, ECF No. 83. The results could not serve as the results on which Dr. Byers relied to show the nature of Tessie's immune system prior to her vaccination.

Tessie's SED rate test results closest in time to the alleged date of symptom onset, August 25, 2005, were all normal. See Table 1, below.

Table 1 - SED rate laboratory results in the record			
Date	**SED rate (Normal reference range listed as 0 – 20)**	**Source**	**Days prior / after August 25, 2005 alleged onset date**
June 1, 2005	32 (high)	Pet'r's Ex. 6 at 27	85 days prior
Sept. 2, 2005	11	Pet'r's Ex. 1 at 67	8 days after
Sept. 9, 2005	19	Pet'r's Ex. 1 at 81	15 days after
Sept. _, 2005[29]	9	Pet'r's Ex. 1 at 54	
Oct. 5, 2005	4	Pet'r's Ex. 3 at 79	41 days after
Oct. 25, 2005	16	Pet'r's Ex. 1 at 51	61 days after
Nov. 28, 2005	10	Pet'r's Ex. 3 at 81	95 days after
June 2, 2006	25 (high)	Pet'r's Ex. 1 at 38	281 days after

An antinuclear antibody (ANA) test is ordered to help screen for autoimmune disorders. A review of this record shows a range of positive ANA tests. Dr. Byers refers to the speckled pattern as a relatively nonspecific, but consistent, pattern. Tr. 28-29. Looking at the ANA test results most closely following Tessie's August 15, 2005 vaccination, which were respectively 1:80 and 1:40, Dr. Byers observed that "it's not unusual for these [results] to kind of flicker back and forth." Tr. 29. But Dr. Byers acknowledged that the medical literature, on which she relied, did not provide a "good profile as to what the pattern of the ANA is going to be" in POTS. Tr. 30. Thus, the significance of Tessie's ANA results is unclear. See Table 2, below.

Table 2 - ANA (antinuclear antibody) laboratory results in the record			
Date	**ANA (Normal reference range listed as Negative; titer <1:40)**	**Source**	**Days prior / after August 25, 2005 alleged onset date**
June 1, 2005	Positive; speckled pattern; titer 1:160	Pet'r's Ex. 6 at 54	85 days prior

[29] The collection date of this blood sample is unknown.

Table 2 - ANA (antinuclear antibody) laboratory results in the record			
Date	**ANA (Normal reference range listed as Negative; titer <1:40)**	**Source**	**Days prior / after August 25, 2005 alleged onset date**
Sept. 2, 2005	Positive; speckled pattern; titer 1:80	Pet'r's Ex. 1 at 79	8 days after
Sept. 9, 2005	Positive; speckled pattern; titer 1:40	Pet'r's Ex. 1 at 65	15 days after
Sept. __, 2005	Positive; speckled pattern; titer 1:40	Pet'r's Ex. 1 at 57	
Oct. 25, 2005	Positive; speckled pattern; titer 1:160	Pet'r's Ex. 1 at 49-50	61 days after

Centromere antibodies may occur in patients with certain autoimmune diseases. Dr. Byers pointed to evidence of what she characterized as Tessie "moving to a centromere pattern," as furnished by the test results of Tessie's centromere B antibody test. Tr. 29. Dr. Byers considered the test results to be telling because, as she explained, a centromere pattern may be observed in patients with autoimmune diseases, but is rarely found in the normal population. Id. A finding of centromere antibodies in Tessie's blood work indicated to Dr. Byers that Tessie was "starting to move towards trying to speciate [her] autoimmune disease, and that's one of the other reasons that [Dr. Byers thought] that the etiology of [Tessie's] POTS [was] autoimmune." Id. See Table 3, below.

Table 3 - Centromere B antibody laboratory results in the record			
Date	**Centromere B Antibody (Positive response is > 120)**	**Source**	**Days prior / after August 25, 2005 alleged onset date**
Sept. 9, 2005	15 (within range)	Pet'r's Ex. 1 at 65	15 days after
Sept. __, 2005	6 (within range)	Pet'r's Ex. 1 at 57	
Oct. 25, 2005	218 (out of range)	Pet'r's Ex. 1 at 49-50	61 days after

The test results on which Dr. Byers is relying would seem to point to a process that predated vaccination, and the sole autoimmune disease Tessie has is her POTS condition. As understood by the undersigned, Tessie's lab test results appear to undercut rather than support petitioner's claim of vaccine-related causation.

Because Dr. Byers focused on the record evidence that in her view implicated a vaccine-mediated mechanism of injury, she discounted any immunologic impact from the presumed viral illness documented in Tessie's records.

3. Tessie's August 1, 2005 Illness

The record indicates that Tessie was treated in the emergency room on August 1, 2005, after becoming ill the previous night. Pet'r's Ex. 20 at 27-29. Tessie awakened feeling nauseated in the middle of the night and vomited approximately six times. Id. at 27. Still feeling weak and nauseous in the morning, she rose to use the restroom, and fell to the ground. Id. Upon her arrival at the hospital, she continued to feel very weak. Id.

The treating physician suspected that dehydration had led to Tessie's "vasovagal episode." Pet'r's Ex. 20 at 28. Although her attending physician considered the possibility of a seizure, the doctor decided "it [was] unlikely. . . [and recommended that Tessie] take Phenergan as needed for her probable viral syndrome." Id. (emphasis added).

Dr. Byers testified that her review of the medical records did not disclose the underlying cause of Tessie's illness that day. Tr. 35-36. She speculated that the illness could have been a viral gastroenteritis or an environmentally-triggered toxin which can lead to gastritis. Tr. 36. While petitioner's other expert, Dr. Kinsbourne, acknowledged that "reports of vir[al] infections [preceding] the disorder POTS," he agreed with Dr. Byers that it was not clear that Tessie's August 1, 2005 illness was a viral one. Tr. 109.

Dr. Byers testified that she would consider the August 15, 2005 hepatitis B vaccine as more likely the trigger of her POTS than the August 1, 2005, "primarily because of the timeframe." Tr. 36. Dr. Byers said that the 10-day onset from the August 15, 2005 vaccination was "exactly consistent" with that of an [anamnestic] reaction, which usually takes "about four days, and then the damage takes a little bit extra." Tr. 36-37. An anamnestic reaction allows the rapid production of antibody to an antigen that has been encountered previously. See The Free Dictionary, http://www.thefreedictionary.com/anamnestic+reaction (last visited July 18, 2013). Dr. Byers essentially argued that Tessie's earlier hepatitis B vaccinations allowed her

immune system to respond more quickly to the one–of interest here–that she received on August 15, 2005.[30]

The literature supports the possibility of a viral infection preceding the onset of POTS. Review of 2007 Thieben shows that of the 38 out of 152 patients in the Mayo Clinic study were found to have a viral illness, either gastrointestinal, upper respiratory tract or unspecified, prior to the onset of their POTS. Pet'r's Ex. 40 at 310 tbl. 2. Of the remaining patients, 109 had no history of preceding illness, 4 were postoperative at onset of their POTS, and 1 patient was omitted from this analysis. Id. Dr. Byers agreed with the authors of the 2002 Grubb article that the etiology of POTS is unclear, but she also said the authors reported that "symptoms appear after a severe viral infection, suggesting that an immune-mediated mechanism may be involved." Tr. 48 (citing Pet'r's Ex. 59 at 49).

Indeed, as addressed earlier in this decision, viral infections as well as immunizations may precede symptom presentations for the immune-mediated partial dysautonomic form of POTS. The difficulty, however, with petitioner's claims regarding this primary form of POTS is that the record does not support a finding that this is the subtype from which she suffered. Rather the weight of the record evidence indicates that Tessie suffered from the congenital condition joint hypermobility syndrome, which as the medical community has recognized, may be accompanied by POTS–as a secondary condition.

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[30] Dr. Byers testimony on the timing of the reaction was amplified by Dr. Kinsbourne's testimony about the appropriate time interval.

Dr. Kinsbourne offered:

> [t]here was some discussion earlier about the time interval. I defer to Dr. Byers as to the details of the evolving nature of the disorder, but typically we accept a fairly wide range of timeframe for autoimmune responses, and in other cases, one has cited the figure five days to 42 days, and I think that's reasonable. Certainly 10 days is well within that timeframe.

Tr. 109. The reference to "other cases" is likely a reference to other Vaccine Program cases, however no citations are offered. As neither party has brought forward any successful cases in which a hepatitis B vaccine was shown to cause POTS (other than Dunbar, which is addressed separately), there is no reason to believe that the time range provided is specific to POTS.

4. Tessie's Joint Hypermobility Syndrome

At hearing, Dr. Kinsbourne attempted to minimize Tessie's diagnosed congenital JHS as a possible cause of her POTS. Dr. Byers said nothing about Tessie's JHS, in either her expert report or her hearing testimony.

Initially, in his expert report, Dr. Kinsbourne stated that "[t]here [is] . . . no evidence for any alternative or underlying disorder that might account for her symptoms in Tessie's medical records." Kinsbourne Expert Rpt. 4. Dr. Kinsbourne made no mention of Tessie's diagnosed JHS in his report.

In his hearing testimony, however, Dr. Kinsbourne did discuss Tessie's JHS. Dr. Kinsbourne described how in a healthy person, blood vessels constrict (vasoconstriction) particularly in the legs and pelvis, to help push blood out of the lower body so that more blood returns to the heart. Tr. 89. The heart, in turn, sends more blood to the brain, and a healthy person does not faint upon standing. See Id. In a person with POTS, however, blood settles in the legs and lower body, which as Dr. Kinsbourne explained can occur when specific fibers in the nervous system are damaged and no longer properly contract blood vessels, thus pushing blood up to the heart. See Id.

Dr. Kinsbourne also testified that Tessie has "hyperextensible joints," and that it is "quite possible that the collagen in the walls of the blood vessels in Tessie's case is also weakened." Tr. 90.

> So you have a situation which is like a double whammy, in a way, triple actually. You've got a genetic predisposition [JHS], undoubtedly, and then you have an attack on the part of the sympathetic nervous system which does the specific job that I've described [pushing blood from the legs up to the heart] and the vessels in which it works are themselves at risk because of the apparent collagen deficit [due to the JHS], so then that causes the problem.

Id. In response to signals that an inadequate amount of blood is flowing to the brain, the heart starts beating faster, in an effort to send more blood to the brain. Tr. 91. Dr. Kinsbourne continued with his discussion of Tessie's JHS and its relationship to her POTS.

> I think she must have been susceptible to [POTS] because this is a very unusual event. I mean you don't normally react like this to a hepatitis B vaccination. When one looks for susceptibility factors, yes, I think that the joint hyperextensibility is viable as a risk factor; however, that's congenital. It's been there since before she was born. I don't see how it can explain the

> event at the time it happened. But I think it sort[] of sets up for it, to some extent.

Tr. 110.

Respondent then asked Dr. Kinsbourne about the 2006 Grubb article in which the authors discussed a subtype of POTS in which hypermobility was the "cause" of the POTS. Tr. 128 (citing to Pet'r's Ex. 29 at 109). Dr. Kinsbourne appeared to be unaware of this portion of the 2006 Grubb article, replying "That's amazing." Tr. 128. According to the Grubb authors,

> Orthostatic intolerance develops in these patients due to the presence of abnormally elastic connective tissue in the vasculature, which results in an increase in vessel distensibility in response to the augmented hydrostatic pressure that occurs during orthostatic stress. This leads to excessive peripheral venous pooling with a resultant compensatory tachycardia.

Pet'r's Ex. 29 at 109.

Upon reviewing this portion of the 2006 Grubb article, Dr. Kinsbourne noted that the mechanism described by the authors as to how JHS affects the vasculature was "exactly what [he] explained" in his earlier testimony. Tr. 129.

Confronted with a "cause" for POTS that he appeared not to have previously considered, Dr. Kinsbourne then attempted to rehabilitate his position that it was the hepatitis B vaccine that caused Tessie's POTS. First agreeing that Tessie had joint hypermobility, Dr. Kinsbourne continued:

> My point was that she had that [JHS] for 15 years and it didn't trigger the severe symptom [POTS]. And what I was thinking was that this was a predisposition and then the vaccine was what we call a second hit. In many condition[s] where you have a predisposition or some early event which puts you at risk, and this would be such an event for sure, and then you have a second event which it will reach its pinpoint and you get the disease. That's my hypothesis, you know? I'm not saying it's the only possible way to think.

Id. (emphasis added).

The problem with Dr. Kinsbourne's hypothesis, offered for the first time during cross-examination at the July 2012 hearing, is that it is contradicted by the literature filed by both petitioner and respondent in this matter. As noted in the earlier discussion on Tessie's JHS, nothing in the literature suggests that an external trigger is necessary for

those with JHS to develop POTS. Instead, the medical literature indicates that a congenital JHS condition alone is sufficient to prompt the appearance of POTS symptoms. See Pet'r's Ex. 29 at 109; Resp't's Ex. A-3 at 37.

Despite the best effort of petitioner's expert, Dr. Kinsbourne, to account for Tessie's JHS in a way that would still allow for the hepatitis B vaccine to be the cause of her POTS, the record simply does not support the interpretation of her JHS as merely a predisposition. Rather, the record as a whole supports the interpretation that Tessie's JHS was the cause of her POTS.

Considering the record as a whole, petitioner has failed to carry her burden on Althen prong two.

E. Althen Prong Three

On the facts of this case, the undersigned is persuaded that the August 15, 2005 hepatitis B vaccine did not cause Tessie's POTS. Nonetheless, out of an abundance of caution, the undersigned addresses petitioner's argument on timing. The undersigned finds that even if petitioner were assumed to have shown that her POTS was immune-mediated–as argued by Dr. Byers–petitioner still cannot carry her burden on Althen prong three.

Under Althen prong three, petitioner must show "a proximate temporal relationship between vaccination and injury." Althen, 418 F.3d at 1278. Petitioner must establish that her injury occurred within a time frame that is medically appropriate for the alleged mechanism of harm. See Pafford, 451 F.3d at 1358 ("Evidence demonstrating petitioner's injury occurred within a medically acceptable time frame bolsters a link between the injury alleged and the vaccination at issue under the 'but-for' prong of the causation analysis."). Petitioner may satisfy this prong by producing "preponderant proof that the onset of symptoms occurred within a time frame for which, given the medical understanding of the disorder's etiology, it is medically acceptable to infer causation-in-fact." de Bazan, 539 F.3d at 1352. The appropriate temporal association will vary according to the particular medical theory advanced in the case. See Pafford, 451 F.3d at 1358.

1. Petitioner's Evidence on Timing

Relying on Dr. Byers' expert report and hearing testimony, petitioner asserts that ten days is an appropriate time period within which to see the onset of POTS after a vaccination. Pet'r's Post-Hr'g Br. 12. Citing Dr. Byers' expert report, petitioner speculated that:

> [the] receipt of her third hepatitis B vaccination . . . probabl[y] . . . stimulated her population of memory cells and this immune challenge triggered the onset of [her] POTS.

Id. (citing Byers Expert Rpt. 2).

Dr. Byers explained that:

> the 10-day lag is appropriate because, as I've described before, [Tessie] already had a population of *T* cells and *B* cells that were specific against hepatitis B and could be easily triggered to produce very active *T* cells and high titer antibodies, and that's the appropriate time. It probably, it would have occurred maybe in about four days, and it would have taken a little bit [of] extra time for the destruction induced by the – inflammation mediated by those cells to be seen.

Tr. 31-32 (emphasis added).

Petitioner reiterated in the post-hearing briefing that she:

> would have had a fairly large reservoir of both, of hepatitis B specific surface antigen directed T cells and B cells, [which] could be triggered . . . very rapidly by the next vaccine that she received, which is the [August 15] vaccine. And the temporal relationship of her symptoms starting within 10 days after the vaccine is very consistent with activating those cells and allowing them . . . to start generating their damage.

Pet'r's Post-Hr'g Br. 12 (citing Tr. 26) (emphasis added).

Neither petitioner nor her expert, Dr. Byers, cited any authority regarding the appropriateness of a 10-day onset period. Dr. Byers acknowledged that she has no experience diagnosing or treating POTS patients and that her opinion in this matter is based solely on her review of the medical literature and Tessie's medical records. Absent specific professional experience with the injury alleged and without support from the filed literature addressing POTS, Dr. Byers' opinion must derive from her general knowledge of immunology.

Assuming for the purpose of this analysis that Dr. Byers has sufficient knowledge of immunology to provide a reliable opinion about the onset of autoimmune mediated disorders in general, the Federal Circuit's teaching in Pafford indicates that such knowledge nonetheless is insufficient to provide evidence of the specific temporal onset for POTS. See Pafford, 451 F.3d at 1359.

In Pafford, the special master applied the pre-Althen test then in use–referred to here as the Grant test–which required a petitioner to: first, provide a reputable medical theory causally connecting the vaccination and the injury, and second, prove that the vaccine actually caused the alleged symptoms in her particular case. Pafford v. Sec'y of Health & Human Servs., No. 01–0165V, 2004 WL 1717359 (Fed. Cl. Spec. Mstr. July 16, 2004) (citing Grant v. Sec'y of Health & Human Servs., 956 F.2d 1144, 1148 (Fed. Cir. 1992)), aff'd 64 Fed. Cl. 19 (2005), aff'd 451 F.3d 1352 (Fed. Cir. 2006)). The Federal Circuit considered the special master's application of the second prong of Grant to be "commensurate with the third prong of the Althen test." Pafford, 451 F.3d at 1356 (citing Pafford, 2004 WL 1717359, at *9 ("The link missing from Petitioner's argument . . . was the lack of any defined time period in which one would expect to see the onset of Still's disease subsequent to a triggering event.")). "Thus, this court perceives no significant difference between the Special Master's test and that established by this court in Althen and Shyface." Id.

The assigned special master hearing the claim determined that the petitioner in Pafford failed to satisfy the second prong of the Grant test. Pafford, 2004 WL 1717359, at *9. Petitioner had provided the testimony of two experts, one of whom said nothing about a medically acceptable timeframe for onset. See Pafford, 451 F.3d at 1358. The other expert testified about the medically acceptable time frame for "arthralgia episodes and joint syndromes generally," Id. at 1359, however the alleged injury in Pafford was Still's disease, a condition that is also known as Juvenile Rheumatoid Arthritis (JRA), see id. at 1354. The special master found that the general evidence presented about arthralgia was insufficient to show a specific temporal relationship for the particular rheumatologic condition, Still's disease. See id. at 1359.

On review, the Federal Circuit affirmed the finding of the special master and stated:

> [s]trong temporal evidence is even more important in cases involving contemporaneous events other than the vaccination, because the presence of multiple potential causative agents makes it difficult to attribute "but-for" causation to the vaccination. After all, credible medical expertise may postulate that any of the other contemporaneous events may have been the sole cause of the injury.

Id. at 1358.

Here, the undersigned's acceptance of Dr. Byers as an expert in immunology does not compel the undersigned's acceptance of every postulate offered by that witness, simply because the expert has been found qualified to opine. See Bergman v. Sec'y of Health & Human Servs., No. 90-1252V, 1992 WL 78671, at *7 (Fed. Cl. Spec. Mstr. Mar. 31, 1992). Dr. Byers' testimony on the temporal relationship prong of Althen

amounts to no more than her ipse dixit. She did not testify to any specifics regarding her former patients, and she did not discuss any experience diagnosing patients with autoimmune diseases after a triggering event that might have informed her opinion in this POTS case.

While Dr. Byers more recently has spent many years as a consulting medical director for pharmaceutical companies overseeing clinical drug trials, and has served both as a co-author on numerous articles and as a co-inventor on several patents, petitioner failed to elicit from Dr. Byers any testimony regarding how these experiences informed her view of the temporal relationship in this matter. Absent more, the undersigned cannot find that petitioner has satisfied the Pafford requirement of providing evidence of an appropriate temporal relationship between the vaccine she received and the particular injury from which she suffers.

2. The Dunbar Case

Petitioner invokes another Vaccine Program case in which, according to petitioner, the special master found that a medically appropriate time frame had been shown in a "POTS case." Pet'r's Post-Hr'g Br. 13 (citing Dunbar v. Sec'y of Health & Human Servs., No 98-627V, 2007 WL 2844826 (Fed. Cl. Spec. Mstr. Sept. 14, 2007)). In Dunbar, the petitioner experienced symptom onset three days after he received a hepatitis B vaccine. Dunbar, 2007 WL 2844826 at *1. Petitioner in this case, however, overstates the importance of the POTS diagnosis in the Dunbar case, and grossly misstates the onset date of Mr. Dunbar's POTS symptoms.

In Dunbar, Mr. Dunbar received two hepatitis B vaccinations, respectively in April 1994 and September 1994. Id. Three days after his second vaccination, Mr. Dunbar sought treatment, reporting that he had experienced an adverse reaction after each administered vaccine. Id. Mr. Dunbar claimed that after his first vaccination, he experienced pain under his left arm, headache, nausea, and watering of his left eye. Id. After his second vaccination, he suffered from frontal headache, aches and pains, sweats and chills, twitching of his left eyelid, joint aches, and stiffness.[31] Id.

Mr. Dunbar was eventually diagnosed with five separate immune-mediated syndromes, including an encephalopathy, POTS, autoimmune hepatitis, neuropathy and a

[31] Mr. Dunbar related his adverse vaccine reactions to subsequent treaters who recorded his recollections in their notes. The description of the symptoms was not always recorded in the same manner, although the undersigned found no material differences. The description included here is taken from one of petitioner's earliest post-vaccinal medical appointments, at which time his memory would be expected to be freshest.

lupus-like syndrome. Id. at *10, 27. On review of Mr. Dunbar's medical records, the special master found that twelve different treating physicians had attributed Mr. Dunbar's problems to his hepatitis B vaccines. Id. at *23 n.6, 28.

During a physical exam in November 1994, nearly 40 days after Mr. Dunbar's second hepatitis B vaccine, he complained of "increasing fatigue, marked loss of short-term memory, shortness of breath, and dyspnea on climbing two flights of stairs." Id. at *1. Mr. Dunbar denied any preceding viral prodrome. Id.

Nine months later, in August 1995, Dr. Richard de Shazo, an immunologist, conducted a review of petitioner's medical records. Dr. de Shazo, who often consulted on worker's compensation cases, id. at *26, wrote an opinion that Mr. Dunbar's hepatitis B vaccine caused his encephalopathy, id. at *18. Dr. de Shazo noted that while not all of Mr. Dunbar's treating physicians agreed on his diagnosis, all agreed that he had an "untoward reaction" to the hepatitis B vaccine, with causation supported by the temporal association with the onset of illness. See id. at *4. Dr. de Shazo also was persuaded by an unusual syndrome of local inflammation at the site of Dr. Dunbar's revaccination. See id.

The special master provided a thorough recitation of Mr. Dunbar's medical records. The record summary showed that in the approximately 110 medical visits he had over 13 years (August 1994-June 2007), POTS is mentioned in only 4 of the records. See id. at *1-17.

In October 1996, almost two years after Mr. Dunbar's second hepatitis B vaccine, one of his treating physicians recorded that he had POTS. See id. at *7. Mr. Dunbar had a positive tilt table test four months later in February 1997. Id. at *8. In April 1997, Mr. Dunbar's physician attributed his fatigue, in part, to his POTS. Id. at *9. Ten months thereafter, in February 1998, petitioner was diagnosed with multiple autoimmune syndromes, including POTS. Id. at *10.

The special master's entitlement ruling did not focus on Mr. Dunbar's POTS diagnosis, and there is no indication that Mr. Dunbar's POTS was as long-term and as debilitating an injury as petitioner in this case has endured. Unlike Tessie–who had difficulty with any strenuous activities and was unable to continue attending school–Mr. Dunbar planned a trip to Europe less than three years after his POTS diagnosis. See id. at *12.

While Mr. Dunbar experienced certain symptoms within three days of his second hepatitis B vaccine, none of the symptoms were similar to Tessie's alleged symptoms of POTS onset. Mr. Dunbar developed POTS more than two years after his vaccination. The best possible interpretation of Dunbar, from petitioner's point of view, is that the symptoms of which Mr. Dunbar complained in November 1994–specifically increasing

fatigue, marked loss of short-term memory, shortness of breath, and dyspnea–were early symptoms of his later-diagnosed POTS. But these symptoms occurred well beyond the 10-day period of onset put forth by petitioner in this matter. Applying the same diagnostic principles to Mr. Dunbar that petitioner urges must be applied in this case–which consider when the injured person "actually started to complain of an increased heart rate," Pet'r's Post-Hr'g Reply Br. 2-3[32]–Mr. Dunbar's onset would be in October 1996, more than two years after his second hepatitis B vaccine in September 1994.

When considered closely, the Dunbar case offers petitioner no support for her Althen prong three argument that Tessie's alleged period of symptom onset was an appropriate one within which to expect the onset of a POTS condition following a hepatitis B vaccine. Upon review of the record as a whole, the undersigned is not persuaded that petitioner has carried her burden of proving that 10 days is a medically acceptable time period within which to expect the onset of an immune-mediated POTS subtype following a hepatitis B vaccine.

Nonetheless, as previously stated, even if 10 days were an appropriate time period within which to expect such onset, petitioner still has failed to carry her burden on causation, because she has failed to show that her POTS was an immune-mediated form of POTS, as explained by the 2006 Grubb article relied upon by her expert, Dr. Kinsbourne. Without this finding, petitioner's theory of causation must fail.

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[32] In an effort to show that she was not suffering from POTS prior to her hepatitis B vaccine, petitioner pointed to the absence of any pre-vaccine medical record that documented an increase in her heart rate. See Pet'r's Post-Hr'g Reply Br. 1-2. Without an increase in heart rate, according to petitioner, there can be no POTS diagnosis, and thus no POTS. See Pet'r's Post-Hr'g Reply Br. 1-2. Petitioner's argument suggests that the date of onset cannot be defined until a diagnosis can be made. But in Tessie's case, petitioner asserted an onset date of August 25, 2005, see, e.g., Byers Expert Rpt. 2, despite first receiving a POTS diagnosis from Dr. Wong on October 4, 2005, see Pet'r's Ex. 7 at 5. If Tessie's onset was defined as the date on which Tessie started to complain of an increased heart rate, as documented in the record, this date would be October 4, 2005, see Pet'r's Ex. 7 at 5, 50 days after her hepatitis B vaccination, and well beyond the 10-day time period defined by Dr. Byers as the expected onset of an immune-mediated form of POTS.

V. CONCLUSION

For the foregoing reasons, petitioner has not established by preponderant evidence her claim for Program compensation, and the petition **SHALL BE DISMISSED**. The Clerk of Court shall enter judgment consistent with this decision.[33]

IT IS SO ORDERED.

s/Patricia E. Campbell-Smith
Patricia E. Campbell-Smith
Chief Special Master

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