

In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

Filed: February 17, 2023

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CARA SPECKS,

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No. 15-491V

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Petitioner,

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Special Master Sanders

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v.

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Denial of Entitlement; Influenza

SECRETARY OF HEALTH
AND HUMAN SERVICES,

*

(“Flu”) Vaccine; Postural Orthostatic

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Tachycardia Syndrome (“POTS”);

*

Hypovolemia

*

Respondent.

* * * * *

Edward Kraus, Kraus Law Group, LLC, Chicago, IL, for Petitioner.

Debra A. Filteau Begley, United States Department of Justice, Washington, DC, for Respondent.

ENTITLEMENT DECISION¹

On May 13, 2015, Cara Specks (“Petitioner”) filed a petition for compensation pursuant to the National Vaccine Injury Compensation Program.² Pet. at 1, ECF No. 1; 42 U.S.C. §§ 300aa-1 to -34 (2012). Petitioner alleges that the influenza (“flu”) vaccine she received on October 8, 2013, was the cause-in-fact of her “hyperadrenergic postural orthostatic tachycardia syndrome (“POTS”)³ with hypovolemia[.]”⁴ Pet. at 1.

¹ This Decision shall be posted on the United States Court of Federal Claims’ website, in accordance with the E-Government Act of 2002, 44 U.S.C. § 3501 note (2012) (Federal Management and Promotion of Electronic Government Services). In accordance with Vaccine Rule 18(b), a party has 14 days to identify and move to delete medical or other information that satisfies the criteria in § 300aa-12(d)(4)(B). Further, consistent with the rule requirement, a motion for redaction must include a proposed redacted Decision. If, upon review, I agree that the identified material fits within the requirements of that provision, such material will be deleted from public access.

² National Childhood Vaccine Injury Act of 1986, Pub L. No. 99-660, 100 Stat. 3755. Hereinafter, for ease of citation, all “§” references to the Vaccine Act will be to the pertinent subparagraph of 42 U.S.C. § 300aa (2012).

³ Postural orthostatic tachycardia syndrome (“POTS”) is “a group of symptoms (not including hypotension) that sometimes occur when a person assumes an upright position, including tachycardia, tremulousness, lightheadedness, sweating, and hyperventilation; this is seen more often in women than in men, and the etiology is uncertain.” *Dorland’s Illustrated Medical Dictionary* 1, 1844 (32nd ed. 2012) [hereinafter “*Dorland’s*”]. Hyperadrenergic refers to the “excessive activity of adrenergic nerve fibers with an increase in the effects of adrenergic receptors.” *Id.* at 886.

⁴ Hypovolemia is “abnormally decreased volume of circulating blood in the body; the most common cause is hemorrhage.” *Dorland’s* at 908.

After carefully analyzing and weighing all the evidence and testimony presented in this case in accordance with the applicable legal standards,⁵ I find that Petitioner has failed to provide preponderant evidence that the flu vaccine she received on October 8, 2013, was the cause-in-fact of her POTS and/or hypovolemia. Accordingly, Petitioner's claim is hereby **DISMISSED**.

I. Procedural History

Petitioner filed her petition for compensation on May 13, 2015. Pet. at 1. On June 17, 2015, Petitioner filed a notice of intent to file exhibits on a compact disc, including medical records, Petitioner's affidavit, and an expert report from David Axelrod, M.D.⁶ Pet'r's Exs. 1–22, ECF No. 7. Petitioner filed a statement of completion on June 24, 2015. ECF No. 8. On September 29, 2015, Petitioner submitted an outstanding medical record and an amended statement of completion. Pet'r's Ex. 23, ECF Nos. 15–16.

Respondent filed his Rule 4(c) report on January 19, 2016, recommending that compensation be denied. Resp't's Report at 1, ECF No. 21. The same day, Respondent filed an expert report and supporting medical literature from Phillip Low, M.D. Resp't's Exs. A, A Tabs 1–11, ECF No. 22. The presiding special master held a status conference with the parties on January 28, 2016. Min. Entry, docketed Jan. 28, 2016. The presiding special master “articulated a concern with the timing of onset . . . [and] that notations in some medical records . . . imply that Petitioner's symptoms may predate vaccination.” ECF No. 23 at 1 (citing Pet'r's Ex. 4). Petitioner “attempted to clarify which of the various symptoms, including shortness of breath [(“SOB”)] and dizziness, were related to [her] alleged injury.” *Id.* She also indicated a desire to amend her petition to include a claim of significant aggravation. *Id.* The presiding special master ordered Petitioner to file an affidavit, supplemental expert report, and an amended petition. *Id.*

On March 3, 2016, Petitioner filed additional medical records. Pet'r's Exs. 24–27, ECF No. 24. The next day, Petitioner filed an affidavit. Pet'r's Ex. 28, ECF No. 25. On March 4, 2016, the presiding special master ordered Petitioner to file a supplemental expert report and an amended petition, if necessary. ECF No. 26. On April 28, 2016, Petitioner filed a supplemental expert report from Marcel Kinsbourne, M.D. Pet'r's Exs. 29–30, ECF No. 27. The presiding special master held a status conference with the parties on May 19, 2016, to discuss the ongoing dispute concerning onset. ECF No. 28; *see also* Min. Entry, docketed May 19, 2016. The parties also addressed Petitioner's “assertion that the medical records misrepresented Petitioner's medical history.” ECF No. 28. The presiding special master ordered Petitioner to file a supplemental expert report from Dr. Kinsbourne “addressing the symptoms documented in Petitioner's medical history and their

⁵ While I have reviewed all of the information filed in this case, only those filings and records that are most relevant to the decision will be discussed. *Moriarty v. Sec'y of Health & Hum. Servs.*, 844 F.3d 1322, 1328 (Fed. Cir. 2016) (“[w]e generally presume that a special master considered the relevant record evidence even though he does not explicitly reference such evidence in his decision.”) (citation omitted); *see also Paterek v. Sec'y of Health & Hum. Servs.*, 527 F. App'x. 875, 884 (Fed. Cir. 2013) (“[f]inding certain information not relevant does not lead to—and likely undermines—the conclusion that it was not considered.”).

⁶ On June 29, 2015, Petitioner moved to strike Petitioner's Exhibit 17, the expert report from Dr. Axelrod, due to it containing an incorrect version of the document. *See* ECF No. 9. Petitioner refiled her expert report the same day. Pet'r's Ex. 17, ECF No. 10.

relationship with orthostatic intolerance and POTS[.]” *Id.* Petitioner filed a supplemental expert report from Dr. Kinsbourne on September 14, 2016. Pet’r’s Ex. 31, ECF No. 31.

This case was reassigned to me on January 11, 2017. ECF Nos. 33–34. On January 19, 2017, Respondent filed a supplemental expert report from Dr. Low and supporting medical literature. Resp’t’s Exs. C, C Tabs 1–7, ECF No. 36. I held a status conference with the parties on March 23, 2017. Min. Entry, docketed Mar. 23, 2017. Following the conference, I ordered Petitioner to file a supplemental expert report addressing “whether [Petitioner] had any evidence of autonomic neuropathy, in order to proceed on an immune-mediated causation theory.” ECF No. 37. I agreed with Petitioner’s suggestion for her expert to address a significant aggravation theory. *Id.* On June 21, 2017, Petitioner filed a supplemental expert report and supporting medical literature. Pet’r’s Exs. 32–39, ECF Nos. 39–40. Respondent submitted his supplemental expert report and supporting medical literature on October 23, 2017. Resp’t’s Exs. D, D Tabs 1–6, ECF No. 42. Petitioner filed additional medical records on December 21, 2017. Pet’r’s Exs. 40–42, ECF No. 44. On March 13, 2018, Respondent filed a joint status report requesting that this case proceed to an entitlement hearing. ECF No. 47.

I scheduled this matter for an entitlement hearing to take place on April 16–17, 2020. Hearing Order, ECF No. 49. Petitioner filed additional medical records on January 31, 2020. Pet’r’s Exs. 43–45, ECF No. 52. The same day, Petitioner filed a supplemental expert report from Dr. Kinsbourne, along with supporting medical literature. Pet’r’s Exs. 46–61, ECF Nos. 53–56. Petitioner also filed her pre-hearing brief on January 31, 2020. Pet’r’s Br., ECF No. 58. Respondent filed his pre-hearing response brief and a supplemental expert report from Dr. Low on March 6, 2020. Resp’t’s Resp., ECF No. 60; Resp’t’s Ex. E, ECF No. 61.

I held a status conference with the parties on March 11, 2020, to discuss the implications of the COVID-19 pandemic. *See* Min. Entry, docketed Mar. 18, 2020. On March 23, 2020, I cancelled the entitlement hearing and ordered Respondent to submit any supporting medical literature referenced in his last supplemental expert report. Non-PDF Order, docketed Mar. 23, 2020. Respondent filed medical literature on March 25, 2020. Resp’t’s Exs. E Tabs 1–18, ECF No. 62.

I rescheduled the entitlement hearing to take place remotely on May 19–20, 2021. Hearing Order, ECF No. 63. Petitioner filed an updated medical record on January 15, 2021. Pet’r’s Ex. 62, ECF No. 64. The hearing was held remotely as scheduled on May 19, 2021. Min. Entry, docketed May 19, 2021. Following the entitlement hearing, Petitioner filed an outstanding medical record. Pet’r’s Ex. 67, ECF No. 79.

Petitioner filed an opening post-hearing brief on August 24, 2021. Pet’r’s Br., ECF No. 84. On September 8, 2021, Respondent filed his post-hearing response brief. Resp’t’s Resp., ECF No. 85. Petitioner filed her post-hearing reply brief on September 14, 2021. Pet’r’s Reply, ECF No. 86. This matter is now ripe for consideration.

II. Factual Background

A. Medical Records

a. Pre-vaccination history

Petitioner's pre-vaccination history is relevant for anxiety, depression, insomnia, laryngopharyngeal reflux ("LPR"),⁷ and asthma. Pet'r's Ex. 1 at 5. On January 12, 2011, Petitioner presented to the emergency room ("ER") for a two-day long anxiety attack. Pet'r's Ex. 21 at 149. The ER physician noted her history of anxiety and panic attacks. *Id.* She complained that it "fe[lt] like [her] heart rate ke[pt] beating fast." *Id.* at 150. Her EKG showed that she had sinus tachycardia⁸ and that her heart rate was 114 beats per minute. *Id.* at 152. The ER physician gave Petitioner Xanax, and her symptoms improved. *Id.* at 149.

Approximately one year later, on January 23, 2012, Petitioner presented to her primary care physician ("PCP") and reported a recent hospitalization for an abnormal EKG. Pet'r's Ex. 13 at 1.⁹ Petitioner's PCP referred her to a cardiologist¹⁰ for her palpitations and another specialist for her "allergic rhinitis."¹¹ *Id.* Five days later, on January 28, 2012, Petitioner returned to her PCP reporting that she "fe[lt] like [her] breathing [had] not improved[]" despite "[u]sing [an] inhaler every [four] hours." *Id.* at 3. Her PCP noted that Petitioner complained of increased respiratory issues over the last two years. *Id.* Petitioner's PCP also wrote that Petitioner quit smoking five weeks ago. *Id.* Her PCP's assessment of Petitioner included allergic rhinitis and asthma. *Id.*

On June 10, 2012, Petitioner called emergency personnel to her home after feeling "lightheaded" and experiencing tachycardia. Pet'r's Ex. 67 at 5.¹² When personnel arrived, her heart rate was measured in the 150s. *Id.* Petitioner was taken to the ER where a history of "feeling 'lightheaded' and tachy[cardia]" was noted. *Id.* Petitioner reported she thought she might be anxious or dehydrated. *Id.* at 6. She also "said she smoked marijuana earlier" that she felt was causing her heart rate to "go up[.]" *Id.* Petitioner's physical examination was normal, and her

⁷ Laryngopharyngeal reflux ("LPR") is "a complication of gastroesophageal reflux caused by reflux from the esophagus into the pharynx, characterized by a variety of intermittent chronic symptoms, including hoarseness, cough, throat clearing, globus pharyngeus, and dysphagia" (difficulty swallowing). *Dorland's* at 1616.

⁸ Sinus tachycardia is "tachycardia originating in the sinus node; it is normal during exercise or anxiety and occurs abnormally associated with shock, hypotension, hypoxia, congestive heart failure, fever, and various high output states." *Dorland's* at 1867. Tachycardia is "excessive rapidity in the action of the heart; the term is usually applied to a heart rate above 100 beats per minute in an adult and is often qualified by the locus of origin as well as by whether it is paroxysmal or nonparoxysmal." *Id.*

⁹ Petitioner did not file medical records documenting a recent hospitalization at Northwest Community Emergency Room as noted by her PCP. *See* Pet'r's Ex. 13 at 1; Pet'r's Ex. 31 at 1–20. The records from Northwest Community Emergency Room are from Petitioner's visit on June 10, 2012. *See* Pet'r's Ex. 67 at 1–20.

¹⁰ Petitioner did not file records from a cardiologist for dates following this referral. She testified during the hearing that she did not see a cardiologist following this visit. *See* Tr. 33:13–15.

¹¹ Allergic rhinitis is "a general term used to denote any allergic reaction of the nasal mucosa; it may occur perennially (annually) or seasonally[.]" *Dorland's* at 1639.

¹² Petitioner originally introduced this exhibit as Petitioner's Exhibit 31, but she then realized that was an error. Petitioner then re-introduced the exhibit as Petitioner's Exhibit 67. *See* Tr. 38:17–19. This medical record was not filed prior to the entitlement hearing in May of 2021. When it was ultimately filed, Petitioner designated it as "Exhibit 31." Since Petitioner's Exhibit 31 is one of Dr. Kinsbourne's expert reports, I will refer to this exhibit as "Exhibit 67."

symptoms resolved with fluids while in the ER. *Id.* at 7. Petitioner received discharge instructions for dizziness and palpitations. *Id.* at 11–12. The ER attending listed Petitioner’s diagnoses including palpitations, anxiety disorder, and significant sinus tachycardia. *Id.* at 12.

Petitioner returned to her PCP on February 27, 2013.¹³ Pet’r’s Ex. 13 at 4. Petitioner reported that had been seen three times for sinus pressure and pain and “then developed asthma.” *Id.* Her PCP noted that Petitioner received oral steroids to treat her symptoms but that Petitioner was worried that “steroids worsen her anxiety.” *Id.* On March 21, 2013, Petitioner presented to her PCP reporting that she had SOB “off/on since Dec[ember].” *Id.* at 5. Petitioner also reported a pain under her left ribcage and that she “c[ould not] finish her breaths.” *Id.*

On April 24, 2013, Petitioner returned to her PCP for “allergic rhinitis, asthma[,] and symptoms.” *Id.* at 22. Petitioner reported that “about [one] week ago[,] she developed a headache [] then . . . sinus pressure.” *Id.* Petitioner then “got a lot of fatigue . . . a sore throat and swollen throat on the left . . . a very stuffy nose with clear discharge . . . sneez[ing] . . . [and t]hen her asthma flared up[.]” *Id.* She reported she needed her inhaler every three hours and “was very low energy.” *Id.* Petitioner noted that she “got prednisone 50 mg for [three] days until she was seen[,]” which “worked right away for her.” *Id.* Her PCP noted that such treatment with prednisone alleviated her symptoms. *Id.* at 27. Petitioner’s PCP also wrote that Petitioner was no longer wheezing, but she “fe[lt] very short of breath and [] gets very winded.” *Id.* at 22. Upon examination, Petitioner exhibited nasal congestion, pharyngitis, post-nasal drainage, dyspnea¹⁴ (occurring one to two times per day), and an irregular heartbeat/palpitations. *Id.* at 23. Her PCP reiterated Petitioner’s diagnoses of asthma and allergic rhinitis. *Id.* at 25. Petitioner returned to her PCP on June 24, 2013, reporting the same issues of SOB and related them to her asthma and allergic rhinitis. *Id.* at 27.

b. Vaccination

Petitioner received the seasonal flu vaccine at issue on October 8, 2013. Pet’r’s Ex. 1 at 8. Petitioner’s PCP noted Petitioner’s chronic conditions including “asthma [and] allergic rhinitis, cause unspecified,” but indicated no other concerns during this visit. *Id.*

c. Post-vaccination history

On October 14, 2013, Petitioner reported to Jess Duyka, M.D., “with a greater than [six] mo[nth] [history of] throat clearing, SOB, dry cough, nocturnal choking, globus sensation, [and] hoarseness.” Pet’r’s Ex. 23 at 1, ECF No. 15-1. Upon examination, Dr. Duyka noted no concerns except for inflammation of Petitioner’s larynx. *Id.* at 1–2. Dr. Duyka assessed Petitioner with a cough, dyspnea, and LPR and she recommended a low acid diet. *Id.* at 2. Petitioner followed up with Dr. Duyka on October 23, 2013, and reported no improvement since her last visit. *Id.* at 5. Upon examination, Dr. Duyka noted that the inflammation in Petitioner’s larynx had resolved. *Id.*

¹³ The records from Lake County Health Department and Community Health Center Primary Care Services are mostly handwritten. The records for this date are extremely illegible and difficult to read. *See* Pet’r’s Ex. 13.

¹⁴ Dyspnea is “breathlessness or shortness of breath; difficult or labored respiration.” *Dorland’s* at 582.

Dr. Duyka opined that “[t]his could be a laryngospasm brought on by transient reflux, but [Dr. Duyka did not] see any signs of th[at] on [] exam.” *Id.*

Petitioner returned to her PCP on November 8, 2013, with complaints of a ten-day history of abdominal pain, cramping, and severe diarrhea approximately ten times per day. Pet’r’s Ex. 1 at 3. She reported that she had experienced recent weight loss “due to [a decrease in] intake [and] diarrhea.” *Id.* Petitioner underwent imaging and testing, including an abdominal X-ray, a fecal stain, and labs to test for the presence of bacteria, including salmonella, parasites, and *H. pylori*, which all yielded negative results. *Id.* at 11, 13–16. Petitioner’s PCP assessed her with abdominal pain and diarrhea. *Id.* at 3.

Later the same day, November 8, 2013, Petitioner presented to the ER with the same complaints of abdominal pain, cramping, and diarrhea plus light-headedness, nausea without vomiting, chills, and weakness that “started yesterday.” Pet’r’s Ex. 4 at 155. She explained that she “ke[pt] twitching” and “fe[lt] strange.” *Id.* at 169. Petitioner expressed that she thought her diarrhea “might be related to Protonix,”¹⁵ which she took for her LPR. *Id.* at 155. She reported her history of sinus tachycardia one year prior. *Id.* at 156, 165. Petitioner underwent an EKG, which was normal. *Id.* at 169–70. The ER physician informed Petitioner that “she likely ha[d] a viral syndrome[.]” *Id.* at 170. The impression included “malaise, weakness, diarrhea, dehydration, [and] hypertension.” *Id.* The physician noted that Petitioner was “very difficult to reassure and want[ed] an ‘answer[.]’ which [wa]s not likely forthcoming[.]” but the physician admitted Petitioner. *Id.*

During her hospital stay, Petitioner saw gastroenterologist Jeffrey Nathanson, M.D., on November 9, 2013. *Id.* at 159. Petitioner reported that she had not been “feeling well” and had intermittent SOB “for the last few months.” *Id.* Petitioner stated that she had seen an ENT specialist prior to her hospitalization and flu vaccination and that the ENT suspected her symptoms “might be due to LPR[.]” so she began taking Prilosec.¹⁶ *Id.* Petitioner reported that when she switched to Protonix a month earlier, her SOB “somewhat improved.” *Id.* Dr. Nathanson noted that Petitioner had not had diarrhea since her admission. *Id.* He also noted that Petitioner “fe[lt]” strongly [that her] anxiety is not [the] cause of [her] symptoms but rather [is] secondary to the symptoms themselves.” *Id.* Dr. Nathanson wrote that he “suspect[ed Petitioner’s] symptoms [were] functional with a likely anxiety component” *Id.* at 161. He opined that it was “unclear if [Petitioner] truly ha[d] reflux, as [there were] nonspecific findings on [her] laryngoscopy [that] often correlate poorly with true acid reflux.” *Id.* Dr. Nathanson ordered lab work, including stool studies for infectious etiologies, celiac serologies, and obstructive series, which were normal except for an elevated thyroid stimulating hormone (“TSH”). *Id.* at 157–58, 161, 375–401.

Petitioner also presented to a physical therapist while hospitalized due to her complaints of weakness. *Id.* at 162. Upon examination, Petitioner exhibited decreased balance, gait, functional endurance, and functional strength. *Id.* at 163. The physical therapist noted that Petitioner

¹⁵ Protonix refers to the trademark preparations of pantoprazole sodium. *Dorland’s* at 1537. Pantoprazole sodium is “a proton pump inhibitor . . . used in the treatment of . . . gastroesophageal reflux disease, administered orally or intravenously[.]” *Id.* at 1371.

¹⁶ Prilosec is the trademark preparation of omeprazole. *Dorland’s* at 1514. Omeprazole is a “proton pump inhibitor used in the treatment of dyspepsia, gastroesophageal reflux disease, and gastric hypersecretory conditions[.]” *Id.* at 1319.

“ambulate[d] very slowly[.]” and that she “appear[ed] to be increasingly fatigued[.]” *Id.* at 162. The physical therapist recommended that Petitioner receive physical therapy (“PT”) for “gait training” once or twice more prior to discharge. *Id.* at 163.

On November 10, 2013, Petitioner was discharged from the hospital with diagnoses including suspected functional irritable bowel syndrome (“IBS”),¹⁷ possible LPR, resolved diarrhea, resolved abdominal pain, and elevated TSH. *Id.* at 158. The attending physician opined that Petitioner’s light-headedness, generalized weakness, and diarrhea were “likely” related to viral gastroenteritis.¹⁸ *Id.* at 156. The physician also noted that Petitioner could ambulate normally at the time of discharge. *Id.*

Four days later, on November 14, 2013, Petitioner presented to internist Kimberly Schaefer, M.D., for complaints of dizziness, diarrhea, nausea, vomiting, increased blood pressure (“BP”), and tachycardia. *Id.* at 151. Petitioner reported that she had recently seen Dr. Nathanson, who “felt her symptoms were [related to] autonomic dysfunction.” *Id.* Petitioner also reported that she “fe[lt] her BP gets high when she stands up.” *Id.* Petitioner described feelings of flushing, shaking, waves of nausea, headaches, and changes in temperature, and she stated that “[l]oud noises and bright lights make her sick.” *Id.* Dr. Schaefer recorded Petitioner’s BP as 140/90 when laying down and 128/88 when standing. *Id.* Dr. Schaefer noted Petitioner’s pulse was “too fast to count.” *Id.* Dr. Schaefer wrote that Petitioner saw a psychiatrist during this visit who opined that her symptoms were not psychiatric. *Id.* Dr. Schaefer also noted that Petitioner had a low appetite and had lost twenty pounds over the last two months, some purposefully, but that her weight loss became more “rapid over the last month.” *Id.* Petitioner’s family reported that Petitioner was “starving herself,” and Dr. Schaefer encouraged her to eat and hydrate. *Id.* at 153.

On November 18, 2013, Petitioner returned to the ER with complaints including palpitations, flushing, dizziness, diarrhea, nausea, vomiting, and sluggish speech. *Id.* at 146. Petitioner reported her symptoms as “waxing and waning” for the past two months and that they “were getting progressively worse.” *Id.* She also stated that she was under stress “as her family th[ought] she [wa]s making up [her] symptoms.” *Id.* The ER physician admitted Petitioner for further evaluation. *Id.* at 148–49.

During her hospital stay, on November 19, 2013, Petitioner saw cardiologist Jonathan Gilbert, M.D., who noted that Petitioner’s BP and heart rate were elevated. *Id.* at 138. Dr. Gilbert noted her BP as 170/101 and her heart rate as 134 beats per minute. *Id.* Dr. Gilbert wrote that Petitioner reported her symptoms beginning on November 8, 2013. *Id.* Petitioner indicated that her symptoms worsened when she was upright, she had an “unsteady gait,” and tingling and numbness in her hands. *Id.* Dr. Gilbert opined that Petitioner suffered from sinus tachycardia and “possible

¹⁷ Irritable bowel syndrome (“IBS”) is “a common, chronic, noninflammatory condition characterized by abdominal pain and altered bowel habits (diarrhea or constipation or both), but no detectable pathologic change; there may be spasms of the intestinal muscles. A variant form is characterized by painless diarrhea. It is usually due to a combination of psychologic and physiologic factors.” *Dorland’s* at 1835.

¹⁸ Gastroenteritis is “inflammation of the lining of the stomach and intestines, characterized by anorexia, nausea, diarrhea, abdominal pain, and weakness. Causes include food poisoning . . . ; viral infections . . . ; consumption of irritating food or drink; and sometimes psychological factors such as anger, stress, or fear.” *Dorland’s* at 764.

POTS-[a]utonomic [d]ysfunction.” *Id.* at 140. Dr. Gilbert noted that other etiologies for her condition include “anxiety [and] bronchodilators[.]” *Id.* He prescribed beta-blockers. *Id.*

The same day, Petitioner saw neurologist Janet Choi, M.D., for concerns of “autonomic symptoms.” *Id.* at 140–41. Petitioner reported that she had “a bad cold and [SOB] that required steroids . . . prior to the onset of all her problems.” *Id.* at 141. Dr. Choi wrote that Petitioner experienced “spells consisting of multiple symptoms of anxiety, lightheadedness, slowing of speech and cognition, clamminess and coldness of hands and feet, diaphoresis,¹⁹ palpitations, flushing, [and] tinnitus[.]”²⁰ but that Petitioner “denie[d] any associated mental anxiety.” *Id.* Dr. Choi noted that Petitioner’s BP had been “variable upon standing, from as high as 175/83 to low . . . [and that t]hese spells usually improve[d] upon laying back down.” *Id.* Petitioner underwent a brain CT and an EEG, which were normal. *Id.* at 143. Dr. Choi noted that Petitioner’s use of Coreg²¹ was helping to reduce her tachycardia. *Id.* at 134. Dr. Choi’s impression of Petitioner included malaise and fatigue, nausea, and anorexia. *Id.* at 135. Dr. Choi opined that Petitioner “could have [POTS], or some other autonomic dysfunction, such as an autoimmune etiology.” *Id.* at 143. Dr. Choi recommended further testing. *Id.* Petitioner’s serum testing and labs on November 19, 2013, for autoimmune dysautonomia, paraneoplastic antibodies, cortisol levels, and Lyme disease were all normal or negative. *Id.* at 352–54. These included tests for acetylcholine receptors (“AChRs”) and ganglionic AChR antibodies. *See id.*

On November 20, 2013, Petitioner saw psychiatrist Susanna Kovari, M.D., to discuss her anxiety. *Id.* at 135. Petitioner reported that “when [her] symptoms happen[,] she is not ‘mentally anxious’ but her body feels like it is anxious.” *Id.* Dr. Kovari diagnosed Petitioner with an anxiety disorder and recommended outpatient mental health treatment. *Id.* at 137. Petitioner was discharged that day. *Id.*

The next day, November 21, 2013, Petitioner presented to cardiologist Manu Chander, M.D., to follow up from her recent hospitalization. *Id.* at 129. Petitioner described her recent symptoms and “insist[ed that] she does[not] have anxiety and [that] the POTS [wa]s triggering her [symptoms].” *Id.* Petitioner reported that her use of Coreg was making her “sedated and more dizzy” but was helping her tachycardia. *Id.* Dr. Chander reduced Petitioner’s Coreg dosage and recommended a tilt-table test. *Id.* Dr. Chander also gave Petitioner a psychiatric referral, which Petitioner declined. *Id.* at 130.

Petitioner returned to Dr. Gilbert on November 23, 2013, for a follow-up. *Id.* at 126–29. Dr. Gilbert reviewed Petitioner’s echocardiogram performed on November 19, 2013, and noted that it was normal. *Id.* at 128. Dr. Gilbert indicated that Petitioner’s heart function was normal. *Id.*

¹⁹ Diaphoresis is “sweating, sometimes specifically that [was] induced artificially.” *Dorland’s* at 509.

²⁰ Tinnitus is “a noise in the ears, such as ringing, buzzing, roaring, or clicking. It is usually subjective in type[.]” *Dorland’s* at 1930.

²¹ Coreg is the trademark preparation of carvedilol. *Dorland’s* at 414. Carvedilol is “a beta-adrenergic blocking agent used in the treatment of essential hypertension and as an adjunct in the treatment of mild or moderate congestive heart failure[.]” *Id.* at 301.

Dr. Gilbert assessed Petitioner with POTS, prescribed Midodrine,²² and referred her to a POTS clinic. *Id.*

Petitioner underwent a tilt-table test on November 29, 2013. *Id.* at 177. Petitioner's baseline BP and heart rate were 127/78 and 87, respectively. *Id.* The testing revealed sinus tachycardia beginning two minutes after Petitioner was placed in a head-up tilt, "with heart rates in the 113 to 140 beats per minute range." *Id.* The technician noted that "[t]here was no concomitant significant change in blood pressures. Specifically, there was no associated orthostatic hypotension." *Id.* Petitioner reported "multiple somatic complaints" during the head-up portion of the test, including "hand shaking, lightheadedness, anxiousness, hyperventilation, lightheadedness, and nausea." *Id.* Petitioner indicated that such symptoms improved when she was placed in a supine position. *Id.* The technician noted that "[i]mmmediately prior" to being placed in a supine position, her BP was 125/83. *Id.* After two minutes in a supine position, Petitioner's BP was 133/73, and her heart rate was 94 beats per minute. *Id.* After five minutes, her BP decreased to 110/64. *Id.* Such findings were "consistent with [POTS]." *Id.*

Petitioner followed up with Dr. Chander on December 2, 2013. *Id.* at 126. Dr. Chander agreed that the tilt-table test was "suggestive of POTS." *Id.* Petitioner reported feeling better on Coreg and "especially since she started [M]idodrine." *Id.* Dr. Chander encouraged Petitioner to hydrate, eat well, wear pressure stockings, and continue taking her medications. *Id.*

On December 20, 2013, Petitioner returned to the ER complaining of ongoing POTS symptoms, including that she had been "bed-ridden for the last month[]" and had left calf pain, tingling in her left lower extremity, and dehydration. *Id.* at 123. The attending physician noted that when Petitioner did not hydrate, her POTS symptoms worsened. *Id.* at 120. Petitioner received IV fluids. *Id.* Petitioner returned to the ER on December 31, 2013, and January 2, 2014, reporting "flare up[s]" of her POTS symptoms, including nausea, "generalized weakness, dizziness, and 'feel[ing] like she will pass out[.]'" *Id.* at 116. Petitioner also reported that she was "unable to keep up with [her two to three liter] hydration requirement." *Id.* at 113, 116. Each time she presented with these complaints Petitioner received IV fluids to successfully treat her symptoms. *See id.*

On January 6, 2014, Petitioner presented to neurologist Alexander Barboi, M.D., as he specializes in autonomic disorders. Pet'r's Ex. 6 at 8. He wrote that Petitioner "seem[ed] to have long standing symptoms that were present for a while and then got better[,] such as intermittent [SOB] after a bout of respiratory infection in December 2012, episodes of palpitations at night[,] and dizzy spells in 2011[.]" *Id.* He also recorded a "more remote history of intermittent flushing[,] abdominal pain[,] and diarrhea." *Id.* Dr. Barboi noted that Petitioner's "increased symptoms" of "dizziness and presyncopal [sic] episodes[]" began in November of 2013. *Id.* He indicated that since Petitioner's November 2013 hospitalizations, she "has been quite restricted in her daily activities with [an] inability to work and drive[.]" *Id.* Dr. Barboi's impression of Petitioner was "long-standing background autonomic dysfunction syndrome[,] acquired versus inherited." *Id.* at

²² Midodrine hydrochloride is "a direct-acting sympathomimetic agent, that stimulates the a-adrenergic receptors of the arteriolar and venous vasculature; used as a vasopressor in the treatment of orthostatic hypotension." *Dorland's* at 1165.

12. He also recorded his impression of possible “[s]icca syndrome”²³ and “mastocyte activation syndrome.”²⁴ *Id.* Dr. Barboi wrote that there were “[u]nclear reasons for [Petitioner’s] worsening [symptoms] in the past year.” *Id.* He recommended exercise, continued hydration, to take Florinef²⁵ instead of Coreg, and only to take Midodrine “sparingly.” *Id.*

Petitioner presented to the hospital for placement of a port-a-catheter to receive IV fluids on January 17, 2014. Pet’r’s Ex. 4 at 88, 100. On January 20, 2014, Petitioner obtained approval for home health services for IV fluids to treat her continued dehydration because she was homebound as a result of her POTS and could not drive herself. Pet’r’s Ex. 3 at 50. Petitioner received IV fluids every other day. *See id.*

On January 27, 2014, following Dr. Barboi’s suspicion, Petitioner underwent a lip biopsy to rule out a possible Sjögren’s syndrome²⁶ diagnosis. Pet’r’s Ex. 2 at 27. The clinical impression of the biopsy indicated that the test “rule[d] out Sjögren’s.” Pet’r’s Ex. 4 at 57. Petitioner presented to neurologist Hoyee Chan, M.D., on February 9, 2014. *Id.* at 65. Dr. Chan noted Petitioner’s lip biopsy on January 27, 2014, and “[d]oubted [that] Sjögren’s [wa]s the cause of her POTS[.]” *Id.* at 67. Dr. Chan referred Petitioner to an endocrinologist to “[rule out] any adrenal insufficiency as the cause of [her] POTS related symptoms.” *Id.*

Petitioner presented to endocrinologist Lisa Purdy, M.D., on February 11, 2014. *Id.* at 59. Petitioner reported that she had been “homebound” for the past three months. *Id.* Petitioner underwent cortisol testing, which did not suggest Addison’s disease,²⁷ and her anti-Sjögren’s titer was negative.²⁸ *Id.* at 61, 276. Dr. Purdy wrote that Petitioner “has considerable anxiety associated with her [POTS] condition, which exacerbates her other symptoms[,] including her BP.” *Id.* at 59.

²³ Sicca syndrome is “keratoconjunctivitis and xerostomia without connective tissue disease[.]” also called Sjögren’s syndrome. *Dorland’s* at 1848. Sjögren’s syndrome is “a symptom complex of unknown etiology, usually occurring in middle-aged or older women, marked by the triad of keratoconjunctivitis sicca with or without lacrimal gland enlargement, xerostomia with or without salivary gland enlargement, and the presence of a connective tissue disease, usually rheumatoid arthritis but sometimes systemic lupus erythematosus, scleroderma, or polymyositis. An abnormal immune response has been implicated.” *Id.*

²⁴ Mastocyte activation syndrome or mastocytosis syndrome is “an episodic syndrome occurring in certain patients with systemic mastocytosis, usually those with skin lesions, bone lesions, and hepatosplenomegaly, presumably associated with histamine release from degranulation of mast cells, and characterized mainly by intense pruritus, flushing, headache, tachycardia, hypotension, and syncope.” *Dorland’s* at 1838.

²⁵ Florinef is the trademark preparation of fludrocortisone acetate. *Dorland’s* at 718. Fludrocortisone acetate is “the acetate salt of a synthetic steroid with potent mineralocorticoid and high glucocorticoid activity, used in replacement therapy for primary or secondary adrenocortical insufficiency in Addison disease and for the treatment of salt-losing adrenogenital syndrome; administered orally.” *Id.* at 719.

²⁶ *See supra*, note 23 (explaining that Sjögren’s syndrome is sicca syndrome).

²⁷ Addison disease is “a chronic type of adrenocortical insufficiency, characterized by hypotension, weight loss, anorexia, weakness, and a bronzelike hyperpigmentation of the skin. It is due to tuberculosis- or autoimmune-induced destruction of the adrenal cortex, which results in deficiency of aldosterone and cortisol and is fatal in the absence of replacement therapy[.]” *Dorland’s* at 528.

²⁸ Petitioner’s medical records and filings contain several notations past this date that reflect she believed she had Sjögren’s syndrome (based on Dr. Barboi’s impression) despite her negative lip biopsy and anti-Sjögren’s titer. *See, e.g.*, Tr. 30:6–12. Despite Petitioner and Dr. Barboi’s belief, the evidence fails to show

On March 6, 2014, Petitioner consulted with rheumatologist Kenneth Crane, M.D. *Id.* at 34; Pet'r's Ex. 2 at 9. Petitioner explained her medical history, including, among other things, weight loss, weakness, fatigue, hoarseness and frequent sore throats, chest pain, rapid and sudden changes in heartbeat, high BP, SOB, nausea, constipation, headaches, and dehydration. Pet'r's Ex. 2 at 14–15. Dr. Crane assessed Petitioner with hyperadrenergic POTS. *Id.* at 13. Dr. Crane ordered additional lab testing. *Id.*

On March 20, 2014, Petitioner underwent spirometry testing at the direction of allergist/immunologist Paul Kentor, M.D. Pet'r's Ex. 4 at 196. The spirometry test revealed no evidence of asthma. *Id.* Petitioner also underwent a panel of tests, including an autoimmune dysautonomia evaluation, on March 25, 2014. *Id.* at 227. This repeat test included serum testing for AChR and g-AChR antibodies. *Id.* The results of this testing were normal. *Id.* On March 27, 2014, Petitioner presented for the additional lab work previously ordered by Dr. Crane. Pet'r's Ex. 2 at 9. Petitioner's lab results from this date revealed elevated C3 and C4 levels, SED rate, ANA titer (of 1:160), and alpha-2 globulins. *Id.* at 17–35.

Petitioner followed up with Dr. Chan on March 28, 2014, to discuss her recent positive ANA titer and Petitioner's concern that this could be reflective of multiple sclerosis (“MS”).²⁹ *Id.* at 16. Dr. Chan wrote that Petitioner's positive ANA was “very non-specific” and “could be [a] false positive” in light of prior negative testing. *Id.* at 18. On April 25, 2014, Petitioner returned to Dr. Chan reporting SOB with an “associated cough” and “burning” in her chest. Pet'r's Ex. 7 at 73. On examination, Petitioner exhibited normal lung function. *Id.* at 76. Dr. Chan told Petitioner that Petitioner's symptoms were “most likely anxiety related.” *Id.* Petitioner underwent a pulmonology consultation for her SOB and chest pain with Jeffrey Hamilton, M.D., on April 30, 2014. *Id.* at 64. Dr. Hamilton indicated that Petitioner's physical exam was normal, and a chest CT was “clear.” *Id.* at 68–69.

by a preponderant standard that Petitioner does, in fact, suffer from Sjögren's. For example, when Petitioner presented to rheumatologist Dr. Crane on March 6, 2014, she told Dr. Crane that she had been diagnosed with Sjögren's, confirmed by a lip biopsy. *See* Pet'r's Ex. 2 at 9, 14–15. Based on Petitioner's self-reported history, Dr. Crane assessed her with Sjögren's. *Id.* at 13. Petitioner also told Dr. Hamilton on April 30, 2014, that she had been diagnosed with Sjögren's, which prompted him to make the same assessment and to unsuccessfully look for an association between Petitioner's POTS and Sjögren's. Pet'r's Ex. 7 at 64, 69. Drs. Crane and Hamilton's assessments do not provide support for a Sjögren's syndrome diagnosis. In fact, Petitioner's reports to treaters are inconsistent with her laboratory testing that was non-diagnostic for Sjögren's. *See, e.g.,* Pet'r's Ex. 4 at 57. When rheumatologist Dr. Gan reviewed the results of Petitioner's lip biopsy first-hand on August 4, 2014, he, consistent with the original interpretation, determined the results conclusively showed she did not have Sjögren's. Pet'r's Ex. 7 at 13–14. Additionally, other treaters opined Petitioner did not have Sjögren's. *See, e.g.,* Pet'r's Ex. 4 at 18, 67; Pet'r's Ex. 7 at 73–74. Petitioner Sjögren's syndrome diagnosis is therefore not supported by a preponderance of the evidence, and I will not credit Dr. Barboi's unsubstantiated conclusion or discuss this issue further.

²⁹ Multiple sclerosis is “a disease in which there are foci of demyelination throughout the white matter of the central nervous system, sometimes extending into the gray matter; symptoms usually include weakness, incoordination, paresthesias, speech disturbances, and visual complaints. The course of the disease is usually prolonged, so that the term *multiple* also refers to remissions and relapses that occur over a period of many years The etiology is unknown.” *Dorland's* at 1680.

Petitioner had a follow-up with Dr. Barboi on July 10, 2014. *Id.* at 159. Petitioner reported “a chief complaint of [an] adrenergic flare” and that she was “in a constant [feeling of] fight or flight.” *Id.* Petitioner explained that she was “unable to take care of herself” and that she “ha[d] difficulty standing up for fear of passing out.” *Id.* at 159–60. Petitioner’s physical examination was normal. *Id.* Dr. Barboi noted his impression as a “POTS flare.” *Id.* at 162–63. Dr. Barboi directed Petitioner to the ER “for evaluation and admission, and medication titration.” *Id.* at 149. Petitioner remained in the hospital from July 10 to July 13, 2014, and was treated with Ativan³⁰ and IV fluids until her symptoms resolved. *Id.* at 134.

On August 4, 2014, Petitioner returned to Dr. Chan with complaints of bleeding gums. *Id.* at 21. The same day, Petitioner saw rheumatologist Justin Gan, M.D., to address her bleeding gums and dry mouth. *Id.* at 10. Petitioner reported that her gums were also swollen and painful. *Id.* Dr. Gan noted his impression that Petitioner’s dry mouth, dry eyes, and gum disease “may be related to [her] POTS[.]” *Id.* at 14. The next day, on August 5, 2014, Petitioner returned to the ER with complaints of nausea, fever, neck pain, bleeding gums, and dehydration and the need for IV fluids. *Id.* at 164. Throughout 2015 and 2016, Petitioner presented to the ER on several occasions reporting, among other things, SOB, joint pain, chest tightness, and difficulty swallowing. Pet’r’s Ex. 12 at 17, 19–20, 26; Pet’r’s Ex. 11 at 7, 29, 31, 46, 55–56; Pet’r’s Ex. 24 at 50, 174, 183, ECF No. 24-1. Petitioner was routinely treated with IV fluids. *See id.*

Petitioner had a follow-up with Dr. Barboi on June 14, 2016, during which he noted his impression of hyperadrenergic POTS.³¹ Pet’r’s Ex. 42 at 174, ECF No. 44-3. Dr. Barboi did not order further testing for autonomic nervous system dysfunction or opine that Petitioner’s POTS was immune-mediated. *Id.* at 174–78. Petitioner underwent testing for anti-adrenergic antibodies on July 14, 2020, which yielded negative or normal results. Pet’r’s Ex. 62 at 1, ECF No. 64-1. Petitioner has not filed any additional medical records.

B. Petitioner’s Affidavits & Fact Testimony

Petitioner submitted two affidavits and testified at the entitlement hearing. *See* Pet’r’s Exs. 18, 28, ECF No. 25; *see also* Tr. 11–53. Petitioner wrote that she was “in good health” prior to her October 8, 2013 vaccination. Pet’r’s Ex. 18 ¶ 2. Petitioner noted that she had received the flu vaccine in the past “and never had a problem with it.” *Id.* ¶ 4; Tr. 17:12–17.

Petitioner attested that “[a]bout three weeks” post vaccination she developed symptoms, including abdominal cramping, diarrhea, nausea, lightheadedness, tremors, and chills. Pet’r’s Ex. 18 ¶ 5. Petitioner was asked to further clarify when her gastrointestinal (“GI”) symptoms began. She acknowledged that she presented to ENT Dr. Duyka on October 23, 2013, and testified that she would have told Dr. Duyka of any “symptoms of gastrointestinal distress” if she had been having them at that time, as Petitioner was “very thorough[.]” Tr. 18:6–14. Based on this

³⁰ Ativan is the trademark preparation of lorazepam. *Dorland’s* at 173. Lorazepam is “a benzodiazepine with anxiolytic and sedative effects . . . for the treatment of anxiety disorders and short-term relief of anxiety symptoms[.]” *Id.* at 1074.

³¹ Dr. Barboi also noted his impression of sicca syndrome based on Petitioner’s lip biopsy, despite negative serologies. Pet’r’s Ex. 42 at 174.

discussion, Petitioner stated it would be fair to say her gastrointestinal symptoms began “sometime after seeing Dr. Duyka in late October [of] 2013[.]” Tr. 18:15–18.

She continued that she had her “first hypertensive crisis” later, on November 8, 2013. Pet’r’s Ex. 18 ¶ 5. Petitioner wrote that she returned to the ER for the second time that day “with [an] extremely elevated [BP] and heart rate, slurred speech, and dizziness.” *Id.* She testified that she was experiencing weakness and nausea without vomiting, which also began that day. Tr. 19:12–17. Petitioner explained that her symptoms of dizziness and weakness began while she was sitting down, “relaxing” watching television. Tr. 19:18–22. She stated she then “suddenly[had] a sensation that [her] heart was racing[, and she i]mmediately[began] to have palpitations.” Tr. 19:22–24. Petitioner indicated that “[s]ince that date,” she has had “chronic POTS symptoms[,] including tachycardia, dizziness, flushing, tremors, and hypovolemia.” Pet’r’s Ex. 18 ¶ 5. Petitioner later stated that when she reported symptoms of flushing, shaking, high BP, nausea, jitteriness, and coldness to Dr. Schaefer on November 14, 2013, this was the first time she experienced this “constellation of symptoms.” Tr. 22:22–23:1–4 (citing Pet’r’s Ex. 4 at 151).

Petitioner discussed several notations in her medical records that she asserted were inaccurate. She addressed the November 9, 2013 note from Dr. Nathanson that indicated Petitioner “had not been feeling well for the last few months.” Tr. 20:16–21 (citing Pet’r’s Ex. 4 at 159). Petitioner testified that description “does[not] sound accurate in its entirety.” Tr. 20:22. Petitioner explained she was referring to her asthma and allergy symptoms in an attempt “to be thorough with [Dr. Nathanson].” Tr. 21:2–5. But she was not referring to the symptoms of an elevated BP, heart rate, dizziness, and weakness she experienced on November 8, 2013, which prompted her to go to the hospital. Tr. 21:6–9.

Petitioner wrote that she is “aware that in the medical records from [her] hospitalization on November 19, 2013, there is a notation that [she] had been having symptoms of ‘palpitations, increased heart rate[,], flushing, diarrhea . . . for [the] past [two] months.’” Pet’r’s Ex. 28 ¶ 6 (citing Pet’r’s Ex. 4 at 146). Petitioner attested that she “do[es] not specifically recall what [she] reported at that time[] but that is not an accurate description of when [her] symptoms started.” *Id.* Instead, she maintained her symptoms started “in very early November [of] 2013 and perhaps as early as the very end of October 2013.” *Id.* Petitioner stated Dr. Choi’s November 19, 2013 note that Petitioner reported a bad cold and SOB prior to the onset of her symptoms “is not accurate.” Tr. 24:4–11. Petitioner “believe[d Dr. Choi] was referring to [Petitioner’s] thorough explanation of [her] previous medical issues . . . where [she] explained [she] had issues with asthma and then separately explained to her that [she] had issues with allergies . . . sinuses and things of that nature.” Tr. 24:12–21. Petitioner wrote that she “was never diagnosed with any viral illness during this time.” Pet’r’s Ex. 18 ¶ 3; Pet’r’s Ex. 28 ¶ 3.

Petitioner discussed the visit notes from her January 6, 2014 encounter with Dr. Barboi. Pet’r’s Ex. 28 ¶ 7 (citing Pet’r’s Ex. 6 at 8). Petitioner wrote that she does not “specifically recall” what she said to Dr. Barboi on this occasion. *Id.* ¶ 8. She indicated that she “was having trouble thinking clearly at that time” as she “had not yet started receiving proper treatment to enhance proper profusion of blood to [her] brain.” *Id.* When confronted with the visit notes, she acknowledged that the notation includes references to Petitioner’s “long standing symptoms” of palpitations, dizzy spells, and SOB since 2011 and 2012, respectively. *Id.* ¶ 7 (citing Pet’r’s Ex. 6 at 8); Tr. 28:5–13. Petitioner attested that she was “sure” she told Dr. Barboi about “episodes of

palpitations at night and dizzy spells” but that such symptoms did not begin until November of 2013. Pet’r’s Ex. 28 ¶ 8. She instead attributed her SOB complaints to her asthma and her palpitations or dizziness to her anxiety “to make sure [she] was being thorough.” Tr. 28:17–22.

Petitioner attested that she “do[es] recall that in the summer of 2012,” she went to the ER after feeling “ill” after being on an “airplane with no air conditioning for several hours.” Pet’r’s Ex. 28 ¶ 9. Petitioner testified this occurred the same day she went to the ER, June 10, 2012. Tr. 30:17–25 (citing Pet’r’s Ex. 4 at 59; Pet’r’s Ex. 67). Petitioner described the circumstances that caused her to go to the ER. She stated that after being in an airplane all day, she used cannabis at night because she could not sleep. Tr. 39:16–22. She then had a coughing fit, her heart was racing, and she was shaking. Tr. 39:23–24. Petitioner testified that her heartrate did not change depending on her position during this time. Tr. 31:9–21. Instead, it was “consistent throughout.” Tr. 31:21–23. She testified the ER doctors told her the cause of her symptoms was “probably dehydration[,]” and she received fluids. Tr. 32:9–11, 39:21. She also clarified the circumstances surrounding her January 12, 2011 ER visit. Tr. 41:23–42:1–25. She stated she presented with a high heart rate and anxiety due to stress in her personal life. Tr. 42:2–17. Petitioner testified her heart rate was “consistent no matter what position [she] was in[.]” Tr. 43:1–6. She stated that the attending physician told her it was anxiety. Tr. 42:18–25.

She also acknowledged that Dr. Barboi recorded “a more remote history of intermittent flushing[,] abdominal pain[,] and diarrhea.” Pet’r’s Ex. 28 ¶ 7 (citing Pet’r’s Ex. 6 at 8); Tr. 28:6–13. She wrote that she “do[es] not know what [she] told Dr. Barboi about [her] intermittent flushing” during this visit. Pet’r’s Ex. 28 ¶ 10. She indicated she “believe[s]” she told him that, since childhood, she “occasionally experience[s] splotchiness on [her] chest and neck when [she is] nervous.” *Id.* Petitioner recalled telling Dr. Barboi about her abdominal pain and diarrhea she experienced before October of 2013, but she explained that she was “referring to the time period when [she] was first diagnosed with laryngeal reflux[.]” and was having a reaction to her medications. *Id.* ¶ 11.

Petitioner described the difference between her pre- and post-vaccination anxiety symptoms. Pet’r’s Ex. 18 ¶ 6. She explained that her pre-vaccination anxiety “was more a feeling of worry” and “stress over [her] relationships.” *Id.* She noted that she “would feel shaky, have a sense of . . . impending doom . . . [SOB,] and an elevated heart rate.” *Id.*; Pet’r’s Ex. 28 ¶ 4; Tr. 13:16–21. Petitioner testified that she was “able to discern” such symptoms were related to her anxiety because they “would coincide with the emotions that [she] was feeling and anxious thoughts.” Tr. 13:22–14:1. She wrote that her post-vaccination anxiety is “a constant feeling of agitation and ‘fight or flight.’” Pet’r’s Ex. 18 ¶ 6; Pet’r’s Ex. 28 ¶ 4.

III. Experts

A. Expert Review

1. Petitioner’s Expert, David Axelrod, M.D.

Dr. Axelrod is a “[c]linical [i]mmunologist, trained at McGill University . . . and at the National Institutes of Health [(“NIH”).]” Pet’r’s Ex. 17 at 1. He served as a principal investigator at the Walter Reed Army Institute of Research, where his laboratory “participated in vaccine development.” *Id.* Dr. Axelrod did not submit a curriculum vitae with his expert report. He

authored one written report in support of Petitioner's claim and did not testify at the entitlement hearing. *See id.*

2. Petitioner's Expert, Marcel Kinsbourne, M.D.

Dr. Kinsbourne received his medical degree from Guy's Hospital in London, England in 1955. Tr. 56:11–13; Pet'r's Ex. 30, ECF No. 27-2. He did "nine years of post-graduate training in neurology, pediatrics, and pediatric neurology." Tr. 56:13–15. Dr. Kinsbourne spent three additional years "working and teaching on comprehensive neuroscience" at Oxford University. Tr. 56:15–17. He came to the United States in 1967 to be a professor of neurology and pediatrics and later the director of pediatric neurology at Duke University Medical Center. Tr. 56:18–21; Pet'r's Ex. 30 at 2. Dr. Kinsbourne served as a professor of pediatric neurology and psychology at the University of Toronto from approximately 1979–1985. Pet'r's Ex. 30 at 2. He was the director of the behavioral neurology department at the Eunice Kennedy Shriver Center from 1980–1991. *Id.* He served as a lecturer in neurology at Harvard Medical School and as a clinical associate in neurology at Massachusetts General Hospital from 1981–1991. *Id.* Dr. Kinsbourne joined the faculty at the New School in New York in 1995, which "is not a medical school" but instead he was "working in the effort to teach psychology, the essentials of neuroscience." Tr. 57:5–9. He testified he has been studying neuroscience for "all of [his] adult life." Tr. 57:14–16.

Dr. Kinsbourne has received numerous honors and awards, has served on advisory committees and editorial boards, and holds memberships in scientific societies. Pet'r's Ex. 30 at 3–6. His curriculum vitae includes over four-hundred peer-reviewed articles, book chapters, and books of which he is a listed author. *See id.* at 7–40. Dr. Kinsbourne testified that he is retired from treating patients but stays up to date by reading "everything pertinent to his interests" in neuroscience and by participating in the Vaccine Program. Tr. 59:8–19. He noted that he still participates in peer reviewing for medical journals. Tr. 59:23–25. Dr. Kinsbourne submitted four expert reports and testified at the entitlement hearing. *See* Pet'r's Exs. 29, 31, 32, 46; Tr. 56–153. Petitioner offered Dr. Kinsbourne as an expert in neurology without objection, and I recognized him as such. Tr. 60:12–21.

However, during his testimony, Dr. Kinsbourne discussed principles of immunology, to which Respondent noted a continuous objection. *See* Tr. 62–73. Respondent argued Dr. Kinsbourne had no specific training or expertise in neuroimmunology that allows him to testify as an expert in that field. Tr. 66:17–21. Under voir dire, Dr. Kinsbourne testified that "[y]ou could[not] do neurology in some way where you are ignorant of such basically related sciences as neuroimmunology." Tr. 63:19–21. Dr. Kinsbourne stated that "at the level which [he is] discussing [immunology], any qualified neurologist would be perfectly capable of doing it." Tr. 66:14–15. He noted that throughout his career as a neurologist, he has "frequently" treated patients with autoimmune neurological conditions. Tr. 68:10–13. Dr. Kinsbourne testified that he has only assessed a patient with POTS as part of his participation in the Vaccine Program. Tr. 118:11–13. Based on Dr. Kinsbourne's representations during voir dire, I allowed Dr. Kinsbourne to testify to matters related to immunology. *See* Tr. 72–73. Respondent agreed it would be proper to admit the full testimony of Dr. Kinsbourne and for me to assign appropriate weight, rather than to strike portions of his testimony. *See* Tr. 229–30. The hearing continued under that premise.

3. Respondent's Expert, Phillip Low, M.D.

Dr. Low received his medical degree from the University of Sydney in Sydney, Australia in 1965. Resp't's Ex. B, ECF No. 22-13. His relevant post-graduate training includes residencies in neurology at the Royal Prince Alfred Hospital in Australia and the Mayo Clinic in Rochester, Minnesota in 1973 and 1980, respectively. *Id.* at 1–2. Dr. Low also completed a research fellowship in neurology at the Mayo Clinic in 1977. *Id.* at 2. Dr. Low has held numerous appointments at the Mayo Clinic. *See id.* at 2–4. Dr. Low served as an assistant and then associate professor of neurology from 1978–1982 and 1982–1984, respectively. *Id.* at 2–3. Dr. Low trained physicians in the field of autonomic neuropathy, including several of the authors of the submitted literature. Tr. 157:18–20. From 1989–2004, Dr. Low was the Chairman of the Division of Clinical Neurophysiology. Resp't's Ex. B at 3. He is board certified in “psychiatry and neurology” and neurology with a subspecialty in clinical neurophysiology. *Id.* He explained that his certification in clinical neurophysiology includes a specialization in autonomic disorders. Tr. 161:8–17. Dr. Low has received numerous honors and awards, holds memberships in honorary societies and committees, and serves on editorial boards. Resp't's Ex. B at 3–5. His curriculum vitae includes approximately four-hundred peer-reviewed articles, and hundreds of edited textbooks, book chapters, studies, and editorials of which he is a listed author. *See id.* at 5–101.

Dr. Low founded the Autonomic Reflex Laboratory at the Mayo Clinic in 1982. *Id.* at 3. He stated that in this lab, he discovered the test that is used to “assess patients with autonomic conditions” called the “QSART.” Tr. 155:8–16. He was also involved in the development of the tilt-table test. Tr. 155:17–19. He served as the head of the Peripheral Nerve Center from 1994–2002. Resp't's Ex. B at 3. Dr. Low testified that this is “a center that focuses on autonomic disorders.” Tr. 155:4–7. He also headed an “NIH-funded program project . . . that was aimed at autoimmune disorders.” Tr. 156:13–19. Dr. Low testified that he has evaluated “thousands” of patients with autonomic disorders and “thousands” with POTS throughout his career. Tr. 159:8–15. He has treated patients with “autoimmune disorders related to the autonomic nervous system.” Tr. 159:17–20. Dr. Low noted that he is one of many who has and is currently investigating whether there is an autoimmune basis for POTS and that he was the first to “identify the presence of an antibody in POTS.” Tr. 160:20–23. He noted that he later determined that the antibody, AChR, is a “bystander antibody” and that it “does nothing.” Tr. 161:1–6. He indicated he currently devotes half of his clinical practice to research and the other half to treating patients. Tr. 158:13–25. Dr. Low submitted four expert reports and testified at the entitlement hearing. Resp't's Exs. A, C, D, E; Tr. 153–229. Respondent offered Dr. Low as an expert in neurology, neurophysiology, and autonomic neuropathies without objection, and I recognized him as such. Tr. 162:6–11.

B. Expert Reports and Testimony

1. Petitioner's Expert, Dr. Axelrod

Dr. Axelrod submitted one written report early in this case, without medical literature, and did not testify at the entitlement hearing. *See Pet'r's Ex. 17.* Dr. Axelrod noted that Petitioner's medical records reflect that she experienced symptoms consistent with POTS within twenty-one days of her October 8, 2013 flu vaccination. *Id.* at 1. Such symptoms included Petitioner's diarrhea, abdominal cramping, anorexia, LPR, chest pressure, hypertension, tachycardia, slurred speech,

profound weakness, and weight loss. *Id.* Dr. Axelrod opined that the twenty-one-day period between Petitioner's flu vaccination and the development of her POTS establishes a causal relationship. *Id.* at 3.

He proposed a biological mechanism and argued that after Petitioner received the flu vaccine, "she experienced [] an innate immune response to the vaccine, which included the release of cytokines that would have allowed her adaptive peripheral immune response to the vaccine to enter the central nervous system through a more permeable blood brain barrier," and to cause her POTS with autonomic neuropathy. *Id.* at 4. Dr. Axelrod noted that generally "vaccination results in elevated levels of Interleukin-1 β , Interleukin-6, Tumor Necrosis Factor- α ["TNF α "], and G-CSF." *Id.* at 3. He continued that "TNF α and Interleukin 6 result in disruption of the blood brain barrier through down regulation of interendothelial adherens and tight junction proteins, leading to elevation of paracellular permeability." *Id.* at 3–4. He cited articles to support these claims but did not provide them for consideration along with his report. He continued that "[t]his permeability allows blood borne chemicals, such as cytokines, and cells produced in the peripheral circulation, to enter the environment of the brain, and to act upon cells within the brain . . . [and] central nervous system." *Id.* at 4.

Dr. Axelrod relied on the concept of molecular mimicry and argued that there are "lipid structures on the influenza vaccine that are homologous to lipids on nervous tissues." *Id.* He referred to the P2 protein, syntaxin, and hemagglutinin specific immune cells as the potential homologous structures between the influenza vaccine and nerve tissues. *Id.* He continued that "[g]anglioside GM1b on nerve tissues may act as an influenza receptor, to which the influenza vaccine products can attach." *Id.* Once this happens, the immune response to the flu vaccine could result in damage to nerve tissues. *Id.* Dr. Axelrod also referred to the concept of "epitope spreading" and argued that the damage to Petitioner's nervous system triggered by her immune response to the vaccine "expose[d] other structures of the nervous tissues[.]" *Id.* This continued to cause damage to the nervous system "even after the vaccine products [] disappeared from [her] body[.]" *Id.*

2. Petitioner's Expert, Dr. Kinsbourne

Dr. Kinsbourne summarized Petitioner's clinical history consistent with her medical records and Petitioner's corrections. *See* Pet'r's Ex. 29 at 1–3; Pet'r's Exs. 18, 28. Dr. Kinsbourne wrote that Petitioner's POTS diagnosis "is not in question." Pet'r's Ex. 29 at 3. He opined that Petitioner's POTS was caused by her October 8, 2013 flu vaccine "to a reasonable degree of medical probability." *Id.* at 8.

In support of his conclusion, Dr. Kinsbourne endorsed Dr. Axelrod's proposed biological mechanism. *Id.* at 6. Dr. Kinsbourne acknowledged that "[i]t is certainly the case that scientific certainty on the specifics of vaccine causation of [an] immune-mediated nerve injury is currently out of reach." *Id.* However, he maintained that Dr. Axelrod's proposed theory involving a "peripheral nerve injury via neuroinflammation and possible molecular mimicry is quite specific enough for purposes of formulating a medically reasonable mechanism of injury[.]" *Id.* Dr.

Kinsbourne cited a study by Blitshteyn et al.,³² which found that molecular mimicry is a “possible pathogenesis” of the new onset of POTS post vaccination due to the “formation of cross-reacting autoantibodies to the potential targets of the autonomic ganglia, neurons, cardiac proteins or vascular receptors.” Pet’r’s Ex. 39 at 2, ECF No. 67-6.

Dr. Kinsbourne expanded on Dr. Axelrod’s theory of causation. Dr. Kinsbourne testified that there is currently a consensus in the medical community that POTS can be an immune-mediated condition. Tr. 80:10–12. Dr. Kinsbourne cited medical literature to show that “many investigators [] regard POTS as immune mediated.” Pet’r’s Ex. 29 at 5 (citing Pet’r’s Ex. 39; Pet’r’s Ex. 66, ECF No. 70-5).³³ He cited a year 2000 study by Vernino et al.³⁴ and argued that it showed “a direct demonstration of autoimmunity among patients with POTS.” *Id.* (citing Pet’r’s Ex. 52, ECF No. 68-4). In that study, Vernino et al. tested serum from 157 patients with varying types of dysautonomia, including POTS. Pet’r’s Ex. 52 at 1. The authors found ganglionic acetylcholine receptor (“gAChRs”) antibodies in 6 out of 67 patients with either POTS, idiopathic gastrointestinal dysmotility, or diabetic autonomic neuropathy for a total of 9%. *Id.* at 1, 3. Based on their study, the authors determined that “[s]eropositivity for antibodies that bind to or block ganglionic acetylcholine receptors identifie[d] patients with various forms of autoimmune autonomic neuropathy[.]” *Id.* at 1. They continued that “[t]he positive correlation between high levels of ganglionic-receptor antibodies and the severity of autonomic dysfunction suggests that the antibodies have a pathogenic role in these types of neuropathy [sic].” *Id.* The authors concluded that autonomic neuropathy has “a presumed autoimmune basis.” *Id.* Dr. Kinsbourne opined that Petitioner suffered from autonomic neuropathy in addition to POTS. Pet’r’s Ex. 29 at 4. However, on cross-examination, Dr. Kinsbourne abandoned his reliance on AChRs. He testified that acetylcholine receptor antibodies are no longer relevant to his theory of vaccine causation. Tr. 120:10–14. Instead, Dr. Kinsbourne explained that his theory is focused on autoantibodies to G protein coupled receptors (“GPCRs”), including particular adrenergic antibodies. Tr. 120:14–19.

Dr. Kinsbourne explained that autoantibodies against GPCRs are “receptor surfaces which the autonomic nervous system uses to implement its commands” Tr. 95:11–14. They “are on the surface of the cell and they conduct the stimulus given [to] them by the antibody to the internal part of the cell.” Tr. 95:16–18. He continued that the “antibody either enhances the function involved of that cell or inhibits it, in both cases, causing disease.” Tr. 95:18–20. He testified that a “POTS population has a higher incidence of anti-A-adrenergic receptor antibodies and anti-B2 receptor surfaces.” Tr. 97:6–9. Dr. Kinsbourne explained that an adrenergic receptor antibody is a type of G-protein antibody. *See* Tr. 120.

Dr. Kinsbourne argued that as autoantibodies to GPCRs are frequently seen in patients with POTS, this supports his assertion that POTS has an autoimmune trigger. *See, e.g.*, Pet’r’s Ex. 46 at 2. He testified that GPCRs have been associated with autonomic function or disease, such as autoimmune autonomic disorders. Tr. 95:25–96:12. Dr. Kinsbourne noted that “in cardiovascular

³² S. Blitshteyn, *Postural tachycardia syndrome following human papillomavirus vaccination*, 21 EUR. J. NEUROL. 135–39 (2014).

³³ S. Blitshteyn, *supra*, note 32; M. Thieben et al., *Postural Orthostatic Tachycardia Syndrome: The Mayo Clinic Experience*, 82(3) MAYO CLIN. PROC. 308–13 (2007).

³⁴ S. Vernino et al., *Autoantibodies to Ganglionic Acetylcholine Receptors in Autoimmune Autonomic Neuropathies*, 343 N. ENG. J. MED. 847–55 (2000).

disorders other than POTS[,]” these autoantibodies against GPCRs “have been associated with disorders of autonomic dysfunction such as inappropriate sinus tachycardia and orthostatic hypotension.” Pet’r’s Ex. 46 at 2 (citing Pet’r’s Ex. 56 at 1, ECF No. 68-8).³⁵ The authors of the Chiale et al. study analyzed patients with inappropriate sinus tachycardia (an arrhythmia) and healthy controls and found that “no anti-autonomic receptor antibodies were detected in healthy controls[,]” but “[i]n marked contrast, anti- β adrenergic receptor antibodies were found in 11 of 21 patients affected by the arrhythmia.” Pet’r’s Ex. 56 at 3. They concluded that there is a link between inappropriate sinus tachycardia and circulating anti- β adrenergic receptor antibodies. *Id.* at 1.

Dr. Kinsbourne cited articles showing that such antibodies to adrenergic alpha-1 adrenergic, beta-adrenergic, muscarinic receptors, and cardiac lipid raft-associated proteins have also been identified in POTS patients. Pet’r’s Ex. 46 at 2 (citing Pet’r’s Ex. 47 at 1, ECF No. 67-8; Pet’r’s Ex. 49, ECF No. 68-1; Pet’r’s Ex. 57 at 3, ECF No. 68-9).³⁶ For example, in 2019, the Gunning et al. study “looked at [] whether th[ere] were elevated, G protein coupled adrenergic antibodies [in POTS] and they found them.” Tr. 102:8–10 (citing Pet’r’s Ex. 47). The Gunning et al. study examined 55 patients with POTS and found elevated serum levels of autoantibodies against alpha-1 adrenergic receptors and muscarinic cholinergic receptors in 89% and 51% of patients, respectively. Pet’r’s Ex. 47 at 5. Dr. Kinsbourne testified that the Gunning et al. study noted that a “well documented association with vaccination preceding the development of POTS is known.” Tr. 102:12–15 (citing Pet’r’s Ex. 47 at 8). The 2019 Hineno et al. study cited by Dr. Kinsbourne sought to investigate the presence of autoantibodies against G protein coupled receptors in Japanese girls who complained of symptoms including orthostatic dysregulation following receipt of the HPV vaccine. Pet’r’s Ex. 57 at 1. The authors found that serum levels of autoantibodies against various adrenergic receptors and muscarinic acetylcholine receptors were elevated in girls who had received the HPV vaccine compared to those who did not receive the vaccine. *Id.* Hineno et al. determined that the “serum levels of these autoantibodies tended to decrease with the time course of the illness,” however, “there was no statistically meaningful association between the clinical symptoms and elevated serum levels of these autoantibodies.” *Id.* The authors concluded that this study provided evidence that “post-vaccination abnormal autoimmunity plays an important role in the development of unique symptoms after HPV vaccination.” *Id.* Dr. Kinsbourne argued these adrenergic receptors documented in such studies are the same GPCRs that affect the regulation of the immune system and may increase inflammatory responses. Pet’r’s Ex. 46 at 2. Dr. Kinsbourne cited the 2016 study by Fedorowski et al.,³⁷ which examined 17 POTS patients and found 47% had alpha-1 receptor antibodies, 65% had beta-1 receptor antibodies, and 71% had beta-2 receptor autoantibodies. Pet’r’s Ex. 51 at 7, ECF No. 68-3. The authors concluded that based on the percentage of POTS patients with autoantibodies, there

³⁵ P. Chiale et al., *Inappropriate sinus tachycardia may be related to an immunologic disorder involving cardiac β adrenergic receptors*, 3 HEART RHYTHM 1182–86 (2006).

³⁶ W. Gunning et al., *Postural Orthostatic Tachycardia Syndrome is Associated with Elevated G-Protein Coupled Receptor Autoantibodies*, X J. AM. HEART ASSOC. 1–10 (2019); H. Li et al., *Autoimmune Basis for Postural Tachycardia Syndrome*, X J. AM. HEART ASSOC. 1–10 (2014); A. Hineno et al., *Autoantibodies against Autonomic Nerve Receptors in Adolescent Japanese Girls after Immunization with Human Papillomavirus Vaccine*, 2(2) ANN. ARTHRITIS CLIN. RHEUMATOL. 1014–20 (2019).

³⁷ A. Fedorowski et al., *Antiadrenergic autoimmunity in postural tachycardia syndrome*, 19 EUR. SOC. CARDIOL. 1211–19 (2017).

is “an apparent autoimmune diathesis that supports the concept that these autoantibodies play a role in the pathophysiology of this entity.” *Id.*

Dr. Kinsbourne also relied on the 2014 Li et al.³⁸ study that used a bioassay and “measured blood levels of various adrenergic receptor autoantibodies in 14 POTS patients.” Pet’r’s Ex. 46 at 2 (citing Pet’r’s Ex. 49 at 1). The authors found 50% of patients had alpha-1 adrenergic receptor antibodies, 50% had beta-2 adrenergic receptor antibodies, and all patients had beta-1 autoantibodies. Pet’r’s Ex. 49 at 7. Li et al. explained that this finding supported their hypothesis that POTS patients manifest “autoantibodies to the pressor [alpha-1 adrenergic receptor] and could partially block the effectiveness of the normal [alpha-1 adrenergic receptor] endogenous ligand norepinephrine central to the homeostatic response to upright posture.” *Id.* at 2. Doing so impairs vasoconstriction, thereby increasing baroreceptor activation and sympathetic nervous system activity. *Id.* The authors determined that the beta-1 adrenergic receptors “would respond to this increased sympathoneural output and circulating norepinephrine with an exaggerated tachycardia[.]” resulting in POTS. *Id.* In other words, their findings supported the relationship between such antibodies and POTS because alpha-1 adrenergic antibodies “act by rendering these receptors partially inactive” causing peripheral blood vessels to be “unable to fully constrict on standing, producing a postural tachycardia.” *Id.* The authors indicated that beta-1 and beta-2 adrenergic receptor autoantibodies increase the severity of the tachycardia. *See id.*

In another animal model by Li et al.³⁹ published in 2019, the authors immunized rabbits with alpha-1 and beta-1 adrenergic receptor peptides. Pet’r’s Ex. 48 at 1, ECF No. 67-9. The authors found that they were able to induce an exaggerated postural tachycardia (measured using a tilt-table test) with such receptors. *Id.* at 2–3. They also found that they were able to block the alpha-1 and beta-1 autoantibodies from interacting with the receptors, and this caused the heart rates of the rabbits to return to normal. *Id.* at 3. Dr. Kinsbourne argued this was “no coincidence” because “if you then get rid of the autoantibodies, then the effect is reversed.” Tr. 104:7–9. The authors concluded that their study “supports the concept that cardiovascular autoantibodies play an important role in POTS pathophysiology.” Pet’r’s Ex. 48 at 8; Tr. 99:18–20. Dr. Kinsbourne was asked how this study supported his theory that a flu vaccine can cause POTS, and he stated it is because “vaccines stimulate antibodies.” Tr. 104:2. He continued that in the Li et al. animal model, “we see that if the antibody that[is] stimulated happens to be of the two kinds mentioned[,], then even in animals, you get a tilt[-]test result [indicative of POTS] very similar to [that] in humans.” Tr. 104:3–6.

Dr. Kinsbourne noted that a 2015 study by Blitshteyn et al.⁴⁰ documents a report of 31 out of 100 POTS patients who had “one or more markers of autoimmunity.” Pet’r’s Ex. 46 at 2 (citing Pet’r’s Ex. 33 at 1, ECF No. 67-2). Such markers primarily consisted of elevated ANA titers. Pet’r’s Ex. 33 at 2–3. The authors wrote that “the question of whether POTS itself is an autoimmune disorder needs to be answered.” *Id.* at 6. They confirmed that “adrenergic

³⁸ H. Li et al., *Autoimmune Basis for Postural Tachycardia Syndrome*, X J. AM. HEART ASSOC. 1–10 (2014).

³⁹ H. Li et al., *Adrenergic Autoantibody-Induced Postural Tachycardia Syndrome in Rabbits*, X J. AM. HEART ASSOC. 1–9 (2019).

⁴⁰ S. Blitshteyn, *Autoimmune markers and autoimmune disorders in patients with postural tachycardia syndrome (POTS)*, 24 LUPUS 1364–69 (2015).

autoantibodies . . . appear to be good candidates mechanistically, in that these antibodies may explain the lack of proper vasoconstriction and increased resting and postural tachycardia in patients with POTS.” *Id.* However, on cross-examination, Dr. Kinsbourne admitted that “we do not know if G protein antibodies are causative of a disease process or induced by the disease.” Tr. 135:18–21.

Dr. Kinsbourne testified regarding the Kharraziha et al.⁴¹ article. Tr. 106:3–6 (citing Pet’r’s Ex. 64, ECF No. 70-3). He explained this article was published recently in 2020 and that the authors “looked at the receptor surfaces for the POTS relevant adrenergic receptors.” Tr. 106:19–20. Kharraziha et al. examined 48 patients with POTS, and 25 healthy individuals, using a “commercial cell-based assay.” Pet’r’s Ex. 64 at 1. The authors found that sera from POTS patients contained adrenergic receptor antibodies “to a higher degree compared with controls.” *Id.* Based on this finding, the authors concluded that “[s]erum-mediated activation of these receptors has high predictive value for POTS.” *Id.* The authors found that “these receptor surfaces had been activated[.]” Tr. 106:20–21. Dr. Kinsbourne explained that this is “what you would expect if there had been autoantibodies attacking them.” Tr. 106:22–24. Dr. Kinsbourne testified that the authors “direct[ly] demonstrate[ed]” that the “degree of activation of the adrenergic A receptor was associated with the severity of orthostatic symptoms in POTS.” Tr. 107:3–7. The authors posited that their findings “provide new insights in the pathophysiology of POTS and pondered further research on a possible autoimmune involvement in POTS.” Tr. 107:18–20 (citing Pet’r’s Ex. 64 at 2). Dr. Kinsbourne opined that while the medical literature does not provide scientific certainty for POTS being immune-mediated, it provides “a very high probability” that it is. Tr. 108:4–6.

On cross-examination, Respondent confronted Dr. Kinsbourne with the 2018 article by Vernino and Stiles.⁴² Tr. 132:6–13 (citing Pet’r’s Ex. 53 at 4, ECF No. 68-5). Vernino and Stiles proposed that an autoimmune basis for POTS “has been suggested based on . . . the occasional association of POTS with . . . autoimmune disorders.” Pet’r’s Ex. 53 at 1–2. They cited a study of 3,300 POTS patients, which found only 16% had a comorbid autoimmune disease. *Id.* at 2. They summarized the “current state of knowledge on the role of autoimmunity in POTS[.]” *Id.* at 1. The authors indicated that “[t]he presence of GPCR or low titers of g-AChR autoantibodies alone are insufficient proof of an autoimmune cause for POTS based on the current research.” *Id.* at 4. They also noted that “[a]t this time, adrenergic, muscarinic, and angiotensin receptor antibodies have not been proven to be causative or useful in confirming a POTS diagnosis.” *Id.* at 3. Vernino and Stiles concluded that “[f]urther research is needed to understand the pathological significance, if any, of GPCR autoantibodies in POTS.” *Id.* Dr. Kinsbourne read the authors’ conclusion which indicated that “the evidence for an autoimmune cause is insufficient at this time . . .” Tr. 132:14–19 (citing Pet’r’s Ex. 53 at 4). Dr. Kinsbourne maintained the article showed support for an autoimmune etiology for POTS. Tr. 132:6–13. He eventually agreed that while some studies have shown antibodies have been found in patients with POTS, such “evidence is not sufficient to declare POTS an autoimmune disease[.]” Tr. 132:21–25.

⁴¹ I. Kharraziha et al., *Serum Activity Against G Protein-Coupled Receptors and Severity of Orthostatic Symptoms in Postural Orthostatic Tachycardia Syndrome*, 9 J. AM. HEART ASSOC. 1–17 (2020).

⁴² S. Vernino & L. Stiles, *Autoimmunity in postural orthostatic tachycardia syndrome: current understanding*, 215 AUTONOMIC NEURO. BASIC & CLIN. 78–82 (2018).

Dr. Kinsbourne further relied on the Vernino and Stiles article's extensive list of autoimmune disorders that are, according to the authors, "comorbid with POTS[.]" including, among others, inflammatory bowel diseases such as Crohn's⁴³ and ulcerative colitis,⁴⁴ MS, Sjögren's syndrome, rheumatoid arthritis ("RA"),⁴⁵ and connective tissue disease,⁴⁶ to argue that "POTS too is autoimmune[.]" See Pet'r's Ex. 46 at 1 (citing Pet'r's Ex. 53 at 2). Dr. Kinsbourne wrote that this "impl[ies]" that POTS has "underlying mechanisms that overlap with" such autoimmune diseases. *Id.* Dr. Kinsbourne wrote that "patients with POTS have a higher prevalence of autoimmune markers and co-morbid autoimmune disorders than the general population." *Id.* at 3. He noted that Petitioner did too, as she "had a positive ANA blood test." *Id.*

Dr. Kinsbourne cited several case reports, which he argued support Petitioner's theory of vaccine causation. Pet'r's Ex. 29 at 7. Several reports contain evidence of patients who experienced the abrupt onset of POTS or orthostatic hypotension/intolerance following the receipt of a HPV vaccine. *Id.* (citing Pet'r's Ex. 34, ECF No. 67-3; Pet'r's Ex. 39; Pet'r's Ex. 55, ECF No. 68-7; Pet'r's Ex. 57).⁴⁷ He also cited a case report by Tsai et al.,⁴⁸ which documented a single case of a patient who developed POTS after receiving an influenza (H1N1) vaccination. *Id.* (citing Pet'r's Ex. 14, ECF No. 67-1). Dr. Kinsbourne attacked Respondent's expert Dr. Low's assertion that such data has "little scientific merit" since it was not developed in large epidemiologic studies. *Id.* Dr. Kinsbourne wrote it "would indeed be convenient to be able to refer to large[,] controlled studies for corroboration of vaccine causation in POTS cases." *Id.* However, he acknowledged that no epidemiological studies related to POTS onset post flu vaccination, "or any vaccination," have been published. *Id.* Dr. Kinsbourne could not point to evidence that showed that the flu vaccine

⁴³ Crohn disease is "one of the principal forms of inflammatory bowel disease, a chronic granulomatous disease of the gastrointestinal tract of unknown etiology; it can involve any part of the tract, but most often is found in the terminal ileum. Characteristics include scarring and thickening of the bowel wall that frequently leads to intestinal obstruction, abscesses, and fistula formation. There is a high rate of recurrence after treatment." *Dorland's* at 531.

⁴⁴ Ulcerative colitis is "one of the principal types of inflammatory bowel disease, consisting of chronic, recurrent ulceration in the colon, chiefly of the mucosa and submucosa, having an unknown cause. It is manifested clinically by cramping abdominal pain, rectal bleeding, and loose discharges of blood, pus, and mucus with scanty fecal particles. Complications include hemorrhoids, abscesses, fistulas, perforation of the colon, pseudopolyps, and carcinoma." *Dorland's* at 384.

⁴⁵ Rheumatoid arthritis is "a chronic systemic disease primarily of the joints, usually polyarticular, marked by inflammatory changes in the synovial membranes and articular structures and by muscle atrophy and rarefaction of the bones. In late stages, deformity and ankylosis develop. The cause is unknown, but autoimmune mechanisms and virus infection have been postulated." *Dorland's* at 157.

⁴⁶ Connective tissue disease or mixed connective tissue disease is "a disorder combining features of scleroderma, myositis, systemic lupus erythematosus, and rheumatoid arthritis, and marked serologically by the presence of antibody against extractable nuclear antigen." *Dorland's* at 539.

⁴⁷ S. Dahan et al., *Postural Orthostatic Tachycardia Syndrome (POTS) – A novel member of the autoimmune family*, 0 LUPUS 1–4 (2016); S. Blitshteyn, *Postural tachycardia syndrome following human papillomavirus vaccination*, 21 EUR. J. NEUROL. 135–39 (2014); L. Brinth, *Orthostatic intolerance and postural tachycardia syndrome as suspected adverse effects of vaccination against human papillomavirus*, 33 VACCINE 2602–05 (2015); A. Hineno et al., *Autoantibodies against Autonomic Nerve Receptors in Adolescent Japanese Girls after Immunization with Human Papillomavirus Vaccine*, 2(2) ANN. ARTHRITIS CLIN. RHEUMATOL. 1014–20 (2019).

⁴⁸ C. Tsai et al., *Novel H1N1 Influenza Vaccine the Cause of Postural Orthostatic*, 31(2) J. MED. SCI. 91–93 (2011).

could trigger the G protein antibodies implicated in his proposed biological mechanism. Tr. 136:22–137:17. Instead, he stated he was “sure” that he did not “file[] evidence specifically that the flu vaccine can trigger G protein antibodies.” Tr. 137:15–17, 138:2–139:2.

Nonetheless, he argued Petitioner’s POTS was more likely than not immune-mediated. Tr. 92:18–20. He based this opinion, in part, on the fact that “there is no alternative reasonable alternative explanation[.]” Tr. 93:5–6. Specifically, Dr. Kinsbourne opined that Petitioner’s October 8, 2013 flu vaccine “stimulated an immune response . . . which gave rise to antibodies that happened, in her case, to attack certain regulatory mechanisms of autonomic function . . . that regulate the sympathetic [immune] system’s response to certain challenges and stressors.” Tr. 64:3–9. He explained that Petitioner’s immune response caused two things. Tr. 64:10–11. First, it disrupted the regulation of her blood flow so that when she stood up, she lacked a “hydrostatic gradient” wherein blood drains from the brain and settles in the abdominal organs and legs. Tr. 64:11–16. Her autonomic system failed to counteract that by contracting her blood vessels and keeping the blood from draining into her legs away from the brain. Tr. 64:16–19, 80:3–9. He explained that “there are receptors in the sympathetic nervous system which cause the distal contractions which keep the blood flowing to the brain.” Tr. 64:20–22. But if an antibody blocks the receptor sites, blood pools in the legs and abdomen away from the brain, and “results in the person feeling faint and losing consciousness.” Tr. 64:23–65:2. Such stress stimulates the sympathetic nervous system and “causes the heart rate to accelerate.” Tr. 65:3–4, 79:10–14.

Dr. Kinsbourne indicated that Petitioner’s medical records do not contain procedures “that could verify tissue injury” as Dr. Low required to validate Petitioner’s medical theory of autoimmunity. Pet’r’s Ex. 32 at 3. Dr. Kinsbourne argued that adrenergic autoantibodies “modulate the function of [GPCRs], regardless of whether they produce tissue injury.” Pet’r’s Ex. 46 at 4. He testified that electrodiagnosis, such as EMGs, are capable of reaching and reading large fibers. Tr. 109:8–22. However, “autonomic nerve fibers are very different. They are thin. They are either unmyelinated or very likely myelinated. And in them, the EMG . . . is negative.” Tr. 109:22–25. He therefore argued that electrodiagnosis cannot determine whether autonomic nerves are damaged or not. Tr. 109:25–110:2. He also noted that one cannot biopsy the autonomic nerves like they can in cases of small fiber neuropathy, because to do so one would have to delve “deep in the body[,]” which standard hospitals do not do. Tr. 110:3–17. On cross-examination, Dr. Kinsbourne testified that Petitioner’s clinical testing, both post vaccination and more recently in 2020, did not show evidence of G protein antibodies. Tr. 133:17–23. He argued this is not surprising as antibodies “tend to fade away over time.” Tr. 134:9–135:3 (citing Pet’r’s Ex. 57). He cited the Hineno et al.⁴⁹ article, which noted that autoantibodies dwindle over time, as support. Tr. 105:10–25 (citing Pet’r’s Ex. 57 at 4); *see also* Pet’r’s Ex. 62. Aside from the presence of antibodies, Dr. Kinsbourne testified that B and T cells can also be responsible for autoimmune damage. Tr. 144:23–145:2. He argued that even though antibodies “may fade away[,]” the T cells specifically “may continue to do damage.” Tr. 145:3–4. He sees POTS as a condition where “there is an attack which causes the damage and the agent may go away, but the damage remains.” Tr. 143:2–7. Dr. Kinsbourne opined that the T cells were therefore responsible for Petitioner’s active injury seven years post vaccination. Tr. 145:8–10. However, he stated that the understanding of such cellular

⁴⁹ A. Hineno et al., *Autoantibodies against Autonomic Nerve Receptors in Adolescent Japanese Girls after Immunization with Human Papillomavirus Vaccine*, 2(2) ANN. ARTHRITIS CLIN. RHEUMATOL. 1014–20 (2019).

immunity “is a work in progress[.]” and there has not been “much written about it at this time.” Tr. 145:11–15. Dr. Kinsbourne argued that “[i]n view of her clear-cut diagnosis of POTS and the extensive and still growing support for an autoimmune mechanism [] in POTS in the medical literature,” Petitioner’s POTS was caused by an autoimmune reaction to her October 8, 2013 flu vaccine. Pet’r’s Ex. 32 at 4.

He was asked which subtype of POTS Petitioner suffers from. Dr. Kinsbourne argued that Petitioner suffers from hyperadrenergic POTS. Tr. 120:23–25. He stated that “there[is] only one subtype of POTS[,] and it[is] hyperadrenergic POTS.” Tr. 123:3–124:17. Dr. Kinsbourne indicated that he does not think that there are other subtypes or classifications of POTS but rather that “they overlap or are the same.” Tr. 121:16–19, 122:2–3. On cross-examination, Dr. Kinsbourne was asked if he knew about POTS associated with hypovolemia, and he testified, “[w]ell, hypovolemia is one of the – is one of the many – one of the parts of the mechanisms of causing the disability. Hypovolemia is[not] a particular type of POTS which by itself causes the condition.” Tr. 122:4–9. He was also asked if any of Petitioner’s submitted literature discusses hypovolemic POTS, and he testified that he “d[id not] think there was occasion to discuss it because there[is] no evidence that [Petitioner] was hypovolemic at the onset[,]” only “subsequently.” Tr. 122:11–18. Dr. Kinsbourne stated that if there is hypovolemia with POTS, “you correct it, [but] you have[not] cured the POTS.” Tr. 124:5–14. As an example, he testified that Petitioner had “been hypovolemic many times and had infusions to correct that.” Tr. 125:12–15.

Regarding timing for the onset of an autoimmune disease post vaccination, Dr. Kinsbourne testified that “within an accepted time margin of less than 42 days, [Petitioner] began to show symptoms compatible with POTS[.]” Tr. 111:22–24. He indicated that “it[is] generally accepted that when vaccines cause . . . the onset of autoimmune disease, that the onset of clinical manifestations occurs within the framework of six weeks[.]” Tr. 113:5–8. Dr. Kinsbourne argued that Petitioner’s onset of symptoms is “well within that framework.” Tr. 113:8–9.

As support, he attributed Petitioner’s nausea, diarrhea, and abdominal pain symptoms beginning around October 29, 2013, to “part of the presentation of [her] POTS.” Pet’r’s Ex. 29 at 4; Tr. 80:19–25. Dr. Kinsbourne noted that vomiting and diarrhea are “themselves symptoms of POTS and may precede complaints of orthostatic instability.” Pet’r’s Ex. 32 at 2. He relied on an article by Parsaik et al.,⁵⁰ which indicates that the clinical presentation of POTS can include “orthostatic, nonorthostatic (i.e.[,] nausea, vomiting, diarrhea, constipation, bladder and pupillary dysfunction), and generalized (fatigue and sleep disturbances) symptoms.” Pet’r’s Ex. 29 at 4 (citing Pet’r’s Ex. 61, ECF No. 69-3). The authors noted that nausea occurs in 59% of patients with orthostatic intolerance; abdominal pain in 24%; and diarrhea in 32%. *See id.* Dr. Kinsbourne cited an abstract of a study by Sullivan et al.,⁵¹ which documented that the most common presenting gastrointestinal symptoms associated with the onset of POTS were abdominal pain, nausea, and vomiting. Pet’r’s Ex. 32 at 2 (citing Pet’r’s Ex. 38 at 1, ECF No. 40-6). Dr. Kinsbourne

⁵⁰ A. Parsaik et al., *Deconditioning in patients with orthostatic intolerance*, 79 NEUROL. 1435–40 (2012).

⁵¹ S. Sullivan et al., *Gastrointestinal Symptoms Associated with Orthostatic Intolerance*, 40(4) J. PED. GASTRO. & NUTRITION 1–2 (2005).

also relied on one of the case studies by Blitshteyn et al.,⁵² documenting six patients with POTS triggered by the HPV vaccine. *Id.* (citing Pet'r's Ex. 39). Patient 2 in the study experienced the onset of diarrhea, nausea, and weight loss two months following receipt of the third HPV vaccine. Pet'r's Ex. 39 at 2. The authors summarized that the six patients “developed new onset of POTS 6 days to 2 months following” receipt of the HPV vaccine. *Id.* at 1. Dr. Kinsbourne opined that Petitioner's diarrhea and GI issues around this time could also be related to Petitioner's medications used to treat her LPR. Pet'r's Ex. 29 at 4. He did not argue such symptoms were caused by a viral illness, and he noted that Petitioner's testing did not support that conclusion. *Id.*

Dr. Kinsbourne addressed Dr. Low's contention that Petitioner's POTS began prior to her October 8, 2013 flu vaccine. *Id.* Dr. Kinsbourne called Dr. Low's claim “untenable[.]” Pet'r's Ex. 32 at 1. He argued Petitioner was not suffering from symptoms of POTS prior to late October of 2013, when her GI issues began. *Id.*; Tr. 86:9–13. Dr. Kinsbourne discussed the clinical significance of Petitioner's symptoms and “their relationship with orthostatic intolerance and POTS.” Pet'r's Ex. 31 at 1. He did not agree with Dr. Low's argument that some of her symptoms “retrospectively meet the diagnostic criteria for POTS[.]” *Id.* at 1–2. Dr. Kinsbourne maintained that any symptoms she experienced pre vaccination did “not at all amount to POTS as defined in medical literature.” *Id.* at 2. As support, he cited the Arnold et al.⁵³ article, which defined POTS as an increased heart rate of “ ≥ 30 [beats per minute] within 10 minutes of assuming an upright posture and in the absence of orthostatic hypotension.” *Id.* (citing Pet'r's Ex. 58 at 2, ECF No. 69-1). The authors wrote that orthostatic intolerance symptoms must last for ≥ 6 months. *See id.*; *see also* Tr. 77–78. Dr. Kinsbourne defined orthostatic hypotension as “where a person may stand up and faint.” Tr. 75:18–20. But he described POTS “different[ly] from that because when a POTS person stands up, they do[not] immediately . . . experience a problem.” Tr. 76:1–3. Instead, over five or ten minutes, the “heart rate gets faster and faster and faster and the point is reached when the pulse rate is so quick that the emptying of the heart into the aorta and the supplying of blood is insufficient[.]” Tr. 76:3–9. Such patients have to sit down to avoid passing out. Tr. 76:9–12. Dr. Kinsbourne “scrutinize[d]” Petitioner's pre-vaccination medical records to determine if they showed evidence of symptoms consistent with that definition. Pet'r's Ex. 31 at 2. He argued “[t]here is no evidence in contemporaneous medical records of POTS prior to the influenza vaccination.” *Id.* at 4. Dr. Kinsbourne also indicated that Petitioner had never been diagnosed with POTS pre vaccination. *Id.* at 1.

Dr. Kinsbourne opined that by the time Petitioner's POTS diagnosis was confirmed with her tilt-table test on November 29, 2013, she had been experiencing symptoms of orthostatic intolerance for “about four weeks.” Tr. 81:6–9. However, he maintained that the fact that she did not have symptoms of orthostatic intolerance for six months or more does not detract from the validity of her POTS diagnosis. Tr. 81:10–12. Instead, he testified that “strictly speaking,” her diagnosis on November 29, 2013, would more appropriately be “presumptive POTS to be confirmed on a timescale[.]” once such symptoms had been present for six months as required for the diagnosis of POTS. Tr. 81:15–19.

⁵² S. Blitshteyn, *Postural tachycardia syndrome following human papillomavirus vaccination*, 21 EUR. J. NEUROL. 135–39 (2014).

⁵³ A. Arnold et al., *Postural tachycardia syndrome – Diagnosis, physiology, and prognosis*, 215 AUTONOMIC NEURO. BASIC & CLIN. 3–11 (2018).

He attacked Dr. Low's reliance on Dr. Barboi's notation reflecting "long-standing" autonomic symptoms, including flushing, abdominal pain, palpitations, dizzy spells, and SOB to say her condition preceded her vaccination. Pet'r's Ex. 29 at 4. He addressed each symptom in turn. Dr. Kinsbourne wrote that "flushing and abdominal pain are not remotely diagnostic of POTS[.]" *Id.* Dr. Kinsbourne attributed Petitioner's SOB to her asthma. *Id.* Dr. Kinsbourne maintained that he had no reason to doubt Petitioner's asthma diagnosis. Tr. 126:10–23. However, without specifically referring to the results of Petitioner's March 20, 2014 spirometry testing, he testified that if Petitioner had undergone spirometry testing that contradicted an asthma diagnosis, then he would agree with such results. Tr. 127:10–16. Following that course of questioning, Dr. Kinsbourne opined that if Petitioner did not have asthma, her pre-vaccination SOB "could well [have] be[en] part of a panic attack." Tr. 129:2–7. He generally attributed Petitioner's SOB reported from December 2012 to March 2013 to her asthma "playing up" and noted that asthma "can be precipitated by anxiety." Tr. 130:14–25 (citing Pet'r's Ex. 13 at 5). Dr. Kinsbourne testified that reflux can also cause SOB. Tr. 151:3–6.

Dr. Kinsbourne addressed Petitioner's remaining symptoms of palpitations and dizzy spells and wrote they can "have many causes[.]" Pet'r's Ex. 29 at 4. He argued that "[o]ne cannot base a diagnosis on such scant and non-specific information." *Id.*; Tr. 142:9–14. Dr. Kinsbourne opined that Petitioner's history of symptoms from 2011 noted by Dr. Barboi "have no apparent relevance to [the] onset of [Petitioner's] POTS" because they are non-specific symptoms. Pet'r's Ex. 32 at 1. He wrote that "Dr. Barboi made a clear distinction between these non-specific episodes and the acute onset of [her] POTS" by noting that "in November of 2013[, Petitioner] started having increased symptoms of dizziness and presyncopal episodes." Pet'r's Ex. 29 at 4. Dr. Kinsbourne argued that Dr. Barboi's notation therefore does not show that Petitioner's POTS began before November of 2013. *Id.*

Dr. Kinsbourne admitted, however, that Dr. Barboi's notation reflected long-standing symptoms of autonomic dysfunction, just not long-standing POTS. Pet'r's Ex. 31 at 3. Dr. Kinsbourne maintained that there is no evidence that Petitioner suffered from dysautonomia prior to late October of 2013. Tr. 86:14–18, 89:13–15. He testified that dysautonomia "is ongoing" and that Petitioner's "medical records would have recorded such a state if it were the case." Tr. 88:20–21. Dr. Kinsbourne explicitly stated that "[i]f there had been a prior dysautonomia[,] one would invoke very significant aggravation of that prior condition, but prior POTS is not in evidence." Pet'r's Ex. 32 at 2.

Dr. Kinsbourne continued his discussion of Petitioner's medical records seeking evidence to disprove a pre-vaccination dysautonomia. He discussed Petitioner's pre-vaccination episodes of tachycardia in detail to differentiate such symptoms from her post-vaccination POTS. *See, e.g.*, Tr. 73–74, 86:19–20 (citing Pet'r's Ex. 21 at 149–50). Dr. Kinsbourne described Petitioner's history of supraventricular tachycardia and noted that while her heartbeat was rapid, it was overall regular and was not affected by orthostasis, or whether she was sitting, standing, or lying down. Tr. 74:17–22. Dr. Kinsbourne testified that "this happens in people who have anxiety disorders" and it is not specifically related to POTS. Tr. 74:22–25. Dr. Kinsbourne stated that Petitioner's pre-vaccination history of panic attacks and anxiety could both in themselves aggravate POTS. Tr. 126:3–9. Regarding her 2011 visit to the ER, Dr. Kinsbourne described Petitioner's condition as "a typical panic attack in a person who has anxiety." Tr. 87:6–10. He agreed with Petitioner's

treaters' assessment of anxiety during that visit. Tr. 87:13–17. He stated he would not have been concerned about dysautonomia in 2011 because “there[is] no statement that [her symptoms] came on when she stood up from lying down.” Tr. 87:18–22. Dr. Kinsbourne also addressed Petitioner’s June 10, 2012 ER visit following being in a hot airplane and smoking marijuana. Tr. 87:25–88:21 (citing Pet’r’s Ex. 67 at 5). Dr. Kinsbourne stated that marijuana can cause tachycardia. Tr. 88:8–9. He testified that her medical records show no evidence of dysautonomia because her condition was not dependent on her posture and this “was an isolated attack.” Tr. 88:10–17. Rather, “[t]hese were occasional, brief attacks of anxiety or panic.” Tr. 88:18.

He also relied on Petitioner’s extensive visits with treaters for her pre-vaccination conditions, such as asthma, to opine that if Petitioner were having orthostatic intolerance or syncope, these complaints would not have “escaped [her treater’s] attention.” Pet’r’s Ex. 31 at 2–3. He applied the same logic to Petitioner’s October of 2013 visits with Dr. Duyka that occurred post vaccination, but before the onset of her POTS. Dr. Kinsbourne noted that Dr. Duyka also did not include complaints of POTS or orthostatic intolerance. *Id.* (citing Pet’r’s Ex. 23 at 1–7). Specifically, he testified regarding Petitioner’s October 23, 2013 visit with Dr. Duyka and noted that under history of present illness, it indicated “intermittent episodes of [SOB] associated with changes in her voice, episodes of coughing, waking up at night with a salty, bitter taste in her mouth.” Tr. 90:10–13 (citing Pet’r’s Ex. 22 at 9). Dr. Kinsbourne stated that was “clearly reflux.” Tr. 90:15. He also stated that Dr. Duyka was “very specific” and noted no cardiovascular symptoms, including chest pain, palpitations, lightheadedness, or syncope. Tr. 90:19–21.

Dr. Kinsbourne addressed Dr. Low’s contention that dehydration and deconditioning caused Petitioner’s POTS. Dr. Kinsbourne wrote that the “ingredients” for Dr. Low’s theory are “dehydration and deconditioning secondary to diarrheas and hypervolemia.”⁵⁴ Pet’r’s Ex. 29 at 8. Dr. Kinsbourne argued that “[t]hese handicaps are indeed consequences of POTS, but hardly explain it.” *Id.* He stated that deconditioning and hypovolemia are secondary aggravating factors of POTS, but in themselves are “not sufficient to cause POTS.” Tr. 122:21–25. He relied on medical literature to argue such conditions would not cause POTS. Pet’r’s Ex. 29 at 8 (citing Pet’r’s Ex. 66; Pet’r’s Ex. 54, ECF No. 68-6). Thieben et al.⁵⁵ indicated that neuropathic or autoimmune bases exist for a substantial percentage of POTS cases. Pet’r’s Ex. 66. However, “hyperadrenergic and hypovolemic correlates are likely compensatory or exacerbating.” *See id.* Benarroch⁵⁶ noted that “there is evidence that bed rest or deconditioning do not primarily affect the reflex control of muscle sympathetic activity.” Pet’r’s Ex. 54. Dr. Kinsbourne relied on a study by Figueroa et al.⁵⁷ that studied exercise capacity in POTS patients and concluded that “not all patients with POTS are deconditioned,” which “raises the possibility that varying degrees of deconditioning may result

⁵⁴ Dr. Kinsbourne referred to hypervolemia, but it is not clear why when the petition alleges POTS with hypovolemia. Hypervolemia is an “abnormal increase in the volume of circulating blood plasma[.]” whereas hypovolemia is the inverse. *See Dorland’s* at 898, 908; *see also supra*, note 4 (defining hypovolemia).

⁵⁵ M. Thieben et al., *Postural Orthostatic Tachycardia Syndrome: The Mayo Clinic Experience*, 82(3) *MAYO CLIN. PROC.* 308–13 (2007).

⁵⁶ E. Benarroch, *Postural Tachycardia Syndrome: A Heterogeneous and Multifactorial Disorder*, 87(12) *MAYO CLIN. PROC.* 1214–25 (2012).

⁵⁷ R. Figueroa et al., *Acute volume loading and exercise capacity in postural tachycardia syndrome*, 117(6) *J. APPL. PHYSIOL.* 663–68 (2014).

secondary to orthostatic tachycardia, rather than as a primary pathophysiological phenomenon.” Pet’r’s Ex. 32 at 2 (citing Pet’r’s Ex. 35, ECF No. 40-3). Figueroa et al. also noted that “[m]any patients with POTS exhibit hypovolemia coupled with cardiac atrophy[.]” Pet’r’s Ex. 35 at 2. Instead, Dr. Kinsbourne maintained that Blitshteyn and Fries⁵⁸ showed that deconditioning “as a sufficient cause for the new onset of POTS has itself been called into serious question.” Pet’r’s Ex. 32 at 2 (citing Pet’r’s Ex. 40, ECF No. 44-1). The authors noted that “[d]econditioning can occur secondary to prolonged bed rest and chronic inactivity in patients with POTS, but it does not appear to be a primary underlying mechanism.” Pet’r’s Ex. 40 at 1. Dr. Kinsbourne opined that deconditioning is a “big factor in the secondary effects of orthostatic intolerance.” Tr. 97:20–21 (citing Pet’r’s Ex. 61).⁵⁹

He argued that deconditioning “cannot be a preponderant theory of causation[.]” in Petitioner’s case. Pet’r’s Ex. 32 at 2. Dr. Kinsbourne posited that prior to November 8, 2013, there was no evidence of deconditioning because there was no evidence that Petitioner “was immobilized to be deconditioned.” Tr. 108:18–21. He testified that Petitioner was functioning normally prior to this time and was able to work. Tr. 83:21–25. Dr. Kinsbourne noted that she “was only in [the] hospital for two days (November 8–10, 2013).” Pet’r’s Ex. 32 at 2. This, Dr. Kinsbourne maintained, “falls well short of” Dr. Low’s proposed timeframe of two to four weeks bedrest “sufficient to induce deconditioning.” *Id.* at 3. Dr. Kinsbourne posited that dehydration or deconditioning would not “themselves bring [POTS] about[.]” Pet’r’s Ex. 29 at 8. He argued that “Dr. Low’s hypothesis of alternative causation cannot succeed based on dehydration and deconditioning alone, but requires an antecedent diagnosis of POTS, which is not in evidence.” *Id.*

Dr. Kinsbourne acknowledged other triggers for POTS. *Id.* at 6. He cited an article by Grubb,⁶⁰ which documents a case study of a 34-year-old woman with POTS following a febrile illness. *Id.* (citing Pet’r’s Ex. 15 at 1). Dr. Kinsbourne cited the Parsaik et al.⁶¹ study, wherein the authors noted that 30% of patients with POTS “identified a preceding event as [a] possible trigger for their symptoms, with viral illness being the most common.” *Id.* (citing Pet’r’s Ex. 61). Dr. Kinsbourne addressed Dr. Low’s assertion that Petitioner’s viral illness was the cause of her POTS. *Id.* Dr. Kinsbourne agreed that infection is a possible cause of POTS. Tr. 91:25. However, while he opined that Dr. Low’s list of potential causes of POTS, including trauma, surgery, childbirth, infections, and immunizations, is “indeed diverse[.]” Petitioner “did not experience trauma, did not have surgery, did not give birth, was not shown to be infected, not stressed out of the ordinary, but she was indeed immunized.” Pet’r’s Ex. 29 at 6.

Under my questioning, Dr. Kinsbourne testified that it “could be the case” that Petitioner’s POTS was “relapsing because it [wa]s exacerbated by her other conditions, specifically her asthma and her anxiety[.]” Tr. 145:16–20. He further opined that “one should[not] forget” the fact that

⁵⁸ S. Blitshteyn & D. Fries, *Postural tachycardia syndrome is not caused by deconditioning*, 6(3) PUL. VASC. RES. INST. 401 (2016).

⁵⁹ A. Parsaik et al., *Deconditioning in patients with orthostatic intolerance*, 79 NEUROL. 1435–40 (2012).

⁶⁰ B. Grubb, *Postural Tachycardia Syndrome*, 117 CLIN. UPDATE 2814–17 (2008).

⁶¹ A. Parsaik et al., *Deconditioning in patients with orthostatic intolerance*, 79 NEUROL. 1435–40 (2012).

Petitioner “seems to have Sjögren’s syndrome[,]”⁶² which made her “vulnerable to POTS.” Tr. 145:21–23. He stated that such a vulnerability is “not a question of what ought to trigger [POTS,]” because one can have a vulnerability that does not lead to POTS. Tr. 145:23–25. Dr. Kinsbourne continued that a vulnerability could still “trigger the actual POTS, which is [his] theory in this case.” Tr. 145:25–146:2. He clarified that his theory is that Petitioner had a “latent” vulnerability to POTS, and he argued that the trigger was her flu vaccine. Tr. 145:25–146:10. He maintained that he was not incorporating a rechallenge theory into his argument. Tr. 149:19–21.

3. Respondent’s Expert, Dr. Low

Dr. Low did not dispute Petitioner’s post-vaccination POTS diagnosis. Resp’t’s Ex. A at 4. Rather, he testified that Petitioner’s October 8, 2013 flu vaccine did not cause her POTS. Tr. 196:1–2. Dr. Low opined that “the likely sequence of events” is that Petitioner “had orthostatic intolerance and some autonomic instability for a significant duration before her vaccination.” Resp’t’s Ex. A at 5. Dr. Low testified that in 2013, Petitioner experienced a “presumed viral illness with gastroenteritis, . . . and about that time, she had dehydration and that exacerbated . . . both the hypovolemia, as well as her anxiety.” Tr. 184:13–18. He noted that diarrhea could also lead to dehydration. Tr. 178:22–25. Dr. Low continued that Petitioner then became less active leading to her deconditioning, which impacted her POTS symptoms. Tr. 184:19–24. Dr. Low opined that Petitioner’s November 8, 2013 hospitalization resulting in her being bedridden contributed to the manifestation of her POTS. Tr. 185:17–22. Dr. Low argued both deconditioning and dehydration “magnif[ied]” Petitioner’s POTS symptoms. Resp’t’s Ex. A at 5. Dr. Low argued that he sees “no obvious linkage” between the worsening of Petitioner’s condition and the receipt of her flu vaccine. Tr. 195:18–22. Dr. Low indicated that he has seen “many” patients who presented like Petitioner. Tr. 185:24–25.

Dr. Low opined that Dr. Kinsbourne “has a very limited and distorted understanding of POTS.” Tr. 164:20–21. Dr. Low discussed relevant information to the “condition” of POTS based on his expertise as an autonomic specialist. Resp’t’s Ex. A at 2–3. He defined POTS as “a syndrome in which – where patients have symptoms of orthostatic intolerance, coupled with orthostatic tachycardia.” Tr. 163:2–4. He explained that POTS is “characterized by an increase in heart rate of >30 beats per minute associated with symptoms of orthostatic intolerance, when the person stands up, and clears when the person sits back down.” Resp’t’s Ex. A at 3. He described orthostatic intolerance as “symptoms of reduced cerebral perfusion,” including lightheadedness, dimming of vision, and cognitive difficulties. *Id.* Orthostatic intolerance also includes symptoms of sympathetic activation such as palpitations, tremulousness, nausea, and diaphoresis. *Id.* He described POTS as the “classic example of orthostatic intolerance.” *Id.* (citing Resp’t’s Ex. A, Tab 1, ECF No. 73-1; Resp’t’s Ex. E, Tab 13, ECF No. 74-11).⁶³ Dr. Low testified that a POTS patient’s sympathetic nervous system is overactive upon standing and that POTS symptoms, such

⁶² See *supra*, note 28 (explaining that the record does not contain preponderant evidence that Petitioner suffers from Sjögren’s syndrome). Further, Dr. Kinsbourne did not otherwise make a connection between the autoimmune mechanism of Sjögren’s or explain how it could act as an autoimmune comorbidity or vulnerability in the development of POTS.

⁶³ E. Benarroch, *Postural Tachycardia Syndrome: A Heterogeneous and Multifactorial Disorder*, 87(12) MAYO CLIN. PROC. 1214–25 (2012); M. Thieben et al., *Postural Orthostatic Tachycardia Syndrome: The Mayo Clinic Experience*, 82(3) MAYO CLIN. PROC. 308–13 (2007).

as dizziness, occur when the person stands, not when they are seated. Tr. 165:1–2, 178:6–15. Dr. Low noted that this is because BP and heart rate increase during sympathetic activation. Resp't's Ex. A at 3. Dr. Low also wrote that POTS patients have “more than just orthostatic intolerance[,]” including chronic fatigue, pain, and headaches, GI complaints, insomnia, and somatic hypervigilance. *See id.* at 4.

He disagreed with Dr. Kinsbourne's assertion that the diagnosis of POTS requires six months of sustained orthostatic intolerance. *See* Tr. 200. Instead, even when confronted with medical literature that indicates the six-month severity requirement, he maintained that POTS requires “the presences of symptoms for six months, of which it does[not] all have to be orthostatic intolerance.” Tr. 201:7–9; *see also* Pet'r's Ex. 58 at 2. As an example, he noted that the astronauts in one of his studies had POTS without sustained orthostatic intolerance for more than six months. Tr. 207:23–22. He explained that the six-month severity requirement in Petitioner's purported definition of POTS is not the main diagnostic criterion since treaters “do[not] wait six months before [] mak[ing] the diagnosis. You take into consideration all of the symptoms that they have had for the previous duration and that[is] where the six months comes in.” Tr. 183:8–12. Dr. Low characterized Dr. Kinsbourne's claim that a POTS diagnosis requires a six-month history of orthostatic intolerance as “surprising[.]” because if one were to “strictly follow[] the guidelines that [Dr. Kinsbourne] claims, then [Petitioner] does not have POTS, the primary claim that [Dr. Kinsbourne] makes.” Resp't's Ex. D at 2.

Dr. Low acknowledged that there is a difference between a symptom of dysautonomia and POTS. Tr. 201:19–22. He wrote that the term dysautonomia refers to abnormal function of the autonomic nervous system. Resp't's Ex. D at 1. He defined dysautonomia as “an imbalance of the autonomic nervous system” wherein “the sympathetic [nervous system] rears its ugly head and causes symptoms.” Tr. 163:10–18. Dr. Low explained that such an imbalance is “not necessarily” a damaged autonomic nervous system, “[i]t[is] just a lack of control.” Tr. 163:19–22.

Next, Dr. Low described the subtypes of POTS. He stated that neuropathic POTS is classified as “regular POTS” and is an example of when POTS can occur as a result of damage to the autonomic nervous system. Tr. 165:10–13, 166:13–15. He defined neuropathic POTS as when “someone has a limited autonomic neuropathy where the nerves to the extremities are partly damaged.” Tr. 165:14–15. He continued, “because of that [damage], [the patient's] blood pressure would try to drop, but [because of] sympathetic overactivity . . . [it is] prevent[ed] from dropping[,]” causing tachycardia. Tr. 165:15–18. Dr. Low stated that blood pressure drops approximately five milliliters in cases of neuropathic POTS. Tr. 166:13–18. Dr. Low then described hyperadrenergic POTS and noted that to meet such classification of POTS, the patient must have “a plasma norepinephrine that[is] excessive when they stand up.” Tr. 167:2–4. Dr. Low wrote that a hyperadrenergic state can result from “increased sympathetic activity that can be caused by POTS and hypovolemia” but it can also be caused by anxiety/panic attacks. Resp't's Ex. A at 4. Dr. Low acknowledged that someone can have a “hyperadrenergic event[,]” such as anxiety or panic that causes tachycardia, separate from POTS. Tr. 167:18–22. He stated the “clue” for this occurrence is “that that person will have a tachycardia when they[are] sitting down” in addition to upon standing, and elevated blood pressure. Tr. 167:20–168:5. In hyperadrenergic POTS, the surge in blood pressure “goes up quite a bit . . . 10, 15, 20, milliliters[s].” Tr. 166:15–

18. Dr. Low testified that two other subtypes of POTS include “constitutional or POTS associated with deconditioning[,]” and POTS associated with anxiety panic. Tr. 166:22–167:10.

He addressed the results of Petitioner’s tilt-table test consistent with his criteria for the classifications of POTS. Dr. Low opined that Petitioner’s tilt-table test showed “regular POTS, not hyperadrenergic POTS.” Tr. 166:21–22. In light of this determination, he disagreed with Dr. Barboi’s diagnosis of hyperadrenergic POTS. Tr. 204:4–9 (citing Pet’r’s Ex. 44 at 146). Dr. Low testified that he understood why Dr. Barboi made such a diagnosis because Petitioner had episodes of hypertension. Tr. 204:21–23. He said that this is “reasonable[,]” but it does not “make him right. He actually made a mistake.” Tr. 204:23–24. Dr. Low posited that there is no debate surrounding the categorizations of POTS and instead, “Dr. Barboi was just a bit sloppy here.” Tr. 205:9–14. Dr. Low was confronted with the Arnold et al.⁶⁴ article which indicated that subtypes of POTS “are not mutually exclusive of each other and many patients have features consistent with more than one subtype.” Tr. 205:15–206:8 (citing Pet’r’s Ex. 58 at 2). He testified that he had “no problem with that” statement. Tr. 206:9. Dr. Low argued that, to him, since Petitioner’s clinical testing did not support a diagnosis of hyperadrenergic POTS, he “found a better way to explain her episodic symptoms[]” and opined that Petitioner had POTS with anxiety-panic. Tr. 204:14–19.

Dr. Low put forth multiple potential causes of POTS, including primary overactivity of the sympathetic nervous system due to deconditioning, reduced plasma volume associated with hypovolemia, and venous pooling. Tr. 165:3–9; Resp’t’s Ex. A at 3. He argued that deconditioning is “the prime cause of POTS[,]” including each subtype. Tr. 209:21–210:9. He explained this is the case because patients improve with reconditioning. Tr. 210:10–11. Dr. Low disagreed with Dr. Kinsbourne’s assertion that deconditioning has not been described as a cause of POTS. Resp’t’s Ex. D at 2. Dr. Low acknowledged that “the focus” of Petitioner’s cited literature “might have been restricted to another mechanism, such as hypovolemia or neuropathy, but not to the exclusion of deconditioning.” *Id.* Dr. Low did not cite to specific literature filed by Petitioner. *See id.* He supported his argument with the fact that he was the “lead/senior author in the majority of the publications that [Dr. Kinsbourne] cites.” *Id.* For example, he explained that early on, he tried to divide the mechanisms into groups, including deconditioning, neuropathic, and hyperadrenergic. *Id.* (citing Resp’t’s Ex. D, Tab 2, ECF No. 74-2).⁶⁵ Then, he tried to “quantify how often deconditioning was the underlying mechanism in POTS.” *Id.* (citing Resp’t’s Ex. A, Tab 7, ECF No. 73-6).⁶⁶ To quantify this, authors, including Dr. Low, conducted a study of 184 patients with POTS who underwent exercise testing to show evidence of deconditioning. Resp’t’s Ex. A, Tab 7 at 3. They found that 95% of the patients exhibited deconditioning and that it “may play a central role in pathophysiology.” *Id.* at 1. They also noted that the patients’ deconditioning improved and was reversed with exercise. *Id.* Dr. Low eventually agreed that deconditioning can also be a secondary effect of POTS. Tr. 211:13–19.

⁶⁴ A. Arnold et al., *Postural tachycardia syndrome – Diagnosis, physiology, and prognosis*, 215 AUTONOMIC NEURO. BASIC & CLIN. 3–11 (2018).

⁶⁵ P. Low et al., *Postural Tachycardia Syndrome (POTS)*, 20 J. CARDIOVASC. ELECTROPHYSIOL. 352–58 (2009).

⁶⁶ A. Parsaik et al., *Deconditioning in patients with orthostatic intolerance*, 79 NEUROL. 1435–43 (2012).

In support of his theory on causation, Dr. Low argued that “[t]ypical of [POTS],” Petitioner became physically inactive post vaccination and “bec[ame] deconditioned[,] further aggravating her POTS and expanding her symptoms” Resp’t’s Ex. A at 5 (citing Resp’t’s Ex. A, Tab 7). Dr. Low cited the Parsaik et al.⁶⁷ article, which indicated that a two-week period of non-continuous bedrest could induce deconditioning. *Id.*; Resp’t’s Ex. D at 3 (citing Resp’t’s Ex. A, Tab 7). Dr. Low wrote that the two-week period is a minimum timeframe. *See id.* Dr. Low relied on Petitioner’s “reported prolonged periods of being bedridden and unable to even care for herself[.]” to highlight evidence of deconditioning. Resp’t’s Ex. A at 5 (citing Pet’r’s Ex. 4 at 60, 124). However, on cross-examination, he stated there was no “good evidence” and that he “honestly d[id not] know” if Petitioner was suffering from deconditioning prior to November 8, 2013. Tr. 206:10–207:2. Dr. Low further relied on two studies showing that when healthy people, without preexisting symptoms of orthostatic intolerance, remain bedridden for as little as two to four weeks, they develop symptoms consistent with POTS. Resp’t’s Ex. C at 1 (citing Resp’t’s Exs. C, Tabs 5–6, ECF Nos. 73-13–73-14).⁶⁸ However, the study by Miller et al. involved male subjects, ages 17 to 23, who “had just completed 8 weeks of basic training in the United States Air Force.” Resp’t’s Ex. C, Tab 5 at 1. The subjects in the Schlegel et al. study had just returned from space. Resp’t’s Ex. C, Tab 6 at 1.

Dr. Low also discussed dehydration as a cause of POTS and opined that Petitioner’s dehydration, experienced as a result of her diarrhea, contributed to her worsening POTS. He explained the process through which dehydration could cause POTS. Tr. 179:2–4. Dr. Low stated that dehydration causes hypovolemia, which is when “the [blood] volume is reduced when you stand up, because of the shift of fluid in the lower half of your body, not enough goes to the brain and that triggers an increase in sympathetic activity.” Tr. 179:5–10 (citing Resp’t’s Exs. C, Tabs 1, 3, ECF Nos. 73-9, 73-11).⁶⁹ He wrote that “[h]ypovolemia (low plasma volume) will regularly cause orthostatic intolerance and orthostatic tachycardia[,]” which improve with fluids in hypovolemic POTS patients. Resp’t’s Ex. C at 1 (citing Resp’t’s Exs. C, Tabs 1, 3). In support of his position, Dr. Low emphasized that Petitioner reported “drinking little water around the time her symptoms worsened[.]” Resp’t’s Ex. A at 5 (citing Pet’r’s Ex. 4 at 152, 170).

Dr. Low’s main argument is that Petitioner’s autonomic disorder predated her vaccination. *See* Resp’t’s Ex. C at 2. Dr. Low argued that Petitioner’s POTS “began a long time ago . . . [p]robably 2011 . . . but it[is] hard to put a specific beginning date.” Tr. 183:18–23. He testified that Petitioner “had some dysautonomia for years and then for a couple of months before the vaccine, she started getting worse[.]” Tr. 177:6–12. He continued that Petitioner then had a more acute illness about three weeks after . . . characterized by gastroenteritis. And by the time she presented to the hospital [on November 8, 2013,] she had a hyperadrenergic response of some sort.” Tr. 177:9–12. He opined that Petitioner’s November 8, 2013 diagnosis of viral gastroenteritis “could be the correct diagnosis” since it was tested for. Tr. 176:16–177:2. Dr. Low therefore opined that Petitioner’s “POTS began with dysautonomia and orthostatic intolerance . . . when

⁶⁷ *See id.*

⁶⁸ P. Miller et al., *Modification of the effects of two weeks of bed rest upon circulatory functions in man*, 35 AEROSP. MED. 931–39 (1964); T. Schlegel et al., *Cardiovascular and Valsalva responses during parabolic flight*, 85(5) J. APPL. PHYSIOL. 1957–65 (1998).

⁶⁹ F. Fouad et al., *Idiopathic Hypovolemia*, 104 ANN. INT. MED. 298–303 (1986); G. Jacob et al., *Relation of blood volume and blood pressure in orthostatic intolerance*, 315(2) AM. J. MED. SCI. 95–100 (1998).

[she] developed vomiting and diarrhea, she developed florid POTS, and this became chronic because of severe deconditioning.” Resp’t’s Ex. C at 3. He argued this progression was all part of “the same condition” of POTS that predated her flu vaccine. *Id.* Dr. Low indicated that preexisting dysautonomia is important because “there is a linked spectrum of autonomic symptoms from dysfunction to POTS.” Resp’t’s Ex. D at 1. He testified that POTS symptoms can wax and wane, and patients experience periods of remission. Tr. 184:2–8.

As support for his contention that Petitioner’s POTS predated her vaccination, he relied on Dr. Barboi’s January 6, 2014 notation indicating Petitioner had “long-standing” autonomic symptoms, such as palpitations and dizziness/lightheadedness. Resp’t’s Ex. C at 2 (citing Pet’r’s Ex. 6 at 8); Tr. 199:8–10. Dr. Low also relied on Petitioner’s two ER visits in 2011 and 2012 for palpitations and dizzy spells, and SOB, respectively, to add context to Dr. Barboi’s notation. Resp’t’s Ex. A at 4. He noted that during Petitioner’s January 12, 2011 ER visit, she had feelings that her “heart ke[pt] beating fast” and that her pulse was 114. Tr. 168:13–169:3 (citing Pet’r’s Ex. 21 at 146, 150). Dr. Low testified that Petitioner “clearly ha[d] dysautonomia” at this time, which was triggered by anxiety-panic. Tr. 169:9–11. He based this assessment on the fact that her pulse was 114 while sitting down, indicating tachycardia. *See* Tr. 169:14–21. Dr. Low discussed Petitioner’s June 10, 2012 ER visit that also showed evidence of tachycardia. Tr. 170:14, 198:7–12 (citing Pet’r’s Ex. 67 at 5–12). He opined that Petitioner “clearly had a sympathetic overactivity” on this occasion, as evidenced by her feelings of lightheadedness and tachycardia “in the 150s.” Tr. 170:20–25. Dr. Low argued this occasion was “more autonomic and not just anxiety” related. Tr. 171:10–11. He based this opinion also on the fact that she improved with IV fluids. Tr. 171:16–19, 199:15–17. However, Dr. Low admitted that there was “not too much evidence of orthostatic intolerance” recorded in the visit notes from this date. Tr. 199:6–8. He conceded the marijuana Petitioner used on June 10, 2012, “could [have] contribute[d] to the lightheadedness[.]” Tr. 199:18–21.

Dr. Low addressed Petitioner’s SOB from early to mid-2013. Tr. 171:20–172:5. He testified that SOB “is a very common symptom of dysautonomia[.]” Tr. 172:1–2. He argued that Petitioner’s breathing issues could be explained by her pre-vaccination dysautonomia. Tr. 174:1–7. Dr. Low argued that the “clue” that Petitioner was experiencing dysautonomia instead of another pulmonary condition, like asthma, was that “she had full respiratory function test[ing] showing that she had no evidence of lung disease or of obstructive airway disease and nothing to suggest asthma.” Tr. 172:2–5 (citing Pet’r’s Ex. 4 at 196). In support of his conclusion that Petitioner did not have asthma, Dr. Low testified regarding Petitioner’s March 20, 2014 spirometry testing and stated that it did not show evidence of “much” asthma. Tr. 172:20–173:11 (citing Pet’r’s Ex. 4 at 196). Dr. Low argued it is not true that a spirometry test would only show evidence of asthma if the patient was having an asthma attack because “[g]enerally, there are some changes even between attacks.” Tr. 173:1–4. Despite the spirometry test results, Dr. Low testified that Petitioner “could have” some degree of asthma. Tr. 202:1–3. He opined that Petitioner “has asthma, but not very bad, and a lot of the difficulty with breathing had to do not with asthma but with anxiety and dysautonomia.” Tr. 202:17–20. Dr. Low further opined that Petitioner’s SOB was not related to her preexisting allergies because she had an allergy test that yielded negative results. Tr. 173:12–16 (citing Pet’r’s Ex. 13 at 44–46).

He stated that Petitioner's preexisting anxiety and panic attacks "[we]re [also] manifestations of [her] dysautonomia." Tr. 203:1–2. He explained that anxiety "is dysautonomia, but it is triggered by emotional factors." Tr. 169:11–13, 203:2–3. Dr. Low testified that "[p]anic is an excellent example of an autonomic stall. The sympathetic[nervous system has] gone haywire during the [attack]. But it is driven by an emotional trigger." Tr. 203:6–8. Dr. Low addressed Petitioner's June 13, 2013 medical record, indicating that she recently discontinued Celexa that she was taking for her anxiety. Tr. 175:18–25 (citing Pet'r's Ex. 13 at 22–25). Dr. Low stated that if patients "stop [taking Celexa] suddenly, it could make the[ir] anxiety worse." Tr. 176:1–2. Dr. Low admitted that a patient can have anxiety symptoms that are unrelated to dysautonomia. Tr. 203:9–11.

Dr. Low wrote that while Dr. Kinsbourne is correct that Petitioner's treaters posited alternative explanations for her pre-vaccination symptoms, such as asthma and anxiety, "this [] is the usual scenario since autonomic disorders are frequently misdiagnosed." Resp't's Ex. C at 2. Dr. Low indicated that it may be hard for a patient with autonomic dysfunction to get a proper diagnosis until they are seen by an autonomic specialist. Tr. 183:1–4. Dr. Low argued that if he, as an autonomic specialist, had seen Petitioner present with a history of dizziness, difficulties breathing, a fast heart rate, and alterations in BP, he would have determined that "combination of symptoms" to "fit into an autonomic diagnosis of dysautonomia" Resp't's Ex. C at 2. Dr. Low opined that such preexisting symptoms "def[y] any of the alternative diagnoses." *Id.* He opined that "in terms of mechanism, . . . one could speculate that [Petitioner] had – her anxiety became worse[.]" Tr. 177:15–17. Dr. Low wrote that Dr. Kinsbourne "does not seem to challenge that [Petitioner] had dysautonomia prior to her current illness." Resp't's Ex. D at 1. What Dr. Kinsbourne does challenge, according to Dr. Low, is whether Petitioner specifically had POTS pre vaccination. *Id.* Dr. Low highlighted that Petitioner did not have autonomic testing "so she obviously could not have been diagnosed as having POTS previously." *Id.*

He cited the articles by Thieben et al. and Benarroch to note that 50% of POTS patients experience "an antecedent event" that can be "quite diverse and non-specific." Resp't's Ex. A at 5 (citing Resp't's Ex. A, Tab 1; Resp't's Ex. E, Tab 13).⁷⁰ These events include trauma, "an illness like [P]etitioner had," surgery, childbirth, infections, stress, and immunizations. *Id.* Dr. Low noted that many POTS patients have "prior symptoms of dysautonomia." Resp't's Ex. C at 3. He argued this "makes the point that although the[patients] might relate onset to some event, such as an infection, surgery, vaccination, stress, childbirth, etc.[,] the onset is not truly acute but dependent in significant part on a predisposition to develop POTS." *Id.* Dr. Low posited that "the diverse nature of the presumed inciting event would argue against the event as the cause of POTS" and in this case that is Petitioner's October 8, 2013 flu vaccine. *Id.*

On cross-examination, Dr. Low was asked to clarify when he believed Petitioner's POTS began. Tr. 197:22–23. In response, Dr. Low stated he "was deliberately a little vague on that simply because dysautonomia [he thinks] began a long time ago." Tr. 197:24–198:1. He continued, "[a]s far as the actual orthostatic intolerance of POTS, that was clearly closer to the vaccine date, and sometime in the previous year . . . when she started getting episodes of tachycardia, et cetera." Tr.

⁷⁰ M. Thieben et al., *Postural Orthostatic Tachycardia Syndrome: The Mayo Clinic Experience*, 82(3) MAYO CLIN. PROC. 308–13 (2007); E. Benarroch, *Postural Tachycardia Syndrome: A Heterogeneous and Multifactorial Disorder*, 87(12) MAYO CLIN. PROC. 1214–25 (2012).

195:13–17, 198:1–5. He argued that Petitioner “was deteriorating” during the two months prior to her October 8, 2013 flu vaccine. Tr. 176:10–11. By three weeks post vaccination, “things really went downhill” with her diarrhea and tachycardia. Tr. 176:11–15. Dr. Low addressed Dr. Kinsbourne’s contention that Petitioner’s diarrhea beginning in late October of 2013 was the onset of Petitioner’s POTS. Dr. Low testified that diarrhea as the first symptom of POTS “would be most unusual” and he has never heard of POTS manifesting that way. Tr. 177:18–21, 178:3–4. He admitted that GI issues are common in POTS patients. Tr. 203:12–14. Dr. Low testified that Petitioner’s gastroenteritis was associated with her POTS but was not a manifestation. Tr. 178:1–3.

Dr. Low attacked Petitioner’s proposed biological mechanism and stated that Dr. Axelrod’s “vague cytokine/molecular mimicry type attribution . . . is quite nonspecific [and] is not a reliable theory in this instance.” Resp’t’s Ex. A at 5. Dr. Low posited that while “loose attribution” is “often made” to cytokines and molecular mimicry or secondary immune responses, such references “are dogged by [a] lack of specificity.” *Id.* Dr. Low argued that, to him, molecular mimicry is “next to meaningless . . . because it[is] so nonspecific.” Tr. 186:9–16. He opined that single case reports like those authored by Tsai et al. or Blitshteyn, “have little scientific merit[]” and are “suspect” because they do not have control data. Resp’t’s Ex. A at 5 (citing Pet’r’s Exs. 14, 39);⁷¹ *see also* Resp’t’s Ex. C at 4. He therefore classified the findings from these articles regarding vaccine causation “into the category of possible but unlikely.” Resp’t’s Ex. A at 5. Dr. Low argued that large, epidemiological studies are more reliable and do not support vaccine causation. *Id.* As an example, Dr. Low cited a study by Zhou et al.,⁷² which showed no relationship between vaccinations and the development of POTS. *Id.* (citing Resp’t’s Ex. A, Tab 10, ECF No. 22-11). The Zhou et al. study analyzed VAERS reports for vaccines generally from 1991 to 2001 and determined that the most reported post-vaccination adverse events included fever, injection-site hypersensitivity, rash, injection-site edema, and vasodilation. Resp’t’s Ex. A, Tab 10 at 2.

Dr. Low argued that POTS is not known to be an autoimmune condition. Tr. 188:4–5. He said there is “an interest” in G proteins as being implicated in the autoimmunity of the condition but such evidence is not conclusive because such antibodies can be found in normal people and/or are present in other disorders besides POTS. Tr. 188:18–189:20 (citing Resp’t’s Ex. E, Tab 17, ECF No. 74-14).⁷³ He testified that G protein antibodies have not been found to be causative of any condition, instead they are secondary or reactive. Tr. 190:9–25. Dr. Low stated that currently there are no causative antibodies in POTS. Tr. 191:1–3.

He discussed the progression of studies regarding the relevant antibodies found in POTS. Dr. Low noted that the scientific community defines the method “by which an autoantibody-mediated autonomic disorder” develops differently than Dr. Kinsbourne proposes. Resp’t’s Ex. E at 1. To make a “designation[,]” that an antibody is the cause of an autoimmune disorder, Dr. Low

⁷¹ C. Tsai et al., *Novel H1N1 Influenza Vaccine the Cause of Postural Orthostatic*, 31(2) J. MED. SCI. 91–93 (2011); S. Blitshteyn, *Postural tachycardia syndrome following human papillomavirus vaccination*, 21 EUR. J. NEUROL. 135–39 (2014).

⁷² W. Zhou et al., *Surveillance for Safety After Immunization: Vaccine Adverse Event Reporting System (VAERS) – United States, 1991–2001*, 52 SURVEILL. SUMM. 1–28 (2003).

⁷³ S. Vernino & L. Stiles, *Autoimmunity in postural orthostatic tachycardia syndrome: current understanding*, 215 AUTONOMIC NEURO. BASIC & CLIN. 78–82 (2018).

wrote that several steps must occur. *Id.* He noted that first, a high titer is necessary “because . . . low antibody titers are often shown to be clinically insignificant.” *Id.* Then, “one must demonstrate that there is a linear relationship between [the] antibody titer and disease severity, which is done by showing that a higher titer is associated with more severe disease.” *Id.* Dr. Low continued that the next step is to show that the disease can be passively transferred. *Id.* He explained this is accomplished through an “animal experiment where the relevant and purified antibody is infused, and the infusion produces the relevant disease in the experimental animal.” *Id.* Dr. Low indicated that the last step “is to characterize the antibody and demonstrate that you can immunize the experimental animal with [the] purified antibody to reproduce the disease.” *Id.* at 1–2. He cited the Thieben et al.⁷⁴ study, which showed that “15% of POTS patients had low titer ganglionic antibody (“AChR”).” Resp’t’s Ex. D at 2–3 (citing Resp’t’s Ex. E, Tab 13). Dr. Low argued that “these are secondary, nonspecific [antibodies that] do not cause tissue injury, and [are] not causally related to POTS.” *Id.* at 3. Dr. Low cited a case by Cutsforth-Gregory et al.⁷⁵ that likewise found that high titer antibodies were associated with autonomic impairment. Resp’t’s Ex. E at 3 (citing Resp’t’s Ex. E, Tab 6, ECF No. 74-4). Dr. Low posited that “[t]here is wide consensus in the medical community that we no longer attempt to measure this [AChR] antibody.” Resp’t’s Ex. D at 3.

As support, Dr. Low relied on the series of studies by Vernino et al.,⁷⁶ which focused on autoimmune autonomic disorders, including autoimmune autonomic ganglionopathy (“AAG”).⁷⁷ Resp’t’s Ex. E at 1–2 (citing Resp’t’s Ex. D, Tab 6, ECF No. 42-7). He used these studies and AAG “as an example of how one goes about demonstrating that an antibody is the cause of an autoimmune disorder.” *Id.* at 1. Vernino et al. demonstrated that patients with AAG had high titers of ganglionic antibodies (AChRs). *Id.* at 2 (citing Resp’t’s Ex. D, Tab 6). The authors also demonstrated a linear relationship between the ganglionic antibody titer and disease severity. *See id.* They noted that “higher levels of [the ganglionic] antibody were significantly associated with greater severity of autonomic dysfunction.” Resp’t’s Ex. D, Tab 6 at 7. Another study by Vernino et al.⁷⁸ found that the passive transfer of the antibody reproduced AAG in an experimental animal model of mice. Resp’t’s Ex. E, Tab 16 at 1, ECF No. 74-13. In that study, mice were injected with IgG containing ganglionic AChR antibodies and developed symptoms of autonomic dysfunction, including GI issues, urinary retention, dilated pupils, reduced heart rate variability, and impaired responses to stress. *Id.* Using the “fully characterized pure antibody,” Vernino et al.⁷⁹ was able to “immunize the experimental animal to reproduce [autonomic neuropathy].” Resp’t’s Ex. E at 2 (citing Resp’t’s Ex. E, Tab 15, ECF No. 74-12).

⁷⁴ M. Thieben et al., *Postural Orthostatic Tachycardia Syndrome: The Mayo Clinic Experience*, 82(3) MAYO CLIN. PROC. 308–13 (2007).

⁷⁵ J. Cutsforth-Gregory et al., *Ganglionic Antibody Level as a Predictor of Severity of Autonomic Failure*, 93(10) MAYO CLIN. PROC. 1440–47 (2018).

⁷⁶ S. Vernino et al., *Autoantibodies to Ganglionic Acetylcholine Receptors in Autoimmune Autonomic Neuropathies*, 343 N. ENG. J. MED. 847–55 (2000).

⁷⁷ Autoimmune autonomic ganglionopathy is “an antibody-mediated disease that classically manifests with widespread autonomic failure [] involving sympathetic, parasympathetic, and enteric functions[.]” *See* J. Cutsforth-Gregory et al., *Ganglionic Antibody Level as a Predictor of Severity of Autonomic Failure*, 93(10) MAYO CLIN. PROC. 1440 (2018).

⁷⁸ S. Vernino et al., *Passive Transfer of Autoimmune Autonomic Neuropathy to Mice*, 24(32) J. NEURO. 7037–42 (2004).

⁷⁹ S. Vernino et al., *Experimental Autoimmune Autonomic Neuropathy*, 90 J. NEUROPHYSIOL. 2053–59 (2003).

However, Dr. Low noted that later studies did not show any correlation between antibody titer and disease severity in POTS patients. *Id.* at 3 (citing Resp't's Ex. E, Tab 13; Resp't's Ex. E, Tab 17; Resp't's Ex. E, Tab 10, ECF No. 74-8; Resp't's Ex. E, Tab 8, ECF No. 74-6).⁸⁰ Dr. Low argued that "evidence suggesting that POTS is autoimmune has not even demonstrated the first step – showing that antibodies are seen in high titers" *Id.* Based on the discrepancy between earlier and later studies, he wrote that the Mayo Laboratory re-evaluated the relationship between "antibody titer to autonomic impairment." *Id.* Dr. Low noted that "[e]ven in a condition that has an established association with these antibodies, [autoimmune autonomic neuropathy], . . . low titers are of no clinical significance." *Id.* Dr. Low addressed the 2018 Vernino and Stiles article which stated that there is evidence of dysregulation of the immune system, including the "presence of autoantibodies directed against targets in the autonomic system." Tr. 214:21–215:11 (citing Resp't's Ex. E, Tab 17 at 4). Dr. Low did not agree that this meant the authors found such autoantibodies had a causative impact. Tr. 215:6–11. He maintained that the research is still developing and as it presently stands, such autoantibodies are bystander antibodies that have no significance. Tr. 215:15–216:6.

Dr. Low was equivocal when asked whether autoantibodies to GPCRs are currently being considered as potentially pathologic in POTS. Tr. 217:2–5. He stated it is true "in that all the evidence we have – we do[not] know if you can measure it accurately." Tr. 217:5–7. He continued that "if it does – if it really exists, then it probably is a reactive or secondary antibody and not a causative antibody[.]" Tr. 217:7–9. As an example, Dr. Low opined that the adrenergic antibody identified in the Li et al.⁸¹ study as being associated with POTS "has never been identified nor characterized" consistent with the methodology described above for determining whether an antibody is causative of an autoimmune disease. Resp't's Ex. E at 3 (citing Pet'r's Ex. 48); Tr. 193:22–23. Dr. Low continued that the Li et al. study did not show any evidence of passive transfer or evidence of tissue injury. *See* Resp't's Ex. E at 3. Thus, the animal model does not establish "that [an] antibody can cause a disease process." *See id.* Dr. Low noted that if there is an autoimmune attack on the sympathetic nervous system, "you expect to see pathology[.]" such as in autoimmune autonomic ganglionopathy, but Li et al. did not show this. Tr. 193:23–194:3. Dr. Low opined that the Li et al. study therefore did not "really provide any insights into the pathogenesis of POTS." Tr. 207:3–9 (citing Pet'r's Ex. 48 at 6).

Dr. Low argued that instead, the methodology used in that study is "seriously flawed." Resp't's Ex. E at 3; Tr. 191:18–21 (citing Pet'r's Ex. 48). As support for this opinion, Dr. Low noted that the animals in that study did not have orthostatic symptoms required for a POTS diagnosis. Resp't's Ex. E at 3. He additionally stated that rabbits are not a good model for studying orthostatic intolerance or hypertension because they are "too short to have significant orthostatic stress." Tr. 191:22–192:3. He also noted "[m]ost importantly" that there was no control group,

⁸⁰ M. Thieben et al., *Postural Orthostatic Tachycardia Syndrome: The Mayo Clinic Experience*, 82(3) MAYO CLIN. PROC. 308–13 (2007); S. Vernino & L. Stiles, *Autoimmunity in postural orthostatic tachycardia syndrome: current understanding*, 215 AUTONOMIC NEURO. BASIC & CLIN. 78–82 (2018); A. McKeon et al., *Ganglionic Acetylcholine Receptor Autoantibody*, 66(6) ARCH. NEUROL. 735–41 (2009); Y. Li et al., *Clinical Experience of Seropositive Ganglionic Acetylcholine Receptor Antibody in a Tertiary Neurology Referral Center*, 52 MUSCLE NERVE 386–91 (2015).

⁸¹ H. Li et al., *Adrenergic Autoantibody-Induced Postural Tachycardia Syndrome in Rabbits*, X J. AM. HEART ASSOC. 1–9 (2019).

“consisting of animals that were not immunized” that could have shown “possible intervening events, apart from immunization, that could result in the modest” symptoms the rabbits experienced, such as dehydration, discomfort, and stress. Resp’t’s Ex. E at 3; Tr. 193:3–19. Dr. Low admitted that the authors were able to show that immunizing rabbits with particular peptides results in altered vasoreactivity. Tr. 192:12–18. However, he said this was not surprising and “has nothing to do with POTS.” Tr. 192:18–19. He therefore disagreed with the authors’ assertion that vasoreactivity is related to POTS. Tr. 192:20–22. Instead, Dr. Low stated that “what [the authors are] saying is that the fact that these peptides do something and when you change – when – the fact that you immunize them, you must be doing something to their receptors.” Tr. 192:23–193:1. Dr. Low thought the authors “could be right[,]” in that assessment, but that still “has nothing to do with POTS.” Tr. 193:1–2. Dr. Low argued that Dr. Kinsbourne “at best” has provided evidence that research regarding an autoimmune basis for POTS is “ongoing.” Resp’t’s Ex. E at 4.

He addressed the Gunning et al.⁸² article, which used the ELISA test to detect autoantibodies against GPCRs, and called the kit “terrible.” Tr. 212:14–213:6 (citing Pet’r’s Ex. 47). He stated that the ELISA test does not work for large surface antibodies and that GPCRs are large proteins. Tr. 214:1–2. Rather, ELISA tests are used for small protein antibodies. Tr. 213:6–23. On cross-examination, Dr. Low was confronted with the article’s mention that “these kits have been validated by the manufacturer and used successfully in a [separate] recent report identifying autoantibodies to beta-adrenergic and muscarinic cholinergic receptors in chronic fatigue syndrome, of which many symptoms overlap with POTS.” Tr. 212:20–25. Dr. Low was “surprised” to be asked about this statement because “these experiments [] do[not] mean very much because . . . many G protein antibodies are increased in many diseases, including chronic fatigue [syndrome.]” Tr. 213:10–14. Dr. Low further argued that “[n]o one has been able to validate the test . . .” or reproduce it, “including Vernino.” Tr. 213:6–10. Dr. Low took issue with this study’s use of a research company that is “selling directly to patients[,]” rather than getting validation or certification from other studies. Tr. 213:15–17.

Dr. Low also addressed the Kharraziha et al.⁸³ article. Tr. 214:15–18, 218:15–219:18 (citing Pet’r’s Ex. 64). Dr. Low opined that the bioassay used in this study was likewise not an adequate test. Tr. 218:3–5. He argued that this is a lesser test than the ELISA and explained that it is “pre-lab type testing where . . . you look at the cremasteric muscle of the rat.” Tr. 218:10–15. He admitted that this study was “a little more sophisticated, looking at tissue.” Tr. 218:15–16. However, he argued “you need to get beyond that to get serious.” Tr. 218:17. He was confronted with Kharraziha et al.’s conclusion that the serum of patients with POTS “demonstrate activity against cardiovascular and nociceptive G protein coupled receptors[,] and such activation is highly predictive of POTS diagnosis.” Tr. 218:18–22. Dr. Low maintained that because the methodology was questionable, “the clinical correlation was not that convincing and to claim it[is] a predictive test . . . is just not correct.” Tr. 219:1–4.

Dr. Low opined that Dr. Kinsbourne “has offered no reliable evidence that a flu vaccine can cause, or does cause, POTS.” Resp’t’s Ex. E at 4. Dr. Low explicitly stated that there is no

⁸² W. Gunning et al., *Postural Orthostatic Tachycardia Syndrome is Associated with Elevated G-Protein Coupled Receptor Autoantibodies*, X J. AM. HEART ASSOC. 1–10 (2019).

⁸³ I. Kharraziha et al., *Serum Activity Against G Protein-Coupled Receptors and Severity of Orthostatic Symptoms in Postural Orthostatic Tachycardia Syndrome*, 9 J. AM. HEART ASSOC. 1–17 (2020).

evidence that the flu vaccine could induce the antibodies posited by Dr. Kinsbourne, and that fact has “been totally skimmed over.” Tr. 194:17–20. Dr. Low testified that “[t]here is no antibody that has produced POTS[.]” Tr. 196:8–9. Dr. Low therefore argued that there is no direct evidence to show that Petitioner’s flu vaccine “ha[d] anything to do with [her] POTS[.]” Resp’t’s Ex. A at 4; Resp’t’s Ex. E at 1.

He wrote that Petitioner’s preexisting orthostatic intolerance “coupled with [her] lack of tissue injury” to show evidence of molecular mimicry, weakens Petitioner’s argument for vaccine causation. Resp’t’s Ex. C at 3–4. In support of this conclusion, Dr. Low testified that “[i]f POTS is autoimmune, because the autoimmune process is so predictable, that [he] would expect to see pathologic change.” Tr. 220:21–24. He argued that “all significant autoimmune autonomic neuropathies” cause tissue injury. Resp’t’s Ex. C at 1–2. Dr. Low maintained that “all proven cases of vaccine injury have resulted in tissue damage[.]” as exemplified by “the beautiful pathology” seen in cases of vaccine-caused Guillain-Barré syndrome.⁸⁴ Resp’t’s Ex. D at 2. He continued, “[e]very case where there is an autoimmune primary injury to the autonomic nervous system has resulted in tissue injury.” *Id.* He explained that “[o]ne reason for this reasonable requirement is that, in many chronic conditions, there are secondary nonspecific, usually minor abnormalities, often described as minor nonspecific abnormalities.” *Id.* Dr. Low argued that evidence of tissue injury is important for “differentiating primary causative mechanism[s] for secondary non-specific abnormalities.” *Id.* at 3. Dr. Low wrote that “low levels of antibodies generally have no linear connection with disease severity. Thus, the antibodies identified by Dr. Kinsbourne fall into the category of minor nonspecific abnormalities.” Resp’t’s Ex. E at 3. He argued that “research has demonstrated that no clinical significance can be placed on such minor abnormalities.” *Id.*

Dr. Low wrote that Petitioner’s “extensive studies” showed no damage to her autonomic nerves, and, in his review of Petitioner’s medical records, he saw “no symptoms or test results that provide any evidence of significant autonomic neuropathy.” Resp’t’s Ex. A at 4. He argued that evidence of damage to autonomic nerves, “such as [that] occurring in [] autoimmune autonomic neuropathies,” would produce “easily identifiable clinical deficits[,] such as orthostatic hypotension, pupillary abnormalities . . . gastroparesis, [and] bladder or bowel failure.” *Id.* (citing Resp’t’s Ex. A, Tab 9, ECF No. 73-8).⁸⁵ Dr. Low wrote that Petitioner “had none of these manifestations[.]” to suggest an autonomic injury. *Id.*; Resp’t’s Ex. E at 4. He continued that “one would not expect vaccine injury to cause just POTS without other manifestations of injury to the sympathetic nervous system.” Resp’t’s Ex. E at 4.

⁸⁴ Guillain-Barré syndrome is “rapidly progressive ascending motor neuron paralysis of unknown etiology, frequently seen after an enteric or respiratory infection. An autoimmune mechanism following viral infection has been postulated. It begins with paresthesias of the feet, followed by flaccid paralysis of the entire lower limbs, ascending to the trunk, upper limbs, and face; other characteristics include slight fever, bulbar palsy, absent or lessened tendon reflexes, and increased protein in the cerebrospinal fluid without a corresponding increase in cells. Variant forms include acute autonomic neuropathy, Miller-Fisher syndrome, acute motor axonal neuropathy, and acute motor-sensory axonal neuropathy.” *Dorland’s* at 1832.

⁸⁵ S. Vernino et al., *Autoantibodies to Ganglionic Acetylcholine Receptors in Autoimmune Autonomic Neuropathies*, 343 N. ENG. J. MED. 847–55 (2000).

Dr. Low maintained that “if you cannot show tissue injury, you do not have a specific immune-mediated complication.” Resp’t’s Ex. C at 2. Dr. Low opined that Petitioner had “quite aggressive treatment and testing[,]” and that if evidence of autoimmunity existed, it would have appeared in her testing, including her norepinephrine testing. Tr. 223:17–224:10, 227:9–14 (citing Pet’r’s Ex. 21 at 46). Dr. Low argued that the reason that an autoimmune etiology was not revealed by Petitioner’s testing is because POTS is “not necessarily autoimmune,” so there is no test that could show that. Tr. 224:11–17. Regarding Petitioner’s July 2020 antibody testing, Dr. Low explained that autoantibodies would fade over time in monophasic illnesses, but POTS is not monophasic so antibodies would not be expected to fade. Tr. 214:8–14. Rather, “POTS is a persistent condition,” so one would expect antibodies to persist. Tr. 191:11–12. Dr. Low argued that “if you look at the testing in the papers that have been presented” by Petitioner, it references the presence of such adrenergic antibodies in POTS patients. Tr. 191:13–16. Such testing was conducted and gathered from the patients at different durations, many of whom “had POTS for many years[.]” *See id.* He did not cite specific articles when making this statement. *See id.* Dr. Low maintained that Dr. Kinsbourne’s “idea that [antibodies] came and then [] disappeared does[not] make any sense.” Tr. 191:15–17. He therefore did not believe Petitioner’s medical records showed any evidence of autoimmunity. *See id.* Dr. Low “fully agree[d]” with Dr. Kinsbourne’s argument that “there need not be tissue injury for POTS to occur.” Resp’t’s Ex. C at 1. Dr. Low argued that this is true because “POTS is a condition and not a disease[.]” and there are mechanisms for POTS, such as deconditioning, medications, hypovolemia, or stress, that do not produce an immune response at all, which is what happened in Petitioner’s case. *Id.*; *see also* Tr. 225:3–5.

Dr. Low discussed the relationship between POTS and other autoimmune disorders. He testified that secondary POTS can occur in patients that are already suffering from an autoimmune disorder. Tr. 165:19–25. He was careful in saying this does not “mean POTS is autoimmune . . . the POTS was purely as a result of damage, clearly secondary.” Tr. 165:25–166:3. He explicitly stated that hyperadrenergic POTS is “definitely not” presumed to be autoimmune-based. Tr. 167:13–15. He indicated he does not “know of any cases of hyperadrenergic POTS that[were] due to [an] autoimmune disorder.” Tr. 167:15–17.

IV. Applicable Legal Standards

To receive compensation under the Vaccine Act, a petitioner must demonstrate either that: (1) the petitioner suffered a “Table injury” by receiving a covered vaccine and subsequently developing a listed injury within the time frame prescribed by the Vaccine Injury Table set forth at 42 U.S.C. § 300aa-14, as amended by 42 C.F.R. § 100.3; or (2) the petitioner suffered an “off-Table injury,” one not listed on the Table, as a result of his receiving a covered vaccine. *See* 42 U.S.C. §§ 300aa-11(c)(1)(C); *Moberly v. Sec’y of Health & Hum. Servs.*, 592 F.3d 1315, 1321 (Fed. Cir. 2010); *Capizzano v. Sec’y of Health & Hum. Servs.*, 440 F.3d 1317, 1319–20 (Fed. Cir. 2006). Petitioner does not allege a Table injury in this case; thus, she must prove that her injury was caused-in-fact by a Table vaccine.

To establish causation-in-fact, a petitioner must demonstrate by a preponderance of the evidence that the vaccine was the cause of the injury. 42 U.S.C. § 300aa-13(a)(1)(A). A petitioner is required to prove that the vaccine was “not only a but-for cause of the injury but also a substantial factor in bringing about the injury.” *Moberly*, 592 F.3d at 1321–22 (quoting *Shyface v. Sec’y of Health & Hum. Servs.*, 165 F.3d 1344, 1352–53 (Fed. Cir. 1999)).

In the seminal case of *Althen v. Sec’y of the Dept. of Health & Hum. Servs.*, the Federal Circuit set forth a three-pronged test used to determine whether a petitioner has established a causal link between a vaccine and the claimed injury. *See* 418 F.3d 1274, 1278–79 (Fed. Cir. 2005). The *Althen* test requires petitioners to set forth: “(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.” *Id.* at 1278. To establish entitlement to compensation under the Program, a petitioner is required to establish each of the three prongs of *Althen* by a preponderance of the evidence. *Id.* “[C]lose calls regarding causation are resolved in favor of injured claimants.” *Id.* at 1280. Further, evidence used to satisfy one prong of the test may overlap to satisfy another prong. *Capizzano*, 440 F.3d at 1326.

A petitioner who satisfies all three prongs of the *Althen* test has established a prima facie showing of causation. *Hammitt v. Sec’y of Health & Hum. Servs.*, 98 Fed. Cl. 719, 726 (2011). A petitioner who demonstrates by a preponderance of the evidence that he suffered an injury caused by vaccination is entitled to compensation unless the respondent can demonstrate by a preponderance of the evidence that the injury was caused by factors unrelated to the vaccination. *See Althen*, 418 F.3d at 1278; *Knudsen v. Sec’y of Health & Hum. Servs.*, 35 F.3d 543, 547 (Fed. Cir. 1994). In such a case, the government must not merely prove the existence of an alternative cause, but that such an alternative actually caused the injury. *Knudsen*, 35 F.3d at 549. Additionally, a factor unrelated “may not include ‘any idiopathic, unexplained, unknown, hypothetical, or undocumentable cause, factor, injury, illness or condition.’” 42 U.S.C. § 300aa-13(a)(2); *see also Doe v. Sec’y of Health & Hum. Servs.*, 601 F.3d 1349 (Fed. Cir. 2010) (explaining that an idiopathic diagnosis cannot be a “factor unrelated,” as it is idiopathic).

In considering the reliability of a petitioner’s evidence of a prima facie case, the special master may consider alternative causes for a petitioner’s condition that are reasonably raised in the record, even if the respondent does not pursue a formal alternative cause argument. *Doe*, 601 F.3d at 1358. Thus, in weighing a petitioner’s case-in-chief, a special master may consider evidence that the petitioner’s alleged injury could have been caused by alternative causes. *Id.*

V. Discussion

A. Experts⁸⁶

Although special masters have the discretion to be informed by past rulings and experiences, case-specific filings and testimony are the most helpful types of evidence, given the fact-specific nature of each decision. *See Doe v. Sec’y of Health & Hum. Servs.*, 76 Fed. Cl. 328, 338–39 (2007). To that end, experts are an essential piece of a petitioner’s claim and Respondent’s defense. Where both sides offer expert testimony, a special master’s decision may be “based on the credibility of the experts and the relative persuasiveness of their competing theories.” *Broekelschen v. Sec’y of Health & Hum. Servs.*, 618 F.3d 1339, 1347 (Fed. Cir. 2010) (citing *Lampe v. Sec’y of Health & Hum. Servs.*, 219 F.3d 1357, 1361 (Fed. Cir. 2000)). However, nothing

⁸⁶ As Dr. Axelrod only submitted one brief expert report and did not testify at the entitlement hearing, I am not relying on his opinions in this Decision, except to the extent that Dr. Kinsbourne adopts or expands upon the basic principles put forth in his report.

requires the acceptance of an expert's conclusion “connected to existing data only by the *ipse dixit* of the expert,” especially if “there is simply too great an analytical gap between the data and the opinion proffered.” *Snyder v. Sec’y of Health & Hum. Servs.*, 88 Fed. Cl. 706, 743 (2009) (quoting *Gen. Elec. Co. v. Joiner*, 522 U.S. 136, 146 (1997)); *see also Isaac v. Sec’y of Health & Hum. Servs.*, No. 08–601V, 2012 WL 3609993, at *17 (Fed. Cl. Spec. Mstr. July 30, 2012), *mot. for review den’d*, 108 Fed. Cl. 743 (2013), *aff’d*, 540 F. App’x. 999 (Fed. Cir. 2013). Weighing the relative persuasiveness of competing expert testimony, based on a particular expert's credibility, is part of the overall reliability analysis to which special masters must subject expert testimony in Vaccine Program cases. *Moberly*, 592 F.3d at 1325–26 (“[a]ssessments as to the reliability of expert testimony often turn on credibility determinations”); *see also Porter v. Sec’y of Health & Hum. Servs.*, 663 F.3d 1242, 1250 (Fed. Cir. 2011) (“[T]his court has unambiguously explained that special masters are expected to consider the credibility of expert witnesses in evaluating petitions for compensation under the Vaccine Act.”).

In determining whether a particular expert's testimony was reliable or credible, a special master may consider whether the expert is offering an opinion that exceeds the expert's training or competence. *Walton v. Sec’y of Health & Hum. Servs.*, No. 04–503V, 2007 WL 1467307, at *17–18 (Fed. Cl. Spec. Mstr. Apr. 30, 2007) (concluding that an otolaryngologist was not well suited to testify about disciplines other than her own specialty). While all testimony of the experts offered at the entitlement hearing was heard and considered, a special master may properly evaluate, and give appropriate weight to, whether certain testimony is beyond a particular expert's purview. *See, e.g., King v. Sec’y of Health & Hum. Servs.*, No. 03-584V, 2010 WL 892296, at *78–79 (Fed. Cl. Spec. Mstr. Mar. 12, 2010) (determining that a petitioner's expert was far less qualified to offer opinion on general causation issues pertaining to autism than specific issues pertaining to the petitioner's actual medical history, given the nature of the expert's qualifications). This case ultimately turns not only on Petitioner’s medical history, but also the persuasiveness of the written reports, supporting documentation, and expert testimony. I therefore must assess each expert’s knowledge in relation to the facts of Petitioner’s case and assign weight accordingly. This assessment will inform my analysis pursuant to each prong of *Althen*.

Petitioner’s expert, Dr. Kinsbourne, is now retired and has been for over 20 years. He spent his career focusing on neurology, and much of his practice dealt specifically with pediatric and behavioral neurology. *See* Pet’r’s Ex. 30; Tr. 56–72. It is true that Dr. Kinsbourne has treated patients with autoimmune conditions generally, but he admitted that any POTS diagnosis he has made has been limited to those within the Vaccine Program. *See* Tr. 68:10–13, 118:11–13. Moreover, although Dr. Kinsbourne’s curriculum vitae reflects that he has an extensive publication history, it is unrevealing of any body of publications directly relevant to the condition of POTS. Conversely, Dr. Low, in addition to a background in neurology, is among the leading autonomic specialists in the medical community and focuses primarily on autonomic conditions, including POTS. *See* Resp’t’s Ex. B; Tr. 155–62. Dr. Low has treated and diagnosed thousands of POTS patients or those suffering from autonomic disorders. *See* Tr. 159:8–15. I must note that I am not accepting the opinion of Dr. Low *carte blanche*, as cautioned against by Petitioner. *See* Pet’r’s Post-Hrg. Br. at 2. However, I base this Decision, in part, on Dr. Low’s credentials and expertise in autonomic conditions, including POTS specifically, as compared to Dr. Kinsbourne’s specialty in pediatric neurology.

Petitioner's medical theory is predicated on POTS having an autoimmune basis. Dr. Kinsbourne is not an expert in immunology. However, I agree with Dr. Kinsbourne that on the level he discussed the immune response to vaccinations, any neurologist would be able to elicit a general understanding of such principles. *See* Tr. 66:14–15. Alternatively, Dr. Low's role in the investigation of an autoimmune etiology for POTS enhances the credibility of his testimony regarding the same. Respondent contemplated but ultimately decided not to move to strike Dr. Kinsbourne's hearing testimony pertaining to immunology.⁸⁷ I will recognize Respondent's request for me to "assign proper weight" to such testimony in accordance with Dr. Kinsbourne's subject-matter expertise. *See* Tr. 62–73, 229–30.

The limitations of Dr. Kinsbourne's knowledge on the subject are evinced by the fact that he authored his expert reports under the premise that AChR autoantibodies are associated with POTS. On the stand, he then completely abandoned his reliance on such antibodies when he presumably realized they are no longer thought to be associated with POTS. I cannot ignore Dr. Kinsbourne's reversal. Furthermore, Dr. Kinsbourne failed to acknowledge that POTS has several subtypes, albeit not mutually exclusive. In Dr. Kinsbourne's opinion, POTS has only one subtype, hyperadrenergic POTS. *See* Tr. 123:3–124:17.

Dr. Kinsbourne is an extremely qualified expert in his field. He has a history of providing useful testimony and persuasive explanations in cases before me, as well as other special masters in the Program. Several special masters have also previously been critical of Dr. Kinsbourne for opining beyond his area of expertise and into the field of immunology. *See, e.g., Kottenstette v. Sec'y of Health & Hum. Servs.*, No. 15-1016V, 2020 WL 4197301, at *13–14 (Fed. Cl. Spec. Mstr. June 2, 2020), *mot. for review den'd*, No. 15-1016V, 2020 WL 4592590 (Fed. Cl. 2020), *rev'd on other grounds*, 861 F. App'x. 433 (Fed. Cir. 2021). In this case, Dr. Kinsbourne's reliance on a seemingly outdated understanding of POTS and his lack of any clinical experience relative to the syndrome is consistent with Respondent's criticism and therefore affects the weight of his testimony. It is also the case that key elements of Dr. Kinsbourne's mechanistic theory are grounded in immunology, a subject that he admits is beyond his area of expertise. Ultimately, his opinion was delivered with less persuasive support and specificity than that of Respondent's expert, Dr. Low. *See Broekelschen*, 618 F.3d at 1347 (citing *Lampe*, 219 F.3d at 1362) (finding that where both sides offer expert testimony, a special master's decision may be "based on the credibility of the experts and the relative persuasiveness of their competing theories[]").

B. *Althen* Prong One

Under the first prong of *Althen*, a petitioner must offer a scientific or medical theory that answers in the affirmative the question: "can the vaccine[] at issue cause the type of injury alleged?" *See Pafford v. Sec'y of Health & Hum. Servs.*, No. 01-0165V, 2004 WL 1717359, at *4 (Fed. Cl. Spec. Mstr. July 16, 2004), *mot. for review den'd*, 64 Fed. Cl. 19 (2005), *aff'd*, 451 F.3d 1352 (Fed. Cir. 2006). To satisfy this prong, a petitioner's theory must be based on a "sound and reliable medical or scientific explanation." *Knudsen*, 35 F.3d at 548. Such a theory must only be "legally probable, not medically or scientifically certain." *Id.* at 548–49. A petitioner is not required to identify "specific biological mechanisms" to establish causation, nor are they required

⁸⁷ Motions to strike expert testimony are rarely granted pursuant the relaxed interpretation of the Federal Rules of Civil Procedure in the Program.

to present “epidemiologic studies, rechallenge[] the presence of pathological markers or genetic disposition, or general acceptance in the scientific or medical communities.” *Capizzano*, 440 F.3d at 1325 (quoting *Althen*, 418 F.3d at 1280). Scientific and “objective confirmation” of the medical theory with additional medical documentation is unnecessary. *Althen*, 418 F.3d at 1278–81; see also *Moberly*, 592 F.3d at 1322. However, as the Federal Circuit has made clear, “simply identifying a ‘plausible’ theory of causation is insufficient for a petitioner to meet her burden of proof.” *LaLonde v. Sec’y of Health & Hum. Servs.*, 746 F.3d 1334, 1339 (Fed. Cir. 2014) (citing *Moberly*, 592 F.3d at 1322). Rather, “[a] petitioner must provide a reputable medical or scientific explanation that pertains specifically to the petitioner’s case.” *Moberly*, 592 F.3d at 1322. In general, “the statutory standard of preponderance of the evidence requires a petitioner to demonstrate that the vaccine more likely than not caused the condition alleged.” *LaLonde*, 746 F.3d at 1339.

Furthermore, establishing a sound and reliable medical theory connecting the vaccine to the injury often requires a petitioner to present expert testimony in support of her claim. *Lampe*, 219 F.3d at 1361. The Supreme Court’s opinion in *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 509 U.S. 579 (1993), requires that courts determine the reliability of an expert opinion before it may be considered as evidence. “In short, the requirement that an expert’s testimony pertain to ‘scientific knowledge’ establishes a standard of evidentiary reliability.” *Id.* at 590 (citation omitted). Thus, for Vaccine Act claims, a “special master is entitled to require some indicia of reliability to support the assertion of the expert witness.” *Moberly*, 592 F.3d at 1324. The *Daubert* factors are used in the *weighing* of the reliability of scientific evidence proffered. *Davis v. Sec’y of Health & Hum. Servs.*, 94 Fed. Cl. 53, 66–67 (2010) (“[U]niquely in this Circuit, the *Daubert* factors have been employed also as an acceptable evidentiary-gauging tool with respect to persuasiveness of expert testimony already admitted[.]”).

Petitioner has failed to meet her burden under *Althen* prong one. Petitioner posited a theory of the flu vaccine’s role in the development of POTS via molecular mimicry.⁸⁸ As discussed in more detail below, this biological mechanism is only minimally supported by the submitted evidence because while Petitioner has shown that POTS can have an autoimmune etiology, she has failed to show that the flu vaccine can trigger an immune-mediated response resulting in POTS.

a. Autoimmune Etiology of POTS

For Petitioner to satisfy her burden as to her proposed biological mechanism, she must establish that POTS has an autoimmune etiology. Petitioner argued that GPCR autoantibodies are found in patients with POTS, which supports an autoimmune “trigger” for the condition. Historically in the Program, petitioners have been unsuccessful in establishing an autoimmune etiology for POTS based on the presence of certain autoantibodies. See, e.g., *L.P. v. Sec’y of Health & Hum. Servs.*, No. 16-1278V, 2021 WL 2373863, at *29 (Fed. Cl. Spec. Mstr. Apr. 26, 2021) (rejecting the petitioner’s claim that the flu vaccine can cause POTS via the induction of

⁸⁸ Petitioner alleged that her flu vaccination caused POTS with hypovolemia. Pet. at 1. However, Petitioner did not provide testimony or evidence regarding the biological mechanism connecting the flu vaccine to hypovolemia. Instead, Dr. Kinsbourne testified that “[w]ell, hypovolemia is one of the – is one of the many – one of the parts of the mechanisms of causing the disability.” Tr. 122:4–9.

antiphospholipid antibodies).⁸⁹ However, we are now confronted with a growing number of studies that place an importance on the role of adrenergic receptor autoantibodies in the development of POTS. This shift in the medical community's understanding of the potential autoimmune etiology of POTS signals that such autoantibodies could be causative of an autoimmune process resulting in POTS.

Indeed, older studies support Petitioner's argument that autoantibodies to adrenergic receptors, including alpha-1 and beta-1 and beta-2 adrenergic receptors, have been found in POTS patients. However, such earlier studies are not determinative, as subsequent studies still questioned the role of autoimmunity in the development of POTS. For example, the 2014 study by Li et al. found at least one subset of adrenergic autoantibodies in each of the study's 14 POTS patients. Pet'r's Ex. 49 at 1, 4, 7. A 2015 study by Blitshteyn et al. determined that 31 out of 100 POTS patients had "markers of autoimmunity." Pet'r's Ex. 33 at 1. While they indicated that adrenergic autoantibodies "appear to be good candidates mechanistically," they concluded at that time that the question of whether POTS is an autoimmune disorder still needed to be answered. *Id.* at 6.

By 2017, the role of such adrenergic autoantibodies was revisited, and small-scale studies showed that such autoantibodies are involved in the pathophysiology of POTS, providing an autoimmune basis for the condition. *See* Pet'r's Ex. 51 at 7. In 2018, Vernino and Stiles undertook efforts to catalog the body of prior research investigating an autoimmune basis for POTS. *See* Pet'r's Ex. 53. While the authors, relying on previously cited studies, admitted that GPCR autoantibodies have been documented in POTS patients, they noted the current literature in 2018 revealed that adrenergic and muscarinic antibodies may have not been causative of POTS in larger studies. *Id.* at 3. Part of the reason for this discrepancy is because GPCR autoantibodies have been found in normal, healthy people. *See id.*; Tr. 189:16–18. Vernino and Stiles concluded that further research is needed in larger cohorts to determine the pathological significance of GPCR autoantibodies in POTS. Pet'r's Ex. 53 at 3.

Notwithstanding Vernino and Stiles' conclusion, the Program does not require evidence from large epidemiological studies for a petitioner's claim under *Althen* prong one to be successful. *See Capizzano*, 440 F.3d at 1325 (quoting *Althen*, 418 F.3d at 1280) (indicating that to satisfy prong one, a petitioner is not required to present "epidemiologic studies, rechallenge[] the presence of pathological markers or genetic disposition, or general acceptance in the scientific or medical communities."). Indeed, subsequent literature, including an animal model, further supports the role of adrenergic autoantibodies in the development of POTS, thus providing preponderant evidence

⁸⁹ *See also Yalacki v. Sec'y of Health & Hum. Servs.*, No. 14-278V, 2019 WL 1061429, at *34 (Fed. Cl. Spec. Mstr. Jan. 31, 2019), *mot. for review den'd*, 146 Fed. Cl. 80 (2019) (finding that the evidence presented to show POTS is autoimmune was thin and that the petitioner failed to show a HPV vaccine likely causes "the production of antibodies associated with autonomic damage or interference sufficient to cause POTS"); *Johnson v. Sec'y of Health & Hum. Servs.*, No. 14-254V, 2018 WL 2051760, at *1 (Fed. Cl. Spec. Mstr. Mar. 23, 2018) (ruling against the petitioner in a case alleging that the HPV vaccine caused POTS and noting that the medical literature suggesting that POTS "might be autoimmune appears [to be] extremely limited"); *L.A.M. v. Sec'y of Health & Hum. Servs.*, No. 11-852V, 2017 WL 527576, at *63 (Fed. Cl. Spec. Mstr. Jan. 31, 2017) (finding that most cases of POTS do not have an autoimmune etiology and that the petitioner's claim that the HPV vaccine caused POTS must fail because she did not provide corroborating evidence of an autoimmune process).

of an autoimmune etiology for the condition. *See, e.g.*, Pet'r's Exs. 47–48. By 2019, autonomic specialists continued to investigate an autoimmune basis for POTS. Gunning et al. used an ELISA test and found elevated titers of alpha-1 adrenergic autoantibodies and M4 muscarinic acetylcholine receptor antibodies in POTS patients. *See* Pet'r's Ex. 47 at 1. I am not persuaded by Dr. Low's attacks on the methodology used in this study. Specifically, he took issue with the authors' use of the ELISA test. He argued it is used for the detection of small proteins but since G proteins are large proteins, the test's ability to measure the presence of such antibodies is unlikely. *See* Tr. 189:4–6, 212–14. Dr. Low demonstrated an outright refusal to acknowledge the authors' findings of adrenergic autoantibodies in POTS patients. Further, Dr. Low seemed to classify Gunning et al.'s findings as isolated and posited that the authors' findings have not been validated or reproduced in subsequent studies, “including [by] Vernino.” *See* Tr. 213:6–10. He did not offer evidence in support of his argument, nor did he identify how many times researchers have unsuccessfully attempted to reproduce Gunning et al.'s results. In fact, his reference to the work of Dr. Vernino here cuts against his argument because the submitted research by Vernino was conducted and published prior to the 2019 Gunning et al. study. *See, e.g.*, Pet'r's Ex. 52 (published in 2000); Resp't's Ex. E, Tab 15 (published in 2003); Resp't's Ex. E, Tab 16 (published in 2004); Pet'r's Ex. 53 (published in 2018). Based on the submitted evidence, it does not appear that Vernino et al. sought to reproduce Gunning et al.'s findings. I am therefore unpersuaded by Dr. Low's arguments regarding the significance of the Gunning et al. study.

Also in 2019, Li et al. purported to show the first animal model of POTS with an autoimmune etiology by immunizing rabbits with alpha-1 and beta-1 adrenergic receptor autoantibodies. The researchers observed that the rabbits then experienced a postural tachycardic response measured on a tilt-table test. *See* Pet'r's Ex. 48 at 3. The authors' determination that they were able to block the adrenergic autoantibodies from interacting with receptors in the rabbits, making their heart rates return to baseline, appears to support their conclusion that such autoantibodies play a causative role in the development of POTS. This finding further supports their claim that POTS is autoimmune. In fact, Dr. Low agreed that these authors sought to, and showed, that immunizing rabbits with these particular antibodies results in changes to their receptors and vasoreactivity. Tr. 192:12–19. Dr. Low then opined that vasoreactivity “has nothing to do with POTS.” Tr. 192:19. When asked how that is, Dr. Low could not explain why vasoreactivity had nothing to do with POTS, instead stating that the authors “could be right” that immunizing the rabbits with such autoantibodies “must be doing something to their receptors.” Tr. 192:20–193:1. He argued, however, that if Petitioner's theory were true, and that antibodies could alter the receptors, he would expect to see “some pathology.” Tr. 194:4–8. Dr. Low attacked the authors' failure to look for evidence of pathology in the rabbits because “[e]very case where there is an autoimmune primary injury to the autonomic nervous system has resulted in tissue injury.” Resp't's Ex. D at 2. He expanded on that argument and maintained that in an autoimmune attack on the nervous system triggered by a vaccine, “you expect to see pathology[,]” such as the “beautiful pathology” visible through clinical testing seen in autoimmune autonomic ganglionopathy or Guillain-Barré syndrome. Tr. 193:23–194:3; Resp't's Ex. D at 2. He did not further elaborate on this argument or provide any supporting evidence in the form of medical literature or otherwise. *See, e.g.*, Resp't's Ex. D at 2. Dr. Low's exacting requirement of clinical evidence of pathologic change and/or tissue injury to show autoimmunity is inconsistent with the Program's standards. *See Capizzano*, 440 F.3d at 1325 (quoting *Althen*, 418 F.3d at 1280) (indicating that to satisfy prong one, a petitioner is not required to identify “specific biological

mechanisms” to establish causation, nor are they required to present “epidemiologic studies, rechallenge[] the presence of pathological markers or genetic disposition, or general acceptance in the scientific or medical communities.”). Therefore, I will not require such of Petitioner.

More recent studies corroborate earlier studies that show POTS can have an autoimmune etiology based on the presence of adrenergic autoantibodies. As recently as 2020, Kharraziha et al. used a cell-based assay and determined that sera from POTS patients contained adrenergic receptor antibodies “to a higher degree compared with [healthy] controls.” Pet’r’s Ex. 64 at 1. The authors found this supported the “predictive value” of the role of such autoantibodies as a cause of POTS. *See id.* Respondent’s expert Dr. Low took issue with the predictive value that these receptors have in causing POTS, primarily because the authors used a bioassay, a lesser test than the ELISA. I do not find Dr. Low’s argument convincing, as he again demonstrated the same blanket refusal to acknowledge the authors’ findings as credible. While Petitioner’s own expert admitted “we do not know if G protein antibodies are causative of a disease process or induced by disease[,]” Tr. 135:18–21, Petitioner’s introduction of a recent study that bolsters earlier findings and the role of such autoantibodies provides support for the autoimmune etiology of POTS. It is true that Dr. Kinsbourne agreed that while some studies have shown antibodies have been found in patients with POTS, such evidence is “not sufficient to declare” POTS an autoimmune disease. Tr. 132:21–25. However, I agree with his statement that while the medical literature does not provide scientific certainty for POTS being immune-mediated, it provides “a very high probability” that it could be. Tr. 108:4–6.

b. Flu Vaccine as Trigger of POTS via Molecular Mimicry

While I have determined that autoimmunity can explain the pathogenesis of POTS, the evidence does not explain how the flu vaccine can trigger such a response. Petitioner relied on a cross-reaction between vaccine-generated autoantibodies and antibodies associated with GPCRs, adrenergic receptor antibodies. This theory is based on the structural similarities between amino acid sequences within the viral protein components of the flu vaccine and the self-protein sympathetic nervous system receptors that might mistakenly get attacked by such autoantibodies triggered by the vaccine. Indeed, Petitioner’s medical literature and expert testimony does not address or explain how the flu vaccine could trigger such autoantibodies and cause POTS. In fact, Petitioner’s own expert provided the best evidence against his theory of vaccine causation. Dr. Kinsbourne could not cite to any evidence that supported his position that the flu vaccine could induce GPCR antibodies. Instead, he stated he was “sure” he did not submit evidence that establishes the flu vaccine can trigger these antibodies. *See* Tr. 137:15–17, 138:2–139:2. He also conceded that no studies have been done that relate to POTS post flu “or any vaccination[.]” Pet’r’s Ex. 29 at 7. While exact certainty and epidemiological studies are not required in the Program, Petitioner was unable to cite to *any* evidence that suggests a reason to find it likely that the proposed autoimmune cross-reaction triggered by the flu vaccine does, in fact, occur. *See Knudsen*, 35 F.3d at 548–49; *Capizzano*, 440 F.3d at 1325 (quoting *Althen*, 418 F.3d at 1280–81) (finding a petitioner does not need to identify specific biological mechanisms or scientific and “objective confirmation” of the medical theory with medical documentation).

The Gunning et al. study notes an association between vaccination generally and POTS. Pet’r’s Ex. 47 at 8. The authors indicated that a number of studies have reported molecular mimicry

associated with autoimmune diseases, and that POTS is such a condition based on the presence of several antibodies in patients. *See id.* Likewise, a case report by Tsai et al. documented a patient who developed POTS following receipt of the H1N1 influenza vaccination. Pet'r's Ex. 14 at 2. The authors concluded that the mechanism of the flu vaccine causing neurological complications is not clear, but they documented the presence of an "unidentified antibody" as the proposed cause of POTS. *Id.* at 3. While such reports reflect the fact that molecular mimicry has been proposed as a potential mechanism in the post vaccination onset of POTS, this conclusion is not applicable to the seasonal flu vaccine at issue here without explanation. The Tsai et al. study documented an association between a type of flu vaccine and POTS, but the authors did not set forth a medical theory casually connecting the vaccine to the development of POTS.

Petitioner's main support was found in case reports that documented an association between the HPV vaccine and POTS via molecular mimicry. *See, e.g.,* Pet'r's Ex. 16. However, Petitioner did not receive the HPV vaccine. While such comparisons can be helpful in certain circumstances, Petitioner's expert did not sufficiently explain the basis for his comparison between the flu and HPV vaccines. Petitioner has therefore failed to show that her proposed theory of molecular mimicry applies to the flu vaccine and POTS. *See W.C. v. Sec'y of Health & Hum. Servs.*, 704 F.3d 1352, 1360 (2013) (finding that a petitioner cannot prevail by simply invoking the term 'molecular mimicry,' or by showing that molecular mimicry is a valid theory to explain how *other* triggers may have induced *other* diseases and determining that a petitioner must produce additional evidence that molecular mimicry can cause the flu vaccine to cause POTS). If I accepted Petitioner's assertion that molecular mimicry could be used to demonstrate an association between any combination of antigens and autoimmune injuries, *Althen* prong one "would be rendered meaningless." *See Caves v. Sec'y of Health & Hum. Servs.*, 100 Fed. Cl. 119, 135 (2011), *aff'd*, 463 F. App'x. 932 (2012); *see also McKown v. Sec'y of Health & Hum. Servs.*, No. 15-1451, 2019 WL 4072113, *50 (Fed. Cl. Spec. Mstr. July 15, 2019) ("[M]erely chanting the words 'molecular mimicry' in a Vaccine Act case does not render a causation theory scientifically reliable, absent additional evidence specifically tying the mechanism to the injury and/or the vaccine in question.").

Lastly, I cannot ignore the fact that to date, no claim has succeeded in the Program that alleged vaccine-caused POTS. Indeed, that pertains to all covered vaccines in the Program. *See, e.g., Hibbard v. Sec'y of Health & Hum. Servs.*, 698 F.3d 1355 (Fed. Cir. 2012) (affirming the special master's dismissal of a case alleging that the flu vaccine caused POTS); *America v. Sec'y of Health & Hum. Servs.*, No. 17-542V, 2022 WL 278151, at *27 (Fed. Cl. Spec. Mstr. Jan. 4, 2022) (ruling against the petitioner's argument that the HPV vaccine can interfere with the nervous system sufficient to cause POTS, autonomic dysfunction or generalized dysautonomia, or vasovagal syncope); *Hughes v. Sec'y of Health & Hum. Servs.*, No. 16-930V, 2021 WL 839092, at *30 (Fed. Cl. Spec. Mstr. Jan. 4, 2021) (denying compensation for a claim involving the HPV vaccine and POTS); *E.S. v. Sec'y of Health & Hum. Servs.*, No. 17-480V, 2020 WL 9076620, at *49–51 (Fed. Cl. Spec. Mstr. Nov. 13, 2020); *Balasco v. Sec'y of Health & Hum. Servs.*, No. 17-215V, 2020 WL 1240917, at *33–34 (Fed. Cl. Spec. Mstr. Feb. 14, 2020); *Combs v. Sec'y of Health & Hum. Servs.*, No. 14-878V, 2018 WL 1581672 (Fed. Cl. Spec. Mstr. Jan. 31, 2017); *Turkopolis v. Sec'y of Health & Hum. Servs.*, No. 10-351V, 2014 WL 2872215 (Fed. Cl. Spec. Mstr. May 30, 2014). This is not to say that a future case alleging vaccine-caused POTS cannot and will not succeed in the Program based on the evolving understanding of the post vaccination

pathogenesis of the condition. However, Petitioner’s claim is not one of those cases. Therefore, Petitioner has failed to satisfy the first prong of *Althen* by a preponderance of the evidence.

C. *Althen* Prongs Two and Three

Under the second prong of *Althen*, a petitioner must prove that the vaccine actually did cause the alleged injury in a particular case. *See Pafford*, 2004 WL 1717359, at *4; *Althen*, 418 F.3d at 1279. The second *Althen* prong requires proof of a logical sequence of cause and effect, usually supported by facts derived from a petitioner’s medical records. *Althen*, 418 F.3d at 1278; *Capizzano*, 440 F.3d at 1326; *Grant v. Sec’y of Health & Hum. Servs.*, 956 F.2d 1144, 1148 (Fed. Cir. 1992). A petitioner does not meet this obligation by showing only a temporal association between the vaccination and the injury; instead, the petitioner “must explain *how* and *why* the injury occurred.” *Pafford*, 2004 WL 1717359, at *4 (emphasis in original). The special master in *Pafford* noted petitioners “must prove [] both that [their] vaccinations were a substantial factor in causing the illness . . . and that the harm would not have occurred in the absence of the vaccination.” 2004 WL 1717359, at *4 (citing *Shyface*, 165 F.3d at 1352). A reputable medical or scientific explanation must support this logical sequence of cause and effect. *Hodges v. Sec’y of Health & Hum. Servs.*, 9 F.3d 958, 961 (Fed. Cir. 1993) (citation omitted). Nevertheless, “[r]equiring epidemiologic studies . . . or general acceptance in the scientific or medical communities . . . impermissibly raises a claimant’s burden under the Vaccine Act and hinders the system created by Congress” *Capizzano*, 440 F.3d at 1325–26. “[C]lose calls regarding causation are resolved in favor of injured claimants.” *Althen*, 418 F.3d at 1280. The record often includes “evidence of possible sources of injury” that can show alternate causes for the alleged vaccine-related injury. *See Stone v. Sec’y of Health & Hum. Servs.*, 676 F.3d 1373, 1379 (Fed. Cir. 2012).

In Program cases, contemporaneous medical records and the opinions of treating physicians are favored. *Capizzano*, 440 F.3d at 1326 (citing *Althen*, 418 F.3d at 1280). Indeed, when reviewing the record, a special master must consider the opinions of treating physicians. *Id.* This is because “treating physicians are likely to be in the best position to determine whether ‘a logical sequence of cause and effect show[s] that the vaccination was the reason for the injury.’” *Id.* In addition, “[m]edical records, in general, warrant consideration as trustworthy evidence. The records contain information supplied to or by health professionals to facilitate diagnosis and treatment of medical conditions. With proper treatment hanging in the balance, accuracy has an extra premium. These records are also generally contemporaneous to the medical events.” *Cucuras v. Sec’y of Health & Hum. Servs.*, 993 F.2d 1525, 1528 (Fed. Cir. 1993). While a special master must consider these opinions and records, they are not “binding on the special master or court.” 42 U.S.C. § 300aa-13(b)(1). Rather, when “evaluating the weight to be afforded to any such . . . [evidence], the special master . . . shall consider the entire record” *Id.* There is no presumption that medical records are accurate and complete as to all the patient’s physical conditions. *Kirby v. Sec’y of Health & Hum. Servs.*, 997 F.3d 1378, 1383 (Fed. Cir. 2021) (finding that “[b]ecause a reasonable fact finder could conclude that [the petitioner’s] testimony [wa]s not inconsistent with her medical records . . . it was not arbitrary and capricious for the special master to credit [the petitioner’s] testimony” over her medical records). Where there are inconsistencies, special masters are within their discretion to award contemporaneous medical records greater weight than later conflicting testimony. *See Cucuras*, 993 F.2d at 1528 (holding that the special master’s

reliance on contemporaneous medical records over conflicting oral testimony given after the fact was not arbitrary or capricious); *see also Burns v. Sec’y of Health & Hum. Servs.*, 3 F.3d 415, 417 (Fed. Cir. 1993) (holding that the decision of whether to accord greater weight to contemporaneous medical records or later given testimony is “uniquely within the purview of the special master”). Indeed, the Court of Federal Claims has outlined four potential explanations for inconsistencies between contemporaneously created medical records and later testimony: (1) a person’s failure to recount to the medical professional everything that happened during the relevant time period; (2) the medical professional’s failure to document everything reported to her or him; (3) a person’s faulty recollection of the events when presenting testimony; or (4) a person’s purposeful recounting of symptoms that did not exist. *LaLonde v. Sec’y of Health & Hum. Servs.*, 110 Fed. Cl. 184, 203–04 (2013), *aff’d*, 746 F.3d 1334 (Fed. Cir. 2014).

Under the third prong of *Althen*, a petitioner must show that the timing of the injury fits with the causal theory. *See Althen*, 418 F.3d at 1278. For example, if a petitioner’s theory involves a process that takes several days to develop after vaccination, an injury that occurred within a day of vaccination would not be temporally consistent with that theory. Conversely, if the theory is one that anticipates a rapid development of a reaction post-vaccination, the development of the alleged injury weeks or months post vaccination would not be consistent with that theory. *See de Bazan v. Sec’y of Health & Hum. Servs.*, 539 F.3d 1347, 1352 (Fed. Cir. 2008). Causation-in-fact cannot be inferred from temporal proximity alone. *See Grant*, 956 F.2d at 1148; *Thibaudeau v. Sec’y of Health & Hum. Servs.*, 24 Cl. Ct. 400, 403–04 (1991); *see also Hasler v. United States*, 718 F.2d 202, 205 (6th Cir. 1983) (“Without more, [a] proximate temporal relationship will not support a finding of causation.”).

a. Petitioner’s Preexisting Symptoms

Petitioner has failed to establish by preponderant evidence a logical sequence of cause and effect showing that her October 8, 2013 flu vaccination was the reason for her development of POTS pursuant to *Althen* prong two. Specifically, the evidence does not establish it more likely than not that Petitioner’s condition began after her vaccination. A petitioner cannot succeed on a claim of causation-in-fact where the alleged condition preexisted the vaccination. *See W.C.*, 704 F.3d at 1354–55 (affirming the special master’s denial of compensation of a claim of causation-in-fact because “[i]f a petitioner has a disorder before being vaccinated, the vaccine logically cannot have caused the disorder[.]”). Therefore, I must begin my analysis of *Althen* prong two with a discussion of Petitioner’s preexisting symptoms.

From the start of the case, Petitioner’s medical records revealed that she was suffering from symptoms prior to her flu vaccination that were similar to her post-vaccination symptoms. In light of this, I (and the special master to whom this case was assigned before me), explicitly afforded Petitioner multiple opportunities to propose a significant aggravation theory. *See* ECF Nos. 23, 26, 37. Despite such opportunities, Petitioner’s expert Dr. Kinsbourne explicitly stated that “[i]f there had been a prior dysautonomia one would invoke very significant aggravation of that prior condition, but prior POTS is not in evidence.” Pet’r’s Ex. 32 at 2. Although Petitioner indicated during a status conference held on January 28, 2016, her intention to amend her claim and include a significant aggravation cause of action, she ultimately did not do so. *See* ECF No. 23 at 1. Furthermore, Petitioner has not offered evidence of a biological mechanism consistent with

significant aggravation. As such, a significant aggravation claim is not before me to consider. *See Hirmiz v. Sec’y of Health & Hum. Servs.*, 119 Fed. Cl. 209, 220 (2014) (rejecting the petitioners’ attempt to raise a significant aggravation claim after a special master issued an entitlement decision because the evidence “cited by petitioners that would support a significant-aggravation theory . . . was submitted in support of separate and distinct theories of causation[] . . . [that involved] neurological dysfunction beginning *after* the administration of the influenza vaccine[]”) (emphasis in original).

Petitioner’s medical record shows by preponderant evidence that for approximately two years prior to her October 8, 2013 flu vaccination, she exhibited symptoms of orthostatic intolerance; and she was subsequently diagnosed with POTS, an orthostatic disorder. Her symptoms of orthostatic intolerance included tachycardia, palpitations, and dizziness/lightheadedness. For example, on January 12, 2011, Petitioner presented to the ER with complaints of palpitations and tachycardia. *See* Pet’r’s Ex. 21 at 49, 150. Petitioner described the sensation as a feeling that her “heart rate kept beating fast.” *Id.* at 150. The next year, on January 23, 2012, Petitioner complained of palpitations to her PCP, for which she received a referral to a cardiologist. *See* Pet’r’s Ex. 13 at 1. On June 10, 2012, Petitioner experienced another episode of tachycardia requiring her to go to the ER. *See* Pet’r’s Ex. 67. Petitioner’s medical records, affidavits, and testimony collectively reflect that she reported palpitations, shaking, dizziness, and lightheadedness on this occasion. *See id.* at 5, 11; Tr. 13:16–21; Pet’r’s Ex. 28 ¶ 4. During a visit on April 24, 2013, Petitioner’s PCP noted that Petitioner exhibited an irregular heartbeat/palpitations on exam. Pet’r’s Ex. 13 at 23.

Post vaccination, Petitioner reported similar complaints of tachycardia and dizziness on several dates during November of 2013, including on November 4, 18, and 19, 2013. *See* Pet’r’s Ex. 4 at 151, 146, 140. In fact, when Petitioner complained of tachycardia and dizziness on November 18, 2013, she indicated that she had been experiencing increased palpitations for the past two months. *See id.* at 146. Petitioner addressed this notation in an affidavit drafted on February 23, 2016, approximately three years after this visit. She merely stated that while she is aware her records reflect such symptoms as persisting for two months, “that is not an accurate description of when [her] symptoms started.” Pet’r’s Ex. 28 ¶ 6. However, Petitioner could not support her assertion that such records were incorrect and wrote that she “d[id] not specifically recall what [she] reported [to treaters] at that time[.]” *Id.*

While there is no presumption that medical records are accurate, in order for Petitioner to overcome the statements in her medical records, she must offer evidence that does not conflict with such statements. *See Kirby*, 997 F.3d at 1383–84 (rejecting the presumption that medical records are accurate and complete as to all the patient’s physical conditions and noting that in the absence of this presumption, the reasonable fact finder was within his discretion to consider the medical and testimonial record to conclude that the petitioner’s medical records did not conflict with later testimony, and to credit such later testimony). Indeed, when witness testimony is offered to overcome the weight of contemporaneous medical records, such testimony must be “consistent, clear, cogent, and compelling.” *Matthews v. Sec’y of Health & Hum. Servs.*, No. 19-414V, 2021 WL 4190265, at *5 (Fed. Cl. Spec. Mstr. Aug. 19, 2021), *mot. for review den’d*, 157 Fed. Cl. 777 (citing *Blutstein v. Sec’y of Health & Hum. Servs.*, No. 90-2808V, 1998 WL 408611, at *5 (Fed. Cl. Spec. Mstr. June 30, 1998)). Further, the Court of Federal Claims has acknowledged that “the

absence of a reference to a condition or circumstance [in contemporaneous medical records] is much less significant than a reference which negates the existence of the condition or circumstance.” See *id.* (citing *Shapiro v. Sec’y of Health & Hum. Servs.*, 101 Fed. Cl. 532, 541 (2011); *Murphy v. Sec’y of Health & Hum. Servs.*, 23 Cl. Ct. 726, 733 (Fed. Cl. 1991), *aff’d*, 968 F.2d 1226 (Fed. Cir. 1992)).

As noted, Petitioner’s medical record from November 18, 2013, indicates that she told treaters her tachycardia, dizziness, and palpitation symptoms had been present for two months. Pet’r’s Ex. 4 at 146. It was only years later, during her written testimony, that she said that is not when her symptoms began. Testimony offered after the events in question is less reliable than contemporaneous reports when the motivation for accurate explication of symptoms is more immediate. See *Reusser v. Sec’y of Health & Hum. Servs.*, 28 Fed. Cl. 516, 523 (1993) (“[W]ritten documentation recorded by a disinterested person at or soon after the event at issue is generally more reliable than the recollection of a party to a lawsuit many years later.”). Petitioner’s medical record therefore directly negates and contradicts her assertion that she was not experiencing such symptoms around or before November 18, 2013. See *Matthews*, 2021 WL 4190265, at *5 (citing *Shapiro*, 101 Fed. Cl. at 541).

More importantly, Petitioner’s reasoning for the discrepancy between her medical record and later testimony is not consistent, clear, cogent, or compelling in as much as she could not explain why such records would incorrectly reflect that her symptoms persisted for two months. See *Matthews*, 2021 WL 4190265, at *5. Instead, she admitted that she does not “specifically recall what [she] reported at that time[.]” Pet’r’s Ex. 28 ¶ 6. It is difficult to credit Petitioner’s statement made in an affidavit authored approximately three years after the date of the visit, especially in light of her admitted inability to remember what she told treaters. See *Reusser*, 28 Fed. Cl. at 523. I must also acknowledge that there is a tendency in human nature to remember things in a way that best fits within the narrator’s perspective of what happened. See *LaLonde*, 110 Fed. Cl. at 203. More so, the Program has long recognized that when witness testimony conflicts with contemporaneous medical records, the Court may accord such testimony lesser weight. *Cucuras*, 993 F.2d at 1528; *Rickett v. Sec’y of Health & Hum. Servs.*, 468 F. App’x. 952, 958 (Fed. Cir. 2011) (holding that when medical records and testimony are “inconsistent, a special master may give greater weight to the medical records”). As a result, I find preponderant evidence that Petitioner’s medical record shows preexisting symptoms of tachycardia, dizziness, and palpitations.

Petitioner’s preexisting symptoms also included SOB. Petitioner experienced numerous episodes of SOB throughout 2012 and pre vaccination in 2013. Petitioner reported increased respiratory issues for the last two years on January 28, 2012, which indicates her respiratory problems began in January of 2010. Pet’r’s Ex. 13 at 3. On March 21, 2013, Petitioner reported SOB and indicated that it had been “off/on since Dec[ember of 2012].” *Id.* at 5. She complained of SOB again on April 24 and June 24, 2013. See *id.* at 22–23, 27. She experienced the same SOB post vaccination in October and November 2013, and even reported that it had been occurring for several months prior. For instance, on October 14, 2013, less than one week post vaccination, Petitioner reported that she had been experiencing SOB for the last six months. Pet’r’s Ex. 23 at 1. On November 19, 2013, Petitioner reiterated that she had been having SOB for the “last few months.” Pet’r’s Ex. 4 at 159. While Petitioner argued her history of SOB could be explained by

her asthma diagnosis, her explanation is not sufficiently supported by the record. Indeed, Dr. Low relied on the results of Petitioner's March 20, 2014 spirometry testing to highlight the lack of evidence of asthma. In fact, Petitioner's spirometry testing showed full respiratory function. *See id.* at 196; *see also* Tr. 172. Without diagnostic evidence of asthma, I find Dr. Low's position that Petitioner's SOB symptoms were instead related to her dysautonomia, to be persuasive.

Petitioner's medical records therefore demonstrate that she experienced several symptoms prior to October 8, 2013, that were similar in nature to the symptoms she experienced post vaccination and are consistent with autonomic dysfunction/dysautonomia and POTS. They also show that she repeatedly reported such symptoms pre vaccination. While Petitioner maintained that her pre vaccination episodes were entirely unrelated to her POTS, her assertions are unavailing. Indeed, Petitioner did not successfully differentiate her pre and post vaccination symptoms of palpitations/tachycardia, dizziness, and SOB in terms of nature or severity, she merely argued her pre vaccination symptoms were caused by factors other than her POTS, such as anxiety and dehydration.

Petitioner attempted to support her position that her POTS began post vaccination with the fact that she was never diagnosed with POTS prior to her October 8, 2013 flu vaccination. Petitioner's date of diagnosis provides no insight into her condition onset, without the context of her medical record. *See W.C.*, 704 F.3d at 1358. In fact, Dr. Low asserted that he, as one of the leading autonomic specialists, likewise would not have diagnosed Petitioner formally with POTS in 2011 because such a "laboratory" diagnosis of the condition can only be confirmed with a tilt-table test. *See Resp't's Ex. C* at 3; Tr. 183:1-4. However, Dr. Low's description of POTS as requiring only orthostatic intolerance associated with tachycardia is persuasive and consistent with the *Dorland's* definition of POTS (noting that POTS refers to a "group of symptoms . . . that sometimes occur when a person assumes an upright position, including tachycardia, tremulousness, [and] lightheadedness . . .").⁹⁰ As Petitioner did not undergo a tilt-table test until late November of 2013 and did not present to an autonomic specialist until 2014, I do not find it more likely than not that she would have received a diagnosis of POTS pre vaccination despite the presence of autonomic symptoms.

Petitioner's claim likewise fails under *Althen* prong three because if a condition began before vaccination, it would be logically impossible to infer that Petitioner's injury occurred "within a timeframe for which . . . it is medically acceptable to infer causation-in-fact." *W.C.*, 704 F.3d at 1358. As I have already determined that Petitioner has not presented preponderant evidence that her condition began post vaccination, and she has failed to establish a biological mechanism within which to assess the onset of her condition, it is impossible for me to analyze or for Petitioner to satisfy her claim under prong three. Therefore, a more thorough discussion of *Althen* prong three is inapplicable.

b. Petitioner's Post-vaccination POTS Manifestations

Petitioner cannot establish a logical sequence of cause and effect connecting her vaccination with her development of POTS, as there is preponderant evidence that her POTS predated her vaccination. Additionally, the submitted evidence, including medical literature and

⁹⁰ *See supra*, note 3 (defining POTS).

credible expert testimony, establishes by preponderant evidence that dehydration, deconditioning,⁹¹ and anxiety are all potential causes of the manifestation of Petitioner's orthostatic intolerance and POTS post vaccination. *See* Resp't's Exs. C, Tabs 1, 3, 5–6; Resp't's Ex. A, Tab 7 at 1, 3; Resp't's Ex. A, Tab 1 at 3–4, 6; *see also* Tr. 165:3–9, 179:2–10, 203, 209–10. I will not go so far as to determine whether either or all of these conditions are alternative cause(s) for Petitioner's POTS. Such a determination is unnecessary pursuant to prong two of *Althen*. Petitioner did not meet her burden with respect to any *Althen* prong and cannot make a prima facie case for entitlement. Therefore, Respondent is under no obligation to establish an alternative cause. I will, however, discuss alternative causation as part of my analysis of Petitioner's medical records and her causation claim. Proof of a "logical sequence of cause and effect" will eliminate potential likely alternatives. *Walther v. Sec'y of Health & Hum. Servs.*, 485 F.3d 1146, 1151 (Fed. Cir. 2007).

When Petitioner presented to the ER on November 8, 2013, she had been experiencing diarrhea ten times per day for the past ten days.⁹² *See* Pet'r's Ex. 1 at 3. Her treater's impression record noted dehydration. *See, e.g.*, Pet'r's Ex. 4 at 170. The record also reflects that Petitioner was experiencing heightened anxiety around this time. *See id.* Petitioner's worsening symptoms on November 8, 2013, caused her to remain in the ER until November 10, 2013. Following this hospitalization, Petitioner then became inactive and eventually homebound and bedridden. In fact, Petitioner repeatedly related this time period as the beginning of her diminished activity and capabilities. For instance, on December 20, 2013, Petitioner reported being bedridden for the past month, roughly since her November 2013 hospitalization. Pet'r's Ex. 4 at 123. By January of 2014, Petitioner received approval for home health services for IV fluids because she was homebound as a result of her POTS symptoms. Pet'r's Ex. 3 at 50. On February 11, 2014, she indicated that she had been homebound for the previous three months. Pet'r's Ex. 4 at 59. The medical literature by Parsaik et al. submitted by Respondent provides preponderant evidence that a one to three month period of discontinuous bedrest is sufficient deconditioning to trigger POTS symptoms. *See, e.g.*, Resp't's Ex. A, Tab 7 (indicating that a two-week, non-continuous period is enough to produce effects of deconditioning).

I do, however, need to delve deeper into Petitioner's arguments on dehydration. Petitioner alleged in her petition that her flu vaccine caused hyperadrenergic POTS with hypovolemia. Pet. at 1. Yet, Petitioner has put forth very limited evidence regarding her hypovolemia. Based on Dr. Kinsbourne's limited testimony, it is not clear to me whether he is referring to hypovolemia interchangeably with dehydration. For example, he testified that Petitioner had "been hypovolemic many times and had infusions to correct that." Tr. 125:14–15. This statement appears to allude to Petitioner's treatment with IV fluids to correct her dehydration caused by her POTS "flare ups."

⁹¹ I must note that some medical literature claims deconditioning in particular to be a secondary factor of POTS, rather than a primary mechanism. *See* Pet'r's Exs. 35, 40.

⁹² Petitioner's treaters indicated that her diarrhea was "likely [caused by a] a viral syndrome" or viral gastroenteritis. Pet'r's Ex. 4 at 156, 170. Petitioner's labs neither confirmed nor denied this assessment. However, Petitioner's treaters' impressions attributable to a specific, albeit ambiguous, cause is consistent with Dr. Low's testimony that POTS would not present for the first time with GI symptoms. Even though the evidence shows GI symptoms are commonly seen in patients with POTS, Dr. Low's testimony that he has never seen POTS present that way among his "thousands" of POTS patients is convincing evidence that Petitioner's POTS likewise did not present that way.

See, e.g., Pet'r's Ex. 4 at 113–16 (noting that Petitioner was unable to keep up with her hydration requirement and that her POTS manifestations improved with IV fluids and hydration). I will not speculate as to Dr. Kinsbourne's understanding of hypovolemia,⁹³ or what he was referring to during such testimony, but I will point out that dehydration carries a different meaning. While dehydration is due to insufficient fluid intake or loss of body water, hypovolemia is defined as an “abnormally decreased volume of circulating blood in the body,” with the most common cause being a hemorrhage. *Dorland's* at 481, 908. The two terms are therefore not synonymous. Further, when asked on cross-examination about POTS associated with hypovolemia, Dr. Kinsbourne admitted that none of the literature he filed discusses hypovolemic POTS because he did not “think there was occasion to discuss it because there[is] not evidence that [Petitioner] was hypovolemic at the onset[.]” only subsequently. Tr. 122:11–15. Again, I do not know if Dr. Kinsbourne was referring to true hypovolemia or if he meant dehydration. It appears that the issue of hypovolemia was essentially glossed over by Petitioner's expert. Without arguments from Petitioner regarding a biological mechanism connecting the flu vaccine to POTS with hypovolemia, I cannot analyze her hypovolemia claim under any prong of *Althen*. Indeed, in light of Petitioner's expert's ambiguous testimony, I must afford Dr. Low's consistent and cohesive argument that dehydration and hypovolemia are separate causes of POTS more weight. *See* Tr. 179:5–10.

In addition to Petitioner's dehydration and deconditioning, which could themselves both have caused her worsening symptoms consistent with POTS, I asked Petitioner's expert Dr. Kinsbourne to tell me if he saw Petitioner's POTS “as relapsing because it [was] exacerbated by her other conditions, specifically her asthma and anxiety[.]” Tr. 145:16–18. He agreed that it “could be the case[.]” that such factors were “working together[.]” Tr. 145:18–20.⁹⁴ Indeed, during Petitioner's November 9, 2013 hospitalization, for what she considered to be the onset of her POTS, Petitioner's treaters thought strongly that her constellation of symptoms was anxiety-related. *See* Pet'r's Ex. 4 at 161. Cardiologist Dr. Gilbert noted on November 19, 2013, that anxiety was a possible cause of Petitioner's symptoms. *See id.* at 140. Even after she received her formal POTS diagnosis and throughout her treatment, Petitioner's treaters maintained that her symptoms were caused by her anxiety. On February 11, 2014, endocrinologist Dr. Purdy opined that anxiety was the cause of her symptoms. *Id.* at 59. Likewise, Petitioner's neurologist Dr. Chan implicated Petitioner's anxiety as the cause of her continued symptoms on April 25, 2014. Pet'r's Ex. 7 at 76. Notably, *none* of Petitioner's treaters attributed her autonomic symptoms and POTS diagnosis to her October 8, 2013 flu vaccination.

⁹³ Dr. Kinsbourne's testimony is minimally supported by Respondent's expert Dr. Low. Dr. Low also testified that symptoms of hypovolemia (orthostatic intolerance and orthostatic tachycardia) can improve with fluids in patients with hypovolemic POTS. Resp't's Ex. C at 1 (citing Resp't's Exs. C, Tabs 1, 3).

⁹⁴ I must reiterate that Petitioner and her expert were afforded several opportunities to present and opine as to any arguments that her October 8, 2013 flu vaccine significantly aggravated her prior condition. In fact, the presiding special master to whom this case was assigned before me explicitly told Petitioner to file an amended petition including a significant aggravation claim, and she did not. ECF No. 23 at 1. I also ordered Petitioner's expert to address a significant aggravation claim through a written report. ECF No. 37. Dr. Kinsbourne did so, but he directly opined against the possibility or viability of a significant aggravation claim and vehemently maintained that Petitioner's POTS began post vaccination. *See* Pet'r's Ex. 29 at 8; Pet'r's Ex. 31 at 1, 4; Pet'r's Ex. 32 at 2. Most notably, Dr. Kinsbourne wrote that “[i]f there had been a prior dysautonomia[.] one would invoke very significant aggravation of that prior condition, but prior POTS is not in evidence.” Pet'r's Ex. 32 at 2. Petitioner has not presented a significant aggravation claim for me to consider, and significant aggravation is therefore not at issue.

c. Autoimmune Response in Petitioner

Petitioner has failed to show that the flu vaccine can cause POTS via autoantibodies to GPCRs pursuant to *Althen* prong one. Additionally, Petitioner is unable to show evidence of an inflammatory or otherwise, immune-mediated response to establish that an autoimmune process occurred in her case pursuant to *Althen* prong two. Evidence of autoimmunity cannot be established merely with symptoms of POTS. Petitioner underwent extensive testing and a complete autoimmune workup on November 19, 2013, which yielded negative results. *See* Pet'r's Ex. 4 at 352–54; Tr. 223–24, 227. Petitioner also underwent additional testing in July of 2020 for the exact GPCR autoantibodies asserted to be causative in this case. Such results were likewise negative. *See* Pet'r's Ex. 62; *see also* Tr. 133:17–23. To show that she experienced an immune-mediated response, Petitioner's expert Dr. Kinsbourne seemingly relied only on the fact that “there is no alternative reasonable alternative explanation[.]” for Petitioner's POTS, other than an autoimmune etiology. *See* Tr. 92:18–20, 93:5–6. Such arguments do not provide persuasive support for evidence of an immune-mediated response following Petitioner's October 8, 2013 flu vaccination.

Likewise, Dr. Kinsbourne's argument that antibodies fade over time so the lack of antibodies in Petitioner's July 2020 tests was not surprising is irreconcilable with Petitioner's current condition. Dr. Kinsbourne was asked to explain how Petitioner's condition continued if her body was not actively engaged in an immune response seen with the presence of autoantibodies. Tr. 142:18–143:1. He stated that POTS is a condition wherein “there is an attack which causes damage and the agent may go away, but the damage remains.” Tr. 143:5–6. Dr. Kinsbourne implicated humoral and cellular immunity but was otherwise unable to explain how Petitioner's POTS continued if her antibodies were negative in July of 2020. *See* Tr. 145:2. In fact, he admitted that “it[is] unlikely that the antibodies were still actively injuring [Petitioner]” seven years later. Tr. 145:8–10. At best, he implicated T cells as responsible for continuing the damage, but he could not say so with any confidence and admitted that “[w]hat the cellular immunity does[, he] do[es not] know because there is[not] much written about it at this time.” Tr. 145:11–12. Alternatively, Dr. Low credibly explained consistent with principles of autoimmunity, that if an antibody is actually the cause of a condition, then the antibody would continue to be present for the duration of the disease. He explicitly stated that “POTS is a persistent condition,” and therefore he would expect to see the antibodies persist. *See* Tr. 191:4–12. Petitioner's argument that antibodies to GPCRs were present post vaccination and then disappeared throughout the course of her disease is not supported by preponderant evidence. Petitioner has failed to satisfy her burden pursuant to *Althen* prong two.

VI. Conclusion

After a careful review of the record, Petitioner has failed to prove by preponderant evidence that her POTS with hypovolemia were caused-in-fact by her October 8, 2013 flu vaccination. Accordingly, Petitioner's claim is hereby **DENIED** and her petition is **DISMISSED**.⁹⁵

IT IS SO ORDERED.

⁹⁵ Pursuant to Vaccine Rule 11(a), entry of judgment is expedited by the parties' joint filing of a notice renouncing the right to seek review.

s/Herbrina D. Sanders
Herbrina D. Sanders
Special Master