In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

Filed: February 13, 2023
Refiled in Redacted Form: April 3, 2023

J. G.,	*	PUBLISHED
	*	
Petitioner,	*	No. 20-664V
	*	
v.	*	Special Master Nora Beth Dorsey
	*	
SECRETARY OF HEALTH AND HUMAN SERVICES,	*	Entitlement; Hepatitis A Vaccine; Guillain-Barré Syndrome ("GBS").
	*	
Respondent.	*	
	*	

Anne Carrion Toale, Maglio Christopher and Toale, Sarasota, FL, for Petitioner.
Julia Marter Collison, U.S. Department of Justice, Washington, DC, for Respondent.

RULING ON ENTITLEMENT[1]

I. INTRODUCTION

On June 1, 2020, J.G. ("Petitioner") filed a petition for compensation under the National Vaccine Injury Compensation Program ("Vaccine Act" or "the Program"), 42 U.S.C. § 300aa-10 et seq. (2012).[2] Petitioner alleges that he suffered Guillain-Barré Syndrome ("GBS") as the result of a hepatitis A vaccination administered on April 19, 2018. Petition at 1-5 (ECF No. 1).

[1] Because this Ruling contains a reasoned explanation for the action in this case, the undersigned is required to post it 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). **This means the Ruling will be available to anyone with access to the Internet.** In accordance with Vaccine Rule 18(b), Petitioner has 14 days to identify and move to redact medical or other information, the disclosure of which would constitute an unwarranted invasion of privacy. If, upon review, the undersigned agrees that the identified material fits within this definition, the undersigned will redact such material from public access.

[2] The National Vaccine Injury Compensation Program is set forth in Part 2 of the National Childhood Vaccine Injury Act of 1986, Pub. L. No. 99-660, 100 Stat. 3755, codified as amended, 42 U.S.C. §§ 300aa-10 to -34 (2012). All citations in this Ruling to individual sections of the Vaccine Act are to 42 U.S.C. § 300aa.

Respondent argued against compensation, stating that "this case is not appropriate for compensation under the [Vaccine] Act." Respondent's Report ("Resp. Rept.") at 1 (ECF No. 18).

After carefully analyzing and weighing the evidence presented in this case in accordance with the applicable legal standards, the undersigned finds that Petitioner has provided preponderant evidence that his hepatitis A vaccine caused his GBS, satisfying Petitioner's burden of proof under Althen v. Secretary of Health & Human Services, 418 F.3d 1274, 1280 (Fed. Cir. 2005). Accordingly, Petitioner is entitled to compensation.

II. ISSUES TO BE DECIDED

Diagnosis and causation are in dispute. As to diagnosis, Petitioner's experts, Dr. S. Sohail Ahmed and Dr. Kazim A. Sheikh, opine Petitioner, more likely than not, developed GBS. Petitioner's Exhibit ("Pet. Ex.") 12 at 20; Pet. Ex. 14 at 1; Pet. Ex. 16 at 6-10. Respondent's expert, Dr. Thomas Leist, opines Petitioner's symptoms are not consistent with GBS and "that more likely than not [Petitioner] sustained or aggravated a lumbar disc herniation and aggravated likely preexisting cervical disc disease while weight training and lifting weights overhead on May 25, 2018." Resp. Ex. A at 7, 9.

Regarding causation, Petitioner contends he has met his burden of proof under all three Althen prongs. Pet. Memorandum of Law in Support of Pet. Motion for Findings of Fact and Conclusions of Law Regarding Entitlement to Compensation ("Pet. Mem."), filed Apr. 4, 2022, at 21-43 (ECF No. 56). Respondent disagrees. Resp. Response to Petitioner's Motion for Ruling on the Record ("Resp. Response"), filed May 9, 2022, at 10-22 (ECF No. 57).

III. BACKGROUND

A. Medical Terminology

GBS is a "rapidly progressive ascending motor neuron paralysis of unknown etiology, frequently seen after an enteric or respiratory infection." Guillain-Barré Syndrome, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=110689 (last visited Dec. 29, 2022). GBS typically "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 [("CSF")] without a corresponding increase in cells." Id.; see also Pet. Ex. 12-2 at 2;[3] Pet. Ex. 18 at 2.[4]

[3] Francine J. Vriesendorp, Guillain-Barré Syndrome in Adults: Clinical Features and Diagnosis, UpToDate, https://www.uptodate.com/contents/guillain-barre-syndrome-in-adults-pathogenesis-clinical-features-and-diagnosis (last updated Dec. 4, 2018).

[4] James J. Sejvar et al., Guillain-Barré Syndrome and Fisher Syndrome: Case Definitions and Guidelines for Collection, Analysis, and Presentation of Immunization Safety Data, 29 Vaccine 599 (2011). Respondent's expert, Dr. Leist, also cited this article. Resp. Ex. E, Tab 5.

Weakness usually begins in the legs but may also begin in the arms or facial muscles. Pet. Ex. 12-2 at 2. "[W]eakness is associated with decreased or absent deep tendon reflexes and tends to be relatively symmetric." Pet. Ex. 18 at 2. "Paresthesias in the hands and feet accompany the weakness in more than 80 percent of patients, but sensory abnormalities on examination are frequently mild." Pet. Ex. 12-2 at 2. "Paresthesias and subjective numbness or tingling may be an early feature and tends to affect the distal extremities." Pet. Ex. 18 at 2. Additionally, "[p]ain due to nerve root inflammation, typically located in the back and extremities, can be a presenting feature and is reported during the acute phase by two-thirds of patients with all forms of GBS." Pet. Ex. 12-2 at 2; see also Resp. Ex. C, Tab 10 at 2 (explaining "many patients with GBS [] report back pain, probably relating to inflammation of nerve roots").[5] "GBS usually progresses over a period of about two weeks. By four weeks after the initial symptoms, [more than] 90 percent of GBS patients have reached the nadir of the disease." Pet. Ex. 12-2 at 3; see also Pet. Ex. 12-24 at 2;[6] Pet. Ex. 18 at 2.

Albuminocytologic dissociation, or elevated CSF protein with a normal white blood cell count, "is present in up to 66 percent of patients with GBS at one week after onset of symptoms." Pet. Ex. 12-2 at 3; see also Pet. Ex. 12-24 at 3. Electrodiagnostic studies may show evidence of GBS and can be used to confirm diagnosis. Pet. Ex. 12-2 at 3; Pet. Ex. 12-24 at 3; Pet. Ex. 18 at 3.

"Although the underlying etiology and pathophysiology of GBS are not completely understood, it is believed that immune stimulation plays a central role in its pathogenesis." Pet. Ex. 18 at 2. GBS "is considered to be an immune-mediated disorder resulting from generation of autoimmune antibodies and/or inflammatory cells which cross-react with epitopes on peripheral nerves and roots, leading to demyelination or axonal damage or both." Id.; see also Pet. Ex. 12-2 at 1 (noting GBS is thought to result from an immune response directed towards the myelin or the axon of peripheral nerve due to molecular mimicry). "Two thirds of cases are preceded by symptoms of upper respiratory tract infection or diarrhea," with *Campylobacter jejuni* ("*C. jejuni*") as the most common precipitating infection. Pet. Ex. 12-24 at 1; see also Pet. Ex. 12-2 at 1; Pet. Ex. 18 at 3; Resp. Ex. A, Tab 1 at 2;[7] Resp. Ex. C, Tab 10 at 2. GBS may also develop after vaccination, surgery, trauma, and bone-marrow transplantation. Pet. Ex. 12 at 5; Pet. Ex. 12-2 at 1; Pet. Ex. 12-22 at 1-2;[8] Pet. Ex. 12-24 at 1-2, 6-7; Pet. Ex. 18 at 3; Resp. Ex. A, Tab 1 at 2; Resp. Ex. C, Tab 10 at 2.

---

[5] Benjamin R. Wakerley & Nobuhiro Yuki, Mimics and Chameleons in Guillain-Barré and Miller Fisher Syndromes, 15 Practical Neurology 90 (2015).

[6] Nobuhiro Yuki & Hans-Peter Hartung, Guillain-Barré Syndrome, 366 New Eng. J. Med. 2294 (2012).

[7] Chuxin Huang et al., Trauma-Related Guillain-Barré Syndrome: Systematic Review of an Emerging Concept, 11 Frontiers Neurology 1 (2020).

[8] Eitan Israeli et al., Guillain-Barré Syndrome—A Classical Autoimmune Disease Triggered by Infection or Vaccination, 42 Clinical Revs. Allergy & Immunology 121 (2012).

B. Procedural History

On June 1, 2020, Petitioner filed his petition, medical records, and an affidavit. Petition; Pet. Exs. 1-7. Petitioner filed additional medical records on September 8, 2020. Pet. Ex. 8. Respondent filed his Rule 4(c) Report on November 10, 2020, arguing against compensation. Resp. Rept. at 1.

Petitioner filed an expert report from Dr. Ahmed on March 12, 2021. Pet. Ex. 12. Respondent filed expert reports from Dr. Leist and Dr. Robert Fujinami on May 11, 2021. Resp. Exs. A, C. On June 9, 2021, Petitioner filed a responsive expert report from Dr. Ahmed. Pet. Ex. 14. Petitioner filed additional records on June 24, 2021. Pet. Ex. 15. On July 26, 2021, Respondent filed a supplemental expert report from Dr. Leist, and Petitioner filed an expert report from Dr. Sheikh on October 20, 2021. Resp. Ex. E; Pet. Ex. 16.

A Rule 5 conference was held on November 2, 2021. Rule 5 Order dated Nov. 2, 2021 (ECF No. 41). The undersigned preliminarily found Petitioner's correct diagnosis is GBS and that Petitioner would be entitled to compensation if this case were to go to hearing. Id. at 1-2. The parties agreed to engage in informal settlement discussions. Id. at 2.

Thereafter, Petitioner filed a declaration and medical records in November and December 2021. Pet. Exs. 20-22. The parties were unable to resolve the case informally and requested that it be resolved through a ruling on the record. Pet. Status Rept., filed Feb. 1, 2022 (ECF No. 52); see also Rule 5 Order at 2.

Petitioner filed her motion for ruling on the record on April 4, 2022. Pet. Mem. Respondent filed his responsive brief on May 9, 2022. Resp. Response. Petitioner did not file a reply.

This matter is now ripe for adjudication.

C. Factual History

1. Medical History

At 38 years of age, Petitioner received a hepatitis A vaccination (HAVRIX) on April 19, 2018. Pet. Ex. 1 at 2. Petitioner had no relevant past medical history. Resp. Response at 1-2.

On June 4, 2018, Petitioner presented to his primary care physician complaining of tingling in his feet, hands, and tongue as well as leg cramps for two weeks. Pet. Ex. 3 at 379. Petitioner reported his symptoms

> started last Friday (10 days ago)[9] when he was working out at the gym. He state[d] that he was lifting kettle bells and felt a weird sensation in his low back.

[9] Ten days before would have been Friday, May 25, 2018.

> He stopped that exercise and sat down on a weight machine and started to feel his feet tingle. This continued throughout the day and then he started feeling tingling in his hands. By Tuesday,[10] he was having cramping in his right leg and hip. This past Saturday,[11] his tongue started tingling.

Id. Petitioner also reported that "when his wife presse[d] deep on his back, he [could] feel the tingling sensation throughout his body." Id. He denied bowel or bladder incontinence. Id. Review of systems was positive for back pain, leg weakness, and numbness. Id. at 380. Physical examination revealed patellar reflexes of 2+ on the right and left side. Id. at 381. Assessments were tingling in extremities and acute right-sided low back pain without sciatica. Id. Petitioner was given a Medrol Dose Pak, labs were ordered, and Petitioner was instructed to stop heavy lifting or exercising and to follow up in four days. Id.

Petitioner returned three days later on June 7, 2018. Pet. Ex. 3 at 338. Petitioner reported worsening back pain, sore neck, and continued tingling in arms and legs. Id. at 339. He had been on a steroid dose pack for three days. Id. Petitioner reported the steroid provided him temporary pain relief and help with walking but wore off after a few hours. Id. He reported that as the steroid wears off, "he feels like his legs are weak and [] like he is going to fall." Id. Physical examination revealed patellar reflexes of 2+ on the right and left side, as well as tenderness in cervical back and bony tenderness in lumbar back. Id. at 340. Assessment included numbness and tingling of both lower extremities, acute bilateral low back pain without sciatica, weakness of both lower extremities, tingling in extremities, cervical pain, and myelopathy. Id. at 341. Magnetic resonance imaging ("MRI") of lumbar and cervical spine were ordered and Petitioner was referred to physical therapy ("PT"). Id.

Later that day, Petitioner had a PT evaluation with physical therapist McKenzie Emrick at Premier Therapy and Health Centers ("Premier"). Pet. Ex. 2 at 3. Petitioner reported symptom onset was May 25, 2018, and he reiterated his history. Id. He complained of increased low back pain and numbness and tingling in bilateral hands and feet. Id. Physical examination revealed decreased lumbar and cervical active range of motion as well as decreased strength bilaterally in hip and knee extensors and flexors, ankle dorsiflexors and plantar flexors, and shoulder flexors. Id. at 4-5. Ms. Emrick noted Petitioner reported increased weakness in bilateral legs, pain, and overall muscle tightness on some movements. Id. at 5. Petitioner also had increased weakness and difficulty with the right side more than the left. Id. Assessment was "bilateral hand and feet numbness/radicular symptoms with low back pain with resultant decrease in patient mobility, strength, [range of motion], and functional [activities of daily living]." Id. Petitioner attended additional PT sessions on June 8 and 11, 2018, until he was discharged on June 26. Id. at 7-14; Pet. Ex. 8 at 39-40, 48-49, 54-61.

MRI of the cervical spine conducted on June 13, 2018 noted degenerative disc disease most prominent at C5/C6 and C3/C4. Pet. Ex. 4 at 35-36. Lumbar spine MRI done the same day showed focal central disc herniation at L5/S1. Id. at 37-38.

---

[10] Tuesday was May 29, 2018.

[11] Saturday was June 2, 2018.

The following day, on June 14, 2018, Petitioner visited Lexington Clinic and saw neurosurgery certified physician assistant ("PA-C") Justin Sammons. Pet. Ex. 4 at 15. In a handwritten form completed the day before, on June 13, Petitioner noted his symptoms had persisted for three weeks. Id. at 20. He indicated his pain, which he described as burning and deep ache, would come and go and was usually a 2/10 on the pain scale. Id. Petitioner also reported symptoms of numbness, tingling, and weakness. Id. In a separate handwritten intake form completed on June 14, Petitioner also reported dizziness, night sweats, unintended weight loss, mouth dryness, stiff or swollen joints, problems sleeping, poor coordination, sexual dysfunction, and difficulty walking, swallowing, and with taste/smell. Id. at 19. Petitioner reiterated his symptoms began "around Memorial Day[12] when he was working out at the gym." Id. at 16. Petitioner reported that "[o]ver the last four days[,] his weakness ha[d] progressed that he [] had to use a rolling walker to help him ambulate. He ha[d] also developed significant difficulty rising from a chair and [was] unable to do so without the use of his arms." Id. Petitioner also reported loss of taste, swallowing difficulty, and inability to stop urinating voluntarily. Id.

Physical examination found 4/5 strength in bilateral lower and upper extremities, poor control of extremities through range of motion, and absent deep tendon reflexes in bilateral upper and lower extremities. Pet. Ex. 4 at 16-17. Assessment was muscle weakness. Id. at 17. PA-C Sammons and neurosurgeon Dr. Matthew Tutt reviewed the MRIs and found no explanation on MRI for Petitioner's symptoms. Id. They noted "[t]here [was] no indication for neurosurgical intervention." Id. Petitioner's "exam[ination] and history suggest[ed] a demyelinating process." Id. Brain and thoracic MRIs were ordered, and Petitioner was directed to see neurologist, Dr. Andrew Schneider for a neurologic evaluation. Id.

Thoracic spine and brain MRIs were done later that day, on June 14, 2018. Pet. Ex. 4 at 33-34. Thoracic spine impression was mid-thoracic spine degenerative joint disease including central protrusion at T7/8. Id. at 33. MRI of the brain was normal. Id. at 34.

The next day, June 15, 2018, Petitioner saw Dr. Schneider. Pet. Ex. 4 at 12. History of present illness reiterated Petitioner's clinical course that began with "tingling of the toes" while at the gym on May 25, 2018. Id. at 14. Petitioner reported that he felt his symptoms had plateaued over the past few days. Id. Petitioner reported he received the hepatitis A vaccine on April 19. Id. Dr. Schneider noted Petitioner's recent MRIs were "unrevealing," showing "no significant abnormality," "no cervical myelopathy," and "no surgical lesion" as indicated by Dr. Tutt. Id. Physical examination "show[ed] weakness in the arms and legs proximally and distally," 3/5 strength in deltoids and biceps, 4/5 strength in triceps, 4-/5 strength in wrist flexion and extension, 3-4/5 strength in first dorsal interosseous, "weak" abductor pollicis brevis muscle, 3/5 strength in hip and knee flexion, 4/5 strength in quadriceps, 4/5 dorsiflexion but better on the right, 3-4/5 plantar flexion, absent deep tendon reflexes, wide-based unsteady gait, and positive for Romberg's. Id. at 15. Assessment was GBS. Id. at 13, 15. Dr. Schneider wrote, "[Petitioner] has had progressive weakness in the arms and legs proximally and distally with distal paresthesias over the past ~3 weeks. He [was] areflexic on exam[ination]. No abnormality

[12] Memorial day was Monday, May 28, 2018.

seen on neuro-imaging." Id. at 15. Dr. Schneider thought Petitioner's case "[was] almost certainly GBS," and noted Petitioner "had hep[atitis] A vaccination a few weeks ago." Id. Dr. Schneider ordered a lumbar puncture[13] and electromyography ("EMG")/nerve conduction study ("NCS"). Id. at 13, 15. "[A]ssuming nothing surprising [was] seen, then [he] would treat with [intravenous immunoglobulin ("IVIG")]."[14] Id. at 15. Dr. Schneider arranged for Petitioner to be admitted to St. Joseph's Hospital. Id.; Pet. Ex. 5 at 10. EMG/NCS was conducted that day prior to admission and findings were "compatible with GBS" in "clinical setting of rapidly progressive weakness." Pet. Ex. 4 at 13, 15, 31-32.

Petitioner was admitted on June 15, 2018 for five days of IVIG. Pet. Ex. 5 at 10. He also received PT and occupational therapy during his stay. Id. Petitioner was discharged on June 19, 2018. Id. He was noted to have "improve[d] his strength and mobility being able to go [up and down] multiple steps." Id. Petitioner "still experience[d] some numbness and tingling of his hands and feet." Id. at 11. He received his fifth and final dose of IVIG prior to discharge. Id. Dr. Derek Henson noted "[Petitioner] has had extensive concern regarding the timing of his hepatitis A vaccine with the onset of this illness and is due for a round two-stage booster within 2 months and I've advised him to not get that" due to Petitioner's "current condition and the IVIG used." Id. Dr. Henson added, "finding direct effect or causation of his vaccine cause[d] GBS is very difficult[,] however, the timing is somewhat suspect." Id. Discharge diagnosis was acute inflammatory demyelinating polyneuropathy ("AIDP")/GBS. Id.

On June 27, 2018, Petitioner presented to King's Daughters Medical Center ("King's Daughters") for an initial PT evaluation with physical therapist Amy Hay. Pet. Ex. 3 at 216. Petitioner's GBS onset was noted as May 25, 2018. Id. Petitioner stated he had an "immediate response to IVIG therapy." Id. He reported muscle soreness particularly in back and calf, neuropathy in hands, numbness in face particularly in top of nose, difficulty with stairs particularly with descending, and fatiguing easier. Id. He was ambulating with a cane. Id. Physical examination revealed "decreased core stability, impaired balance, impaired sensation[,] and functional mobility deficits." Id. at 218.

Petitioner returned to Dr. Schneider on June 29, 2018. Pet. Ex. 4 at 10. Since Petitioner's hospitalization and IVIG, Petitioner was doing better. Id. His strength improved, although he tired easily, still felt "wobbly on his feet [], and ha[d] mild difficulty with descending more than ascending stairs." Id. at 11. Dr. Schneider noted Petitioner was using a cane. Id. Petitioner's "hypersensitivity [was] better in the feet, though they still fe[lt] numb," and "[h]is hands fe[lt] like prunes." Id. Physical examination noted Petitioner's "strength [was] much better today than two weeks ago." Id. Dr. Schneider "[found] mild weakness of biceps bilaterally (4+/5) and knee flexion [was] about 4/5 on the right, but other muscles proximally and

[13] Lumbar puncture test was cancelled "as it was no longer needed following" the results of the EMG/NCS. Pet. Ex. 5 at 10. Dr. Lori McIntosh wrote, "[g]iven the clinical presentation is classic for AIDP will not do lumbar puncture at this time." Id. at 21.

[14] IVIG is immune globulin used to treat GBS as well as various immunodeficiency disorders. Immune Globulin Intravenous (Human), Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=78975 (last visited Jan. 25, 2023).

distally [were] normal or nearly so." Id. Petitioner's deep tendon reflexes remained absent. Id. His tone and coordination were "ok[ay]," "[g]ait [was] much more steady," and Romberg's test was now negative. Id. Dr. Schneider determined Petitioner could return to work part-time and then full-time by the end of July if he continued to improve. Id. He added, "[i]t is possible that this GBS was related to the hep[atitis] A vaccination which he received a few weeks before, and I am going to look into reporting this." Id. at 12.

Later that day, Dr. Schneider submitted a Vaccine Adverse Event Reporting System ("VAERS") report. Pet. Ex. 15 at 4. Date of onset was May 25, 2018. Id. Dr. Schneider wrote "[Petitioner] developed [GBS] in late May, 2018, after receiving hepatitis A vaccination about five weeks before. I am not certain of the exact formulation of the hep[atitis] A vaccine which was given, if this was 'HAVRIX' or the other one." Id.

After 14 PT sessions at King's Daughters, Petitioner was discharged from PT on August 20, 2018. Pet. Ex. 3 at 108. Petitioner reported he was "[d]oing much better" and was "[a]ble to carry son up/down stairs with no difficulty." Id. He "[c]ontinue[d] to have neuropathy in [h]ands, feet[,] and nose." Id. Ms. Hay noted Petitioner was "[a]mbulating independent with no assistive device" and "ha[d] demonstrated significant improvement since initiating PT." Id. at 108-09.

Petitioner returned to Dr. Schneider on August 28, 2018. Pet. Ex. 4 at 8. Petitioner's strength had improved and he was working full-time. Id. at 9. He continued to have tingling in his nose and fingers, sometimes with sharp pains in toes and feet. Id. Physical examination revealed "basically normal strength, perhaps 5-/5 biceps." Id. Deep tendon reflexes were 1+ in biceps bilaterally, diminished/absent in knees, and absent in ankles. Id. Dr. Schneider noted "residual paresthesias are not unexpected and this will probably continue to improve." Id. at 10.

On December 18, 2018, Petitioner followed up with Dr. Schneider. Pet. Ex. 4 at 5. Petitioner "ha[d] been doing better overall" but "ha[d] a few residual symptoms." Id. at 7. He still experienced tingling in nose, feet, and toes, but his "[h]ands [were] largely better, 95% better." Id. Physical examination revealed normal strength in arms and legs, deep tendon reflexes of 1+ at biceps, reduced deep tendon reflexes at knees, and diminished/absent deep tendon reflexes at ankles. Id. at 7-8. Dr. Schneider prescribed Cymbalta[15] to help with Petitioner's "residual tingling and cutaneous burning discomfort." Id. at 8. EMG/NCS was ordered and conducted that day. Id. at 8, 29-30. Study findings were compatible with mild polyneuropathy. Id. at 30. Significant improvement was seen when compared to the prior study done in June 2018. Id.

Petitioner returned to Dr. Schneider for a follow-up visit on May 2, 2019. Pet. Ex. 4 at 3. Petitioner reported no pain, intermittent tingling of feet and nose, and good strength and balance.

[15] Among its various uses, Cymbalta (duloxetine) is prescribed to treat nerve pain as well as chronic pain. Duloxetine (Oral Route), Mayo Clinic, https://www.mayoclinic.org/drugs-supplements/duloxetine-oral-route/description/drg-20067247 (last visited Jan. 25, 2023). In May 2019, at a follow up, Petitioner reported he took only one dose due to side effects. Pet. Ex. 4 at 4. He refilled this prescription next on March 20, 2020, and continued to do so throughout 2020 and 2021. Pet. Ex. 21 at 3, 6-7.

Id. at 4. Physical examination revealed "very normal strength, bulk, [and] tone in arms and legs;" deep tendon reflexes of 2+ at knees, 1+ at biceps, and reduced/absent at ankles; and normal gait. Id. Dr. Schneider noted Petitioner "ha[d] mild residual sensory symptoms" that "may continue to slowly improve," but believed there was nothing else that needed to be done. Id.

At an annual wellness visit on December 17, 2019, Petitioner reported intermittent tingling and numbness. Pet. Ex. 3 at 18-20. Past medical history included "[GBS] after [h]ep[atitis] A [v]accine," with a date of May 2018. Id. at 19. Physical examination was normal, including a normal gait. Id. at 20. Advanced practice registered nurse ("APRN") Amy Sieweke wrote, "No immunizations at this point due to history of [GBS]. I would personally like confirmation from his neurologist when he feels that it is appropriate for him to resume immunizations, should he feel that is appropriate in the future." Id. at 18. "[W]ith his history of [GBS,] he most likely will not be taking immunizations in the future." Id. at 19.

Petitioner returned to PT at Premier on January 15, 2020 for PT for his right elbow. Pet. Ex. 8 at 6. Petitioner related his symptoms back to his GBS diagnosis in May 2018. Id. Physical examination by physical therapist Taylor Ison revealed strength, range of motion, balance, and coordination "within functional limits" except for tenderness to palpation at right lateral epicondyle, positive finger lift test, and pain with manual muscle testing and grip strength testing. Id. at 7. On January 27, 2020, Petitioner began PT for right hip pain he reported was related to his GBS. Id. at 30. PT assessment was "chronic right hip pain secondary to overuse syndrome and GBS that resulted in the following deficits: weakness, decreased [range of motion], pain with functional activities, and ability to perform functional activities." Id. at 31.

By February 17, 2020, Petitioner reported "less pain and some neuropathy [was] gone," but he continued to have neuropathy and weakness in left lower and upper extremity." Pet. Ex. 8 at 33. "He reported the symptoms were worse on the [right], but now that the [right] is getting stronger he feels like the [left] is weaker and throwing him off balance." Id. Physical therapist Rebekah Green noted Petitioner "ha[d] made moderate improvements" since starting PT but continued to demonstrate several impairments. Id. Petitioner attended a total of 15 PT sessions in January and February 2020. Id. at 10-38, 41-47, 50-53.

On October 1, 2020, Petitioner had an annual wellness visit. Pet. Ex. 22 at 29. Petitioner reported intermittent numbness in hands and feet as well as fatigue. Id. at 31. He stated he takes Cymbalta for the numbness. Id. He was given refills for Cymbalta. Id. at 29, 31.

One year later, on October 21, 2021, Petitioner had his annual wellness visit with his primary care physician. Pet. Ex. 22 at 2. Petitioner reported numbness in hands and feet. Id. at 5. Petitioner was up-to-date on Covid-19 vaccines but "desire[d] no additional vaccines due to history of GBS with [h]ep[atitis] A vaccine." Id. at 4. He was given refills for Cymbalta. Id. at 6.

2. Petitioner's Declaration

Petitioner stated he received a hepatitis A vaccine on April 19, 2018, and first noticed tingling in his toes on May 25, 2018, while he was working out at the gym. Pet. Ex. 20 at ¶ 3. "The tingling continued to spread, getting worse over the next 2 days; and then [he] noticed that [his] hands and fingers began to tingle as well. The tingling then started in [his] tongue, [his] mouth, and then [his] nose." Id. During this time, he was also "experiencing general weakness in [his] extremities," having "trouble lifting [his] warmup weights at the gym[,] and was fatiguing very quickly." Id. By May 31, 2018, he "experienced severe cramping from [his] waist down that persisted for approximately 1.5 [hours]." Id. Over that weekend, Petitioner's "tingling and weakness continued to spread and get worse, with the addition of what felt like the occasional electrical current shooting through [his] arms and legs." Id. at ¶ 4. He made his first doctor's appointment for June 4, 2018 "as soon as the cramping subsided." Id.

By June 4, 2018, Petitioner "was struggling to walk and climb stairs, though [he] was still able to manage." Pet. Ex. 20 at ¶ 5. At a visit on June 4, he stated that his doctor said his "heart rate and blood-pressure [were] very high, which was not normal; and that [his] reflexes were not working correctly." Id. At that visit, "they believed it was muscular and began treating accordingly." Id. By June 7, Petitioner's "coordination and balance were failing" and "[i]t was recommended that [he] stop driving and that [he] should not go back to work." Id. Petitioner stated he was "walking like a toddler and struggling to stand from a sitting position" during his PT session on June 11, 2018. Id. On June 13, 2018, he received his first MRIs, but the results were not concerning. Id. at ¶¶ 6, 10.

At this time, he could only "walk short distances with a walker, [his] wife was mostly pushing [him] in a wheelchair when [he] needed to get somewhere, [his] balance and coordination were gone, [his] strength was non-existent, [he] could not stand on [his] own[,] and [he] was spending all [his] time in a chair." Pet. Ex. 20 at ¶ 6. Petitioner was also having trouble using the restroom, bathing, brushing his teeth, and sleeping. Id. "The electrical shock sensations had grown more intense, and [his] skin had grown incredibly sensitive." Id. He "was beginning to experience paralysis in [his] feet and toes." Id. In areas where he lost all feeling, he later developed "ghost" pain, which he "described as a cramp causing your muscles [to] contract, focused mostly on [his] toes and feet." Id.

Petitioner then saw neurosurgeon Dr. Tutt and PA-C Sammons at the Lexington Clinic. Pet. Ex. 20 at ¶ 11. After they ruled out everything that would require surgery, they referred Petitioner to neurologist, Dr. Schneider, who Petitioner saw on June 15, 2018. Id. Petitioner explained Dr. Schneider diagnosed him with GBS based on Petitioner's physical condition, history, and test results. Id. at ¶ 13. Dr. Schneider "explained to [Petitioner] that something always triggers GBS, and asked permission to file the case with VAERS." Id. Dr. Schneider conducted EMG/NCS to confirm diagnosis and had Petitioner admitted to the hospital. Id. Petitioner saw various specialists and began IVIG treatment over his five-day hospital stay. Id. at ¶ 15.

When Petitioner was discharged from the hospital on June 19, 2018, he "was able to support [his] own weight, but still could not walk without a walker." Pet. Ex. 20 at ¶ 16. He began outpatient PT and continued until November 2018. Id. He returned to work with a walker

part-time/light-duty on July 9, 2018, full-time/light-duty with a cane on July 31, 2018, and then his light duty restriction was lifted. Id.

Dr. Schneider conducted an EMG/NCS on May 2, 2019, which confirmed Petitioner still had some nerve damage. Pet. Ex. 20 at ¶ 18. Dr. Schneider indicated Petitioner "could continue to heal and eventually make a full recover[y]." Id. Petitioner "started [PT] again in January 2020 at the recommendation of [his] family doctor for [his] right hip and arm, which continue[d] to have pain and weakness." Id. Petitioner stated his "physical therapist believe[d] that [he] experienced atrophy in [his] hip and forearm during [his] GBS episode[] that [led] to severely underdeveloped muscles." Id. Although he quit PT at the start of the Covid-19 pandemic in March 2020, he "continue[d] the exercises and stretches and ha[s] seen some improvement in both [his] hip and arm." Id.

As of the date of Petitioner's declaration, executed on November 3, 2021, Petitioner "still experience[d] neuropathy in [his] feet, hands[,] and face; the severity varies and can sometime[s] be linked to anxiety and/or stress." Pet. Ex. 20 at ¶ 18. Petitioner takes Cymbalta for his neuropathy, which "increased in severity during the early months of the pandemic, brought on by increased stress." Id. at ¶¶ 19, 21. Petitioner believes he is "back to roughly 90% on the energy level, and 80% of the fitness level that [he] was pre-GBS." Id. at ¶ 20.

D. Expert Reports

1. Petitioner's Expert, Dr. S. Sohail Ahmed, M.D.[16]

a. Background and Qualifications

Dr. Ahmed was board certified in internal medicine and rheumatology,[17] and is board certified in Rome, Italy. Pet. Ex. 13 at 3. After receiving his M.D. from the University of Texas Medical School in Houston, Texas, he completed an internal medicine residency and rheumatology fellowship at the University of Texas Medical School. Id. He has clinical training in general medicine, cardiology, oncology, and rheumatology. Pet. Ex. 12 at 2. Dr. Ahmed has spent his career conducting research and studies and has held academic appointments at the University of Texas Medical School and Boston University School of Medicine. Id. He has spent over eight years in the vaccine industry, where his work "spanned the areas of vaccine Research & Development, vaccine manufacturing, and vaccine subject safety." Id. Dr. Ahmed has also published numerous articles in areas related to vaccines, immune-mediated diseases, and mechanisms triggered by vaccinations. Id. at 2-3.

b. Opinion

[16] Dr. Ahmed provided two expert reports. Pet. Exs. 12, 14.

[17] According to Dr. Ahmed's CV, he was board certified in internal medicine from 2003 to 2013 and rheumatology from 2004 to 2014. Pet. Ex. 13 at 3.

Dr. Ahmed opined Petitioner more likely than not developed GBS following receipt of a hepatitis A vaccination. Pet. Ex. 12 at 20.

i. Diagnosis

Although Dr. Ahmed's expert reports focused on whether the hepatitis A vaccine administered on April 19, 2018 caused Petitioner's GBS, he briefly opined as to diagnosis. Pet. Ex. 12 at 4. After reviewing Petitioner's medical records, Dr. Ahmed opined there was no evidence suggestive of GBS prior to Petitioner's hepatitis A vaccination. Id. at 6. He also opined Petitioner, more likely than not, developed GBS after hepatitis A vaccination. Id. at 6-12.

Citing Vriesendorp, Dr. Ahmed noted that of the common features associated with GBS, Petitioner exhibited (1) weakness in extremities and facial muscles; (2) decreased or absent reflexes in the affected extremities; (3) paresthesias in the hands and feet that accompanied weakness; and (4) "pain due to nerve root inflammation, typically located in the back," and "reported during the acute phase." Pet. Ex. 12 at 5 (quoting Pet. Ex. 12-2 at 2).

In response to Respondent's expert's, Dr. Leist's, opinion that Petitioner developed an L5 radiculopathy and cervical sprain, Dr. Ahmed noted Petitioner's treating neurosurgeon Dr. Tutt and PA-C Sammons determined a demyelinating process was occurring and there was no explanation on MRI to support his symptoms structurally, in contrast with Dr. Leist's opinions. Pet. Ex. 14 at 6 (citing Pet. Ex. 4 at 17; Resp. Ex. A at 9).

ii. Althen Prong One

Dr. Ahmed first explained what occurs when a vaccine is introduced to the body. First, a vaccine activates immune cells, the surface of which contain toll-like receptors ("TLRs"), generating a local pro-inflammatory response at the site of vaccination. Pet. Ex. 12 at 15-16. "[T]he innate immune cells recogniz[e] the 'danger' signals and secret[e] pro-inflammatory cytokines that attract and promote differentiation of immature dendric cells." Id. at 16-17; see also Pet. Ex. 12-14 at 3.[18] "This initial immune response triggers neuronal responses that amplify the local responses to inflammation as well as trigger[s] systemic responses that [] result in the resolution of the inflammatory process and restoration back to the normal homeostatic state." Pet. Ex. 12 at 15; see also Pet. Ex. 12-14 at 4. T cells are required to "maintain[] immunological homeostasis and prevent[] autoimmunity by suppressing self-reactive T cells and abolishing antigen-specific T cell proliferation." Pet. Ex. 12 at 15. "A T-cell only responds to a small antigenic peptide fragment presented by [human leukocyte antigen ("HLA")] molecules on antigen-presenting cells (APCs). T cells subsequently release cytokines that stimulate specific B-cells to produce antibodies to the peptide fragment." Id. at 16.

[18] Jeanette M. Bennett et al., Inflammation–Nature's Way to Efficiently Respond to All Types of Challenges: Implications for Understanding and Managing "the Epidemic" of Chronic Diseases, 5 Frontiers Med. 1 (2018).

Thus, "a successful adaptive immune response is dependent on sufficient co-signals from the innate immune response, the goal being to minimize reactiveness against self-antigens." Pet. Ex. 12 at 15 (emphasis omitted). "However, in certain individuals, reactiveness against self-antigen (autoimmune disease development) occurs in the context of . . . vaccines derived from the wild[-]type virus." Id.

Dr. Ahmed proposed the following mechanism by which the hepatitis A vaccine can cause GBS: molecular mimicry and aluminum ("alum") adjuvant.[19] Pet. Ex. 12 at 15-17. He opined that molecular mimicry combined with the alum in the hepatitis A vaccine can cause GBS. Id. at 17. Specifically, he stated the "alum adjuvant directly influences the adaptive immune response and creates an environment mimicking infection that together with molecular mimicry would induce immune dysregulation and autoimmune disease development in genetically predisposed subjects." Id.

Regarding molecular mimicry, Dr. Ahmed explained that "the initial stimulus for a first antibody response may be a non-self-protein (from an infectious agent)[20] possessing a peptide region that mimics a self-epitope (from normal human tissue)." Pet. Ex. 12 at 16. If the infectious agent has "amino acids identical to a self-epitope, an autoimmune response may result," and "in individuals carrying HLA susceptibility genes, [autoimmunity] can progress to autoimmune disease." Id. Dr. Ahmed acknowledged that "the exact identity of the epitope in HAVRIX that is generating molecular mimicry leading to GBS is still under investigation," but he asserted that "this does not preclude the importance or relevance of this mechanism." Id.

For support, he cited various articles explaining the concept of molecular mimicry and its relationship to GBS. See, e.g., Pet. Ex. 12-18 at 1;[21] Pet. Ex. 12-19 at 1;[22] Pet. Ex. 12-20 at 1 ("Mimicry of host antigens by infectious agents may induce cross-reactive autoimmune responses to epitopes within host proteins which, in susceptible individuals, may tip the balance of immunological response versus tolerance toward response and subsequently lead to autoimmune disease.");[23] Pet. Ex. 12-22 at 2, 6 (noting "viral infections . . . are often associated with [GBS], and both bacterial and viral vaccines have been linked with induction of the

---

[19] The hepatitis A vaccine at issue here (HAVRIX) was an inactivated vaccine that contained alum. Pet. Ex. 9 at 9.

[20] He added, "[i]nfectious agents that display self-like peptides are the source material for the generation of vaccines." Pet. Ex. 12 at 16.

[21] Michael B. A. Oldstone, Molecular Mimicry and Immune-Mediated Diseases, 12 FASEB J. 1255 (1998).

[22] Lou Ann Barnett & Robert S. Fujinami, Molecular Mimicry: A Mechanism for Autoimmune Injury, 6 FASEB J. 840 (1992).

[23] Janet M. Davies, Molecular Mimicry: Can Epitope Mimicry Induce Autoimmune Disease?, 75 Immunology & Cell Biology 113 (1997).

condition," with molecular mimicry as a "[p]ossible mechanism that can [t]rigger GBS"); Pet. Ex. 12-23 at 1-2;[24] Pet. Ex. 12-24 at 6 ("Some evidence supports the presence of molecular mimicry between gangliosides and antecedent infectious agents in patients with [GBS] . . . ."). He also cited articles discussing how infections and vaccines can trigger GBS via molecular mimicry. See, e.g., Pet. Ex. 12-22; Pet. Ex. 12-23.

In an article authored by Dr. Ahmed and others,[25] assessing the safety of adjuvanted vaccines, the authors explained that "a vaccine stimulates some of the same host responses (such as innate immune activation by pattern recognition receptors and T and B cell activation through specific antigen receptors) as an infection," and thus, "vaccines might . . . trigger a clinical manifestation of autoimmune disease in healthy subjects that are genetically predisposed to developing autoimmune disease." Pet. Ex. 12-1 at 2. He argued that "[s]ince the HAVRIX vaccine is derived from the wild-type hepatitis A virus, the development of GBS with . . . vaccination provides confirmatory evidence for the role of commonly shared hepatitis A antigens (involved in molecular mimicry)." Pet. Ex. 14 at 4 (emphasis omitted).

Dr. Ahmed also suggested that the alum adjuvant in the vaccine could contribute to the development of GBS. Pet. Ex. 12 at 16-17. Dr. Ahmed explained that "[a]lum enhances the adaptive immune responses likely by both the formation of a deposit [at the site of administration] from which the antigen is slowly de-absorbed and released, extending the duration of B and T cell activation, as well as the preferential induction of the cytokine IL-4 by [alum] exposed macrophages." Id. at 17 (emphasis omitted) (citing Pet. Ex. 12-3 at 9);[26] see also Pet. Ex. 12-25 at 1-5.[27] With an adjuvanted vaccine like HAVRIX, "the immune stimulation would be even stronger and subsequently the immune response more rapid." Pet. Ex. 12 at 12. He concluded "alum adjuvant directly influences the adaptive immune response and creates an environment mimicking infection that together with molecular mimicry would induce immune dysregulation and autoimmune disease development in genetically predisposed subjects." Id. at 17.

For additional support, Dr. Ahmed opined "[alum]-containing vaccines administered to individuals carrying currently unknown susceptibility genes can trigger [macrophagic myofasciitis] and therefore, it [would not be] unexpected that [alum]-containing vaccines could

[24] Irving Nachamkin et al., Anti-Ganglioside Antibody Induction by Swine (A/NJ/1976/H1N1) and Other Influenza Vaccines: Insights into Vaccine-Associated Guillain-Barré Syndrome, 198 J. Infectious Diseases 226 (2008).

[25] S. Sohail Ahmed et al., Assessing the Safety of Adjuvanted Vaccines, 3 Sci. Translational Med. 1 (2011).

[26] Claire-Anne Siegrist, Vaccine Immunology, in Vaccines 17 (Stanley A. Plotkin et al. eds., 5th ed. 2008).

[27] Mirjam Kool et al., Alum Adjuvant: Some of the Tricks of the Oldest Adjuvant, 61 J. Med. Microbiology 927 (2012).

trigger other autoimmune diseases," such as GBS. Pet. Ex. 14 at 4 (citing Pet. Ex. 14-1).[28] Dr. Ahmed cited two articles he co-authored that discussed safety of adjuvanted vaccines. See Pet. Ex. 12-2; Pet. Ex. 14-3.[29] The articles explained the benefits of alum and other adjuvants in vaccines but did not detail how alum can cause GBS. See Pet. Ex. 12-2; Pet. Ex. 14-3. One article noted that "vaccine antigens are screened for molecular mimicry to exclude autoantigens, using in silico and in vitro studies." Pet. Ex. 12-2 at 2. Dr. Ahmed did not further expand on how alum can specifically enhance molecular mimicry so as to cause GBS.

Respondent's expert, Dr. Fujinami, argued the adjuvant in the hepatitis A vaccine is "very weak" when compared to the adjuvant used in experimental autoimmune encephalomyelitis ("EAE") in animal models for the purpose of studying demyelinating diseases. Pet. Ex. 14 at 9 (citing Resp. Ex. C at 4). Dr. Ahmed disagreed that vaccine adjuvants are "very weak." Id. And he argued Dr. Fujinami failed to take into account human genetic susceptibility. Id. "Adjuvants are potent stimulators of the immune system designed to generate strong immune responses to antigens contained in various vaccines (especially inactivated vaccines that are not replicating)." Id. These adjuvants "can provide the appropriate immunological environment for the development of autoimmune disease in a genetically susceptible subject in the context of a failure of regulatory mechanisms." Id.

Next, Dr. Ahmed opined that both hepatitis A infections and vaccines have been found to trigger autoimmune diseases including GBS. Pet. Ex. 12 at 12-15. First, he noted that "both inactivated and live-attenuated vaccines have been associated with the induction of autoimmune disease," although he acknowledged the hepatitis A vaccine at issue here is an inactivated vaccine. Id. at 12, 17 (citing Pet. Ex. 9 at 9 (package insert)). He then argued that "vaccine-associated signals of rare autoimmune diseases such as GBS may only become evident when large populations (containing individuals with diverse HLA alleles) receive a vaccine in a short time period." Id. at 12. When this scenario is absent, "one can rely on published case reports" due to "their importance as a valuable source of unique, unexpected patient findings." Id. For support, he provided seven articles related to GBS associated with wild-type hepatitis virus (from which the hepatitis A vaccine is derived from) and two articles documenting the development of GBS in the setting of hepatitis A vaccination. Id. at 12-13.

For the hepatitis A infection publications, Dr. Ahmed opined they are relevant "because the symptoms occurring in these subjects parallel those experienced by [Petitioner] and they discuss the mechanisms (including molecular mimicry) that are triggering GBS in these subjects infected by wild-type virus." Pet. Ex. 14 at 2. He added, "[s]ince the vaccine is derived from the wild-type virus and is being given in the context of an adjuvant that would stimulate the immune

[28] R. K. Gherardi et al., Macrophagic Myofasciitis: An Emerging Entity, 352 Lancet 347 (1998). There is no evidence here that Petitioner had macrophagic myofasciitis, which is an inflammatory myopathy of unknown origin, characterized by an infiltration of non-epithelioid histiocytic cells. Pet. Ex. 14-1 at 1.

[29] Béatris Mastelic et al., Mode of Action of Adjuvants: Implications for Vaccine Safety and Design, 38 Biologicals 594 (2010). Dr. Ahmed was a named author in this publication.

system (like the effect of a replicating live virus), it is very likely that GBS can be triggered in genetically susceptible subjects being administered the HAVRIX vaccine." Id. at 2-3.

In Azuri et al.,[30] a three-and-one-half-year-old boy developed GBS after exposure to hepatitis A infection and receipt of immunoglobulin immunization. Pet. Ex. 12-5 at 1. The authors noted "[i]t is possible that there is molecular resemblance between antigens of . . . [hepatitis A] and components of the myelin of peripheral nerves." Id. The authors questioned whether the immunoglobulin immunization led to GBS. Id.

Breuer et al.[31] discussed the case of a 28-year-old pregnant woman who was diagnosed with hepatitis A and then diagnosed with GBS a few days later. Pet. Ex. 12-7 at 1.[32] "The exact mechanism by which the virus causes the disease is not clear," however, "immune mechanisms may be postulated." Id. at 2. And Chitambar et al.[33] reported a case of hepatitis A with GBS in a 17-year-old male. Pet. Ex. 12-8 at 1. The authors noted "[t]he mechanism for [GBS] occurring in viral disease is not clear and is not known for hepatitis A." Id. at 3.

Johnston et al.[34] described a case of a 37-year-old male who developed GBS following infection with hepatitis A. Pet. Ex. 12-9 at 1. Similarly, Bosch et al.[35] reported two of 167 patients with GBS who tested positive for hepatitis A antibodies, indicating recent viral infection. Pet. Ex. 12-6 at 1-2. The authors concluded "[t]he incidence of hepatitis A virus infection in [] patients with GBS . . . was low," which "may be a reflection of the incidence of hepatitis A virus in [the] population." Id. at 2. Marés-Segura et al.[36] reported a 34-year-old woman who was diagnosed with acute hepatitis and developed GBS one week later. Pet. Ex. 12-

[30] J. Azuri et al., Guillain-Barre Syndrome Following Serological Evidence of Hepatitis A in a Child, 158 Eur. J. Pediatrics 341 (1999).

[31] Gabriel S. Breuer et al., A Pregnant Woman with Hepatitis A and Guillain-Barré, 32 J. Clinical Gastroenterology 179 (2001).

[32] The Bates stamp in this article does not match Petitioner's exhibit list. See Pet. Ex. List, filed Nov. 30, 2022 (ECF No. 66-1). For clarity, the undersigned will use the exhibit number that matches the exhibit list.

[33] Shobha D. Chitambar et al., Case Report: Hepatitis A Preceding Guillain-Barré Syndrome, 78 J. Med. Virology 1011 (2006).

[34] C. L. W. Johnston et al., Acute Inflammatory Polyradiculoneuropathy Following Type A Viral Hepatitis, 57 Postgraduate Med. J. 647 (1981).

[35] Vivian V. Bosch et al., Hepatitis A Virus Immunoglobulin M Antibody in Acute Neurological Disease, 14 Annals Neurology 685 (1983).

[36] R. Marés-Segura et al., Guillain-Barré Syndrome Associated with Hepatitis A, 19 Annals Neurology 100 (1986).

10 at 1.[37] The authors noted "acute polyradiculoneuropathy [GBS] could be attributed" to recent infection with hepatitis A virus. Id. In an article authored by Tabor,[38] the author reviewed articles discussing an association of GBS with hepatitis A, including the three cases above. Pet. Ex. 12-11 at 2. The authors noted the mechanism was unknown, "but may include direct cytotoxicity of the virus or immune-mediated damage." Id. at 1.

Dr. Ahmed also cited two case reports of patients who developed GBS following hepatitis A vaccination. Pet. Ex. 12 at 14-15. The first, authored by Blumenthal et al.,[39] reported GBS in a one-and-one-half-year-old child who received a hepatitis A vaccination (HAVRIX)[40] five days before symptom onset. Pet. Ex. 12-12 at 1. They noted recent vaccination has been associated with GBS, with an "underlying pathophysiology [] presumed to involve an immune cascade induced by the precedent agent, leading to demyelination of the large nerve roots." Id. at 2. The authors determined that "[i]n their patient, the association of [GBS] with hepatitis A vaccine is supported by temporal proximity of the vaccination with the onset of symptoms, lack of other precipitating factors[,] and the immune-mediated nature of the manifestation." Id. The authors further explained that the "[h]epatitis A vaccine consists of inactivated hepatitis A viruses that cause an immune response similar to that caused by the infection." Id. Thus, given the "earlier reports of a relationship between [the hepatitis A virus] infection and [GBS], [the authors] assume[d] there may also be a relationship between the [hepatitis A] vaccine and [GBS]." Id.

The second case report, authored by Roux et al.,[41] discussed "the case of a 30-year-old patient with a past medical history of Graves[']' disease, who presented with GBS within the month after receiving an anti-hepatitis A vaccination." Pet. Ex. 12-13 at 1.

According to Dr. Ahmed, these case reports "provide important data on the timeframe of GBS development post-vaccination, the symptoms, potential mechanisms, and the rarity of these signals." Pet. Ex. 14 at 3. He opined that "[t]he fact that observed signals can occur is 'proof' that administration of specific vaccines is causal for certain genetically predisposed subjects in the population." Id. (emphasis omitted). He noted "GBS development is rare after infections and even rarer following vaccination[,] . . . mak[ing] it difficult to estimate precise background

[37] The Bates stamp in this article does not match Petitioner's exhibit list. See Pet. Ex. List, filed Nov. 30, 2022 (ECF No. 66-1). For clarity, the undersigned will use the exhibit number that matches the exhibit list.

[38] Edward Tabor, Guillain-Barré Syndrome and Other Neurologic Syndromes in Hepatitis A, B, and Non-A, Non-B, 21 J. Med. Virology 207 (1987).

[39] Danith Blumenthal et al., Possible Association of Guillain-Barré Syndrome and Hepatitis A Vaccination, 23 Pediatric Infectious Disease J. 586 (2004).

[40] Petitioner received the adult HAVRIX vaccine. Pet. Ex. 1 at 2.

[41] X. Roux et al., Syndrome de Guillain-Barré et vaccination contre l'hépatite A [Guillain-Barré Syndrome and Anti-Hepatitis A Vaccination], 40 Médecine et maladies infectieuses [Med. & Infectious Diseases] 490 (2010) (Fr.).

risk." Id. By way of example, he explained that it was only after the "mass immunization campaign of 1976 for influenza that a strong epidemiological signal was able to be detected[,] subsequently confirming an increased GBS risk of six-to eight-fold in the vaccinated population." Id.

In addition to the case reports, Dr. Ahmed cited to the package insert as "compelling evidence for a causal association between HAVRIX and GBS development." Pet. Ex. 12 at 17. GBS was identified as an adverse event in the "postmarketing experience" section reporting "worldwide voluntary reports of adverse events received for HAVRIX," which "include[d] serious adverse events or events which have a suspected causal connection to components of HAVRIX or other vaccines or drugs." Pet. Ex. 12 at 18 (quoting Pet. Ex. 9 at 7).[42] Dr. Ahmed concluded "the package insert for HAVRIX [] provide[s] information concerning a causal relationship between inactivated hepatitis A vaccine and GBS." Pet. Ex. 14 at 3.

He also quoted the 2012 Institute of Medicine ("IOM")[43] report to explain how "[s]trong mechanistic evidence, which requires at least one case report in which compelling evidence exists that the vaccine indeed did cause the adverse event, always carries sufficient weight for the committee to conclude the evidence convincingly supports a causal relationship." Pet. Ex. 12 at 18-19 (quoting Pet. Ex. 12-26 at 46-47). And thus, based on this statement, Dr. Ahmed opined "if the vaccine did cause the adverse effect in one person, then it can cause the adverse effect in someone else as reflected in the case reports."[44] Id. (internal citation omitted). In his supplemental expert report, Dr. Ahmed recognized that the IOM found "[t]he evidence [] inadequate to accept or reject a causal relationship between hepatitis A vaccine and GBS," but argued "this does not exclude that an association exists" because "the failure to find an increased risk in studies does not equate to zero risk for all vaccinated subjects." Pet. Ex. 14 at 2 (quoting Pet. Ex. 12-26 at 455).

Additionally, Dudley et al.,[45] an article cited by Dr. Fujinami, noted the Agency for Healthcare Research and Quality determined there was "insufficient" evidence that the hepatitis A vaccine could cause GBS. Pet. Ex. 14 at 7 (citing Resp. Ex. C, Tab 6 at 4 tbl.1). In response, Dr. Ahmed argued they were unable to find enough information to assess the role that

[42] The package insert acknowledged that "[b]ecause these events are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to the vaccine." Pet. Ex. 9 at 7.

[43] Inst. of Med., Adverse Effects of Vaccines: Evidence and Causality (Kathleen Stratton et al. eds., 2012). The IOM is now the National Academy of Medicine.

[44] However, he failed to acknowledge "[t]he committee assesse[d] the mechanistic evidence regarding an association between hepatitis A vaccine and GBS as weak based on knowledge about the natural infection." Pet. Ex. 12-26 at 455.

[45] Matthew Z. Dudley et al., The State of Vaccine Safety Science: Systematic Reviews of the Evidence, 20 Lancet Infectious Diseases e80 (2020).

vaccination had in GBS development. Id. This does not discount the role vaccination has in GBS development. Id.

Lastly, Dr. Ahmed disagreed with Dr. Fujinami's reliance on EAE models to compare multiple sclerosis ("MS") and GBS and opined "[MS] and GBS are considered distinct neurological diseases and therefore applying animal models of EAE broadly to include [MS] and GBS is not correct." Pet. Ex. 14 at 9 (emphasis omitted). He argued the EAE models cannot "be reliably expected to predict autoimmune disease induction." Id. Dr. Ahmed noted Dr. Fujinami failed to consider "1) differences between animal models and human disease clinical manifestations, 2) fundamental genetic and physiological differences between humans and commonly used laboratory animals, and finally 3) the poorly understood etiology of human autoimmune diseases in general." Id. at 10.

iii. Althen Prong Two

Dr. Ahmed opined, more likely than not, the hepatitis A vaccine Petitioner received caused him to develop GBS. Pet. Ex. 12 at 15, 19. For support, he cited the above-mentioned articles, case reports, the package insert, and the opinions of Petitioner's treating physicians. Id. at 17-18; Pet. Ex. 14 at 10.

He opined "both the wild-type virus causing hepatitis A infection and vaccines derived from hepatitis A virus have without doubt triggered GBS in subjects. The patients in these reports manifested certain symptoms and a time course that parallel those seen in [Petitioner's] case." Pet. Ex. 12 at 18. Dr. Ahmed summarized Petitioner's clinical course and found it consistent with GBS following hepatitis A vaccination. Id. at 6-12.

Next, Dr. Ahmed cited to Petitioner's treating physicians' statements and opined that "[Petitioner's] treating physicians suspect[ed] causality between HAVRIX and GBS development in his case." Pet. Ex. 12 at 17-18. Dr. Schneider, on June 15, 2018, noted "this is almost certainly GBS. He ha[d] hep[atitis] A vaccination a few weeks ago, of note." Id. at 18 (quoting Pet. Ex. 4 at 15). And on June 29, 2018, Dr. Schneider wrote "[i]t is possible that this GBS was related to the hep[atitis] A vaccination which he received a few weeks before, and I am going to look into reporting this." Id. (quoting Pet. Ex. 4 at 12). Similarly, Dr. Henson noted he "advised [Petitioner] to not get [his hepatitis A booster]." Id. (quoting Pet. Ex. 5 at 11). Dr. Henson also noted that "finding direct effect or causation of his vaccine caus[ing] GBS is very difficult[,] however, the timing is somewhat suspect." Id. (quoting Pet. Ex. 5 at 11).

Lastly, Dr. Ahmed found "no evidence of active autoimmune disease (nor GBS) documented in the medical records of [Petitioner] prior to receipt of HAVRIX vaccine." Pet. Ex. 12 at 5-6, 19. He summarized Petitioner's medical history prior to vaccination, and noted Petitioner reported no active medical issues at his preventative wellness examinations in 2015, 2016, and 2017, the three years prior to vaccination. Id. at 6. No issues were noted at these visits. Id. Laboratory tests from 2015 revealed slightly elevated cholesterol and triglyceride, but levels were normal by his next annual visit in 2016. Id. Thus, he found no evidence of GBS prior to vaccination. Id.

iv. Althen Prong Three

Dr. Ahmed placed onset of Petitioner's GBS on May 25, 2018, 36 days post-vaccination. Pet. Ex. 12 at 6-7, 12. He cited Petitioner's June 4, 2018 visit, where he complained of tingling in his feet, hands, and tongue as well as leg cramps for two weeks. Id. at 6 (citing Pet. Ex. 3 at 379). Also at this visit, Petitioner reported his symptoms "started last Friday (10 days ago) when he was working out at the gym," which references Friday, May 25, 2018. Id. at 6-7 (citing Pet. Ex. 3 at 379).

Dr. Leist opined Petitioner's GBS onset was "after June 4, 2018," or more than 47 days post-vaccination, because "[Petitioner's] symptoms on June 4, 2018 were consistent with lumbar and cervical strain and L5 radiculopathy," and thus, not consistent with GBS. Resp. Ex. A at 8. However, Dr. Ahmed disagreed and opined Petitioner's symptoms that began on May 25, 2018, and were reported on June 4, 2018, were consistent with GBS. Pet. Ex. 12 at 6-7, 12; Pet. Ex. 14 at 5.

Dr. Ahmed opined a 36-day onset "is compatible with the timeframe for a vaccine to generate an immune response and trigger an autoimmune response that progresses to an immune-mediated disease in the genetically predisposed subject," especially given the fact that the vaccine contains an adjuvant that "would boost the immune response." Pet. Ex. 12 at 12, 19. Thus, "a temporal relationship between immunization with the adjuvanted hepatitis A vaccine, HAVRIX, and injury exists." Id. at 19.

For additional support, he stated the International Alliance for Biological Standardization, a society that Dr. Ahmed participated in to discuss vaccine safety, concluded "that the plausible time window in which autoimmune disease development after vaccination can be attributable to the vaccine is < 6 months." Pet. Ex. 14 at 5. Goetz et al.[46] noted "[a]gencies often request long-term follow-up visits up to six months from the start of the trial, depending on the perceived potential risk for long-term events like autoimmunity." Pet. Ex. 14-4 at 6. Additionally, the authors determined "appropriate safety evaluations in vaccinees and regular and extensive follow-up visits suitable to detect late effects (up to several months) must be implemented." Id. at 4-5.

2. Petitioner's Expert, Dr. Kazim A. Sheikh, M.D.[47]

a. Background and Qualifications

Dr. Sheikh is board certified in psychiatry and neurology, with a qualification in muscle pathology and subspecialty certification in clinical neuromuscular pathology. Pet. Ex. 16 at 1; Pet. Ex. 24 at 2. He completed an internship and residency in Pakistan before completing an internship and neurology residency in New York and a post-doctoral fellowship in peripheral

[46] Karen B. Goetz et al., First-in-Human Clinical Trials with Vaccines—What Regulators Want, 28 Nature Biotechnology 910 (2010).

[47] Dr. Sheikh provided one expert report. Pet. Ex. 16.

nerves at Johns Hopkins University. Pet. Ex. 16 at 2; Pet. Ex. 24 at 1. Dr. Sheikh is a tenured Professor of Neurology at the University of Texas Medical School in Houston, where he is also the Director of the Neuromuscular Program. Pet. Ex. 16 at 1; Pet. Ex. 25 at 1-2. Dr. Sheikh is also the Director of the Neuromuscular Disorders Center at the Mischer Neuroscience Institute at Memorial Hermann-Texas Medical Center, Director of Muscle and Nerve Laboratory, and Director of the GBS/CIDP Center of Excellence at the University of Texas Health Science Center at Houston. Pet. Ex. 16 at 1. He has authored or co-authored over 200 publications, has an active clinical practice in neurology, and teaches medical students, residents, and fellows. Id. at 1-2; Pet. Ex. 42 at 6-9, 14-35, 40-41.

b. Opinion

Dr. Sheikh's opinions focused on diagnosis and onset. Pet. Ex. 16 at 1. Dr. Sheikh opined Petitioner's correct diagnosis is GBS and that Petitioner's neurologic symptoms began on May 25, 2018, 36 days post-vaccination. Id. at 6-10. He also specifically addressed Respondent's expert's, Dr. Leist's, arguments that (1) Petitioner's symptoms were not consistent with GBS and (2) Petitioner's onset was outside the accepted timeframe. Id. at 1, 6-10.

i. Diagnosis

Dr. Sheikh opined Petitioner's "clinical features and course, electrodiagnostic findings, and treatment-responsiveness to IVIG were all consistent with GBS." Pet. Ex. 16 at 10. He also concluded Petitioner met the Brighton diagnostic criteria for GBS. Id.

Dr. Sheikh first described how Petitioner's clinical course was consistent with GBS. Pet. Ex. 16 at 2-5. To summarize, Petitioner first complained of neurologic symptoms on June 4, 2018, when he presented with tingling of his feet, hands, and tongue as well as leg cramps. Id. at 2. Petitioner indicated these symptoms began on May 25, 2018, when he was lifting kettle bells in the gym. Id. On June 4, he was diagnosed with tingling in extremities and acute right-sided lower back pain without sciatica. Id. Petitioner's symptoms worsened, particularly his leg weakness, which prompted a follow up visit on June 7. Id. at 2-3. MRIs and PT were recommended. Id. at 3. After reviewing Petitioner's MRIs, neurosurgeon Dr. Tutt determined "[t]here [was] no indication for neurosurgical intervention" and "exam[ination] and history suggest[ed] a demyelinating process." Id. (quoting Pet. Ex. 4 at 17). Petitioner was referred to neurologist Dr. Schneider, who diagnosed Petitioner with GBS on June 15, 2018, due to clinical features that were confirmed with EMG/NCS testing. Id. At the June 15 visit to Dr. Schneider, Petitioner reported his symptoms had plateaued. Id. at 4. Physical examination revealed weakness in arms and legs proximally and distally as well as absent deep tendon reflexes. Id. "Dr. Schneider also categorically stated that degenerative disc disease was unrelated to [Petitioner's] condition." Id. at 3. Dr. Sheikh agreed with Petitioner's treating physician's diagnosis of AIDP/GBS. Id. at 10-11.

Thereafter, Petitioner was admitted to St. Joseph's Hospital. Pet. Ex. 16 at 4. Dr. McIntosh, a neurologist, evaluated Petitioner on June 15, 2018, and diagnosed Petitioner with AIDP. Id. at 4-5. Petitioner started IVIG treatment, and was discharged on June 19, 2018, after

five days of treatment. Id. at 5. "[Petitioner] continued outpatient [PT] and improved over time." Id.

Based on Petitioner's clinical course, Dr. Sheikh opined Petitioner's diagnosis was GBS and that he met the Brighton's level 2[48] of diagnostic certainty criteria[49] and the National Institute of Neurological Disorders and Stroke ("NINDS") criteria.[50] Pet. Ex. 16 at 6 (citing Pet. Exs. 17-18). The following findings are required for level 2 of diagnostic certainty for GBS under the Brighton criteria: (1) "[b]ilateral AND flaccid weakness of the limbs;" (2) "[d]ecreased or absent deep tendon reflexes in weak limbs;" (3) "[m]onophasic illness pattern AND interval between onset and nadir of weakness between 12 h[ours] and 28 days AND subsequent clinical plateau;" (4) a certain "CSF total white cell count" or "[i]f CSF not collected or results not available, electrophysiologic studies consistent with GBS;" and (5) "[a]bsence of identified alternative diagnosis for weakness." Pet. Ex. 18 at 7. The two "[f]eatures required for diagnosis" as per NINDS criteria are (1) "[p]rogressive motor weakness of more than one limb" and (2) areflexia. Pet. Ex. 17 at 1.

Applying the facts to the Brighton diagnostic criteria, Dr. Sheikh noted that Dr. Schneider's examination on June 15, 2018 found Petitioner had weakness in extremities proximally and distally that progressed over the last three weeks as well as absent deep tendon reflexes. Pet. Ex. 16 at 4. He opined Petitioner symptoms began on May 25, 2018, and 21 days later, on June 15, Petitioner reported that over "the past few days he fe[lt] that symptoms have generally plateaued." Id. at 4, 10 (quoting Pet. Ex. 4 at 26). With regard to CSF, Dr. Sheikh noted Dr. McIntosh at St. Joseph's Hospital found a lumbar puncture testing for CSF was not needed given Petitioner's "clinical presentation [was] classic for AIDP" and "[h]is exam[ination] and EMG/NCS were consistent with AIDP." Id. at 5 (quoting Pet. Ex. 5 at 21). Dr. Sheikh also opined Petitioner's EMG/NCS findings were characteristic and confirmatory of AIDP/GBS diagnosis. Id. at 8-9. Additionally, "repeat electrical studies on December 18, 2018 show[ed] significant improvements[,] . . . definitely confirm[ing] recovery of the peripheral neuropathy and the monophasic nature of the disease consistent with GBS." Id. at 9.

Next, Dr. Sheikh explained that Petitioner's symptoms could not be explained by the findings of chronic degenerative disc disease on MRI. Pet. Ex. 16 at 6-8. He found the "MRI findings consistent with chronic degenerative spine disease without acute changes explaining

---

[48] Dr. Sheikh noted that Petitioner's "treating physicians appropriately decided not to do [the] invasive [lumbar puncture] as clinical features and electrodiagnostic testing were typical and consistent with GBS." Pet. Ex. 16 at 6; see Pet. Ex. 5 at 10, 21. Because a lumbar puncture was not done, and CSF not collected, Petitioner could not meet level 1 diagnostic certainty. Pet. Ex. 16 at 6.

[49] James J. Sejvar et al., Guillain-Barré Syndrome and Fisher Syndrome: Case Definitions and Guidelines for Collection, Analysis, and Presentation of Immunization Safety Data, 29 Vaccine 599 (2011).

[50] Arthur K. Asbury & David R. Cornblath, Assessment of Current Diagnostic Criteria for Guillain-Barré Syndrome, 27 Annals Neurology S21 (1990).

new diffuse widespread symptoms." Id. at 7. Dr. Sheikh noted Petitioner showed a "progression of sensory symptoms from feet to hands and then face (ascending pattern)." Id. at 7-8 (citing Pet. Ex. 4 at 14, 26). He found the MRIs showed no evidence of "acute disc herniations externally compressing the nerve roots to explain distribution of new symmetric sensory symptoms." Id. at 7. Moreover, "sensory symptoms on the face cannot be explained [by] lumbar or cervical root disease" but they "reflect[] [an] acute widespread neuropathic process such as GBS." Id. at 8.

Additionally, Dr. Sheikh noted Dr. Tutt, a neurosurgeon, reviewed Petitioner's MRIs and determined they did not explain Petitioner's symptoms. Pet. Ex. 16 at 8 (citing Pet. Ex. 4 at 17). Instead, Petitioner's history and examination "suggest[ed] a demyelinating process." Id. (quoting Pet. Ex. 4 at 17). And Dr. Schneider, Petitioner's neurologist, agreed Petitioner's MRIs "[did] not explain [Petitioner's] clinical features and diagnosed him with GBS." Id. (citing Pet. Ex. 4 at 14, 27). For all these reasons, Dr. Sheikh opined Dr. Leist's assertion that Petitioner's symptoms were due to lumbar and cervical disc disease is unsupported by the MRIs or Petitioner's clinical course. Id.

Dr. Sheikh also disagreed with Dr. Leist's opinion that Petitioner's symptoms reflected lumbar and cervical disc disease. Pet. Ex. 16 at 6 (citing Resp. Ex. A at 7). He opined Petitioner "initially started with typical GBS symptoms and had classic course and developed symmetric severe proximal and distal weakness in arms and legs that cannot be explained on the basis of disc herniations in lumbar and cervical spine[]." Id.

Dr. Sheikh cited an article by Ropper,[51] who found sensory symptoms to be the most common presenting symptom for GBS. Pet. Ex. 16 at 6 (citing Pet. Ex. 19 at 1). Ropper wrote "[a]cute [GBS] typically begins with fine paresthesias in the toes or fingertips, followed within days by leg weakness that makes walking and climbing stairs difficult." Pet. Ex. 19 at 1. Ropper further noted "[e]arly acute [GBS] may be difficult to identify and has no pathognomonic features, but the fully evolved pattern is easily recognized." Id. at 3. "Failure to recognize any neurologic disease is a common error in early [GBS]. Paresthesias are often discounted, reflexes not carefully checked, and pains in the legs or back misinterpreted, leading to emergency room diagnoses of viral syndrome, anxiety, or sciatica." Id.

Additionally, Ropper examined the frequency of features of acute GBS initially and once the illness was "fully developed." Pet. Ex. 19 at 3 tbl.1. One feature, areflexia, or decreased or absent tendon reflexes, was found in 75% of patients initially and 90% of patients once GBS was fully developed. Id. Dr. Sheikh noted areflexia may be seen in limbs without weakness but "must be observed in weak limbs" to meet the Brighton criteria. Pet. Ex. 16 at 6-7 (citing Pet. Ex. 18 at 7 n.9). On initial examination, Petitioner had preserved patellar reflexes, which Dr. Sheikh opined "is not inconsistent with early GBS as [Petitioner] had no weakness in quadriceps muscle at the time of that examination." Id. at 7 (citing Pet. Ex. 3 at 381). "[T]he deep tendon reflexes exam[ination] was restricted to patella and examination at this point [did] not exclude the possibility of hypo- or areflexia in other muscle groups." Id. And "in its fully developed form[,] [Petitioner] was areflexic." Id. at 6.

[51] Allan H. Ropper, The Guillain-Barré Syndrome, 326 New Eng. J. Med. 1130 (1992).

Lastly, Dr. Sheikh opined Petitioner's significant clinical improvement following IVIG supports a diagnosis of GBS. Pet. Ex. 16 at 9-10. Dr. Sheikh and Dr. Leist agreed Petitioner improved during IVIG therapy. Id. at 9. However, Dr. Leist argued Petitioner's improvement while on IVIG was coincident with pain management, PT, and rest, and thus, was to be "expected" and not evidence of GBS. Id. (citing Resp. Ex. A at 8).

Dr. Sheikh disagreed and opined that such "[q]uick recovery in muscle strength with IVIG treatment would not be compatible with radiculopathic disease related [to] spinal disc disease." Pet. Ex. 16 at 10. On discharge, Dr. Henson documented Petitioner's improvement after five days of IVIG and physical and occupational therapy. Id. (citing Pet. Ex. 5 at 10-11). Dr. Henson noted Petitioner "improve[d] his strength and mobility being able to go [up] multiple steps and down multiple step[s] when he could not even go up one [six-]inch step when [he] arrived here." Id. (quoting Pet. Ex. 5 at 10-11). Dr. Sheikh explained that if Petitioner's "weakness was due to lumbar and cervical radiculopathic disease related to degenerative disc disease[,] then quick recovery, within days, related to IVIG treatment would not be expected to occur." Id. He added that "the time course of motor recovery with IVIG treatment is consistent with acquired inflammatory demyelinating injury to motor nerve fibers." Id. at 9-10. He concluded Petitioner's "most striking clinical feature was severe proximal and distal muscle weakness in arms and legs that improved rapidly with IVIG supporting the diagnosis of GBS." Id. at 10.

ii. Onset

Dr. Sheikh opined Petitioner's "neurologic symptoms started with low back pain and numbness in feet on May 25, 2018," or around 36 days after hepatitis A vaccination. Pet. Ex. 16 at 10. He found "the back pain likely reflect[ed] inflammation in the spinal roots related with GBS." Id.

Dr. Sheikh argued that even if Petitioner's foot and back symptoms on May 25, 2018 were not caused by GBS, Petitioner's bilateral hand symptoms began two days later, around 38 days post-vaccination. Pet. Ex. 16 at 10. Dr. Sheikh opined "[t]hese hand symptoms cannot be attributed to degenerative dis[c] disease and radiculopathy as there was no associated neck pain or radiating pain from the neck." Id. Around 40 days post-vaccination, Petitioner's mouth and nose symptoms began, as documented by Dr. Schneider. Id. Dr. Sheikh also opined "that the mouth and nose symptoms cannot be attributed to lumbar or cervical radiculopathies related to dis[c] disease." Id.

Thus, Dr. Sheikh concluded "[Petitioner's] neurologic symptoms started within 3-42 days after vaccination, a time period considered plausible biologic window for GBS after vaccination according to the vaccine injury table." Pet. Ex. 16 at 10.

iii. Causation

Although Dr. Sheikh's opinions focused on diagnosis and onset, he briefly responded to Dr. Leist's suggestion that trauma was a trigger of Petitioner's GBS. Pet. Ex. 16 at 1, 7. Dr. Sheikh opined Petitioner's clinical course does not support trauma as a trigger. Id. at 7.

Dr. Leist opined that "[t]he trauma [Petitioner] sustained shortly after lifting kettle bells on May 25, 2018 would consequentially be the most temporally proximate event to the onset of symptoms of GBS." Pet. Ex. 16 at 7 (quoting Resp. Ex. A at 9). Dr. Leist relied on a meta-analysis from Huang et al., where the authors concluded that "given the current focus on infectious agents as the main cause of GBS, trauma may be neglected as a potential cause of GBS, leading to misdiagnosis or missed diagnosis in clinical practice." Id. (quoting Resp. Ex. A, Tab 1 at 9).

Dr. Sheikh opined this article was not relevant to Petitioner's case for several reasons. Pet. Ex. 16 at 7. First, the interval between Petitioner's symptom onset and the alleged trauma (lifting kettle bells) was immediate. Id. However, Huang et al. found "[t]he median duration from the trauma trigger to onset of the first GBS symptom was 9 ([interquartile range] 6.5-13) days." Resp. Ex. A, Tab 1 at 3. Next, Dr. Sheikh noted the article "[did] not specify inclusion criteria for spinal trauma but include[d] patients with spinal surgery and/or direct spinal or spinal cord trauma." Pet. Ex. 16 at 7. Here, "[t]here [was] no evidence of direct spinal trauma." Id. Lastly, Huang et al. "excluded patients with vaccinations in preceding 6 weeks from the[ir] analysis." Id. (citing Resp. Ex. A, Tab 1 at 2).

3. Respondent's Expert, Dr. Thomas P. Leist, M.D., Ph.D.[52]

a. Background and Qualifications

Dr. Leist is a board-certified neurologist, specializing in the field of neuroimmunology and "regularly involved in the care of patients with neuroimmunological conditions, including [MS], transverse myelitis (TM), neuromyelitis optica spectrum disorder (NMOSD), NMO syndrome, immune disorders of the peripheral nervous system including [GBS], and paraneoplastic neurologic syndromes." Resp. Ex. A at 1. He received a Ph.D. in Biochemistry from the University of Zurich in Switzerland and an M.D. from the University of Miami in Florida. Resp. Ex. B at 1. Thereafter, he completed an internal medicine internship at the University of Miami and a neurology residency at Cornell Medical Center/Sloan Kettering Memorial Cancer Center in New York. Id. Dr. Leist is a neurology professor at Thomas Jefferson University, where he also directs the Division of Clinical Neuroimmunology. Id.; Resp. Ex. A at 1. Additionally, he holds multiple hospital and administrative appointments. Resp. Ex. B at 1. Dr. Leist has authored or co-authored various publications on the subject of immunology, neuroimmunology, and imaging. Id. at 6-11; Resp. Ex. A at 1.

b. Opinion

[52] Dr. Leist provided two expert reports. Resp. Exs. A, E.

Dr. Leist opined, "to a reasonable degree of medical certainty," that "[Petitioner] did not sustain an adverse event as a consequence of the dose of inactivated hepatitis A vaccine he received on April 19, 2018, but rather a sport injury resulting in L5 radiculopathy and a cervical sprain." Resp. Ex. A at 9; see also Resp. Ex. E at 4.

i. Diagnosis

Dr. Leist opined "GBS is not the most likely diagnosis for [Petitioner]" and "that more likely than not [Petitioner] sustained or aggravated lumbar disc herniation and aggravated likely preexisting cervical disc disease while weight training and lifting weights overhead on May 25, 2018." Resp. Ex. A at 7; see also Resp. Ex. E at 1.

For support, Dr. Leist explained that Petitioner's symptoms "are consistent with an injury or aggravation of a preexisting condition." Resp. Ex. A at 7. On May 25, 2018, Petitioner "developed numbness in the feet shortly after lifting kettle bells." Id. Petitioner reported "that about 45 minutes later[,] both of his feet started tingling." Id. (quoting Pet. Ex. 2 at 3). On June 4, 2018, Petitioner reported that on May 25, 2018, "he was lifting kettle bells and felt a weird sensation in his low back. He stopped that exercise and sat down on a weight machine and started to feel his feet tingle. This continued throughout the day and then he started feeling tingling in his hands." Id. (quoting Pet. Ex. 3 at 379). A few days later, he developed "cramping in his right leg and hip." Id. (quoting Pet. Ex. 3 at 379). On June 4, he was found to have "an area in his low back that [was] sore and he state[d] that when his wife presse[d] deep on his back, he [could] feel the tingling sensation throughout his body." Id. (quoting Pet. Ex. 3 at 379). On examination, Petitioner had preserved patellar reflexes. Id. (citing Pet. Ex. 3 at 381). Dr. Leist opined the June 4, 2018 examination "is consistent with L5 radiculopathy and cervical sprain." Id. Additionally, he cited to the June 16, 2018 PT intake examination that found "greater weakness in the proximal than in the distal muscles of the lower extremity," which he argued is "the opposite of what would have been expected with GBS." Id. at 9 (citing Pet. Ex. 3 at 238).

Dr. Leist found Petitioner's June 13, 2018 MRIs consistent with an L5 radiculopathy. Resp. Ex. A at 7; Resp. Ex. E at 1. The lumbar spine MRI "showed an annular tear at L5-S1 level with central disc herniation and bilateral foraminal narrowing and a diffuse disc bulge with lateral prominence at L3-L4." Resp. Ex. A at 7 (citing Pet. Ex. 4 at 37-38). And the cervical spine MRI "showed degenerative changes at C3-C4 and C5-C6." Id. (citing Pet. Ex. 4 at 35-36).

He also opined that the EMG performed by Dr. Schneider on June 15, 2018, was consistent with an L5 radiculopathy. Resp. Ex. A at 7; Resp. Ex. E at 1. Dr. Leist noted the EMG "showed reduced recruitment for the right tibialis anterior muscle."[53] Resp. Ex. A at 7

[53] The tibialis anterior muscle is an anterior tibial muscle originates in the lateral condyle and lateral surface of tibia, interosseous membrane and inserts into the medial cuneiform and base of first metatarsal that dorsiflexes and inverts the feet. Musculus Tibialis Anterior, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=90989 (last visited Jan. 25, 2023).

(citing Pet. Ex. 4 at 32). Citing Wright and Inbody,[54] Dr. Leist explained that "[i]nvolvement of the L5 nerve root can cause sharp or shooting feeling in the buttock, thigh, leg, and foot, numbness in the foot and toe, and weakness of the movement of the ankle and the big toe." Id. (citing Resp. Ex. A, Tab 5 at 3-4). Wright and Inbody explained that the "signs of an L5 radiculopathy" include (1) "pain radiating to the posterolateral buttock, lateral posterior thigh, and lateral leg;" (2) "[s]ensory loss [] most likely in a triangular wedge involving the great toe, second toe, and adjacent skin on the dorsum of the foot;" and (3) "[w]eakness [] in the muscles innervated by the L5 root (gluteus medius, tibialis anterior and posterior, peronei, and extensor hallucis longus)," resulting "in difficulty in ankle dorsiflexion, eversion, inversion, and hip abduction." Resp. Ex. A, Tab 5 at 3-4. The authors also noted an L5 radiculopathy "is most easily identified by weakness in the extensor hallucis longus (extension of the big toe)" and "ankle reflex is usually normal." Id. at 4.

Dr. Leist also noted that "Dr. Schneider documented normal action potentials for the vastus medialis[55] and the tibialis anterior in the limited EMG of the right lower extremity," which is "not consistent with GBS." Resp. Ex. A at 7-8 (emphasis omitted). Dr. Leist argued Dr. Schneider "relied only on the [NCS], and not the limited [EMG]" when diagnosing Petitioner with GBS. Id. at 8 (emphasis omitted).

Next, Dr. Leist opined "[t]he treatments that alleviated [Petitioner's] symptoms are consistent with an injury or aggravation of a preexisting condition." Resp. Ex. A at 7. He noted Petitioner's symptoms were alleviated when he used an inversion table. Id. (citing Pet. Ex. 2 at 3 (noting Petitioner reported "he was symptom free for [one] minute" after using an inversion table)). While Dr. Leist acknowledged that Petitioner improved while on IVIG treatment, he noted Petitioner was also receiving pain management, PT, and rest during this time. Id. at 8. He asserted "[i]t is expected that the symptoms of lumbar and cervical sprain would improve with pain management, [PT], and rest." Id. Dr. Leist concluded that "[t]he improvement [Petitioner] experienced during the hospitalization does not serve as evidence that he had GBS." Id.

Lastly, Dr. Leist opined "that [Petitioner's] case does not meet Brighton criteria for GBS" because "the June 4, 2018 exam[ination] findings and the June 15, 2018 partial EMG, specifically the finding of normal actional potentials for the vastus medialis and the tibialis anterior, are inconsistent with a diagnosis of GBS." Resp. Ex. E at 1, 4.

Dr. Leist concluded that Petitioner's clinical symptoms, imaging, EMG/NCS, physical examination and history, and response to treatment were "consistent with [Petitioner] having suffered L5 radiculopathy and a cervical sprain, not GBS." Resp. Ex. A at 7-9 (emphasis omitted); see also Resp. Ex. E at 1, 4.

---

[54] Randall Wright & Steven B. Inbody, Radiculopathy and Degenerative Spine Disease, in Neurology Secrets 121 (5th ed. 2011).

[55] The vastus medialis muscle is a common tendon of the quadriceps used to extend the knees. Musculus Vastus Medialis, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=91014 (last visited Jan. 25, 2023). The muscle originates in the medial aspect of the femur and inserts into the patella. Id.

ii. Althen Prong One

Dr. Leist addressed Dr. Ahmed's proposed mechanism and opined there is no evidence that the hepatitis A vaccine can cause GBS. Resp. Ex. A at 5-6. He opined "[t]here is no evidence of molecular mimicry as a mechanism for GBS caused by inactivated hepatitis A vaccine." Id. For support, he agreed with the IOM that "molecular mimicry may contribute to the symptoms of GBS; however, the publications did not provide evidence linking these mechanisms to hepatitis A vaccine." Id. (quoting Resp. Ex. A, Tab 4 at 2).[56] He noted "that no research published since 2012 has provided reliable information to the contrary." Id. Dr. Leist acknowledged certain literature cited in this case discussed the theory molecular mimicry. Resp Ex. E at 2. In fact, in an article cited by Dr. Leist, authored by Huang et al., the authors noted "molecular mimicry has been proposed as a trigger, along with direct damage to the myelin, or axonal membranes from the vaccine or exposure of cryptogenic epitopes." Resp. Ex. A, Tab 1 at 2. However, he argued that "[d]iscussion of potential mechanisms of injury in a case report describing temporality neither proves that the discussed mechanisms were relevant in the specific case nor does it establish causation." Resp. Ex. E at 2.

As for the alum adjuvant, Dr. Leist opined "[t]here is no evidence that [alum] adjuvant contained in inactivated hepatitis A vaccine causes neurologic complications." Resp. Ex. A at 6. For support, he cited a 2008[57] report from the Global Advisory Committee on Vaccine Safety ("GACVS")[58] of the World Health Organization ("WHO"). Id. (citing Resp. Ex. A, Tab 2). The GACVS found "no evidence of a health risk from [alum]-containing vaccines or any justification for changing current vaccination practices." Resp. Ex. A, Tab 2 at 1. GACVS further wrote, "[f]rom the most recent evidence available, there is no reason to conclude that a health risk exists as a result of administration of [alum]-containing vaccines, nor is there any good reason for changing current vaccination practice." Id. at 2.

Next, Dr. Leist explained that the inactivated hepatitis A vaccine is not known to cause or be associated with GBS. Resp. Ex. A at 5-6; Resp. Ex. E at 4. He cited the 2012 IOM report that determined "the epidemiologic evidence was insufficient or absent to assess an association between hepatitis A vaccine and GBS." Resp. Ex. A at 5 (quoting Resp. Ex. A, Tab 4 at 2). Regarding mechanistic evidence, the IOM noted that "[w]hile rare, hepatitis A infection has been associated with the development of GBS," and they "consider[ed] the effects of natural infection [as] one type of mechanistic evidence" between the hepatitis A vaccine and GBS. Resp. Ex. A, Tab 4 at 2. However, the IOM determined "the mechanistic evidence regarding an association between hepatitis A vaccine and GBS [is] weak based on the knowledge of the natural

---

[56] Inst. of Med., Hepatitis A, in Adverse Effects of Vaccines: Evidence and Causality, supra note 43, at 421, 426-27.

[57] Dr. Leist stated there have been no changes over the past 13 years to this guidance. Resp. Ex. A at 6.

[58] Global Vaccine Safety: Statement from the Global Advisory Committee on Vaccine Safety on Aluminium-Containing Vaccines, World Health Org., https://archive.ph/KA6aS (last reviewed Dec. 3, 2008).

infection." Id. Relying on this information, Dr. Leist opined that "a causal relationship between hepatitis A virus and GBS has not been established." Resp. Ex. E at 2 (citing Resp. Ex. A, Tab 4 at 2). Additionally, Dr. Leist asserted there have been no epidemiologic studies suggesting an association between hepatitis A vaccine and GBS since the IOM report published in 2012. Resp. Ex. A at 5-6.

In response to Dr. Ahmed's reliance on Blumenthal et al.[59] and Roux et al., Dr. Leist argued "[n]either report provides evidence beyond temporality." Resp. Ex. A at 5 (citing Pet. Ex. 12-12; Pet. Ex. 12-13). Additionally, Dr. Ahmed's other "case reports do not provide evidence beyond temporality either." Id. Although Dr. Ahmed argued his case reports provide "'proof' that administration of specific vaccines is causal for certain genetically predisposed subjects," Dr. Leist opined that to accept such a statement would mean "temporal relationship alone would be sufficient to establish causality as any unnamed and unrecognized genetic predisposition could be invoked in any case occurring after vaccination." Resp. Ex. E at 2 (quoting Pet. Ex. 14 at 3 (emphasis omitted)).

Lastly, Dr. Leist opined the package insert "does not provide information concerning a causal relationship between inactivated hepatitis A vaccine and GBS." Resp. Ex. A at 6. He acknowledged GBS is listed in the package insert under "postmarketing experience" in a list of "serious adverse events or events which have a suspected causal connection to components of [the hepatitis A vaccine] or other vaccines or drugs." Id. (quoting Pet. Ex. 9 at 7). But Dr. Leist, quoting the package insert, explained that "[b]ecause these events are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to the vaccine." Id. (quoting Pet. Ex. 9 at 7). Thus, he opined "[t]he reports from the postmarketing experience do not establish or infer a causal relationship between hepatitis A vaccine and the listed events including GBS and do not provide information beyond temporality." Id.

Dr. Leist concluded that "it has not been established that the hepatitis A vaccine can cause GBS." Resp. Ex. E at 2.

iii. Althen Prong Two

Regarding Althen prong two, Dr. Leist opined that even if "the symptoms [Petitioner] experienced after May 25, 2018 were due to GBS, then trauma as [the] cause of his GBS would have to be considered." Resp. Ex. A at 9. The trauma sustained on May 25, 2018 would be "the most temporally proximate event to the onset of symptoms of GBS." Id. He quoted Huang et al., who stated "trauma may be neglected as a potential cause of GBS, leading to misdiagnosis or missed diagnosis in clinical practice." Id. (quoting Resp. Ex. A, Tab 1 at 9).

In their study, Huang et al. "conducted a systematic review to summarize documented cases of GBS following various trauma-related triggers and discuss[ed] potential immunological and pathological mechanisms." Resp. Ex. A, Tab 1 at 2. The authors proposed a new subtype of

[59] Dr. Leist noted this report was reviewed by the IOM in their 2012 report. Resp. Ex. A at 5; see Resp. Ex. A, Tab 4 at 2.

"trauma-related GBS" due to the increasing reports of GBS following various injuries, including "high-intensity exercise" or "strenuous exercise." Id. at 2, 9. "Although the underlying pathophysiological mechanisms of the association between injury and GBS ha[ve] not yet been completely elucidated, [they] consider[ed] that injury-related GBS may involve various biochemical cascades and immunologic responses resulting from psychological stress, physical damage, and pain." Id. at 3, 8 fig.2 (proposing multiple mechanisms of trauma-related GBS).

iv. Althen Prong Three

Dr. Leist opined "[Petitioner's] symptomology fits the timeline for an injury or aggravation of pre-existing injury." Resp. Ex. A at 8. Dr. Leist explained "[Petitioner] sprained his back on May 25, 2018, experienced initial symptoms shortly after that[,] and presented with findings consistent with right greater than left L5 radiculopathy on June 4, 2018[,] or 47 days after the vaccination." Id. He opined that the "symptoms present on June 4, 2018 were consistent with L5 radiculopathy and cervical sprain he sustained on May 25, 2018." Id.

If Petitioner had GBS, then Dr. Leist opined Petitioner's GBS onset would have been "after June 4, 2018,"[60] or more than 47 days after vaccination because "[Petitioner's] symptoms on June 4, 2018 were consistent with lumbar and cervical strain and L5 radiculopathy." Resp. Ex. A at 8. He explained that an onset of more than 47 days post-vaccination would be five days outside the three- to 42-day timeframe in the Vaccine Injury Table for GBS following influenza vaccine. Id.

Dr. Leist opined that because "[there is] no reliable medical theory explaining how inactivated hepatitis A vaccine causes GBS and no epidemiological evidence establishing causation, . . . there [is] no way to know what a medically appropriate timeframe for post-vaccine onset of symptoms would be." Resp. Ex. A at 8.

If Petitioner is found to have developed GBS, and trauma is found to be the trigger of his GBS, then Dr. Leist found "[t]he trauma [Petitioner] sustained [occurred] shortly after lifting kettle bells on May 25, 2018." Resp. Ex. A at 9. According to the findings in Huang et al., the time from trauma trigger to GBS onset was a median of nine days. Resp. Ex. A, Tab 1 at 3, 4 tbl.1.

4. Respondent's Expert, Dr. Robert Fujinami, Ph.D.[61]

a. Background and Qualifications

In 1977, Dr. Fujinami received his Ph.D. in immunology-microbiology from Northwestern University. Resp. Ex. D at 1. He worked at the Scripps Clinic and Research Foundation in the Department of Immunopathology from 1977 to 1985. Id. While at Scripps, he and Dr. Michael Oldstone "first introduced the concept of molecular mimicry in the early 1980's

[60] Dr. Leist did not specify an exact date. See Resp. Ex. A at 8-9.

[61] Dr. Fujinami provided one expert report. Resp. Ex. C.

involving viruses and autoimmunity." Resp. Ex. C at 1. Thereafter, he was an Associate Professor in the Department of Pathology at the University of California, San Diego before moving to the University of Utah School of Medicine in 1990, where he currently teaches in both the neurology and pathology departments. Resp. Ex. D at 1. While at the University of California, he "studied virus triggers for autoimmune disease and demyelinating diseases caused by autoimmune mechanisms and viruses." Resp. Ex. C at 1. He "continue[s] to investigate viral-host interactions that can lead to nervous system inflammatory disease." Id. Throughout his career, Dr. Fujinami has won various awards, has held numerous editorial and administrative positions, and has authored or co-authored over 400 publications. Resp. Ex. D at 1-7, 20-52. He also has relevant experience in viral infections, vaccines, and autoimmune diseases. Resp. Ex. C at 1-2.

b. Opinion

Dr. Fujinami focused his opinions on whether the hepatitis A vaccine can trigger autoimmune diseases and whether Petitioner's purported mechanism of molecular mimicry in combination with alum is the most likely mechanism to explain Petitioner's GBS. Resp. Ex. C at 2. Dr. Fujinami is "neither a physician nor [a] neurologist," and thus, he did not provide an opinion as to diagnosis. Id.

i. Althen Prong One

Dr. Fujinami opined "[t]here is no evidence for hepatitis A vaccine containing alum inducing GBS by molecular mimicry." Resp. Ex. C at 3. Citing articles he co-authored, Dr. Fujinami

> described molecular mimicry as a sharing of an immunologic determinant/epitope between a microbe and host protein/epitope. The two epitopes would cross-react, such that infection with the microbe would generate an immune response that would recognize an epitope in the microbe as well as the mimicking epitope in the host's tissue, resulting in an autoimmune disease.

Id. at 4 (citing Resp. Ex. C, Tab 7;[62] Resp. Ex. C, Tab 8).[63] He indicated "there is a clear causal role for the microbe, [*C.*] *jejuni* infection, an identified cross-reacting epitope between the bacteria and host peripheral nerve myelin, and a particular type of autoimmune nervous system disease, within the GBS classification." Id. (citing Resp. Ex. C, Tab 10 at 2). Dr. Fujinami argued Dr. Ahmed's theory that the alum in the hepatitis A vaccine drove a cross-reactive

[62] Robert S. Fujinami & Michael D. Oldstone, Amino Acid Homology Between the Encephalitogenic Site of Myelin Basic Protein and Virus: Mechanism for Autoimmunity, 230 Science 1043 (1985).

[63] Robert S. Fujinami et al., Molecular Mimicry in Virus Infection: Crossreaction of Measles Virus Phosphoprotein or of Herpes Simplex Virus Protein with Human Intermediate Filaments, 90 Proc. Nat'l Acad. Scis. U.S. 2346 (1983).

inflammatory demyelinating immune response due to molecular mimicry between epitopes in the hepatitis A virus and epitopes in peripheral nerve myelin is inconsistent with the literature. Id.

As for alum, Dr. Fujinami explained that the "very weak adjuvant" contained in the hepatitis A vaccine could not have contributed to the development of a demyelinating illness like GBS. Resp. Ex. C at 4. Citing an article he co-authored, Dr. Fujinami explained that EAE, a model for MS, has been shown to occur in rodents when myelin components are mixed with "powerful adjuvants," leading to the animals' immune system attacking its own myelin and resulting in signs of inflammation and demyelination. Id. (citing Resp. Ex. C, Tab 7). He opined that in GBS, like MS, "immune cells such as T and B cells/antibodies contribute to the pathogenesis of [the] disease[]." Id.

He next cited to Sicotte et al.,[64] a study where mice were specifically immunized with the alum adjuvant along with a neuroantigen. Resp. Ex. C, Tab 9 at 1. None of the mice showed signs of EAE. Id. at 4-5. Instead, the addition of the alum adjuvant prevented EAE and was thought to be effective in promoting antibody production and regenerative responses. Id. at 11. Dr. Fujinami opined that Sicotte et al. is "strong evidence" against Dr. Ahmed's theory, making his theory "scientifically implausible," because none of the mice immunized with the alum adjuvant developed a clinical disease or inflammation of the nervous system. Resp. Ex. C at 5.

Lastly, Dr. Fujinami cited Wållberg et al.,[65] another study that immunized mice with recombinant myelin oligodendrocyte glycoprotein ("rMOG") mixed with alum. Resp. Ex. C, Tab 11 at 1. Seven days after immunization, the authors induced EAE in the mice. Id. at 2, 2 fig.1. Only one out of ten mice that received rMOG and alum developed EAE symptoms, which were mild. Id. at 2 fig.1. The authors determined that immunization with rMOG and alum could protect from EAE. Id. at 1. Dr. Fujinami concluded that Sicotte et al. and Wållberg et al. "support the premise of a vaccine having a disease-relevant mimicry with nervous system myelin adsorbed to alum would be expected to significantly decrease the induction of disease," which is at odds with Dr. Ahmed's theory. Resp. Ex. C at 5 (internal citations omitted).

Dr. Fujinami also criticized Dr. Ahmed's reliance on nine case reports when opining there is evidence that acute infection by the hepatitis A virus and/or vaccine can trigger GBS. Resp. Ex. C at 2-3. Dr. Fujinami noted that based on data from WHO, millions of people have been infected with hepatitis A virus. Id. at 3 (citing Resp. Ex. C, Tab 2 at 2-3;[66] Resp. Ex. C,

---

[64] Maryline Sicotte et al., Immunization with Myelin or Recombinant Nogo-66/MAG in Alum Promotes Axon Regeneration and Sprouting After Corticospinal Tract Lesions in the Spinal Cord, 23 Molecular & Cellular Neuroscience 251 (2003).

[65] Maja Wållberg et al., Vaccination with Myelin Oligodendrocyte Glycoprotein Adsorbed to Alum Effectively Protects DBA/1 Mice from Experimental Autoimmune Encephalomyelitis, 33 Eur. J. Immunology 1539 (2003).

[66] World Health Org. [WHO], WHO Position Paper on Hepatitis A Vaccines (2012).

Tab 3 at 1).[67] A WHO position paper stated, "no serious adverse events occurred that were considered to be associated with administration of the vaccine." Resp. Ex. C, Tab 2 at 10-11. Further, Dr. Fujinami stated that the CDC has not reported GBS or any other autoimmune disease following hepatitis A infection or vaccination. Resp. Ex. C at 3. The CDC stated "the hepatitis A vaccine is safe" and "[n]o serious side effects have been reported." Id. (quoting Resp. Ex. C, Tab 5 at 5);[68] see also Resp. Ex. C, Tab 4 at 13 ("No serious adverse reactions have been reported.").[69] Thus, Dr. Fujinami argued that since millions have been infected or vaccinated with hepatitis A, "there would have been a plethora of articles making such a link or association, not just [nine] case reports." Resp. Ex. C at 3. Dr. Fujinami added that "[c]ase reports do not on their own form any basis for the assumption of a cause-effect relationship[] because the purported cause (vaccination) and the effect (e.g., GBS) may be closely associated in time due to coincidence alone." Id.

Further, Dr. Fujinami cited to Dudley et al., mentioned above. Resp. Ex. C at 3 (citing Resp. Ex. C, Tab 6). They reviewed data from the 2012 IOM report and the 2014 Agency for Healthcare Research and Quality report that assessed possible causal associations of adverse events, including GBS, following vaccinations. Resp. Ex. C, Tab 6 at 1. The IOM did not provide a conclusion as to an association between GBS and hepatitis A vaccination, while the Agency for Healthcare Research and Quality determined there was "insufficient" evidence that the hepatitis A vaccine could cause GBS.[70] Id. at 4 tbl.1, 6-7. Dudley et al. concluded vaccines other than influenza "have not been shown to cause [GBS]." Id. at 4 tbl.1. They explained "a temporal association alone, even with a hypothesis as to how the vaccine might have caused an [adverse effect following immunization], does not establish a causal relationship." Id. at 7.

ii. Althen Prongs Two and Three

Dr. Fujinami opined "more likely than not" the hepatitis A vaccine did not cause Petitioner to develop GBS. Resp. Ex. C at 5. Dr. Fujinami did not otherwise discuss Petitioner's clinical course, onset, or perform an analysis as to Althen prongs two and three.

IV. DISCUSSION

[67] Immunization, Vaccines and Biologicals: Hepatitis A, World Health Org., https://www.who.int/teams/immunization-vaccines-and-biologicals/diseases/hepatitis#hepa (last updated Oct. 19, 2015).

[68] Hepatitis A Questions and Answers for the Public, Ctrs. for Disease Control & Prevention, https://www.cdc.gov/hepatitis/hav/afaq.htm (last reviewed July 28, 2020).

[69] Ctrs. for Disease Control & Prevention, Epidemiology and Prevention of Vaccine-Preventable Diseases 135-48 (Jennifer Hamborsky eds., 13th ed. 2015).

[70] Dr. Fujinami noted there was also "insufficient" evidence linking the hepatitis A vaccine with acute disseminated encephalomyelitis, Bell's palsy, chronic inflammatory disseminated polyneuropathy, MS, transverse myelitis, and other neuroinflammatory immune mediated diseases. Resp. Ex. C at 3 (citing Resp. Ex. C, Tab 6 at 4 tbl.1, 5-6 tbl.2).

A. Standards for Adjudication

The Vaccine Act was established to compensate vaccine-related injuries and deaths. § 10(a). "Congress designed the Vaccine Program to supplement the state law civil tort system as a simple, fair and expeditious means for compensating vaccine-related injured persons. The Program was established to award 'vaccine-injured persons quickly, easily, and with certainty and generosity.'" Rooks v. Sec'y of Health & Hum. Servs., 35 Fed. Cl. 1, 7 (1996) (quoting H.R. Rep. No. 908 at 3, reprinted in 1986 U.S.C.C.A.N. at 6287, 6344).

Petitioner's burden of proof is by a preponderance of the evidence. § 13(a)(1). The preponderance standard requires a petitioner to demonstrate that it is more likely than not that the vaccine at issue caused the injury. Moberly v. Sec'y of Health & Hum. Servs., 592 F.3d 1315, 1322 n.2 (Fed. Cir. 2010). Proof of medical certainty is not required. Bunting v. Sec'y of Health & Hum. Servs., 931 F.2d 867, 873 (Fed. Cir. 1991). Petitioner need not make a specific type of evidentiary showing, i.e., "epidemiologic studies, rechallenge, the presence of pathological markers or genetic predisposition, or general acceptance in the scientific or medical communities to establish a logical sequence of cause and effect." Capizzano v. Sec'y of Health & Hum. Servs., 440 F.3d 1317, 1325 (Fed. Cir. 2006). Instead, Petitioner may satisfy his burden by presenting circumstantial evidence and reliable medical opinions. Id. at 1325-26.

In particular, Petitioner must prove that the vaccine was "not only [the] but-for cause of the injury but also a substantial factor in bringing about the injury." Moberly, 592 F.3d at 1321 (quoting Shyface v. Sec'y of Health & Hum. Servs., 165 F.3d 1344, 1352-53 (Fed. Cir. 1999)); see also Pafford v. Sec'y of Health & Hum. Servs., 451 F.3d 1352, 1355 (Fed. Cir. 2006). The received vaccine, however, need not be the predominant cause of the injury. Shyface, 165 F.3d at 1351. A petitioner who satisfies this burden is entitled to compensation unless Respondent can prove, by a preponderance of the evidence, that the vaccinee's injury is "due to factors unrelated to the administration of the vaccine." § 13(a)(1)(B). However, if a petitioner fails to establish a prima facie case, the burden does not shift. Bradley v. Sec'y of Health & Hum. Servs., 991 F.2d 1570, 1575 (Fed. Cir. 1993).

"Regardless of whether the burden ever shifts to the [R]espondent, the special master may consider the evidence presented by the [R]espondent in determining whether the [P]etitioner has established a prima facie case." Flores v. Sec'y of Health & Hum. Servs., 115 Fed. Cl. 157, 162-63 (2014); see also Stone v. Sec'y of Health & Hum. Servs., 676 F.3d 1373, 1379 (Fed. Cir. 2012) ("[E]vidence of other possible sources of injury can be relevant not only to the 'factors unrelated' defense, but also to whether a prima facie showing has been made that the vaccine was a substantial factor in causing the injury in question."); de Bazan v. Sec'y of Health & Hum. Servs., 539 F.3d 1347, 1353 (Fed. Cir. 2008) ("The government, like any defendant, is permitted to offer evidence to demonstrate the inadequacy of the [P]etitioner's evidence on a requisite element of the [P]etitioner's case-in-chief."); Pafford, 451 F.3d at 1358-59 ("[T]he presence of multiple potential causative agents makes it difficult to attribute 'but for' causation to the vaccination. . . . [T]he Special Master properly introduced the presence of the other unrelated contemporaneous events as just as likely to have been the triggering event as the vaccinations.").

B. Factual Issues

A petitioner must prove, by a preponderance of the evidence, the factual circumstances surrounding his claim. § 13(a)(1)(A). To resolve factual issues, the special master must weigh the evidence presented, which may include contemporaneous medical records and testimony. See Burns v. Sec'y of Health & Hum. Servs., 3 F.3d 415, 417 (Fed. Cir. 1993) (explaining that a special master must decide what weight to give evidence including oral testimony and contemporaneous medical records). Contemporaneous medical records, "in general, warrant consideration as trustworthy evidence." Cucuras v. Sec'y of Health & Hum. Servs., 993 F.2d 1525, 1528 (Fed. Cir. 1993). But see Kirby v. Sec'y of Health & Hum. Servs., 997 F.3d 1378, 1382 (Fed. Cir. 2021) (rejecting the presumption that "medical records are accurate and complete as to all the patient's physical conditions"); Shapiro v. Sec'y of Health & Hum. Servs., 101 Fed. Cl. 532, 538 (2011) ("[T]he absence of a reference to a condition or circumstance is much less significant than a reference which negates the existence of the condition or circumstance." (quoting Murphy v. Sec'y of Health & Hum. Servs., 23 Cl. Ct. 726, 733 (1991), aff'd per curiam, 968 F.2d 1226 (Fed. Cir. 1992))), recons. den'd after remand, 105 Fed. Cl. 353 (2012), aff'd mem., 503 F. App'x 952 (Fed. Cir. 2013).

There are situations in which compelling testimony may be more persuasive than written records, such as where records are deemed to be incomplete or inaccurate. Campbell v. Sec'y of Health & Hum. Servs., 69 Fed. Cl. 775, 779 (2006) ("[L]ike any norm based upon common sense and experience, this rule should not be treated as an absolute and must yield where the factual predicates for its application are weak or lacking."); Lowrie v. Sec'y of Health & Hum. Servs., No. 03-1585V, 2005 WL 6117475, at *19 (Fed. Cl. Spec. Mstr. Dec. 12, 2005) ("[W]ritten records which are, themselves, inconsistent, should be accorded less deference than those which are internally consistent." (quoting Murphy v. Sec'y of Health & Hum. Servs., 23 Cl. Ct. 726, 733 (1991), aff'd per curiam, 968 F.2d 1226 (Fed. Cir. 1992))). Ultimately, a determination regarding a witness's credibility is needed when determining the weight that such testimony should be afforded. Andreu v. Sec'y of Health & Hum. Servs., 569 F.3d 1367, 1379 (Fed. Cir. 2009); Bradley, 991 F.2d at 1575.

Despite the weight afforded medical records, special masters are not bound rigidly by those records in determining onset of a petitioner's symptoms. Valenzuela v. Sec'y of Health & Hum. Servs., No. 90-1002V, 1991 WL 182241, at *3 (Fed. Cl. Spec. Mstr. Aug. 30, 1991); see also Eng v. Sec'y of Health & Hum. Servs., No. 90-1754V, 1994 WL 67704, at *3 (Fed. Cl. Spec. Mstr. Feb. 18, 1994) (Section 13(b)(2) "must be construed so as to give effect also to § 13(b)(1) which directs the special master or court to consider the medical records (reports, diagnosis, conclusions, medical judgment, test reports, etc.), but does not require the special master or court to be bound by them").

C. Causation

To receive compensation through the Program, Petitioner must prove either (1) that he suffered a "Table Injury"—i.e., an injury listed on the Vaccine Injury Table—corresponding to a vaccine that he received, or (2) that he suffered an injury that was actually caused by a vaccination. See §§ 11(c)(1), 13(a)(1)(A); Capizzano, 440 F.3d at 1319-20. Petitioner must

show that the vaccine was "not only a but-for cause of the injury but also a substantial factor in bringing about the injury." Moberly, 592 F.3d at 1321 (quoting Shyface, 165 F.3d at 1352-53).

Because Petitioner does not allege he suffered a Table Injury, he must prove a vaccine he received caused his injury. To do so, Petitioner must establish, by preponderant evidence: "(1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of a proximate temporal relationship between vaccination and injury." Althen, 418 F.3d at 1278.

The causation theory must relate to the injury alleged. Petitioner must provide a sound and reliable medical or scientific explanation that pertains specifically to this case, although the explanation need only be "legally probable, not medically or scientifically certain." Knudsen v. Sec'y of Health & Hum. Servs., 35 F.3d. 543, 548-49 (Fed. Cir. 1994). Petitioner cannot establish entitlement to compensation based solely on his assertions; rather, a vaccine claim must be supported either by medical records or by the opinion of a medical doctor. § 13(a)(1). In determining whether Petitioner is entitled to compensation, the special master shall consider all material in the record, including "any . . . conclusion, [or] medical judgment . . . which is contained in the record regarding . . . causation." § 13(b)(1)(A). The undersigned must weigh the submitted evidence and the testimony of the parties' proffered experts and rule in Petitioner's favor when the evidence weighs in his favor. See Moberly, 592 F.3d at 1325-26 ("Finders of fact are entitled—indeed, expected—to make determinations as to the reliability of the evidence presented to them and, if appropriate, as to the credibility of the persons presenting that evidence."); Althen, 418 F.3d at 1280 (noting that "close calls" are resolved in Petitioner's favor).

Testimony that merely expresses the possibility—not the probability—is insufficient, by itself, to substantiate a claim that such an injury occurred. See Waterman v. Sec'y of Health & Hum. Servs., 123 Fed. Cl. 564, 573-74 (2015) (denying Petitioner's motion for review and noting that a possible causal link was not sufficient to meet the preponderance standard). The Federal Circuit has made clear that the mere possibility of a link between a vaccination and a petitioner's injury is not sufficient to satisfy the preponderance standard. Moberly, 592 F.3d at 1322 (emphasizing that "proof of a 'plausible' or 'possible' causal link between the vaccine and the injury" does not equate to proof of causation by a preponderance of the evidence); Boatmon v. Sec'y of Health & Hum. Servs., 941 F.3d 1351, 1359-60 (Fed. Cir. 2019). While certainty is by no means required, a possible mechanism does not rise to the level of preponderance. Moberly, 592 F.3d at 1322; see also de Bazan, 539 F.3d at 1351.

V. ANALYSIS

A. Diagnosis

As Federal Circuit precedent establishes, in certain cases it is appropriate to determine the nature of an injury before engaging in the Althen analysis. Broekelschen v. Sec'y of Health & Hum. Servs., 618 F.3d 1339, 1346 (Fed. Cir. 2010). Since "each prong of the Althen test is decided relative to the injury[,]" determining facts relating to the claimed injury can be significant in a case like this, where Petitioner's diagnosis is not clear. Id. Thus, before

determining if Petitioner has met each prong of Althen, the undersigned addresses whether Petitioner has established, by a preponderance of the evidence, that he suffers from GBS.

The undersigned finds Petitioner suffers from GBS. First, a brief review of Petitioner's medical records shows Petitioner's treating physicians diagnosed him with GBS. They did not attribute his condition to trauma, degenerative disc disease, radiculopathy, or cervical sprain. On April 19, 2018, Petitioner received a hepatitis A vaccine. Petitioner first reported neurologic symptoms that began on May 25, 2018 to his primary care physician on June 4, 2018. He experienced tingling in feet, hands, and tongue and cramping in right leg and hip. Assessments were tingling in extremities and acute right-sided low back pain without sciatica.

Petitioner returned three days later, on June 7, 2018, complaining of worsening pain and continued tingling in arms and legs. Assessment included numbness and tingling of both lower extremities, acute bilateral low back pain without sciatica, weakness of both lower extremities, tingling in extremities, cervical pain, and myelopathy.

On June 14, 2018, Petitioner presented to neurosurgeon Dr. Tutt and neurosurgery PA-C Sammons. Petitioner complained of burning and deep aching pain, numbness, tingling, and weakness. Petitioner reported that "[o]ver the last four days[,] his weakness ha[d] progressed that he [] had to use a rolling walker to help him ambulate. He has also developed significant difficulty rising from a chair and is unable to do so without the use of his arms." Pet. Ex. 4 at 16. Dr. Tutt opined that Petitioner's "exam[ination] and history suggest[ed] a demyelinating process." Id. at 17.

The next day, on June 15, 2018, Petitioner saw neurologist Dr. Schneider. Physical examination showed weakness and decreased strength in the arms and legs proximally and distally, absent deep tendon reflexes, wide-based unsteady gait, and positive Romberg's. Dr. Schneider's diagnosis was GBS. Pet. Ex. 4 at 15.

EMG/NCS was conducted that day, June 15, and the findings were "compatible with GBS." Pet. Ex. 4 at 31-32. Dr. McIntosh opined that Petitioner's "clinical presentation" was "classic for AIDP." Id. at 21.

Petitioner was admitted to St. Joseph's Hospital on June 15, 2018 for IVIG. Discharge diagnosis on June 19, 2018 was AIDP/GBS.

Numerous specialists examined and treated Petitioner and all of them agreed that his diagnosis was GBS. Respondent's expert, Dr. Leist, opined Petitioner's symptoms, imaging, testing, and physical examination findings were consistent with an L5 radiculopathy and cervical sprain. However, Petitioner was not diagnosed with radiculopathy or cervical sprain. Moreover, none of Petitioner's treating physicians ever suggested that the cause of his GBS was trauma or exercise.

Further, Petitioner's expert, Dr. Sheikh opined that Petitioner had a classic course of GBS, with symptoms that could not be explained by the MRI findings.

Although Petitioner's MRIs showed degenerative disc disease and a focal central disc herniation with annular fissure at L5/S1, the undersigned determines these findings do not negate Petitioner's GBS diagnosis. When assessing Petitioner, his treating neurosurgeon considered whether the MRIs could explain Petitioner's symptoms. Neurosurgeon Dr. Tutt specifically opined that the MRI findings did not explain Petitioner's symptoms. Dr. Tutt stated "[t]here [was] no indication for neurosurgical intervention on these images." Pet. Ex. 4 at 17. And Dr. Tutt opined that Petitioner's physical examination and history suggested "a demyelinating process." Id. The same is true for Dr. Schneider, Petitioner's neurologist, who after reviewing the MRIs and examining Petitioner, concluded "this is almost certainly GBS." Id. at 15.

In reaching his opinions as to diagnosis, Dr. Leist failed to recognize that Petitioner's treating neurosurgeon and neurologist both reviewed Petitioner's MRIs and found no abnormality that could explain Petitioner's symptoms. Nor did he acknowledge that Petitioner's neurosurgeon "suggest[ed] a demyelinating process" was at play or that Petitioner's neurologist opined Petitioner "almost certainly" has GBS. Pet. Ex. 4 at 15, 17. Therefore, the undersigned finds Dr. Sheikh's opinions here more persuasive as they are consistent with those held by Petitioner's treating physicians.

Both Dr. Leist and Dr. Sheikh agreed Petitioner improved while on IVIG. Dr. Leist argued this improvement is not evidence that Petitioner has GBS since Petitioner was also receiving occupational therapy, PT, and rest at the same time. However, Dr. Sheikh opined Petitioner's significant clinical improvement following IVIG supports a diagnosis of GBS because such "[q]uick recovery in muscle strength with IVIG treatment would not be compatible with radiculopathic disease related [to] spinal disc disease." Pet. Ex. 16 at 10. The undersigned agrees with Dr. Sheikh's opinion here, and finds the combination of Petitioner's medical records, clinical course, treating physician statements, and improvement on IVIG supports a diagnosis of GBS.

Lastly, Dr. Sheikh opined Petitioner met the Brighton and NINDS criteria for a diagnosis of GBS. He explained that Petitioner had bilateral and flaccid weakness of the extremities; absent deep tendon reflexes; a monophasic illness, with an interval of 21 days between onset and nadir; an EMG/NCS consistent with GBS; and his weakness could not be explained by his MRI findings, for the reasons stated above. See Pet. Ex. 16 at 4-10.

Dr. Leist disagreed and argued that Petitioner's June 4, 2018 examination and EMG/NCS were inconsistent with GBS. Resp. Ex. E at 1, 4. However, the undersigned disagrees and finds Dr. Sheikh's and Dr. Schneider's opinions more persuasive here. Thus, the undersigned finds the overall weight of the evidence preponderates in favor of Petitioner.

For the reasons described above, the undersigned finds by preponderant evidence that Petitioner's diagnosis after vaccination was GBS.

B. Althen Prong One

Under Althen prong one, Petitioner must set forth a medical theory explaining how the received vaccine could have caused the sustained injury. Andreu v. Sec'y of Health & Hum.

Servs., 569 F.3d 1367, 1375 (Fed. Cir. 2009); Pafford, 451 F.3d at 1355-56. Petitioner's theory of causation need not be medically or scientifically certain, but it must be informed by a "sound and reliable" medical or scientific explanation. Boatmon, 941 F.3d at 1359; see also Knudsen, 35 F.3d at 548; Veryzer v. Sec'y of Health & Hum. Servs., 98 Fed. Cl. 214, 223 (2011) (noting that special masters are bound by both § 13(b)(1) and Vaccine Rule 8(b)(1) to consider only evidence that is both "relevant" and "reliable"). If Petitioner relies upon a medical opinion to support his theory, the basis for the opinion and the reliability of that basis must be considered in the determination of how much weight to afford the offered opinion. See Broekelschen, 618 F.3d 1339 at 1347 ("The special master's decision often times is based on the credibility of the experts and the relative persuasiveness of their competing theories."); Perreira v. Sec'y of Health & Hum. Servs., 33 F.3d 1375, 1377 n.6 (Fed. Cir. 1994) (stating that an "expert opinion is no better than the soundness of the reasons supporting it" (citing Fehrs v. United States, 620 F.2d 255, 265 (Ct. Cl. 1980))).

The undersigned finds Petitioner provided preponderant evidence that molecular mimicry is a sound and reliable theory to explain how the hepatitis A vaccination can cause GBS.[71] There are several reasons for this finding, including expert opinions and medical literature.

The experts do not dispute the theory of molecular mimicry, or that it is a sound and reliable theory generally as it relates to GBS, but disagree as to whether a hepatitis A vaccine can trigger molecular mimicry and cause GBS. Respondent's experts opined there is no evidence that the hepatitis A vaccine can cause GBS via molecular mimicry.

For support, Dr. Ahmed cited a number of articles explaining the theory of molecular mimicry and how it can cause GBS. To summarize, molecular mimicry occurs when "agents [] induce cross-reactive autoimmune responses to epitopes within host proteins which, in susceptible individuals, may tip the balance of immunological response versus tolerance toward response and subsequently lead to autoimmune disease." Pet. Ex. 12-20 at 1. "[B]oth bacterial and viral vaccines have been linked with induction of [GBS]," with molecular mimicry as a "[p]ossible mechanism that can [t]rigger GBS." Pet. Ex. 12-22 at 2, 6. Vaccines can trigger an autoimmune disease in individuals that are genetically predisposed because "a vaccine stimulates some of the same host responses . . . as an infection." Pet. Ex. 12-1 at 2. Because the hepatitis A vaccine, HAVRIX, "is derived from the wild-type hepatitis A virus, the development of GBS with . . . vaccination provides confirmatory evidence for the role of commonly shared hepatitis A antigens (involved in molecular mimicry)." Pet. Ex. 14 at 4 (emphasis omitted).

Molecular mimicry has been accepted as a sound and reliable theory in many Vaccine Program cases dealing with demyelinating conditions, including GBS, forming the basis for petitioners to be entitled to compensation. See, e.g., Conte v. Sec'y of Health & Hum. Servs., No. 17-403V, 2020 WL 5743696, at *23 (Fed. Cl. Spec. Mstr. July 27, 2020) (noting the theory of molecular mimicry in a GBS case is "well-established and well-settled in the Vaccine

[71] The undersigned does not find Petitioner provided preponderant evidence that the alum adjuvant in the hepatitis A vaccine plays a role in causing GBS. The literature provided does not articulate any role played by the alum adjuvant in inducing GBS. Thus, the undersigned finds the evidence insufficient to find alum played a role here.

Program"); Barone v. Sec'y of Health & Hum. Servs., No. 11-707V, 2014 WL 6834557, at *8-9 (Fed. Cl. Spec. Mstr. Nov. 12, 2014) (noting molecular mimicry "has been accepted in other Program cases as a reliable medical explanation for how various autoimmune conditions could develop after the receipt of different kinds of vaccinations"); Pierson v. Sec'y of Health & Hum. Servs., No. 17-1136V, 2022 WL 322836, at *23, *25 (Fed. Cl. Spec. Mstr. Jan. 19, 2022) (listing cases that have linked molecular mimicry to several demyelinating illnesses and various vaccines).[72] Although decisions of other special masters are not binding, the undersigned finds these cases instructive and agrees with the reasoning of other special masters who have generally found molecular mimicry to be a sound and reliable mechanism for GBS. See Boatmon, 941 F.3d at 1358; Hanlon v. Sec'y of Health & Hum. Servs., 40 Fed. Cl. 625, 630 (1998), aff'd, 191 F.3d 1344 (Fed. Cir. 1999).

More specifically, Dr. Ahmed also cited a number of case reports documenting GBS following hepatitis A infection. For example, Azuri et al. documented GBS in a three-and-one-half-year-old boy following exposure to hepatitis A infection and receipt of immunoglobulin immunization. The authors noted "[i]t is possible that there is molecular resemblance between antigens of . . . [hepatitis A] and components of the myelin of peripheral nerves." Pet. Ex. 12-5 at 1. Breuer et al. similarly noted an immune mechanism may be postulated after reporting on a case of GBS in a 28-year-old pregnant woman diagnosed with hepatitis A. The Tabor article reviewed cases of GBS following hepatitis A infection and noted the mechanism leading to GBS "may include direct cytotoxicity of the virus or immune-mediated damage." Pet. Ex. 12-11 at 2.

Chitambar et al. reported a case of GBS following hepatitis A in a 17-year-old male. Johnston et al. described a case of a 37-year-old who developed GBS following hepatitis A infection. And Bosch et al. found two of 167 patients with GBS also tested positive for hepatitis A antibodies, indicating recent infection with hepatitis A. The authors in Bosch et al. acknowledged "[t]he incidence of hepatitis A virus infection in [] patients with GBS . . . was low," but found it "may be a reflection of the incidence of hepatitis A virus in [the] population." Pet. Ex. 12-6 at 2. Marés-Segura et al. also found the GBS in their 34-year-old patient "could be attributed" to her recent hepatitis A infection. Pet. Ex. 12-10 at 1.

GBS has also been reported after hepatitis A vaccination. Dr. Ahmed cited two reports of patients who developed GBS following hepatitis A vaccination. Roux et al. discussed a 30-year-old patient who developed GBS after receiving anti-hepatitis A vaccination. Blumenthal et al. reported a case of GBS in a one-and-one-half-year-old following vaccination with hepatitis A (HAVRIX). Blumenthal et al. noted the "underlying pathophysiology is presumed to involve an immune cascade induced by the precedent agent, leading to demyelination of the large nerve roots." Pet. Ex. 12-12 at 2. They also added that the hepatitis A vaccine, HAVRIX, contains inactivated hepatitis A viruses that can cause a similar immune response to the hepatitis A infection. The authors concluded that "[i]n their patient, the association of [GBS] with hepatitis A vaccine is supported by temporal proximity of the vaccination with the onset of symptoms, lack of other precipitating factors[,] and the immune-mediated nature of the manifestation." Id.

[72] The undersigned acknowledges these cases involve a different vaccine, although the same illness.

And due to the reports of GBS following hepatitis A infection, "there may also be a relationship between the [hepatitis A] vaccine and [GBS]." Id.

The lack of supportive epidemiological evidence is not dispositive, as "[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, in which close calls regarding causation are resolved in favor of injured claimants." Andreu, 569 F.3d at 1378 (quoting Capizzano, 440 F.3d at 1325-26); see also Althen, 418 F.3d at 1280 (noting that "close calls" are resolved in petitioner's favor). Generally, case reports alone may be insufficient to prove causation. However, where robust epidemiology studies are not available, they provide some evidence of causation. And here, where the medical literature reported GBS cases associated with hepatitis A infection and vaccination, the evidence weighs in favor of causation.

Lastly, the package insert is some evidence that the hepatitis A vaccine can cause GBS.[73] See Cottingham ex rel. K.C. v. Sec'y of Health & Hum. Servs., 971 F.3d 1337, 1346 (Fed. Cir. 2020) (finding "medical records paired with the [] package insert [] constitute at minimum circumstantial, objective evidence supporting causation" in determining whether there was a reasonable basis for the claim, a lower standard than preponderance). Here, GBS was identified as an adverse event in the "postmarketing experience" section of the package insert, which "include[d] serious adverse events or events which have a suspected causal connection to components of HAVRIX or other vaccines or drugs." Pet. Ex. 9 at 7.

In summary, this is a close case. Althen, 418 F.3d at 1280 (noting that "close calls" are resolved in Petitioner's favor). However, looking at the evidence as a whole, the undersigned finds Petitioner has offered a sound and reliable medical theory and by preponderant evidence with respect to the first Althen prong.

C. Althen Prong Two

Under Althen prong two, Petitioner must prove by a preponderance of the evidence that there is a "logical sequence of cause and effect showing that the vaccination was the reason for the injury." Capizzano, 440 F.3d at 1324 (quoting Althen, 418 F.3d at 1278). "Petitioner must show that the vaccine was the 'but for' cause of the harm . . . or in other words, that the vaccine was the 'reason for the injury.'" Pafford, 451 F.3d at 1356 (internal citations omitted).

In evaluating whether this prong is satisfied, the opinions and views of the vaccinee's treating physicians are entitled to some weight. Andreu, 569 F.3d at 1367; Capizzano, 440 F.3d at 1326 ("[M]edical records and medical opinion testimony are favored in vaccine cases, as treating physicians are likely to be in the best position to determine whether a 'logical sequence of cause and effect show[s] that the vaccination was the reason for the injury.'" (quoting Althen, 418 F.3d at 1280)). Medical records are generally viewed as trustworthy evidence, since they are created contemporaneously with the treatment of the vaccinee. Cucuras v. Sec'y of Health &

[73] The undersigned acknowledges the language in a package insert in and of itself would not constitute preponderant evidence of causation.

Hum. Servs., 993 F.2d 1525, 1528 (Fed. Cir. 1993). Petitioner need not make a specific type of evidentiary showing, i.e., "epidemiologic studies, rechallenge, the presence of pathological markers or genetic predisposition, or general acceptance in the scientific or medical communities to establish a logical sequence of cause and effect." Capizzano, 440 F.3d at 1325. Instead, Petitioner may satisfy his burden by presenting circumstantial evidence and reliable medical opinions. Id. at 1325-26.

The undersigned finds Petitioner has proved Althen prong two by preponderant evidence for three reasons: Petitioner's clinical course was consistent with vaccine-related GBS; his treating physicians suspected that the hepatitis A vaccine played a causal role; and there is no persuasive evidence of an alternative cause.

First, the records show a clinical course consistent with the mechanism of molecular mimicry as described in the medical literature that described vaccine related GBS. Petitioner received a hepatitis A vaccine on April 19, 2018. His neurological symptoms first presented on May 25, 2018. His symptoms progressed and he first complained of these symptoms to his primary care physician on June 4, 2018. On June 14, 2018, Dr. Tutt's physical examination revealed decreased strength in all extremities as well as absent deep tendon reflexes in all extremities. He determined Petitioner's "exam[ination] and history suggest[ed] a demyelinating process." Pet. Ex. 4 at 17. On June 15, 2018, Dr. Schneider found weakness and decreased strength in all extremities, absent deep tendon reflexes, and wide-based unsteady gait. At this visit, Petitioner reported that he felt his symptoms plateaued over the past few days. Assessment was GBS. Petitioner's EMG/NCS was "compatible with GBS" in "clinical setting of rapidly progressive weakness." Id. at 31-32. Petitioner was admitted on June 15, 2018 for five days of IVIG. His discharge diagnosis was AIDP/GBS.

Petitioner's medical records show Petitioner experienced bilateral flaccid limb weakness and absent deep tendon reflexes in those extremities. He also had a monophasic course, with an interval of 21 days between onset (May 25, 2018, when Petitioner first felt tingling in his extremities) and nadir (June 15, 2018, when Petitioner reported he felt his symptoms had plateaued). Thus, Petitioner's clinical course is consistent with that reported in the literature and case reports of vaccine-related GBS.

Second, Petitioner's treating physicians questioned whether Petitioner's GBS was caused by his hepatitis A vaccine. For example, Dr. Schneider, on June 15, 2018, found Petitioner had GBS and noted he had a hepatitis A vaccination a few weeks prior. Pet. Ex. 4 at 15. On discharge from the hospital on June 19, 2018, Dr. Henson noted "[Petitioner] has had extensive concern regarding the timing of his hepatitis A vaccine with the onset of this illness and is due for a round two-stage booster within 2 months and I've advised him to not get that" due to Petitioner's "current condition and the IVIG used." Pet. Ex. 5 at 11. Dr. Henson added, "finding direct effect or causation of his vaccine caus[ing] GBS is very difficult[,] however, the timing is somewhat suspect." Id.

At a follow-up appointment with Dr. Schneider on June 29, 2018, Dr. Schneider noted "[i]t is possible that this GBS was related to the hep[atitis] A vaccination which he received a few weeks before, and I am going to look into reporting this." Pet. Ex. 4 at 12. Later that day,

Dr. Schneider submitted a VAERS report, writing "[Petitioner] developed [GBS] in late May, 2018, after receiving hepatitis A vaccination about five weeks before." Pet. Ex. 15 at 4.

At an annual wellness visit on December 17, 2019, Petitioner's past medical history included "[GBS] after [h]ep[atitis] A [v]accine," with a date of May 2018. Pet. Ex. 3 at 19. APRN Sieweke wrote, "No immunizations at this point due to history of [GBS]. I would personally like confirmation from his neurologist when he feels that it is appropriate for him to resume immunizations, should he feel that is appropriate in the future." Id. at 18. "[W]ith his history of [GBS,] he most likely will not be taking immunizations in the future." Id. at 19. On October 21, 2021, at an annual wellness visit, Petitioner was noted to be up-to-date on Covid-19 vaccines but "desire[d] no additional vaccines due to history of GBS with [h]ep[atitis] A vaccine." Pet. Ex. 22 at 4.

The undersigned acknowledges Dr. Schneider wrote this association is "possible," and an opinion that causation is "possible" is insufficient to establish causation. However, Dr. Schneider also submitted a VAERS report, indicating concern about vaccine causation. Additionally, Dr. Henson advised Petitioner to not get the booster. And APRN Sieweke withheld future vaccinations given Petitioner's history of GBS. These statements from Dr. Henson and APRN Sieweke are more persuasive. Thus, the undersigned finds that collectively, these statements constitute circumstantial evidence that the Petitioner's treating physicians associated his hepatitis A vaccine with the development of his GBS.[74]

Further, there is no persuasive evidence of an alternative cause. Petitioner did not have any signs or symptoms of an infection around the time of onset. Nor was he diagnosed with any infection or any antecedent condition that could have caused his GBS. There is evidence that Petitioner has degenerative disc disease. However, as described above in the diagnosis section, this does not explain his neurological symptoms. Dr. Tutt found "no indication for neurosurgical intervention" on MRI. Pet. Ex. 4 at 17. And thus, he concluded Petitioner's "exam[ination] and history suggest[ed] a demyelinating process." Id. Dr. Schneider agreed Petitioner's recent MRIs were "unrevealing," showing "no significant abnormality," "no cervical myelopathy," and "no surgical lesion" as indicated by Dr. Tutt. Id. at 14. He then diagnosed Petitioner with GBS. Thus, Petitioner's MRI findings cannot explain his neurologic symptoms.

Dr. Leist opined that if Petitioner had GBS, then his GBS could have been caused by trauma sustained on May 25, 2018, which he found to be "the most temporally proximate event to the onset of symptoms of GBS." Resp. Ex. A at 9. However, the undersigned is not persuaded by Dr. Leist here. First, there is no treating physician support for this theory. Petitioner consistently reported his symptoms began while he was working out, and none of his treating physicians questioned whether such "trauma" could have caused his GBS. Second, Huang et al., the only literature article Dr. Leist filed in support of his theory, is not supportive. The clinical course described by their patients does not match that of Petitioner's. Lastly, Huang et al. found the time from trauma trigger to GBS onset was a median of 9 days, but as described below, Petitioner's GBS onset was May 25. This would mean that Petitioner's onset would have

[74] See Maloney v. Sec'y of Health & Hum. Servs., No. 19-1713V, 2022 WL 1074087, *33 (Fed. Cl. Spec. Mstr. Mar. 17, 2022).

been immediate under this theory, which is inconsistent with the timing in Huang et al. and inconsistent with the undersigned's experience in dealing with demyelinating illnesses.

For all of the reasons described above, the undersigned finds that Petitioner has provided preponderant evidence of a logical sequence of cause and effect required under Althen prong two.

D. Althen Prong Three

Althen prong three requires Petitioner to establish a "proximate temporal relationship" between the vaccination and the injury alleged. Althen, 418 F.3d at 1281. That term has been defined as a "medically acceptable temporal relationship." Id. Petitioner must offer "preponderant proof that the onset of symptoms occurred within a time frame for which, given the medical understanding of the disorder's etiology, it is medically acceptable to infer causation-in-fact." de Bazan, 539 F.3d at 1352. The explanation for what is a medically acceptable time frame must also coincide with the theory of how the relevant vaccine can cause the injury alleged (under Althen prong one). Id.; Koehn v. Sec'y of Health & Hum. Servs., 773 F.3d 1239, 1243 (Fed. Cir. 2014); Shapiro, 101 Fed. Cl. at 542; see Pafford, 451 F.3d at 1358. A temporal relationship between a vaccine and an injury, standing alone, does not constitute preponderant evidence of vaccine causation. See, e.g., Veryzer, 100 Fed. Cl. at 356 (explaining that "a temporal relationship alone will not demonstrate the requisite causal link and that [P]etitioner must posit a medical theory causally connecting the vaccine and injury"), aff'd, 475 F. App'x 765 (Fed. Cir. 2012).

Dr. Ahmed and Dr. Sheikh opine Petitioner's GBS onset was May 25, 2018, or 36 days post-vaccination, while Dr. Leist opines Petitioner's GBS onset would have been "after June 4, 2018," or more than 47 days post-vaccination. Based on the medical records, opinions of Petitioner's treating physicians, and expert opinions, the undersigned finds Petitioner's onset to be May 25, 2018, or 36 days post-vaccination.

Petitioner received his hepatitis A vaccine on April 19, 2018. Petitioner first presented to a medical provider after his hepatitis A vaccination on June 4, 2018. On that date, he reported a history of tingling in his feet, hands, and tongue that began "last Friday (10 days ago)," which was May 25, 2018. Pet. Ex. 3 at 379. On June 7, 2018, Petitioner reported symptom onset of May 25, 2018. Pet. Ex. 2 at 3. On June 14, 2018, Petitioner saw neurosurgeon Dr. Tutt and reported his symptoms began "around Memorial Day when he was working out at the gym." Pet. Ex. 4 at 16. The following day, on June 15, 2018, Petitioner presented to Dr. Schneider and reiterated his "tingling of the toes" began on May 25, 2018, while at the gym. Id. at 14. Thus, Petitioner's contemporaneous medical records place onset on May 25, 2018, consistent with the opinions of Dr. Ahmed and Dr. Sheikh.

Dr. Leist did not explain his reasoning for concluding that Petitioner's GBS onset was "after June 4, 2018" other than to state the "symptoms on June 4, 2018 were consistent with lumbar and cervical strain and L5 radiculopathy." Resp. Ex. A at 8. Further, Dr. Leist did not specify an exact or approximate date for GBS onset, or provide an opinion as to whether a 36-

day onset would be inappropriate for vaccine-induced GBS. Thus, the undersigned finds Dr. Leist's opinions less persuasive.

Moreover, the undersigned finds an onset of 36 days to be medically appropriate and supported by the opinions of Dr. Ahmed and Dr. Sheikh. This temporal association is consistent with the onset period of three to 42 days as set forth in the Vaccine Injury Table for GBS following influenza vaccination. 42 C.F.R. § 100.3(a)(XIV)(D). Additionally, this time frame has been acknowledged as appropriate in other Vaccine Program cases in which molecular mimicry has been proffered as the causal mechanism in a GBS case. See, e.g., Barone v. Sec'y of Health & Hum. Servs., No. 11-707V, 2014 WL 6834557, at *13 (Fed. Cl. Spec. Mstr. Nov. 12, 2014) ("[S]pecial masters have never gone beyond a two-month (meaning eight week) interval in holding that a vaccination caused a demyelinating illness."); Pierson, 2022 WL 322836, at *32-33, *37 (finding a temporal relationship between vaccination and GBS when onset was within "the outermost medically appropriate onset date for vaccine-caused GBS at eight weeks, or 56 days, post-vaccination").

Therefore, the undersigned finds the temporal association is appropriate given the mechanism of injury and Petitioner has satisfied the third Althen prong.

E. Alternative Causation

Because the undersigned concludes that Petitioner has established a prima facie case, Petitioner is entitled to compensation unless Respondent can put forth preponderant evidence "that [Petitioner's] injury was in fact caused by factors unrelated to the vaccine." Whitecotton v. Sec'y of Health & Hum. Servs., 17 F.3d 374, 376 (Fed. Cir. 1994), rev'd on other grounds sub nom., Shalala v. Whitecotton, 514 U.S. 268 (1995); see also Walther v. Sec'y of Health & Hum. Servs., 485 F.3d 1146, 1151 (Fed. Cir. 2007). As discussed above in the analysis related to Althen prong two, the undersigned found Respondent failed to establish evidence to show that Petitioner's GBS was caused by a source other than vaccination. Thus, Respondent did not prove by a preponderance of evidence that Petitioner's injury is "due to factors unrelated to the administration of the vaccine." § 13(a)(1)(B).

VI. CONCLUSION

For the reasons discussed above, the undersigned finds that Petitioner has established by preponderant evidence that his hepatitis A vaccine caused his GBS. Therefore, Petitioner is entitled to compensation. A separate damages order will issue.

IT IS SO ORDERED.

s/Nora Beth Dorsey
Nora Beth Dorsey
Special Master