In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

No. 13-709V

(to be published)

KRISTINE R. BELL, Petitioner, v. SECRETARY OF HEALTH AND HUMAN SERVICES, Respondent.	Special Master Corcoran Filed: December 1, 2016 Decision; Hepatitis B ("Hep B") Vaccine; Acute Disseminated Encephalomyelitis ("ADEM").

Richard H. Moeller, Moore, Heffernan, et al., Sioux City, IA, for Petitioner.

Althea Walker Davis, U.S. Dep't of Justice, Washington, DC, for Respondent.

DECISION DENYING ENTITLEMENT[1]

On September 12, 2013, Kristine Bell filed this action seeking compensation under the National Vaccine Injury Compensation Program (the "Vaccine Program")[2], alleging that she experienced acute disseminated encephalomyelitis ("ADEM") after receiving the second of three doses of the Hepatitis B ("Hep B") vaccine. Petition ("Pet.") (ECF No. 1) at 1, 4-5. An entitlement hearing was held in this matter on January 28-29, 2016. After considering the record as a whole, I find that Petitioner has failed to carry her burden establishing causation, and therefore has not demonstrated entitlement to compensation under the Vaccine Program. As discussed in greater

[1] Because this decision contains a reasoned explanation for my action in this case, it will be posted on the United States Court of Federal Claims' website, in accordance with the E-Government Act of 2002, 44 U.S.C. § 3501 (2012). As provided by 42 U.S.C § 300aa-12(d)(4)(B), however, the parties may object to the decision's inclusion of certain kinds of confidential information. To do so, Vaccine Rule 18(b) permits each party fourteen (14) days within which to request redaction "of any information furnished by that party: (1) that is a trade secret or commercial or financial in substance and is privileged or confidential; or (2) that includes medical files or similar files, the disclosure of which would constitute a clearly unwarranted invasion of privacy." Vaccine Rule 18(b). Otherwise, the decision will be available to the public. *Id.*

[2] The National Vaccine Injury Compensation Program comprises Part 2 of the National Childhood Vaccine Injury Act of 1986, Pub. L. No. 99-660, 100 Stat. 3755 (codified as amended at 42 U.S.C. § 300aa-10 through 34 (2012)).

detail below, Petitioner's entire claim hinges on the factual finding that she had ADEM – but the record, as amplified by both side's experts, suggests she did not.

I. FACTUAL BACKGROUND

The record in this case consists of Ms. Bell's medical records, the testimony of four experts, and medical or scientific literature submitted by the parties in support of their respective positions. I have reviewed the entire record as required by the Vaccine Act. In this ruling I address the sufficiency of Petitioner's evidence in support of an award of compensation.

A. Receipt of First and Second Hep B Vaccines

Petitioner was born on July 7, 1975. Petitioner's Exhibit ("Pet'r's Ex.") 2 at 1. Her prior relevant medical history includes migraine headaches, depression, anxiety, adult attention deficit disorder (ADD), and two miscarriages. Pet'r's Ex. 1 at 2. The only prescribed medication Petitioner took was Zoloft. *Id*.

Ms. Bell was seen at St. Luke's Hospital on December 6, 2011 for her yearly physical, at which time she received the first of three Hep B vaccine doses. Pet'r's Ex. 1 at 1. There is no record evidence of any notable reaction to that dose, and indeed (as was underscored at hearing) Petitioner's experts could not point to any either. *See, e.g.*, Transcript ("Tr.") at 23, 159-60.

The second dose of the Hep B vaccine was administered to Petitioner on January 16, 2012. Pet'r's Ex. 1 at 1. Fifteen days later, on January 31, 2012, Petitioner saw an optometrist because she was suddenly experiencing blurred vision, burning, tearing, itching, and photophobia. Pet'r's Ex. 2 at 5. Specifically, she reported that she had noticed the blurriness and red eye for one week. *Id*. At this visit, the doctor noted a history of Meniere's disease,[3] and that Petitioner had experienced a cold two weeks before. *Id.* Ms. Bell was prescribed Tobradex[4] for possible conjunctivitis and a corneal abrasion. A few days later, on February 2, 2012, at her follow up appointment, Ms. Bell presented with improved symptoms, allowing her to restart use of her contact lenses. *Id*.

B. Symptoms Following Second Hep B Vaccine Dose

Thirty-three days after receiving the second Hep B vaccine, on February 18, 2012, Ms. Bell

[3] Meniere's disease consists of hearing loss, tinnitus, and vertigo resulting from non-supperative disease of the labyrinth with edema. *Dorland's Medical Dictionary* 539 (32nd ed. 2012) (hereinafter "*Dorland's*").

[4] Tobradex is a combination of an antibiotic and a corticosteroid, used in the eye (as an eye drop) to prevent permanent eye damage. *Drugs and Supplements: Tobramycin And Dexamethasone*, Mayo Clinic (Jan. 01, 2016), http://www.mayoclinic.org/drugs-supplements/tobramycin-and-dexamethasone-ophthalmic-route/description/DRG-20062827 (last visited Nov. 2, 2016).

visited Unity Point Urgent Care complaining of left-sided weakness. Pet'r's Ex. 10 at 1. At this visit, the records indicate, Petitioner informed her treater that she believed her symptoms were carpal tunnel syndrome, and consequently she had delayed seeking a physician's opinion until her symptoms had progressed over the "last couple of weeks." *Id*. The Urgent Care physician who examined Ms. Bell noted "definite left-sided weakness, probably 3-4/5 in the left arm, hand, left leg and foot," and therefore instructed Ms. Bell to get a "head scan."[5] *Id*. Because Ms. Bell worked in billing for St. Luke's Hospital- where she wanted to go for treatment, she waited until Monday, February 20, 2012 to schedule a head scan. *Id*. On that day, Ms. Bell was first seen by a nurse practitioner, Joan Schlenk, who took Ms. Bell's vitals and reviewed her systems. Petitioner reported that her medical history included Meniere's disease, but she did not disclose having received the Hep B vaccine earlier that year. Pet'r's Ex. 7 at 1. In reviewing Ms. Bell's systems, Nurse Schlenk reported that Ms. Bell presented with a number of symptoms including fatigue, "feelings of weakness on exertion," "inability to cope with daily activities," and a previous history of dizziness. *Id*. at 2.

Based on those symptoms, Ms. Bell was instructed to report to the Emergency Room at St. Luke's Hospital in Cedar Rapids, Iowa for an evaluation by a neurologist. Pet'r's Ex. 7 at 2. She did so on February 20, 2012, and saw Laurence Krain, M.D., a neurologist, for an evaluation and CT scan. Pet'r's Ex. 6B at 348. The written record of that evaluation documents Petitioner's verbal report to Dr. Krain that she felt "flulike," with fatigue, abdominal pain, and nausea, but also reported that "it all started with blurred vision in her left eye associated with redness and pain about 4 to 5 weeks ago." *Id.* at 343, 347. The CT scan was normal, leading Dr. Krain to propose that Ms. Bell had a "subtle suggestion of the left spastic hemiparesis…subacute course consistent with progressive spastic left hemiparesis. This could be hemispheric or myelopathy. Major consideration demyelinating disease." *Id*. at 347. Dr. Krain's treatment plan included an MRI[6] of the cervical spine and head, along with an evaluation of Petitioner's B12 levels[7]. *Id.*

An MRI was performed on February 21, 2012, and showed an "abnormal mass-like signal centered in the region of the right basal ganglia, caudate nucleus, and centrum semiovale." Pet'r's Ex. 6B at 369. That finding led Dr. Krain to include in his differential diagnosis low grade neoplasm or tumefactive demyelinating disease as possible explanations for Petitioner's

[5] The treating physician did not specify if the "head scan" would be an MRI or CT scan, however. Mrs. Bell's first test once at St. Luke's Hospital was a CT scan. Pet'r's Ex. 10 at 1.

[6] MRI stands for Magnetic Resonance Imaging. *Dorland's* at 1184.

[7] Dr. Krain's notes do not explain his rationale for measuring Petitioner's B12 levels. A B12 deficiency, however, "frequently causes macrocytic anemia, glossitis, peripheral neuropathy, weakness, hyperreflexia, ataxia, loss of proprioception, poor coordination, and affective behavioral changes," and it is therefore likely that Dr. Krain was trying to rule out B12 deficiency as a cause of Petitioner's symptoms. *Test ID: B12, Vitamin B12 Assay, Serum*, Mayo, http://www.mayomedicallaboratories.com/test-catalog/Clinical+and+Interpretive/9154 (Last visited Nov. 4, 2016).

condition, whereas cerebritis[8] or an area of subacute ischemia were now considered less likely. *Id*. Dr. Krain began treating Ms. Bell with IV steroids, which were to be tapered off with the use of oral steroids. *Id.* at 381. This treatment plan came with a diagnosis of multiple sclerosis ("MS"). *Id*.

Ms. Bell reported to her follow-up appointment on March 21, 2012, and presented with increased stiffness, dystonic posturing on her right upper extremities, and other movement impairment, reporting no improvement despite the steroid treatments. Pet'r's Ex. 6B at 180-81. Dr. Krain noted that Ms. Bell's previously-observed brain lesion was "difficult to categorize fully." *Id.* at 180. A second MRI he had ordered had been performed the day before, on March 20, 2012, and it showed that the previous hyper-intense T2 signal in the lentiform nucleus and caudate nucleus had diminished, as well as less swelling in the right caudate nucleus. *Id*. at 185; Pet'r's Ex. 5 at 501. At the same time, the MRI revealed a new, T1 hyper-intensity in the lentiform and caudate nucleus, but with no abnormal enhancement (which would show inflammation).[9] Pet'r's Ex. 6B at 185; Pet'r's Ex. 5 at 501. The radiologist who performed new MRI, Dr. Glenn Hammer, overall noted some "internal improvement in edema and . . . swelling," and this, plus the changes in signal intensity, suggested "petechial hemorrhage or necrosis within a previous ischemic infarct," while deeming MS or neoplasm unlikely. Pet'r's Ex. 5 at 501.

Based on the above, Dr. Krain proposed a new diagnosis of extrapyramidal disorder,[10] which required substantiation through blood tests, a lumbar puncture, and a third brain MRI, accompanied by occupational and physical therapy and botox injections.[11] Pet'r's Ex. 6B at 180. The lumbar puncture was conducted on April 12, 2012 and showed normal results. *Id*. at 135-138. Tests for oligoclonal bands, cryptococcal antigen, IgG and syphilis were also normal. *Id.* The repeat MRI ordered by Dr. Krain was performed on April 30, 2012, and revealed reduced

[8] Cerebritis is inflammation of the cerebrum. *Dorland's* at 332.

[9] Lesions revealed by an MRI that are suggestive of ADEM are "hyperintense (have a greater signal) on T2-weighted and FLAIR sequences," but "are usually inconspicuous or unenhanced T1-weighted sequences (black holes)." Waldman, A. and D. Jacobs, *Acute Disseminated Encephalomyelitis in Adults*, UpToDate, F. Gonzalez-Scarano, Editor Accessed on February 12, 2015, Wolters Kluwer Health: Waltham MA. Filed as Resp't's Ex. I.

When a patient is suspected of having inflammation in the brain, a physician will inject paramagnetic dye in their veins while the patient undergoes an MRI. Tr. at 221-22. If the dye goes through the blood vessels and gets to the brain then enhancing lesions will appear on the MRI. Id. at 222. If the dye does not reach the brain, or show up on the MRI through enhancing lesions, that is a good indicator that the blood brain barrier was not breached – and hence no inflammation of the brain. *Id.*

[10] Extrapyramidal disorder constitutes any of a group of clinical disorders considered to be attributable to malfunction in the extrapyramidal system (a non-anatomical part of the central nervous system that controls motor activities), and characterized by abnormal involuntary movements, *e.g.* Parkinsonism, athetosis, and chorea. *Dorland's* at 1829, 1859.

[11] The Doctors at the Mayo Clinic who later evaluated Ms. Bell concluded that these botox treatments "caused worsening weakness in the hands." Pet'r's Ex. 9 at 49.

signal size of the right basal ganglia, but was accompanied by an increased signal in the right lentiform nucleus consistent with small vessel ischemia or vasculitis.[12] Pet'r's Ex. 3 at 28. Dr. Krain discussed Ms. Bell's condition with Dr. Mary L. Hlavin.[13] *Id*. at 34. A handwritten note by Dr. Hlavin states "tell [Petitioner] scan continues to look better." *Id.* at 28.

In addition to Dr. Krain, Ms. Bell also sought treatment from Dr. David E. Puk, an ophthalmologist, on May 5, 2012, for her ongoing vision problems first manifesting after her receipt of the second Hep B dose. During that appointment, she complained of diplopia[14] that had begun two days prior, along with intermittent blurriness. Pet'r's Ex. 4 at 6. Dr. Puk acknowledged the improvement in the brain lesion discussed above, and diagnosed Ms. Bell with hypertropia,[15] which could be helped with an eye patch on one eye. *Id*.

Ms. Bell then followed up with Dr. Krain on May 17, 2012, to get his input on the diplopia she had been experiencing for two weeks. Pet'r's Ex. 4 at 17. Dr. Krain's notes from this examination and visit underscore the extent to which Ms. Bell's treaters were uncertain of the cause of her condition – but were slowly but surely moving away from initial concerns about demyelination. Thus, Dr. Krain characterized her right basal ganglia lesion as of "indeterminate etiology," and that "[t]he presentation [of Ms. Bell] does not suggest infectious or autoimmune encephalitis well . . . [d]emyelinating disease presenting with a single lesion has been entertained, but *there are lesions in the gray matter and I have felt this is quite unlikely*." *Id*. at 16 (emphasis added). He also noted that the steroidal treatments had not proven effective. *Id.* at 18.

At this point (about four months post-vaccination), Dr. Krain ordered further testing, including an MRI and chest X-ray, and also referred Petitioner to specialists in the neurology department at the University of Iowa Hospital ("Iowa"). Pet'r's Ex. 4 at 27. The first of those specialists that Ms. Bell saw was Dr. Robert Rodnitzky, a neurologist, on May 23, 2012. Pet'r's Ex. 8 at 24. Dr. Rodnitzky was tasked with evaluating Petitioner for right basal ganglia pathology with new cranial nerve palsies. To do so, he reviewed Petitioner's medical history and summarized it as consistent with what is stated above. *Id.* However, an additional piece of information was added to Ms. Bell's history of migraines: Ms. Bell had experienced paresthesia[16]

[12] Small vessel ischemia is a deficiency of blood flow in certain smaller vessels, usually due to functional constriction or actual constriction of the blood vessel, while vasculitis is inflammation of the blood or lymph vessel. *Dorland's* at 961, 2026.

[13] Dr. Hlavin's name is mentioned sporadically throughout the record, mainly by Dr. Krain when he is describing Ms. Bell's past medical history, although the medical record does not reveal any instances in which Dr. Hlavin herself directly examined Ms. Bell. Pet'r's Ex. 5 at 60. It is also unclear what type of medicine is Dr. Hlavin's specialty.

[14] Diplopia means double vision. *Dorland's* at 525.

[15] Hypertropia is a permanent upward deviation of the visual axis of the eye. *Dorland's* at 898.

[16] Paresthesias are the sensations of burning, numbness, tingling, or prickling. *Dorland's* at 1383.

in both hands, expressive aphasia,[17] and difficultly writing with her migraines - the most recent occurrence of such problems having happened several years before. *Id.* at 24.

Dr. Rodnitzky performed several tests, and repeated some that had already been conducted, including a cell count, an MS screen, an MRI, and a lumbar puncture. The blood tests revealed three oligoclonal bands[18], normal protein, and negative tests for histoplasma, cytomegalovirus, enterovirus, cryptococcal, and angiotensin-converting enzyme. Pet'r's Ex. 8 at 40. The newest MRI was compared to the MRIs performed in February, March, and April, and the impression in the medical records from August 29, 2012, stated "evolution of the signal abnormalities involving the gray matter …reflect[ing] evolution of an acute process on the original MRI, the differentials of which include viral encephalitis, ADEM[19], or autoimmune encephalitis.[20]" *Id.* at 41, 160. Alongside ADEM, Dr. Rodnitzky also considered "para/post-infectious autoimmune encephalitis and mitochondrial disease" as potential diagnoses for Ms. Bell's condition. *Id.*

After completing this testing and evaluation, Dr. Rodnitzky referred Ms. Bell to a neuro-ophthalmologist – Dr. Matthew Thurtell. Dr. Thurtell concluded from his examination of Petitioner that there was "a broad differential diagnosis, including inflammatory, infectious, neoplastic, and paraneoplastic etiologies." Pet'r's Ex. 8 at 68. He also noted that Ms. Bell had a pattern of misalignment consistent with a fourth nerve palsy and slowing of horizontal saccades with impaired gaze-holding. *Id.* Ms. Bell was prescribed a Fresnel prism for her visual disturbance. *Id.*

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[17] Aphasia is any of a large group of language disorders involving defect or loss of the power of expression by speech. *Dorland's* at 115.

[18] "Isoelectric focusing/immunofixation reveals two or more oligoclonal bands in the CSF but no band in the serum. This is consistent with intrathecal synthesis of immunoglobulin and is considered to be a positive result for oligoclonal bands. Oligoclonal bands are present in approximately 95 percent of patients with multiple sclerosis." Pet'r's Ex. 8 at 30-31.

[19] "Acute disseminated encephalomyelitis (ADEM) is an immune-mediated disorder of the CNS [central nervous system] characterized by a widespread demyelination that predominantly involves the white matter of the brain and spinal cord. The condition is usually precipitated by a viral infection or vaccination. The presenting features include an acute encephalopathy with multifocal neurologic signs and deficits." S. Tenembaum, *et al.*, *Acute Disseminated Encephalomyelitis*, Neurology, Apr. 17, 2007; 68 (Suppl 2), S23-S36 at S23 (filed as Pet'r's Ex. 16).

[20] These results were in the record labelled "External MRI-store and Interpret." The record states that the MRI was reviewed by Aaron D. Berg, MD and Toshio Moritani, MD. Pet'r's Ex. 8 at 41. Aaron D. Berg appears to be a board certified radiologist. *Aaron Middle Berg*, Sanford Health, http://www.sanfordhealth.org/find-a-doctor/aaron-berg (last accessed on 11/10/2016). Toshio Moritani is the director of the Clinical Neuroradiology at Iowa who is board certified in medicine and radiology. *Toshio Moritani*, University of Iowa Carver College of Medicine: Radiology, https://www.medicine.uiowa.edu/dept_primary_apr.aspx?appointment=Radiology&id=moritanit (last accessed on 11/10/2016)

C. Third Hep B Dose and Further Progression of Symptoms

Ms. Bell returned to Dr. Krain on June 4, 2012 for a follow-up visit. At this visit, there are inconsistencies in the record about her condition. The medical record begins by stating "returns today with no new complaints," but two sentences later states that "her only new complaint today is decreased hearing on the right side." Pet'r's Ex. 5 at 92. That same paragraph concluded with the statement that Petitioner had "not developed any *other* new problems, nor change in her other conditions…she has not had any *other* new complaints or change in her condition." *Id*. (emphasis added). Accordingly, this record suggests some concern as of June 2012 on Ms. Bell's part about hearing.

Several days later, on June 12, 2012, Ms. Bell received her third Hep B vaccine. Pet'r's Ex. 1 at 1. She thereafter reported for occupational therapy on June 19, 2012, where she stated that she was experiencing continued decline in balance and the use of her left hand, along with further decreased hearing and vision, leading Dr. Krain to order a PET scan.[21] Pet'r's Ex. 6A at 64. The PET scan revealed unilateral absent 18-FDG[22] activity in the right caudate and lentiform nuclei, which was termed an unusual result, as in a few reported cases it could reflect an ischemic event resulting in parenchymal scaring or hyperglycemic-induced regional metabolic failure. Pet'r's Ex. 5 at 496.

Ms. Bell was next seen for a follow-up appointment with Dr. Thurtell on July 2, 2012. By this point, Ms. Bell noted, she was unable to drive, had onset hearing loss on the right side, gaze palsy, and her left hand was not functioning well. Pet'r's Ex. 8 at 105. Dr. Thurtell concluded that "this is a very unusual spectrum of disorders," and adding his view that "considering her progressive symptoms in multiple anatomic locations, an inflammatory cause would be highest on the differential." *Id.* at 111. Given that Petitioner's neurologic deficit had worsened since the last appointment, Dr. Thurtell recommended an MRI with contrast, a CT with contrast, a mammogram, and a pap smear. *Id*. at 112. Despite his reluctance to recommend steroids, Dr. Thurtell also suggested to Ms. Bell that IVIG treatments should be considered again to prevent further neurological decline, although she had tried but discontinued their use previously after experiencing flu-like side effects (and although they had not proven effective otherwise). *Id*.

Following the exam with Dr. Thurtell, Ms. Bell underwent another MRI, plus an additional

[21] A PET scan stands for Positron Emission Tomography, and uses a radioactive drug to show chemical activity in tissues and organs. *Tests and Procedures: Positron Emission Tomography (PET) Scan*, Mayo (2014), http://www.mayoclinic.org/tests-procedures/pet-scan/basics/definition/prc-20014301 (Last visited Nov. 4, 2016).

[22] 18-FDG is a radiopharmaceutical used to help measure abnormal glucose metabolism in the brain. *Review of F-18 Fluoro-2-Deoxyglucose (F-18 FDG) Positron Emission Tomography in the Evaluation of Malignancy*, FDA 1999, http://www.fda.gov/Drugs/DevelopmentApprovalProcess/Manufacturing/ucm182668 htm (Last visited on Nov. 4, 2016).

CT and mammogram. The MRI found a largely "stable examination," with no abnormal enhancement or "areas of restricted diffusion." Pet'r's Ex. 5 at 495. The radiologist responsible for conducting this MRI, after comparing it to the prior MRIs performed on Ms. Bell, proposed that the cause of her many symptoms was "a prior focal insult which may have been due to vasculitis, encephalitis, or small vessel ischemia." *Id*. Dr. Krain reviewed these findings on July 9, 2012, and stated that he still had difficulty categorizing her disease, but was considering non-paraneoplastic autoimmune encephalitis, although the test for paraneoplastic antibodies was negative. *Id.* at 72. In contrast to her improving head MRIs, Dr. Krain noted continuing clinical manifestations such as diplopia with opthalmoparesis and hearing loss. *Id*. Dr. Paulina J. Kunecka[23] ordered the July MRI and recorded the "pertinent clinical findings and specific questions to be answered" as "inflammation (ADEM?) vs. tumor?." Pet'r's Ex. 8 at 114.

Ms. Bell thereafter saw another ophthalmologist, Dr. Mark Granner, who opined that the most likely cause of Ms. Bell's injuries was an autoimmune process because of the evolution of her symptoms over time. Pet'r's Ex. 8 at 134. He noted that Ms. Bell had not responded well to IVIG treatments, but because he could not determine the insulting agent for Ms. Bell's condition, he was unsure of the utility of trying more aggressive treatment such as plasmapheresis.[24] *Id*. at 134-135.

D. Alternative Explanations for Petitioner's Symptoms

On August 16, 2012, Ms. Bell was seen again by Dr. Krain for another follow-up regarding her rigidity and diplopia. Pet'r's Ex. 5 at 58. This is the first instance evident from the record where Ms. Bell (accompanied by her mom) asked if her problems were a result of the Hep B vaccines she had received. *Id*. Dr. Krain stated that given Ms. Bell's presentation, temporally and on imaging, he felt post-vaccinal encephalomyelitis to be unlikely. *Id*. He noted Petitioner's active problems to be abnormal brain scan, dizziness and giddiness, dystonia musculorum deformans idiopathic, extrapyramidal disorders, and inner ear autoimmune disease. *Id*. Later that same month, on August 29, 2012, Ms. Bell saw Dr. Rodnitzky again, who continued to include ADEM (specifically, a recurrent form of the condition) as a diagnostic possibility, although it is not evident from the record why he did so (and in particular if he was relying on any more recent testing for its inclusion in the differential diagnosis). Pet'r's Ex. 8 at 163.

Ms. Bell asked if she should seek an opinion at the Mayo Clinic in Rochester, Minnesota, and Dr. Thurtell concluded that was a reasonable course of action. Pet'r's Ex. 8 at 151.

[23] Dr. Kunecka does not appear to be one of Ms. Bell's treating physicians but rather a Staff, Resident, or Fellow. Pet'r's Ex. 8 at 163.

[24] Plasmapheresis is the removal of plasma from withdrawn blood, with re-transfusion of the formed elements into the donor. *Dorland's* at 1456.

Accordingly, on September 20, 2012, Ms. Bell arrived at the Mayo Clinic for further treatment. At this time, Petitioner saw Dr. Andrew McKeon, a neurologist, who oversaw an initial and comprehensive evaluation, with numerous tests performed, including an MRA, MRI, EEG, EMG, CSF evaluation, echocardiogram, and muscle biopsy of her bicep. Pet'r's Ex. 9 at 67.

Dr. McKeon and the associated Mayo treaters who assisted in this testing largely concluded (consistent with Ms. Bell's prior testing), based on MRI and MRA findings, that the evidence of "vascular, infectious or neoplastic projects [was] unlikely." Pet'r's Ex. 9 at 78. By contrast, the EMG showed evidence of a diffuse, distally predominant myopathic process.[25] These findings were most noticeable in Ms. Bell's arms, and the lack of fibrillation potentials indicated a non-inflammatory process with no evidence for peripheral neuropathy. As a result, congenital myopathy and/or a mitochondrial disorder were deemed to be possible causes for her various symptoms. *Id.*

A biopsy of Ms. Bell's bicep muscle, however, resulted in no evidence indicating a mitochondrial, inflammatory, or active-myopathic process, leading Dr. McKeon to conclude that his proposition of mitochondrial dysfunction was misplaced. Pet'r's Ex. 9 at 23, 79. The records also reveal Dr. McKeon's awareness that Ms. Bell had been referred for evaluation of a possible autoimmune disease, but that, in his review of the records, there was no evidence pointing to that conclusion, noting her lack of response to IVIG or steroids as further supporting the unlikeliness of an autoimmune process (for which either treatment would normally be effective). *Id.* at 49. When Ms. Bell prompted Dr. McKeon about possible vaccine causation, he stated that he was unaware of a specific relation of her illness to the Hep B vaccine. *Id.*

In October 2012, Ms. Bell was seen by four additional doctors at the Mayo Clinic (Drs. Lund, Andrea L. Cheville, Lyell K. Jones, and Ralitza H. Gavrilova) some of whom were from the medical genetics group at Mayo, to further address whether mitochondrial dysfunction might be the cause for Petitioner's condition despite Dr. McKeon's initial take. The visit concluded with a prescription for a prescriptive "cocktail" intended to help ameliorate the impact of a possible mitochondrial disease, and with the recommendation that Ms. Bell obtain a genetics evaluation. Pet'r's Ex. 9 at 35. Dr. Jones performed a neurologic evaluation on Ms. Bell, but in the process also determined that although an autoimmune condition was originally considered as a possible cause for her symptoms, Ms. Bell did not have the markers for neural autoimmunity that would be otherwise expected if the process causing her symptoms were in fact autoimmune. *Id.* at 29.

On January 16, 2013, Ms. Bell appeared for a follow-up with Dr. Gavrilova, who reviewed the testing performed and confirmed that the evidence of an underlying mitochondrial disorder remained scant. Pet'r's Ex. 9 at 11, 16, 18. As a result, Dr. Gavrilova recommended further

[25] Myopathy is any disease of the muscle. *Dorland's* at 1224.

genetics testing, although Ms. Bell was hesitant to participate due to concerns about her insurance coverage. At this visit, Ms. Bell also noted that despite the "mitochondrial cocktail" treatment intended to address an underlying metabolic disorder, she was now experiencing decreased hearing by 50 percent and deterioration in her speech by 25 percent. *Id*. at 8. The diagnosis for Ms. Bell was now "progressive neurological deterioration characterized by dystonia, external ophthalmoplegia, hearing loss, gait imbalance, speech dysarthria, and brain MRI abnormalities of uncertain etiology." *Id*. at 9.

Dr. Gavrilova referred Ms. Bell to Dr. Patricia J. Best in the cardiovascular diseases group at the Mayo Clinic. Pet'r's Ex. 9 at 13. Dr. Best reviewed the results of Ms. Bell's September echocardiogram, determining that she had "very minimal early signs of cardiac involvement likely from her myopathic process." *Id*. at 14. As treatment, Dr. Best recommended that Ms. Bell start on a low dose of ACE inhibitor (Lisinopril), as well as a low dose of carvedilol.[26] *Id.*

E. University of Iowa Treatment and ADEM Diagnosis

One month later, on February 13, 2013, Ms. Bell went back to the treaters at Iowa. She first saw Dr. Rebecca K. Novacek, who reviewed the Mayo Clinic results as well as Ms. Bell's clinical presentation. Dr. Novacek noted that Ms. Bell's hearing had continued to worsen, while her left-side dystonia and vision were stable. Pet'r's Ex. 8 at 179. Because the etiology of Ms. Bell's condition remained unknown, Dr. Novacek ordered yet another MRI and lab work to evaluate copper, ceruloplasmin, ferritin, homocysteine, and a urine screen. *Id*. at 181. All of her lab work returned results within the normal range. *Id.* at 182-185. The MRI in particular showed that the FLAIR signal in the basal ganglia was mostly resolved, there was mild atrophy and iron deposition of the right basal ganglia and substantia nigra, and stable minimal wispy enhancement in the bilateral basal ganglia. *Id*. at 199.

Dr. Bruce J. Gantz, an audiologist at Iowa, also evaluated Ms. Bell. In his clinical notes he stated a "coincident finding with onset of symptoms was completion of Hep B vaccine series and conjunctivitis," although the record is silent as to whether Dr. Gantz found reason himself to connect the two – indeed, he acknowledged that steroid treatments had not been effective either. Pet'r's Ex. 8 at 191-92. He ultimately concluded that she had severe bilateral asymmetric sensorineural hearing loss and facial palsy. *Id*. at 191.

On March 29, 2013, Ms. Bell saw Dr. Pedro Gonzalez-Alegre, a neurologist specializing in movement disorders, at Iowa. The medical record reveals that, although Dr. Gonzalez-Alegre purported to have received the medical history from Ms. Bell and her family and reviewed her prior medical records, he misstated certain relevant facts of the progression of her condition. Pet'r's Ex. 8 at 209. For example, he recorded in the medical history section of the treatment

[26] Lisinopril and Carvedilol are medications used to treat hypertension. *Dorland's* at 301.

notes he prepared that she was doing well until December 2012, when she first received the Hep B vaccines – when in fact she had received all three doses by June 2012, six months earlier. *Id.* He also incorrectly ordered her symptoms chronologically, reciting that Ms. Bell progressed from hearing loss to blurry vision. *Id*. In fact, Ms. Bell's first doctor visit after receiving the second Hep B vaccine was to an ophthalmologist (15 days after vaccination) (Pet'r's Ex. 2 at 5), and she did not report decreased hearing until June. Pet'r's Ex. 10 at 1.

Based on review of testing performed through March 2013, Dr. Gonzalez-Alegre opined (like the doctors at the Mayo Clinic) that Ms. Bell did not have a mitochondrial disorder. Pet'r's Ex. 8 at 210. Rather, in his view she likely suffered from an inflammatory disorder that had produced permanent brain damage, as suggested by the atrophy in the basal ganglia. *Id*. He makes no mention in these records, however, of earlier contrary determinations – not only by Dr. Krain but from the Mayo treaters – that evidence of inflammation was absent, nor does he suggest these findings were in error in light of subsequent testing and analysis of Ms. Bell's symptoms. He also noted that Petitioner's basal ganglia lesion could not account for her visual and auditory symptoms. Not long after, in April 2013, Dr. Gonzalez-Alegre wrote a letter to Ms. Bell stating that the majority of potential etiologies for her condition had been appropriately ruled out by prior providers, with the exception of two rare diseases - - Whipple's disease and Brucellosis[27] - that could be tested for through an additional lumbar puncture. *Id*. at 213.

Ms. Bell was subsequently admitted to Iowa on May 5, 2013, with a chief compliant of "worsening encephalitis." Pet'r's Ex. 8 at 683. By this time, Dr. Gonzalez-Alegre had begun to pursue more testing, including CSF and brain imaging, in order to look for unusual possible additional etiologies such as Nieman-Pick type C.[28] *Id.* at 686. Moreover, he now listed as part of Ms. Bell's differential diagnosis encephalitis, noninfectious acute disseminated encephalomyelitis (ADEM), dysphagia, dysarthria, and memory loss. *Id*. As part of the expansive testing performed during the five day stay at Iowa, Ms. Bell saw Dr. Oleg A. Shchelochkov, a specialist in genetics. Pet'r's Ex. 8 at 710. Dr. Shchelochkov listed a multitude of possible genetic disorders that present with acute adult onset neuro-metabolic disorders with spasticity, recommending further diagnostic testing, especially given the presence of iron in her basal ganglia. *Id*.

On May 24, 2013, Ms. Bell returned to Iowa for a follow up with Dr. Gonzalez-Alegre. After reviewing all the testing results from Ms. Bell's stay at the Hospital, Dr. Gonzalez-Alegre

[27] Whipple's disease is a malabsorption syndrome caused by infection with mentation, arthralgia and arthritis, lymphadenopathy, and sometimes central nervous system involvement with oculofacioskeletal or oculomasticory dysrhythmia. *Dorland's* at 545. Brucellosis is characterized by fever, sweating, weakness, malaise, and weight loss. *Id*. at 255.

[28] Nieman-Pick Type C is a lysomal storage disease due to a deficiency of sphingomyelin phosphodiesterase with sphingomyelin accumulation in the reticuloendothelial system. *Dorland's* at 1276.

(based on consultation with other doctors- Drs. Rodnitzky and Shivapour) proposed that the most likely diagnosis was a monophasic encephalitic process occurring after vaccination. Pet'r's Ex. 8 at 810. Dr. Gonzalez-Alegre also noted that there was "ongoing inflammation in the central nervous system from her CSF," although (other than an increased IgG index from the year before), the basis of this assertion is unclear and not evident from the records. Dr. Gonzalez-Alegre also acknowledged that the plasma exchange treatments he had attempted had not been ameliorative, but proposed to try IV Solu-Medrol for five days, and then consider additional steroid treatments if Ms. Bell showed even the smallest improvement. *Id*. As before, Dr. Gonzalez-Alegre's notes reference Ms. Bell's prior treatments but do not grapple with, contest, or otherwise dispute the determination of earlier treaters that were contrary to his current impressions.

Three months later, on August 12, 2013, Ms. Bell returned again to Iowa for another consultation with a genetics counselor. This visit resulted in extensive clinical notes, including a chart listing all the medical testing she had undergone in the last year, along with proposals for yet more new testing and treatment. Pet'r's Ex. 12 at 21-27. These records also state the remaining possible diagnoses (including ADEM), both genetic and otherwise, concluding that the etiology of Ms. Bell's condition remained unclear. *Id*. at 29-30. Ms. Bell had a follow up appointment on September 6, 2013 at the Movement Disorders Clinic with Dr. Gonzalez-Alegre. He noted that Ms. Bell had been stable (if not slightly better) since her last visit, and his overall impression was that she had an acquired disorder that had not changed despite the general ineffectiveness of all the varied treatments she received. *Id*. at 62. The active symptoms and conditions proposed at this time as part of the differential diagnosis included basal ganglia disorder, dry eyes, decreased hearing, gaze palsy, dystonia, noninfectious ADEM, encephalitis, dysphagia, dysarthria, and memory loss. *Id*. at 63.

Dr. Gonzalez-Alegre saw Ms. Bell again on September 25, 2013 to treat her with botulinum toxin ("Botox") injections in her left adductor pollicis. Pet'r's Ex. 13 at 16. Ms. Bell thereafter requested a visit with a neuro-ophthalmologist because her vision and diplopia were again worsening, and returned to Iowa for that purpose on December 23, 2013. *Id.* at 30. Before Ms. Bell reported for her appointment, Dr. Gonzalez-Alegre noted (in the contemporaneous records from the time) that Ms. Bell was a "38 yo woman with an episode of suspected basal ganglia and brainstem encephalitis following Hep B vaccination. She has shown some progression of symptoms, *which is unusual for such a static process*." *Id*. (emphasis added). Dr. Thurtell also examined Ms. Bell in December, stating that her condition seemed to be stable since her last visit. *Id*. at 45. His treatment plan for her vision was to try aggressive lubrication to help with her dry eye, and he also proposed surgical correction. *Id*. at 50.

Ms. Bell returned for a second Botox treatment on January 8, 2014, because her arm position had improved from her last visit three months ago. Pet'r's Ex. 13 at 58; s*ee also* Pet'r's

Ex. 9 at 49. Her encounter diagnoses at this visit no longer included ADEM, however, but instead listed "encephalitis, postimmunization." Pet'r's Ex. 12 at 60. Moreover, the impression of her status after the MRI performed at this time was deemed most consistent with a neurodegenerative process involving the bilateral basal ganglia. *Id.* at 67. The differential diagnoses were pantothenate kinase associated neuro-generation, multiple system atrophy-parkinsonian, or other atypical Parkinsonism. *Id.*

It appears that Ms. Bell saw Dr. Gonzalez-Alegre one more time, on April 9, 2014. *See generally* Pet'r's Ex. 22 at 2-10. At this visit, Dr. Gonzalez-Alegre characterized her condition as a "complex neurologic syndrome, likely due to basal ganglia encephalitis that may have been triggered by a hepatitis B vaccination." *Id.* at 9. He informed Ms. Bell that he would be moving institutions and would no longer be able to provide her care, but introduced her to Dr. Shivapour, who would be Ms. Bell's treater at her follow-up visit in six months. *Id*. at 5. Ms. Bell's condition remained largely unchanged for this visit, leading Dr. Gonzalez-Alegre to conclude that she would benefit from obtaining a "second opinion" at the Mayo Clinic, from an expert in primary demyelinating disorders of the nervous system. *Id*. Again, however, Dr. Gonzalez-Alegre's impressions and proposed diagnoses showed no awareness of, or grappling with, the Mayo Clinic's fall 2012 fairly comprehensive neurologic work-up for Ms. Bell, which had not found evidence supporting the existence of a demyelinating disorder.

Ms. Bell then went back to the Mayo Clinic on July 23, 2014 and was seen again by Dr. McKeon. Pet'r's Ex. 25 at 46. Dr. McKeon's history characterized the Petitioner as suffering from a "multifocal neurological disorder" which seemed most likely attributable to mitochondrial dysfunction, although he noted that the testing to confirm that hypothesis in later 2012 had been negative. *Id.* He also reiterated that her CSF testing had produced normal results in September 2012, but not in the more recent testing in May 2013. *Id.* Yet the steroidal course prescribed for Ms. Bell had been unsuccessful (contrary to what would be expected if inflammation relating to an autoimmune condition were the source of her various symptoms). Dr. McKeon therefore proposed that the cause for her condition largely remained undiagnosed, and proposed two sets of further care for Ms. Bell - additional testing to be completed within a few days (including an MRI, blood work, CSF evaluation, EMG and nerve conduction studies, and a lumbar puncture), and rehabilitation services, which included seeing a speech pathologist, undergoing a swallow evaluation, and a consultation with physical medicine and rehabilitation groups. *Id*. at 47.

The first of those rehabilitation consultations was with Dr. Joseph Duffy, a speech pathologist. He noted that Ms. Bell's speech difficulty had increased over the last six months and diagnosed her with mixed hypokinetic-ataxic dysarthria, moderately severe. Pet'r's Ex. 25 at 38-39. Shortly thereafter, Ms. Bell saw Dr. Margaret A. Moutvic, a specialist in physical medicine and rehabilitation. Dr. Moutvic performed physical strength testing, concluding that Ms. Bell would benefit from a rolling walker and more physical therapy. *Id*. at 34, 36-37. Ms. Bell then

followed up with her Mayo Clinic geneticist, Dr. Gavrilova, who reiterated the views of prior treaters that there was no specific etiology for Ms. Bell's phenotype. Dr. Gavrilova requested neurotransmitter analysis of the CSF and a repeat echocardiogram, among other things, while also proposing some genetic testing. *Id*. 30-31.

Dr. McKeon reviewed the new findings from Ms. Bell's July 2014 return visit to the Mayo Clinic and associated testing, and concluded that, from a diagnostic standpoint, they were unhelpful in identifying the underlying causes of her overall illness. Pet'r's Ex. 25 at 15. He opined that outside of whole exome sequencing (which would be costly), there was no further testing that could be done. *Id*. His listed differential diagnoses as of September 2014 included external ophthalmoplegia with diplopia, multifocal central nervous system disorder, myopathy, and sudomotor failure – but not ADEM. *Id*. Overall, however, he opined that even with a correct diagnosis, Ms. Bell's condition was unlikely to improve (although it could become stable). *Id*.

II. EXPERT TESTIMONY

In this case, both sides offered two experts, but no fact witness testimony. The opinions and testimony of the relevant experts are set forth below.

A. Dr. Thomas F. Morgan – The first of petitioner's two experts, Thomas Morgan, M.D., provided an opinion as to the etiology of Ms. Bell's condition, along with the purported role the Hep B vaccine played in it.

Dr. Morgan graduated from Meharry Medical College in 1970 (after completing his undergraduate degree at St. Louis University). Pet'r's Ex. 18 at 1. Dr. Morgan went on to complete his residencies in internal medicine at Brown University School of Medicine (1970-1972) and neurology at Boston University School of Medicine (1972-1975). *Id*. at 2. Dr. Morgan is board certified in psychiatry, neurology, and as a medical examiner. *Id.* at 3. He is currently with the Department of Clinical Neuroscience at Brown University as a clinical assistant professor and maintains a clinical practice at a private office as a disability examiner. *Id*. at 4. Dr. Morgan sees about 15 patients a week, but it is uncommon in his practice to treat autoimmune conditions, including ADEM. Tr. at 17. Additionally, Dr. Morgan could not recall having diagnosed anyone with ADEM as part of his clinical practice. *Id*. at 17.

Dr. Morgan's opinion was based on his review of Petitioner's medical records and medical or scientific literature (including articles on the methodology of neurology and ADEM). Tr. at 13-14. He began with testimony about the proper neurologic methodolody employed in coming to a diagnosis, explaining how it was used by Dr. Krain and himself to evaluate Ms. Bell's condition. Tr. at 17-24. This evaluation began with describing the changes observed on the MRIs performed in 2012, after Petitioner's second Hep B dose. *Id*. at 28-29.

As Dr. Morgan testified, the images from Ms. Bell's first MRI revealed lesions in the gray matter of the caudate nucleus region of the brain, along with what appeared to be a tumor that was producing changes in brain white matter, leading Dr. Krain to characterize it as evidence of tumefactive demyelination. Tr. at 26-28. Dr. Morgan also relied on Dr. Krain's initial conclusions that Ms. Bell's condition presented as subacute. *Id.* at 142. The progression of Ms. Bell's condition into the brain stem, associated with her reported worsening vision, further persuaded Dr. Morgan that it was evidence of ADEM – because it affected one side of the brain and the brainstem. *Id.* at 24.

A large portion of Dr. Morgan's opinion was dedicated to review of Ms. Bell's symptoms and the progression of her condition compared to the classical presentation of ADEM. Overall, Dr. Morgan maintained that ADEM was present (Tr. at 22), relying on the clinical factors for the disease as set forth in S. Tenembaum, *et al.*, *Acute Disseminated Encephalomyelitis*, Neurology, Apr. 17, 2007; 68 (Suppl 2), S23-S36, filed as Pet'r's Ex. 16 ("Tenenbaum"). In his opinion, Ms. Bell matched the criteria for ADEM (as stated by Tenembaum) because she had rapid onset of encephalopathy (problems on the left side of her body affecting deep structures), and because the MRIs performed in the first half of 2012 showed confluent tumefactive lesions with extension and edema and mass effect. Tr. at 47.

Respondent challenged several of these factors on cross-examination. As a preliminary matter, both Dr. Morgan and Respondent's primary expert, Dr. Sriram, agreed that a predicate to ADEM is encephalopathy, although they maintained different definitions for what it meant in this context. Dr. Morgan defined encephalopathy as any pathology of the brain presenting with *either* normal or abnormal mental status, while Dr. Sriram's position was that encephalopathy associated with ADEM would present only with behavioral changes or changes in consciousness. Tr. at 74, 79. Thus, when confronted with Respondent's definition of encephalopathy (which relied on Krupp, L.B. and S. Tenembaum, *Consensus definitions proposed for pediatric multiple sclerosis and related disorders*, Neurology, 2007, 68 (16 Suppl. 2): p. S7-12, filed as Resp't's Ex. D), Dr. Morgan conceded that Ms. Bell had not presented with any notable behavioral changes or alterations, but maintained that "they're saying that's a requirement, but I'm going to tell you, in the real world, this [ADEM] is what the lady had." Tr. at 79.

Dr. Morgan agreed, however, with Respondent that Ms. Bell's presentation was otherwise atypical for the disease, given the absence of other symptoms representative of the condition (as described by Krupp), and given that it was not until Dr. Krain received the MRI results that he was able to say there even was a focal problem. Tr. at 77. Dr. Morgan also confronted the errors in Dr. Gonzalez-Alegre's (the treater whose ADEM diagnosis is heavily relied upon by Petitioner) recitation of Ms. Bell's history from 2013, stating "he may have errors, but I think his conclusion is right." Tr. at 115.

Another central issue to Ms. Bell's diagnosis that was highlighted in Dr. Morgan's testimony was the matter of how brain MRIs use enhancement to evaluate the presence of inflammation as discussed above. Dr. Morgan admitted that the first MRI performed on Ms. Bell showed no enhancement - meaning there was nothing that would suggest an ongoing demyelination process, or that the inflammation was so microscopic that it did not appear on the scan. *Id.* at 85. He otherwise pointed to no other instances from the time contemporaneous with the second or third Hep B doses that were contrary.

Dr. Morgan also conceded that many of Ms. Bell's normal testing results (none of which in 2012, for example, corroborated the existence of inflammation) did not support his opinion about the propriety of the ADEM diagnosis, but maintained that this did not make it less likely that ADEM was the appropriate explanation, arguing that test results were "great if they're positive, but not being there does not by any stretch rule out this condition." Tr. at 13. He also proposed that some common testing might not reveal ADEM-related problems. Thus, with respect to the normal CSF results, Dr. Morgan stated that sometimes there are conditions of the brain that do not get "spilled over" into the spinal cord, and thus would not be revealed by a lumbar puncture. *Id.* at 143. Dr. Morgan also acknowledged that, based on his review of the medical records, there was no evidence that Ms. Bell had experienced a reaction to her first dose of Hep B vaccine, but dismissed the significance of that fact. In his view, it was common for individuals to be unaffected by a vaccine's initial dose, since many times the first would merely serve to prime the immune system, leading to a pathologic, inflammatory reaction only after the second dose. *Id*. at 13.

Another debatable aspect of Dr. Morgan's diagnostic opinion was whether demyelinating syndromes such as ADEM are established largely on MRI findings of lesions in gray matter regions of the brain, like the basal stem ganglia. Dr. Morgan proposed that ADEM can so manifest. Tr. at 94. His proposal arose from Tenenbaum, which states that "the gray matter of the thalami and basal ganglia are frequently involved" in ADEM. Tenenbaum at S25. Dr. Morgan supported that statement by discussing how he independently determined that ADEM is the proper diagnosis. Ms. Bell presented with a subacute demyelinated lesion (seen in the first MRI) that was tumefactive, she had a lesion in the basal ganglia, and other conditions were excluded. Tr. at 116.

Dr. Morgan's opinion generally strayed away from discussing the causal role the Hep B vaccine could have played in the development of Ms. Bell's purported ADEM. Although throughout his testimony he stated that the cause was post-vaccinal, he also admitted that he is not an immunologist and relied on molecular mimicry as the mechanism because it is a "touted medical theory." Tr. at 36-38, 121. Dr. Morgan did reference some scientific support for the causal relationship between ADEM and the Hep B vaccine, referencing Langer-Gould, Annette,

et al., *Vaccines and the Risk of Multiple Sclerosis and Other Central Nervous System Demyelinating Diseases*. JAMA Neurol. 2014; 71 (12):1506-1513, filed as Pet'r's Ex. 26-1 ("Langer-Gould"). Thus, he opined that based on Langer-Gould, Ms. Bell "fits the bill" for the results produced in the study. Tr. at 60. Langer-Gould focused on the Hep B and HPV vaccines and their potential relationship to central nervous system and demyelinating syndromes. Langer-Gould at 1. Its authors found "no longer-term association of vaccines with MS or any other central nervous system- acquired demyelinating syndromes ("CNS ADS") but a "short-term increase in risk [that] suggests that vaccines may accelerate the transition from subclinical to over autoimmunity in patient with existing disease." Id. at 1. In Dr. Morgan's opinion, Ms. Bell's circumstances were comparable to the studied patients who experienced some kind of demyelinating condition in the first thirty days after vaccination. Tr. at 15.

Dr. Morgan also proposed, with respect to the period between vaccination and onset of Petitioner's symptoms, that "the timing is pretty classic, certainly the first one [vaccine administered 01/2012], within ten days to two weeks." *Id.* at 10. In his view, Ms. Bell's immune system was re-challenged when she received the third Hep B vaccine, as evidenced by the fact that Ms. Bell got worse after receipt. *Id*. However, when pressed to explain the worsening symptoms in detail, he conceded that her worsening vision and hearing may have been evident before she received the third vaccine. *Id.* at 99.

Dr. Morgan acknowledged the contrary findings of many of Ms. Bell's treaters that did not embrace ADEM as her illness, and instead proposed that there was no explanation yet provided for the cause of her symptoms, or did not believe that the Hep B vaccination was the most likely cause. He nevertheless proposed that the opinions offered by some of the Iowa treaters, like Dr. Gonzalez-Alegre (who, as he noted, had consulted with other Iowa treaters about his views), were more persuasive on the issue of diagnosis. Tr. at 117. As support for this contention, Dr. Morgan stated that the Mayo Clinic treaters only focused on the potential genetic aspect of Ms. Bell's condition, while only performing a more cursory neurologic review (although, as noted above, the record belies that assertion). *Id.* at 145. Dr. Morgan was similarly presented with Ms. Bell's condition as of July 2014, and questioned about the implication of the more-recent treater views that her symptoms did not reflect an acute, monophasic illness like ADEM. *Id* at 48, 128-129. When asked if those records indicated a progression in Ms. Bell's symptoms, Dr. Morgan could only concede that her symptoms were worse. *Id*. at 129.

B. Dr. David Axelrod

Petitioner's second expert, David Axelrod, M.D., provided an immunology opinion about the theoretical causative role the Hep B vaccine could play in developing ADEM or another demyelinating condition. He filed one report in this case, and also testified at hearing. *See* Pet'r's Ex. 23, *see also* Tr. 150-198.

Dr. Axelrod graduated from the University of Michigan Medical School in 1974 (after completing his bachelor's degree at the University of Michigan). Pet'r's Ex. 24 at 1. He completed two residencies in internal medicine, one at the University of Toronto and one at William Beaumont Hospital, followed by additional residencies with a fellowship in allergy, immunology, and rheumatology at McGill University, and then serving as a fellow for the National Institutes of Health in the laboratory of clinical immunology. *Id*. Dr. Axelrod is board certified in medicine, allergy and immunology, adult rheumatology, and medical laboratory immunology. Tr. at 151. He currently works in private practice, with the vast majority of patients having allergies, immunologic conditions, or autoimmune rheumatic diseases. *Id*. at 152. In particular, he largely treats elderly patients who have suffered an allergic reaction to a medication, thus dealing with autoimmune diseases only if his existing patients have that as a previously diagnosed, underlying condition. *Id.* at 173.

Dr. Axelrod's opinions were based mainly on his review of Ms. Bell's medical records and scientific literature. Pet'r's Ex. 23 at 1. He also acknowledged that his opinion assumed that Ms. Bell in fact had a demyelinating condition. Tr. at 155-56. Indeed, he did not purport to have the expertise to propose a diagnosis for Petitioner, and did not attempt to do so in providing an expert report in the case. *See generally Id.* at 150-75. Thus, he agreed that if the assumption about the character of her condition were incorrect – that she did not suffer from ADEM or a similar demyelinating condition affecting her brain - then his testimony would no longer have relevance to the lawsuit, because he would not be able to offer an opinion with respect to the vaccine's causal role in causing a different injury than that alleged. *Id*. at 180.

Most of Dr. Axelrod's opinion focused on the proposed biological mechanism linking the Hep B vaccine to damage in the central nervous system – molecular mimicry. Dr. Axelrod opined that the immune response elicited by a vaccine could damage the myelin sheath around nerves in the brain as a result of homology (which is defined as similarity of nucleotide or amino acid sequence-protein) between the vaccine and the myelin. Tr. at 156, *see also* Merriam-Webster, *Definition of Homology*, http://www.merriam-webster.com/dictionary/homology (last visited Nov. 7, 2016). In support of such homology existing, Dr. Axelrod cited Bogdanos, D.P., et al., *A study of molecular mimicry and immunological cross-reactivity between hepatitis B surface antigen and myelin mimics*. Clinic Dev. Immunology, 2005. 12(3): p. 217-24, filed as Pet'r's Ex. 23-12. ("Bogdanos").

Specifically, the study referenced in Bogdanos found antibodies that inhibited patients' response to the recombinant hepatitis B vaccine that contained an antigen identical to the wild virus. Tr. at 156. In Ms. Bell's case, Dr. Axelrod proposed, the Hep B vaccine, contained protein structures homologous to the myelin protein oligodendrocyte glycoprotein; the interaction between the vaccine homologous antigens and the myelin resulted in the production of antibodies, and the cytokine production stimulated by the vaccine facilitated movement of the antibodies in

Ms. Bell's central nervous system through the blood brain barrier. Pet'r's Ex. 23 at 6. Once the cytokines combined with cells within the brain, damage occurred to her central nervous system. *Id*. And he referenced other literature finding a relationship between the Hep B vaccine and a variety of neurologic conditions.[29] *Id*. at 6-7.

Dr. Axelrod was further questioned on the Bogdanos paper, and especially its conclusions that no one studied in it ever manifested the disease even with the presence of homology. Tr. at 187. He conceded that molecular mimicry is just a theory and there is no practical ability to prove that homology can lead to disease. *Id*. at 187-88.

Dr. Axelrod's expert report and testimony briefly discussed several other factors that he believes support causation in this case. First was the lack of alternative explanations. Ms. Bell's physicians found no preceding infectious or malignant cause of her neurologic symptoms. Pet'r's Ex. 23 at 4. By contrast, Ms. Bell's MRI in March of 2013 showed near complete interval resolution of her lesions from the time of vaccination, thus establishing that she had experienced a de-challenge - the defining aspects of the disorder disappeared with removal of the exposure. *Id*.

Dr. Axelrod's testimony also addressed the temporal association of Ms. Bell's receipt of the vaccine and her reaction. He relied particularly on Abbas, A.K., *Cellular and Molecular Immunology Edition 6*. 6th ed. 2010, Philadelphia: Saunders Else Ier, 566, filed as Pet'r's Ex. 23-4 ("Abbas"), as evidence that Ms. Bell's first reaction was within the proper time frame – 14-21 days following the vaccination. He also found significant Petitioner's purported second reaction after her third dose of Hep B vaccine, noting that a secondary (memory) immune response is known to result more quickly than a first immune response. Pet'r's Ex. 23 at 3; Tr. at 159. Applied to Ms. Bell's case, Dr. Axelrod averred, Ms. Bell's reaction to her third vaccine fit squarely within the time-frame suggested by Abbas. Dr. Axelrod thus concluded that Ms. Bell's reaction to her second and third Hep B vaccinations established that the vaccine played a causative role in her illness. *Id*. at 160.

Indeed, Dr. Axelrod proposed that Ms. Bell got worse after the third vaccination, bolstering his causation opinion because a re-challenge caused her condition to worsen. Pet'r's Ex. 23 at 4-5. However, when cross-examined about instances in the medical record demonstrating that

[29] Thus, Dr. Axelrod cited the following references to show a connection between Hep B and neurologic conditions: Geier, D.A, *et al., A case-control study of serious autoimmune adverse events following hepatitis B immunization. Autoimmunity, 2005*. 38(4): pp. 295-301 (studied subjects suffered neurologic damage after Hep B vaccine); Nam, T.S., *et al*., *Mononeuropathy multiplex in a patient with chronic active hepatitis B*. J. Clinical Neurology, 2010. 6(3): p. 156-8; Matsui, M., et al., *Recurrent demyelinating transverse myelitis in a high titer HBs-antigen carrier*. J. Neurologic Science, 1996. 139(2): p. 235-7 (case study of a patient with recurrent demyelinating transverse myelitis with antibodies to Hep B antigen); and Vital, C., et al., *Postvaccinal inflammatory neuropathy: peripheral nerve biopsy in 3 cases*. J. Peripheral Nervous Syst, 2002. 7(3): p. 163-7 (two cases of demyelinating disease following Hep B vaccination).

Petitioner had experienced worsening prior to the third Hep B dose, Dr. Axelrod conceded that his assumptions about worsening might not in fact have substantiation and "maybe the third vaccine didn't do much of anything else." Tr. at 183.

C. Dr. Subramanian Sriram

Respondent's first expert, Subramanian Sriram, M.D., testified that it was more likely than not that the Hep B vaccinations that Ms. Bell received were unrelated to the neurologic syndrome that she developed. Tr. at 214. He further stated that based on her clinical presentation, he did not think Ms. Bell had ADEM, characterizing her condition instead as of idiopathic origin. *Id.* Like Dr. Morgan, Dr. Sriram filed three expert reports in total. *See* Resp't's Exs. A, Q, and R.

Dr. Sriram completed his bachelors and medical degrees from the University of Madras in India, completing his residency in internal medicine at Wayne State University followed by a neurology residency and at Stanford University. Tr. at 206; Resp't's Ex. B. He then went on to complete a four year neuroimmunology fellowship at Stanford, before becoming director of the MS Center at the University of Vermont for about 10 years. Resp't's Ex. B. Today, Dr. Sriram directs the Multiple Sclerosis Center at Vanderbilt Medical Center, where he sees patients while also serving as a Professor of Neurology and Experimental Therapeutics at Vanderbilt. Tr. at 206-07.

Dr. Sriram sees approximately 35 patients per week, 80 percent of whom have MS, with the remainder having some other neurological disease. Tr. at 209. Relying on his experience treating such patients with autoimmune disorders, Dr. Sriram formulated his opinion in this case after reviewing Petitioner's medical records, and pertinent medical or scientific literature. *Id*. at 215-16.

Dr. Sriram began by describing the characteristic clinical metrics used to diagnose a patient with ADEM. He emphasized that ADEM is a monophasic disorder, typically lasting no more than four to six weeks before the patient recovers. Tr. at 210. ADEM occurs most commonly with children, usually presenting with multiple abnormal areas on an MRI in the white matter of the brain, and with evidence of inflammation (as established by CSF testing). In addition, ADEM can be effectively treated with steroids and immunosuppressive agents. *Id.* at 211-12.

As stated earlier, Dr. Sriram and Dr. Morgan agreed that encephalopathy is a predicate to ADEM. Dr. Sriram, however, took issue with Dr. Morgan's testimony about what factors would establish the existence of an encephalopathy. Tr. at 213-14. In Dr. Sriram's view, encephalopathy manifests as behavioral change, such as irritability, inability to concentrate, loss of consciousness or alertness, or lethargy. *Id*. at 214. He also added seizures to the list of behavioral changes consistent with encephalopathy. *Id.* at 273. He thus firmly disagreed with Dr. Morgan's categorization of encephalopathy as a mere pathology of the brain, stating that "encephalopathy can result from the pathology . . . that does not mean every pathology of the brain has encephalopathy." *Id*. at 215.

After setting out the characteristics of ADEM, Dr. Sriram referenced Ms. Bell's clinical presentation to show how it did not fit the classic clinical factors for the disease. Dr. Sriram placed the most emphasis on ADEM being a disease of the white matter – whereas, according to the MRI results, any abnormal findings from Ms. Bell's first two MRIS appeared only in the gray matter. Tr. at 216-17. Moreover, he opined, based on Ms. Bell's MRIs that her brain abnormalities were located in the deep nuclei or the caudate, the putamen, and the globus pallidus- all deep neurons not found in the white matter regions of the brain. *Id*. at 217. Dr. Sriram admitted that it was possible for ADEM to be present without evidence of white matter lesions, but that it was unlikely that ADEM would present with *only* isolated lesions in the gray matter, as here. *Id*. at 220-21. He also noted that the lack of evidence of inflammation on both the MRIs and from the CSF tests as further diminishing the propriety of the diagnosis. *Id*. Additionally, Dr. Sriram emphasized that if Ms. Bell's condition was part of an immunological process, then he would have expected to see progression in the IgG index and oligoclonal bands, which was not present for Ms. Bell. *Id*. at 298.

Dr. Sriram was confronted on cross-examination with the idea that the criteria for ADEM, which typically appears in children, could be different for adults. Tr. at 270-73. He mentioned that the variations between adults and children could be the amount of lesions appearing on MRIs, and the amount of spinal fluid cells that the patient should have. *Id*. at 273. But he maintained that there were certain clinical criteria that would be expected regardless of the patient's age, such as presenting with encephalopathy or a monophasic course to the disease's symptoms – none of which were evident with respect to Ms. Bell. *Id*. at 273.

Outside of the issues stated above, Dr. Sriram stressed that Ms. Bell's ongoing symptoms over many years, and inability of her treaters to pinpoint the nature of her illness or its source, further undercut the conclusion that she ever suffered from ADEM. Tr. at 290. In a typical ADEM case, Dr. Sriram would expect to see the patient's condition resolve in a matter of weeks. *Id*. He acknowledged the existence of other variations of ADEM that did not adhere to a similar course, including relapse, recurrent, or multiphasic ADEM, although he did not accept that they provided possible explanations for Ms. Bell's illness. *Id*. at 300. Thus, while Dr. Sriram admitted that relapse of ADEM symptoms could occur, he argued that this was mostly present when the demyelinating condition was later determined to be MS, which had a different, more intermittent course. Tr. at 290. He also proposed that purported ADEM relapses were often nothing more than evidence that an ameliorative treatment like steroids had been tapered or discontinued, allowing underlying symptoms to flare back. *Id*. at 289. He acknowledged as well that in very rare cases children had been known to get better from ADEM and then show new symptoms, but distinguished such unusual cases from individuals like Ms. Bell, who could only be said to be experiencing some kind of ongoing process with some demyelinating features, the source of which ultimately could not be known. *Id*. at 290.

Dr. Sriram also referenced portions of the medical record that he believed contained incorrect speculation or conclusions as to Ms. Bell's condition. The first such disagreement was with the differential diagnosis of a tumefactive demyelinating disease after Ms. Bell's first MRI. Tr. at 223. Dr. Sriram described a tumefactive demyelinating disease as presenting with lesions in the white matter that are so large they appear on an MRI much like a tumor. *Id*. at 222. Although Dr. Krain included it in his differential diagnosis from February 21, 2012, Dr. Sriram noted that there was little white matter where the lesions were present in the MRI. *Id*. at 223.

Dr. Sriram further offered his own interpretation of the results of the MRIs performed in May and June 2012. At the time of the May MRI, Ms. Bell was exhibiting horizontal gaze palsy – the inability to look left or right. Tr. at 242. This condition, he proposed, results from a problem in the pons region of the brain and not the cranial nerves. *Id.* at 243. The subsequent June MRI showed stability – Ms. Bell's lesions had changed very little. *Id*. at 244. The findings documented in that MRI stated an abnormal signal extending to the ventral mesencephalon. *Id*. In Dr. Sriram's view, such a finding was demonstrative of basal ganglia damage, which is seen in Parkinson's disease and other similar conditions. *Id*. at 245-47. It was therefore further evidence not supportive of the ADEM diagnosis.

Dr. Sriram also discussed the PET scan Ms. Bell received in June 2012. He described the process of a PET scan, which allows for the measurement of glucose uptake by the cells by injecting FDG and observing the reaction. Tr. at 238. In Ms. Bell's case, there was a total absence of uptake in the right caudate lentiform nucleus, suggesting to Dr. Sriram that those cells were already dead. *Id*. In his opinion, such findings were not consistent with either the presence of a white matter tumor or inflammation, which in either case would require live brain cells capable of division, and thus susceptible to inflammation. *Id*. at 239.

D. Dr. Kathleen Collins

Respondent's final expert, Kathleen Loretta Collins, M.D., Ph. D., offered an opinion mostly aimed at rebutting Dr. Axelrod's assertions about the causal relationship between the Hep B vaccine and ADEM, based both upon the facts of the case as well as science regarding the vaccine.

Dr. Collins received her medical degree and doctorate from Johns Hopkins University School of Medicine (after receiving an undergraduate degree from Wellesley College) in 1993. Resp't's Ex. G at 1, Tr. at 306-63. She then completed her residency in internal medicine at Brigham and Women's Hospital before serving as a clinical fellow of infectious disease at Beth Israel Hospital and served as a research fellow at Harvard University. Tr. at 307. Dr. Collins was also a post-doctoral fellow at MIT researching the immune response to viral infections. *Id*. Dr. Collins is board certified in infectious disease and currently works as a professor of internal

medicine and microbiology and immunology at the University of Michigan. Tr. at 307. Although she is on the faculty at Michigan as an assistant professor, 70 percent of her time is spent on basic science research, leading her to publish over 50 articles. *Id*. at 311. Her opinion in this case was based on review of the medical records, the expert report of Dr. Axelrod, and medical or scientific literature. *Id*. at 313.

Dr. Collins' primary opinion was that the record did not support the conclusion that Ms. Bell had suffered an immune response to any doses of the Hep B vaccine. Tr. at 316. In order to conclude that there was an immune response, there would, in Dr. Collins's experience, need to be evidence of inflammation from the MRI as well as CSF tests. *Id*. at 316-17. Here, however, Ms. Bell showed no enhancement in her MRIs - meaning there was no inflammation. *Id*. The CSF test results were similarly unsupportive of the conclusion that inflammation was present. *Id*. She also reiterated Dr. Sriram's contention that if there is inflammation in the brain, CSF tests would reveal it – and in so doing questioned Dr. Morgan's contention that CSF tests might not be so revealing, noting that the spinal column was akin to a "cistern" that would almost always reveal evidence of inflammatory activity in the brain. Tr. at 304.

Similarly, Dr. Collins noted the difference between the diagnoses of an infection versus an autoimmune disorder, proposing that this distinction highlighted a deficiency in Petitioner's contentions about the nature of her condition. The former would be treated by antibiotics, while the latter would call for suppression of the immune system in order to halt the damaging autoimmune process. Tr. at 312-13. The treatment history here, however, showed that Ms. Bell was treated with anti-inflammatory steroids to suppress her immune system without positive effect, thus suggesting her underling problem was not autoimmune in nature. *Id*.

Finally, Dr. Collins challenged Dr. Axelrod's opinion that molecular mimicry is a mechanism by which the Hep B vaccine can cause ADEM. Tr. at 338. In particular, one of the primary studies he relied upon addressing cytokines opening the blood brain barrier did not relate to the proteins in the Hep B vaccine. *Id*. at 330; *see also* Lawson, C.M., *Evidence for mimicry by viral antigens in animal models of autoimmune disease including myocarditis*. Cell Molecular Life Science, 2000. 57(4): p. 552-60, filed as Pet'r's Ex. 23-11 ("Lawson"). Dr. Collins described how the blood brain barrier works to protect the brain, allowing that in rare cases or particular kinds of viral or bacterial infection (such as meningitis) the barrier will open as a result of excessive inflammation. Tr. at 333. That did not lead to the conclusion, however, that the barrier would necessarily open as a result of vaccine-induced cytokine expression, which could not be shown (and had not been shown by Dr. Axelrod) to have the same inflammatory impact. *Id*. In order to have an immune response that could even involve molecular mimicry as a pathologic mechanism, inflammation was required – but she purports it was completely absent here. *Id*. at 350.

E. Supplemental Reports Interpreting Missing MRIs

During the January 2016 entitlement hearing, it was disclosed that Ms. Bell's initial 2012 MRIs had not been reviewed by the experts, because they were never obtained or filed in the case. Tr. at 138-39. I therefore ordered them produced and filed, if possible, and allowed both sides the opportunity to file a supplemental expert report interpreting the newly-disclosed MRIs. *See* Order dated February 5, 2016; *see also* Non-PDF Order dated March 22, 2016. The parties did so on April 29, 2016.[30]

Petitioner's supplemental report was not merely Dr. Morgan's opinion, but was also based on his consultation with Dr. Roman Klufas, a neuro-radiologist at Brigham & Women's Hospital in Boston, Massachusetts. Pet'r's Ex. 35; *see also* Pet'r's Ex. 35-2. Dr. Morgan stated that the newly-disclosed MRIs demonstrated that Ms. Bell had "classic MRI findings for ADEM," noting the improvement seen on the March 20, 2012, MRI after Ms. Bell was treated with steroids. Pet'r's Ex. 35 at 2. He also discussed the new demyelination findings of the July 2, 2012, MRI and their consistency with a post vaccinal second attack following Ms. Bell's third injection. *Id*. at 3. However, Dr. Morgan pointed out nothing from the MRIs that was different from what the existing contemporaneous record reveals, or that added any shading to his previous testimony.

The supplemental report included a separate piece of correspondence from Dr. Klufas as well. Pet'r's Ex. 35-2. Dr. Klufas noted a large area of T2 abnormality from his review of the first February 2012, MRI which nearly resolves by September 24, 2012. Pet'r's Ex. 35-2 at 2. Regarding the July MRI, Dr. Klufas specifically claimed to discern new white matter findings within the mid pons. *Id*. Dr. Klufas ultimately concluded that the MRI findings were consistent with a diagnosis of ADEM. *Id*. at 2. However, he also stated that he saw little to no evidence of enhancement that would suggest the presence of inflammation. *Id*. at 1-2.

Respondent's supplemental report from Dr. Sriram reached conclusions consistent with his trial testimony about the MRI findings. Thus, Dr. Sriram notes a basal ganglia abnormality in the February 2012 MRI (thus a gray matter abnormality, as testified) and an increase in the T2 signal without inflammation. Resp't's Ex. R. at 2. He emphasized that his review of the unfiled MRIs also showed a gradual decrease of the T2 signal as seen on the March, April, and July MRIs. *Id*. In his opinion, the evolution of the T2 signal from hyper to hypo-intense is characteristic of metal deposits – something typically seen in degenerative and metabolic conditions such as Alzheimer's and Parkinson's, rather than a demyelinating condition. *Id*. Overall, and with the benefit of having seen the original MRI, Dr. Sriram reiterated his opinion

[30] This was the second supplemental report for both Drs. Morgan and Sriram. Dr. Morgan previously filed a supplemental report on February 3, 2015 addressing Respondent's expert reports as well as attempting to provide further evidentiary support for causation as ordered by the court on October 8, 2014. *See* Order dated October 8, 2014. Dr. Sriram filed his first supplemental report responding to Drs. Morgan's and Axelrod's reports on April 1, 2015.

that there was no evidence of lesions in the white matter, making ADEM unlikely in this case, and confirming for him that the true etiology of Ms. Bell's condition remained unknown. *Id*.

III. PROCEDURAL HISTORY

Ms. Bell filed her Petition on September 23, 2013. Pet. at 1. In it, she specifically alleged that she suffers from ADEM, progressive neurological deterioration, gaze palsy, facial palsy, asymmetric sensorineural hearing loss, and other conditions. *Id*. at 4-5.

On January 6, 2014, Respondent filed her Rule 4(c) report denying that Ms. Bell was entitled to compensation. ECF No. 10. Shortly thereafter, the case was reassigned to me. In the ensuing 16 months, Petitioner filed medical records, both sides submitted expert reports, and Petitioner filed an amended petition stating that "regardless of the precise diagnoses of or label of Kristine's illnesses, disabilities, injuries, condition, and/or disorder, one or more of them constitute a vaccine-related injury." *See* Amended Petition Filed on December 15, 2014. Thereafter, in May of 2015, I scheduled a hearing for January 28-29 of 2016, to determine entitlement. ECF No. 43.

The entitlement hearing was held as scheduled, with both sides filing pre-hearing briefs. That hearing included testimony from the experts identified above. After the hearing, I instructed Petitioner to obtain the actual MRI images of Ms. Bell taken during 2012. Both parties were then to have their neurologists review the images and write supplemental reports. The parties filed these reports from Drs. Morgan and Sriram on the same day, April 29, 2016. The parties elected not to file post-hearing briefs.

IV. APPLICABLE LEGAL STANDARDS

A. Petitioner's Overall Burden in Vaccine Program Cases

To receive compensation in the Vaccine Program, a petitioner must prove either: (1) that she suffered a "Table Injury" – *i.e.*, an injury falling within the Vaccine Injury Table – corresponding to one of the vaccinations in question within a statutorily prescribed period of time or, in the alternative, (2) that her illnesses were actually caused by a vaccine (a "Non-Table Injury"). *See* Sections 13(a)(1)(A), 11(c)(1), and 14(a), as amended by 42 C.F.R. § 100.3; § 11(c)(1)(C)(ii)(I); *see also Moberly v. Sec'y of Health & Human Servs*., 592 F.3d 1315, 1321 (Fed. Cir. 2010); *Capizzano v. Sec'y of Health & Human Servs*., 440 F.3d 1317, 1320 (Fed. Cir. 2006).[31] In this case, Petitioner does not assert a Table claim.

[31] Decisions of special masters (some of which I reference in this ruling) constitute persuasive but not binding authority. *Hanlon v. Sec'y of Health & Human Servs.*, 40 Fed. Cl. 625, 630 (1998). By contrast, Federal Circuit rulings concerning legal issues are binding on special masters. *Guillory v. Sec'y of Health & Human Servs.*, 59 Fed. Cl. 121, 124 (2003), *aff'd*, 104 F. App'x 712 (Fed. Cir. 2004); *see also Spooner v. Sec'y of Health & Human Servs.*, No. 13-

For both Table and Non-Table claims, Vaccine Program petitioners bear a "preponderance of the evidence" burden of proof. Section 13(1)(a). That is, a petitioner must offer evidence that leads the "trier of fact to believe that the existence of a fact is more probable than its nonexistence before [he] may find in favor of the party who has the burden to persuade the judge of the fact's existence." *Moberly*, 592 F.3d at 1322 n.2; *see also Snowbank Enter. v. United States*, 6 Cl. Ct. 476, 486 (1984) (mere conjecture or speculation is insufficient under a preponderance standard). Proof of medical certainty is not required. *Bunting v. Sec'y of Health & Human Servs*., 931 F.2d 867, 873 (Fed. Cir. 1991). In particular, a petitioner must demonstrate 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 & Human Servs*., 165 F.3d 1344, 1352-53 (Fed. Cir. 1999)); *Pafford v. Sec'y of Health & Human Servs*., 451 F.3d 1352, 1355 (Fed. Cir. 2006). A petitioner may not receive a Vaccine Program award based solely on her assertions; rather, the petition must be supported by either medical records or by the opinion of a competent physician. Section 13(a)(1).

In attempting to establish entitlement to a Vaccine Program award of compensation for a Non-Table claim, a petitioner must satisfy all three of the elements established by the Federal Circuit in *Althen*: "(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.

Each of the *Althen* prongs requires a different showing. Under *Althen* prong one, petitioners must provide a "reputable medical theory," demonstrating that the vaccine received *can cause* the type of injury alleged. *Pafford*, 451 F.3d at 1355-56 (citations omitted). To satisfy this prong, a petitioner's theory must be based on a "sound and reliable medical or scientific explanation." *Knudsen v. Sec'y of Health & Human Servs.*, 35 F.3d 543, 548 (Fed. Cir. 1994). Such a theory must only be "legally probable, not medically or scientifically certain." *Id*. at 549.

Petitioners may satisfy the first *Althen* prong without resort to medical literature, epidemiological studies, demonstration of a specific mechanism, or a generally accepted medical theory. *Andreu v. Sec'y of Health & Human Servs.*, 569 F.3d 1367, 1378-79 (Fed. Cir. 2009) (citing *Capizzano*, 440 F.3d at 1325-26). Special masters, despite their expertise, are not empowered by statute to conclusively resolve what are essentially thorny scientific and medical questions, and thus scientific evidence offered to establish *Althen* prong one is viewed "not through the lens of the laboratorian, but instead from the vantage point of the Vaccine Act's preponderant evidence standard." *Id.* at 1380. Accordingly, special masters must take care not to increase the burden placed on petitioners in offering a scientific theory linking vaccine to injury. *Contreras v. Sec'y of Health & Human Servs.*, 121 Fed. Cl. 230, 245 (2015) ("[p]lausibility . . . in many cases *may* be

159V, 2014 WL 504728, at *7 n.12 (Fed. Cl. Spec. Mstr. Jan. 16, 2014).

enough to satisfy *Althen* prong one" (emphasis in original)), *appeal docketed*, No. 2015-5097 (Fed. Cir. June 19, 2015). But this does not negate or reduce a petitioner's ultimate burden to establish her overall entitlement to damages by preponderant evidence. *W.C. v. Sec'y of Health & Human Servs.*, 704 F.3d 1352, 1356 (Fed. Cir. 2013) (citations omitted).[32]

The second *Althen* prong requires proof of a logical sequence of cause and effect, usually supported by facts derived from a petitioner's medical records. *Althen*, 418 F.3d at 1278; *Andreu*, 569 F.3d at 1375-77; *Capizzano*, 440 F.3d at 1326; *Grant v. Sec'y of Health & Human Servs.*, 956 F.2d 1144, 1148 (Fed. Cir. 1992). In establishing that a vaccine "did cause" injury, the opinions and views of the injured party's treating physicians are entitled to some weight. *Andreu*, 569 F.3d at 1367; *Capizzano*, 440 F.3d at 1326 ("medical records and medical opinion testimony are favored in vaccine cases, as treating physicians are likely to be in the best position to determine whether a 'logical sequence of cause and effect show[s] that the vaccination was the reason for the injury'") (quoting *Althen*, 418 F.3d at 1280). Medical records are generally viewed as particularly trustworthy evidence, since they are created contemporaneously with the treatment of the patient. *Cucuras v. Sec'y of Health & Human Servs.*, 993 F.2d 1525, 1528 (Fed. Cir. 1993).

However, medical records and/or statements of a treating physician's views do not *per se* bind the special master to adopt the conclusions of such an individual, even if they must be considered and carefully evaluated. Section 13(b)(1) (providing that "[a]ny such diagnosis, conclusion, judgment, test result, report, or summary shall not be binding on the special master or court"); *Snyder v. Sec'y of Health & Human Servs.*, 88 Fed. Cl. 706, 746 n.67 (2009) ("there is nothing . . . that mandates that the testimony of a treating physician is sacrosanct – that it must be accepted in its entirety and cannot be rebutted"). As with expert testimony offered to establish a theory of causation, the opinions or diagnoses of treating physicians are only as trustworthy as the reasonableness of their suppositions or bases. The views of treating physicians should also be weighed against other, contrary evidence also present in the record – including conflicting opinions among such individuals. *Hibbard v. Sec'y of Health & Human Servs.*, 100 Fed. Cl. 742, 749 (2011) (not arbitrary or capricious for special master to weigh competing treating physicians' conclusions against each other), *aff'd*, 698 F.3d 1355 (Fed. Cir. 2012); *Caves v. Sec'y of Dep't of Health & Human Servs.*, 100 Fed. Cl. 119, 136 (2011), *aff'd*, 463 F. App'x 932 (Fed. Cir. 2012); *Veryzer v. Sec'y of Health & Human Servs.*, No. 06-522V, 2011 WL 1935813, at *17 (Fed. Cl. Spec. Mstr. Apr. 29, 2011), *mot. for review den'd*, 100 Fed. Cl. 344, 356 (2011), *aff'd without opinion*, 475 Fed. App'x 765 (Fed. Cir. 2012).

[32] There is ample contrary authority for the more straightforward proposition that the first *Althen* prong, like the overall test itself, simply applies a preponderance standard when evaluating if a reliable and plausible causal theory has been established. *Broekelschen v. Sec'y of Health & Human Servs.*, 618 F.3d 1339, 1350 (Fed. Cir. 2010). For purposes of the present analysis, I am stressing those cases focusing on the *plausibility* of the causal theory proposed, as opposed to whether preponderant evidence supports it, in order to avoid imposing on Petitioners a greater evidentiary burden than the law requires. This does not, however, change the fact that *any* theory's plausibility, for purposes of satisfying the *Althen* test, is properly analyzed by subjecting its components to the *Daubert* tests for scientific reliability. *Terran v. Sec'y of Health & Human Servs*., 195 F.3d 1302, 1316 (Fed. Cir. 1999).

The third *Althen* prong requires establishing a "proximate temporal relationship" between the vaccination and the injury alleged. *Althen*, 418 F.3d at 1281. That term has been equated to the phrase "medically-acceptable temporal relationship." *Id.* A petitioner must offer "preponderant proof that the onset of symptoms occurred within a timeframe which, given the medical understanding of the disorder's etiology, it is medically acceptable to infer causation." *Bazan v. Sec'y of Health & Human Servs.*, 539 F.3d 1347, 1352 (Fed. Cir. 2008). The explanation for what is a medically acceptable timeframe must also coincide with the theory of how the relevant vaccine can cause an injury (*Althen* prong one's requirement). *Id*. at 1352; *Shapiro v. Sec'y of Health & Human Servs.*, 101 Fed. Cl. 532, 542 (2011), *recons. den'd after remand*, 105 Fed. Cl. 353 (2012), *aff'd mem.*, 2013 WL 1896173 (Fed. Cir. 2013); *Koehn v. Sec'y of Health & Human Servs.*, No. 11-355V, 2013 WL 3214877 (Fed. Cl. Spec. Mstr. May 30, 2013), *mot. for review den'd* (Fed. Cl. Dec. 3, 2013), *aff'd*, 773 F.3d 1239 (Fed. Cir. 2014).

B. Law Governing Analysis of Fact Evidence

The process for making determinations in Vaccine Program cases regarding factual issues begins with consideration of the medical records. Section 11(c)(2). The special master is required to consider "all [] relevant medical and scientific evidence contained in the record," including "any diagnosis, conclusion, medical judgment, or autopsy or coroner's report which is contained in the record regarding the nature, causation, and aggravation of the petitioner's illness, disability, injury, condition, or death," as well as "the results of any diagnostic or evaluative test which are contained in the record and the summaries and conclusions." Section 13(b)(1)(A). The special master is then required to weigh the evidence presented, including contemporaneous medical records and testimony. *See Burns v. Sec'y of Health & Human Servs*., 3 F.3d 415, 417 (Fed. Cir. 1993) (it is within the special master's discretion to determine whether to afford greater weight to contemporaneous medical records than to other evidence, such as oral testimony surrounding the events in question that was given at a later date, provided that such a determination is evidenced by a rational determination).

Medical records that are created contemporaneously with the events they describe are presumed to be accurate and "complete" (*i.e*., presenting all relevant information on a patient's health problems). *Cucuras*, 993 F.2d at 1528; *Doe/70 v. Sec'y of Health & Human Servs.*, 95 Fed. Cl. 598, 608 (2010) ("[g]iven the inconsistencies between petitioner's testimony and his contemporaneous medical records, the special master's decision to rely on petitioner's medical records was rational and consistent with applicable law"), *aff'd*, *Rickett v. Sec'y of Health & Human Servs*., 468 F. App'x 952 (Fed. Cir. 2011) (non-precedential opinion). This presumption is based on the linked propositions that (i) sick people visit medical professionals; (ii) sick people honestly report their health problems to those professionals; and (iii) medical professionals record what they are told or observe when examining their patients in as accurate a manner as possible, so that they are aware of enough relevant facts to make appropriate treatment decisions. *Sanchez*

v. Sec'y of Health & Human Servs., No. 11-685V, 2013 WL 1880825, at *2 (Fed. Cl. Spec. Mstr. Apr. 10, 2013); *Cucuras v. Sec'y of Health & Human Servs*., 26 Cl. Ct. 537, 543 (1992), *aff'd*, 993 F.2d 1525 (Fed. Cir. 1993) ("[i]t strains reason to conclude that petitioners would fail to accurately report the onset of their daughter's symptoms. It is equally unlikely that pediatric neurologists, who are trained in taking medical histories concerning the onset of neurologically significant symptoms, would consistently but erroneously report the onset of seizures a week after they in fact occurred").

Accordingly, if the medical records are clear, consistent, and complete, then they should be afforded substantial weight. *Lowrie v. Sec'y of Health & Human Servs*., No. 03-1585V, 2005 WL 6117475, at *20 (Fed. Cl. Spec. Mstr. Dec. 12, 2005). Indeed, contemporaneously medical records are generally found to be deserving of greater evidentiary weight than oral testimony – especially where such testimony conflicts with the record evidence. *Cucuras*, 993 F.2d at 1528; *see also Murphy v. Sec'y of Health & Human Servs.*, 23 Cl. Ct. 726, 733 (1991), *aff'd*, 968 F.2d 1226 (Fed. Cir.), *cert. den'd*, *Murphy v. Sullivan*, 506 U.S. 974 (1992) (citing *United States v. United States Gypsum Co.*, 333 U.S. 364, 396 (1947) ("[i]t has generally been held that oral testimony which is in conflict with contemporaneous documents is entitled to little evidentiary weight.")).

However, there are situations in which compelling oral 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 & Human Servs*., 69 Fed. Cl. 775, 779 (2006) ("like 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*, 2005 WL 6117475, at *19 ("[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 & Human 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*, 569 F.3d at 1379; *Bradley v. Sec'y of Health & Human Servs.*, 991 F.2d 1570, 1575 (Fed. Cir. 1993).

C. Analysis of Expert Testimony

Establishing a sound and reliable medical theory often requires a petitioner to present expert testimony in support of his claim. *Lampe v. Sec'y of Health & Human Servs.*, 219 F.3d 1357, 1361 (Fed. Cir. 2000). Vaccine Program expert testimony is usually evaluated according to the factors for analyzing scientific reliability set forth in *Daubert v. Merrell Dow Pharm., Inc*., 509 U.S. 579, 594-96 (1993). *See Cedillo v. Sec'y of Health & Human Servs.*, 617 F.3d 1328, 1339 (Fed. Cir. 2010) (citing *Terran v. Sec'y of Health & Human Servs.*, 195 F.3d 1302, 1316 (Fed. Cir. 1999)). "The *Daubert* factors for analyzing the reliability of testimony are: (1) whether a theory or

technique can be (and has been) tested; (2) whether the theory or technique has been subjected to peer review and publication; (3) whether there is a known or potential rate of error and whether there are standards for controlling the error; and (4) whether the theory or technique enjoys general acceptance within a relevant scientific community." *Terran*, 195 F.3d at 1316 n.2 (citing *Daubert*, 509 U.S. at 592-95).

The *Daubert* factors play a slightly different role in Vaccine Program cases than they do when applied in other federal judicial fora (such as the district courts). *Daubert* factors are usually employed by judges (in the performance of their evidentiary gatekeeper roles) to exclude evidence that is unreliable and/or could confuse a jury. In Vaccine Program cases, by contrast, these factors are used in the *weighing* of the reliability of scientific evidence proffered. *Davis v. Sec'y of Health & Human Servs.*, 94 Fed. Cl. 53, 66-67 (2010) ("uniquely in this Circuit, the *Daubert* factors have been employed also as an acceptable evidentiary-gauging tool with respect to persuasiveness of expert testimony already admitted"). The flexible use of the *Daubert* factors to evaluate the persuasiveness and reliability of expert testimony has routinely been upheld. *See, e.g.*, *Snyder*, 88 Fed. Cl. at 742-45. In this matter (as in numerous other Vaccine Program cases), *Daubert* has not been employed at the threshold, to determine what evidence should be admitted, but instead to determine whether expert testimony offered is reliable and/or persuasive.

Respondent frequently offers one or more experts of her own in order to rebut a petitioner's case. Where both sides offer expert testimony, a special master's decision may be "based on the credibility of the experts and the relative persuasiveness of their competing theories." *Broekelschen v. Sec'y of Health & Human Servs.*, 618 F.3d 1339, 1347 (Fed. Cir. 2010) (citing *Lampe*, 219 F.3d at 1362). However, nothing requires the acceptance of an expert's conclusion "connected to existing data only by the *ipse dixit* of the expert," especially if "there is simply too great an analytical gap between the data and the opinion proffered." *Snyder*, 88 Fed. Cl. at 743 (quoting *Gen. Elec. Co. v. Joiner*, 522 U.S. 146 (1997)); *see also Isaac v. Sec'y of Health & Human Servs.*, No. 08-601V, 2012 WL 3609993, at *17 (Fed. Cl. Spec. Mstr. July 30, 2012), *mot. for review den'd*, 108 Fed. Cl. 743 (2013), *aff'd*, 540 Fed. App'x 999 (Fed. Cir. 2013) (citing *Cedillo*, 617 F.3d at 1339).

Weighing the relative persuasiveness of competing expert testimony, based on a particular expert's credibility, is part of the overall reliability analysis to which special masters must subject expert testimony in Vaccine Program cases. *Moberly*, 592 F.3d at 1325-26 ("[a]ssessments as to the reliability of expert testimony often turn on credibility determinations"); *see also Porter v. Sec'y of Health & Human Servs*., 663 F.3d 1242, 1250 (Fed. Cir. 2011) ("this court has unambiguously explained that special masters are expected to consider the credibility of expert witnesses in evaluating petitions for compensation under the Vaccine Act"). It is in the exercise of my duties as a special master to weigh competing expert testimony. *Copenhaver v. Sec'y of Health & Human Servs.*, No. 13-1002V, 2016 WL 6947389, at *5 (Fed. Cl. Oct. 20, 2016) ("Special

Masters may use their discretion in weighing expert testimony, and case law supports that discretion").

In determining whether a particular expert's testimony was reliable or credible, I may consider whether the expert offers an opinion that exceeds his training or competence. *Walton v. Sec'y of Health & Human Servs.*, No. 04-503V, 2007 WL 1467307, at *17-18 (Fed. Cl. Spec. Mstr. Apr. 30, 2007) (otolaryngologist not well suited to testify about disciplines other than her own specialty). While (in keeping with the liberality with which evidence offered in Vaccine Program cases is treated) I heard and have considered all of the testimony of the experts offered at the entitlement hearing, I may properly evaluate, and give appropriate weight to, whether certain testimony is beyond a particular expert's purview. *See, e.g.*, *King v. Sec'y of Health & Human Servs.*, No. 03-584V, 2010 WL 892296, at *78-79 (Fed. Cl. Spec. Mstr. Mar. 12, 2010) (petitioner's expert far less qualified to offer opinion on general causation issues pertaining to autism than specific issues pertaining to the petitioner's actual medical history, given the nature of the expert's qualifications).

D. Consideration of Medical Literature

Both parties filed medical and scientific literature in this case, including some articles (such as those discussing molecular mimicry and protein sequences in vaccines) that do not factor into the outcome of this decision. I have reviewed all of the medical literature submitted in this case, but I only discuss those articles that are most relevant to my determination and/or are central to Petitioners' case – just as I have not exhaustively discussed every individual medical record filed. *Moriarty v. Sec'y of Health & Human Servs.*, No. 2015-5072, 2016 WL 1358616, at *5 (Fed. Cir. Apr. 6, 2016) ("[w]e generally presume that a special master considered the relevant record evidence even though he does not explicitly reference such evidence in his decision") (citation omitted); *see also Paterek v. v. Sec'y of Health & Human Servs.,* 527 F. App'x 875, 884 (Fed. Cir. 2013) ("[f]inding certain information not relevant does not lead to — and likely undermines — the conclusion that it was not considered").

V. ANALYSIS

Based on consideration of the record and the testimony of both side's experts, I conclude that Petitioner has not carried her burden under the Federal Circuit's test for non-Table causation claims established in *Althen.* I address the *Althen* prongs out of order, in order to highlight the deficiency in Petitioner's proof or arguments in order of importance.

A. *Althen* Prong Two

The Vaccine Act requires a petitioner to show that she has suffered from as least one defined and recognized injury. *Lombardi v. Sec'y of Health & Human Servs.,* 656 F3d. 1343, 1353

(Fed. Cir. 2011). In the context of *Althen* prong two, which requires a showing that the vaccine caused petitioner's injuries, it follows that "in the absence of a showing of the very existence of any specific injury of which the petitioner complains, the question of causation is not reached." *Id*. Appellate courts have upheld the decisions of other special masters that focused their inquiry on determining the injury. *Broekelschen,* 618 F.3d at 1345. Indeed, where the petitioner cannot show that she "suffer[s] the injury that she claims was caused by the vaccine, there is no reason why the special master should be required to undertake and answer the separate (and frequently more difficult) question whether there is a medical theory, supported by 'reputable medical or scientific explanation' by which a vaccine can cause the kind of injury that the petitioner claims to have suffered." *Hibbard v. Sec'y of Health & Human Servs.,* 689 F.3d 1355, 1365 (Fed. Cir. 2012).

The facts of this case do not permit the conclusion that Ms. Bell "more likely than not" suffered from ADEM, or any other central nervous system demyelinating condition. Rather, the evidence allows for no conclusion as to the etiology of her condition – consistent with Dr. Sriram's testimony – making it impossible to find preponderant evidence supporting this factual allegation. Because Petitioner's theory was heavily dependent upon the finding that she suffered from ADEM -- for as her immunologic expert admitted, he could not opine to a relationship with any other condition and the relevant vaccine -- this failure is fatal to Ms. Bell's entire claim.

Discussion of the medical records and expert opinions above illustrates the complex nature of Ms. Bell's condition, and why ADEM is not the most likely explanation for it. During initial treatment (between receipt of the second and third Hep B doses), ADEM was not deemed likely. Ms. Bell did not present with symptoms suggestive of the disease (and the fact that it is typically an acute and rapidly progressing disease makes those earlier treater views significant). The MRIs performed on her in the first three months after the January 2012 Hep B dose did not reveal white matter lesions, demyelination, or inflammation, nor did any of the technicians performing the MRIs, or neurologists interpreting their result, propose ADEM as part of the differential diagnosis. Other tests that could have corroborated ADEM, such as the CSF testing (which should have shown brain inflammation were it occurring), were similarly negative. And treatments that would be effective if an individual were suffering from a demyelinating condition, such as steroids, did not assist Ms. Bell either, providing further confirmation that an inflammatory autoimmune response to some prior insult was not the likely cause of her symptoms. *National Institute of Neurological Disorders and Stroke: Acute Disseminated Encephalomyelitis Information Page*, NIH, http://www.ninds.nih.gov/disorders/acute_encephalomyelitis/acute_encephalomyelitis.htm (last visited Nov. 3, 2016).

In the months after the second Hep B dose, and from the time of Ms. Bell's initial treatment with Dr. Krain to when she first saw physicians at Iowa (from February to August, 2012), the only treater to suggest ADEM as part of a differential diagnosis was Dr. Rodnitzky - after the May 2012 MRI, where the radiologist performing the MRI proposed it. Pet'r's Ex. 8 at 160. It remained a consideration for Dr. Rodnitzky up until August 2012. At that point, however, Dr. Rodnitzky began also considering a mitochondrial disorder and wanted to pursue further testing in that area. *Id*.

However, and as the medical records make clear, the thorough evaluation and testing performed by the Mayo Clinic treaters essentially ruled out mitochondrial dysfunction – while at the same time rejecting earlier proposals that a demyelinating condition was to blame. Pet'r's Ex. 9 at 11, 16, 18. Thus, as Ms. Bell's condition continued to evolve in a worsening manner, ADEM was slowly abandoned as an explanation for her symptoms.

Ms. Bell's subsequent history only underscores the difficulty with accepting the ADEM diagnosis proposed by Petitioner. Rather than proceeding in an acute and monophasic pattern, as would be expected for ADEM, Ms. Bell continued to display a slower progression in a variety of symptoms from the spring to fall in 2012. Ms. Bell's treatment and related work-up at the Mayo Clinic is especially telling. Despite a full neurologic evaluation, the highly-qualified Mayo treaters found little to no evidence of demyelination or inflammation, and therefore largely rejected explanations for her state along the lines urged here by Petitioner in favor of an entirely new diagnosis (also embraced by Dr. Rodnitzky, the treater who first proposed ADEM) – that she had some kind of mitochondrial disorder. Pet'r's Ex. 8 at 160. Yet even that diagnosis was later not found to be supported by test results, and was therefore reasonably abandoned.

Petitioner places great stock in the subsequent 2013 determinations of Dr. Gonzalez-Alegre at Iowa, who breathed new life into ADEM as a possible explanation for her condition. As noted above, however, the mere fact that a treater proposes a possible diagnosis or explanation for a petitioner's condition does not require its acceptance. *Snyder*, 88 Fed. Cl. at 746 n.67. Rather, I must evaluate such a treater opinion in light of the overall evidence, and conduct an analysis that properly conforms to the preponderant evidentiary test governing Vaccine Program claims.

Although Respondent has suggested that errors in Dr. Gonzalez-Alegre's factual assumptions about Ms. Bell's medical history cast doubt on his suppositions, the context for his analysis is more persuasive grounds for determining that it is not well-founded. Here, it is evident that Dr. Gonzalez-Alegre's suppositions were not tested by consideration of Ms. Bell's prior medical history, which contained a host of test results and relevant MRI readings that were not supportive of his proposed diagnosis. It also flies in the face of the understanding, as the literature offered herein confirms, that ADEM is more often than not acute and monophasic – adjectives that do not capture the long term, progressive nature of Ms. Bell's still-undiagnosed condition.

I thus do not give significant weight to the fact that a year after Ms. Bell first sought treatment for her initial symptoms, and after numerous relevant tests had been performed that should have shed light on the diagnosis, another treater began to propose ADEM as Petitioner's illness. Indeed, were his after-the-fact view meritorious from an evidentiary standpoint, it should have been confirmed by additional test results or treatment evidence – but the subsequent treatment record after Dr. Gonzalez-Alegre first saw Ms. Bell does not provide such confirmation.[33] Indeed,

[33] Other special masters have dealt with the issue of treater disagreement as to the existence of ADEM, giving more evidentiary weight to the diagnoses of early treaters along with the petitioner's test results. *See Carter v. Sec'y of Health & Human Servs.*, No. 14-1500V, 2007 WL 415185 at *23 (Fed. Cl. Spec. Mstr. Jan. 19, 2007)("[t]he treating doctors saw [petitioner], ran tests, treated him for a virus, noted [his] improvement to the treatment and diagnosed him

as noted above Petitioner returned a second time to the Mayo Clinic, and its subsequent findings in no way confirm Dr. Gonzalez-Alegre's diagnosis (which itself only included ADEM as a possibility, rather than centering on it as likely).

Petitioner's experts did not effectively rebut any of the above. Rather, Dr. Morgan offered a piecemeal reading of the record, emphasizing the facts that helped Petitioner's claim (for example, that ADEM can infrequently present with gray matter lesions) while downplaying or ignoring other facts that called out for evaluation – in particular, both the lack of classic presenting symptoms suggestive of ADEM, as well as that testing of the CSF did not confirm inflammation and unsuccessful steroidal treatments. He offered no record support for the contention that Ms. Bell was experiencing an autoimmune condition, and his acceptance of Dr. Gonzalez-Alegre's opinion was conclusory in nature. Dr. Morgan did not grapple with the overarching suggestion the record makes about the inability of Ms. Bell's treaters generally to identify her illness.

While Dr. Morgan was steadfast in his opinion, I gave more weight to Dr. Sriram's view (based on frequent patient exposure, and more expertise in evaluating CNS demyelinating conditions like MS) that Ms. Bell's presentation was not consistent with ADEM. Among the problems with her clinical presentation, or lack thereof, was encephalopathy. Dr. Sriram was persuasive in stating that he would expect to see major behavioral changes as evidence of encephalopathy. Here, the only slight indication of a behavioral change is the note by Nurse Schlenk indicating that Ms. Bell was experiencing fatigue and feelings of weakness - symptoms that are not equivalent to the behavioral changes contemplated by Dr. Sriram. Additionally, Petitioner's initial MRIs did not support an ADEM diagnosis. Dr. Sriram was also persuasive in emphasizing that an individual suffering from ADEM would not have only lesions in gray matter areas of the brain, without some corresponding white matter lesions. Dr. Axelrod, by his own admission, lacked the qualifications to offer a diagnostic interpretation of the record.

Petitioner's arguments that she experienced a reaction the third Hep B dose in June 2012 are also inadequately supported by the record. That record more persuasively establishes that she was already experiencing problems with her vision and hearing prior to this date, as discussed above – and, as Dr. Axelrod admitted, if the record showed prior symptoms, then the Petitioner's entire worsening theory was demolished. Tr. at 182. Dr. Collins's testimony was more consistent with this record – and as she testified, it revealed that Ms. Bell's symptoms were simply progressing on throughout the time of her third Hep B dose, before and afrer, rather than flaring up in response. *Id.* at 351. Again – if the third dose had functioned as Petitioner proposed, some

with a viral cause. No doctor, until Dr. Griesemer, diagnosed ADEM. The radiologist did state that the MRI findings may be seen in processes such as ADEM, but did not diagnose ADEM. Importantly, the treatment of [petitioner] did not change in light of the MRI scan and interpretation. In the face of this evidence, it is illogical to conclude that [petitioner] should be re-diagnosed with ADEM and find that the vaccine was its cause").

evidence of an ongoing autoimmune process, such as inflammation, would be expected, but was not seen in this case. *Id.* at 314-18, 326.[34]

Other special masters have previously dealt with the propriety of an ADEM diagnosis as a threshold matter to entitlement. One such claim was determined by former Chief Special Master Patricia Campbell-Smith in *Stillwell v. Sec'y of Health & Human Servs.,* No. 11-77V, 2013 WL4540013, at *11 (Fed. Cl. Spec. Mstr. June 17, 2013). *Stillwell* (which involved the flu vaccine rather than Hep B) set forth six factors for whether ADEM was present, including (1) the statistical improbability that petitioner has the disease, given its propensity to affect children; (2) the absence of an ADEM diagnosis from her treaters; (3) the appearance of her brain lesion; (4) the timing of her symptom onset; (5) the nature and severity of her symptoms; and (6) the protracted course of her illness and her limited recovery. *Stillwell*, 2013 WL 4540013, at *11. Petitioner's condition was found to "diverge in too many respects and by too great a degree from the presentation of ADEM to even be deemed an atypical form of ADEM. Yet, Petitioner does appear to suffer from another, unspecified illness that has bewildered her physician." *Id.*

Those same *Stillwell* factors suggest a similar conclusion herein. The probability that Ms. Bell developed ADEM - a condition more commonly found in children – in her adulthood makes the diagnosis unlikely at the outset, although this is not a dispositive factor. Moreover, as mentioned above, none of Ms. Bell's treaters firmly opined that ADEM was the proper diagnosis until Dr. Gonzalez-Alegre a year later, basing that finding primarily on the findings of the MRIs that were inconsistent with ADEM, while ignoring the rich treatment history that did not support ADEM as an explanation. Thus, the immediate and initial evidence relevant to the diagnosis, from the time Ms. Bell first presented with her symptoms in early 2012, did not support the diagnosis. Finally, the protracted nature of Ms. Bell's condition further diminishes the likelihood of ADEM. *See also Saunders v. Sec'y of Health & Human Servs.,* No. 97-808V, 2001 WL 1135035 at *4 (Fed. Cl. Spec. Mstr. Sept. 4, 2001) (the lack of supporting ADEM MRI results and ADEM not appearing in the differential diagnosis led to the conclusion that ADEM was not a proper diagnosis-and thus no link to vaccination existed).[35]

My decision in this case does not reflect my own judgment as to the proper diagnosis for Ms. Bell's condition. Not only is this a task that special masters are not called upon to perform,

[34] I also note again that, as Petitioner's experts admitted, there is no evidence that Ms. Bell experienced any reaction at all to the first dose of Hep B vaccine. *See, e.g.,* Tr. at 197-98 (no evidence of immunologic "priming" between first and second dose). While Petitioner's experts explained this away as insignificant or commonplace when a vaccine is administered in multiple doses (Tr. at 160), I find this fact has some bearing on their argument that the second dose primed Ms. Bell to experience a renewing, or exacerbation, of symptoms after the third. Petitioner did not persuasively set forth why the first dose would cause no reaction, but the second and third would.

[35] The instant case can also be contrasted with *Brown v. Secretary of Health and Human Services*, No. 09-426V, 2011 WL 5029865, at *41 (Fed. Cl. Spec. Mstr. Sept. 30, 2011), which found that a petitioner's flu vaccine did cause his ADEM. The Special Master in that case relied on the "unwavering" diagnosis of ADEM among the many treaters that Petitioner saw, unlike here, where ADEM was no more than a brief differential diagnosis until Ms. Bell was seen by Dr. Gonzalez-Alegre almost a year later.

but it is something that no qualified medical treater in this case has yet to do successfully. Rather, I have found that Petitioner has failed to meet her burden of offering sufficient preponderant evidence establishing it more likely than not that she had ADEM.

B. *Althen* Prongs One and Three

Given my finding above, it is unnecessary to discuss Petitioner's showings under the other two *Althen* prongs. *See, e.g., Lasnetski v. Sec'y of Health & Human Servs.,* 128 Fed. Cl. 242, 64 (2016) (not error for special master to forego *Althen* analysis after determining that a petitioner had not in fact experienced the disease or illness alleged to have been vaccine-caused), *citing Hibbard*, 698 F.3d at 1365. I will nevertheless briefly consider the evidentiary showing made by Ms. Bell for each of them.

With respect to the first, "can cause" prong, Petitioner's theory that Hep B could cause ADEM has both scientific reasonableness and plausibility. While Respondent identified some weaknesses in the theory,[36] Petitioner has offered sufficient scientific grounding for this aspect of her claim. Indeed, there are numerous instances in the Vaccine Program in which other special masters, in cases also involving the Hep B vaccine and similar injuries, have also determined that a petitioner successfully established a plausible causation theory. *See, e.g., Werderitsh v. Sec'y of Health & Human Servs.*, No. 99-310V, 2006 WL 1672884, at *26 (Fed. Cl. Spec. Mstr. May 26, 2006) (discussing ADEM's similarity to MS, and finding that Hep B could cause a demyelinating disease like MS)*; Stevens v. Sec'y of Health & Human Servs*, No.99-594V, 2006 WL 659525 (Fed. Cl. Spec. Mstr. Feb. 24, 2006) (Hep B can cause transverse myelitis, a subset of ADEM). Unfortunately, this does not aid Petitioner – for success in establishing the first prong does not help her if, as here, her theory applies to an illness the evidence does not suggest she has, as Dr. Axelrod admitted. Tr. at 180 ("if it turns out she doesn't have a demyelinating disease, then whether I'm right or wrong about [causation], it's irrelevant.").

Petitioner's *Althen* three arguments were less persuasive, however. Petitioner offered insufficient evidence, whether record medical documents or literature, supporting the assertion that the timeframe in which her symptoms developed was medically acceptable. Thus, Dr. Axelrod assumed that the timing of the development of Petitioner's symptoms after the second Hep B dose was medically acceptable, simply because of the temporal relationship between symptom (like left side weakness) and vaccine (TR. at 175-76, 178), but cited no record evidence that would corroborate his assertion that an immunologic reaction was occurring in the interval (while again admitting he lacked the neurologic expertise even to identify what evidence would show the

[36] For example, Dr. Collins noted that Lawson did not involve the Hep B vaccine, and therefore its findings about how a different vaccine had the capacity to pry open the blood brain barrier could not be assumed to be applicable herein. Tr. at 328-29. She also proposed that it could not be assumed that inflammation stemming from the upregulation of cytokines induced by a vaccine would have the same persistent and elevated inflammatory effect as a live virus. *Id.* at 333, 359-60. And Dr. Axelrod admitted that "we don't know" if in fact Hep B can cause ADEM (*Id.* at 183), although a lack of scientific certainty does not mean that a claimant's theory is not sufficiently reliable or plausible to satisfy the first prong of the *Althen* test.

demyelinating process was occurring). *Id.* at 185. Dr. Collins, by contrast, both identified what she would expect to see (e.g. inflammation based on MRIs or CSF testing) were Petitioner's theory occurring in "real time," and established based on the record how this evidence was lacking. *Id.* at 315-18. Accordingly, even if I had found that Petitioner's illness was more likely than not ADEM, and credited her theory as well, I would still find a lack of preponderant evidence on the third prong.

CONCLUSION

The Vaccine Act permits me to award compensation only if a Petitioner alleging a "non-Table Injury" can show by medical records or competent medical opinion that the injury was more likely than not vaccine-caused. Here, Petitioner's causation theory depends upon my finding that she experienced a particular injury, but the weight of the evidence does not support that conclusion. Thus – and even if the theory itself has plausibility – there is insufficient evidence to support an award of compensation, leaving me no choice but to hereby **DENY** this claim.

In the absence of a timely-filed motion for review (see Appendix B to the Rules of the Court), the Clerk shall enter judgment in accord with this decision.

IT IS SO ORDERED.

/s/ Brian H. Corcoran
Brian H. Corcoran
Special Master