In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

Filed: December 19, 2019

HEIDI WHITE *and* DAVID WHITE, *Parents of Minor* A.C.W.,	*	Published
Petitioners,	*	No. 15-1521V
v.	*	Special Master Gowen
SECRETARY OF HEALTH AND HUMAN SERVICES,	*	Human Papillomavirus Vaccine ("HPV"); Acute Transverse Myelitis; Molecular Mimicry.
Respondent.	*	

Anthony M. Carr, Shaheen & Gordon, P.A., Concord, NH, for petitioner.
Adriana R. Teitel, U.S. Dept. of Justice, Washington, D.C., for respondent.

RULING ON ENTITLEMENT[1]

On December 15, 2015, Heidi White and David White ("petitioners"), on behalf of their minor child, A.C.W., filed a petition in the National Vaccine Injury Compensation Program.[2] Petitioners allege that A.C.W.[3] developed transverse myelitis which was caused in fact by the human papillomavirus vaccination ("HPV") received on July 30, 2013. Petition at Preamble

[1] In accordance with the E-Government Act of 2002, 44 U.S.C. § 3501 (2012), because this opinion contains a reasoned explanation for the action in this case, **this opinion will be posted on the website of the United States Court of Federal Claims**. This means the opinion will be available to anyone with access to the internet. As provided by 42 U.S.C. § 300aa-12(d)(4)B), however, the parties may object to the published Decision's inclusion of certain kinds of confidential information. Specifically, under Vaccine Rule 18(b), each party has 14 days within which to request redaction "of any information furnished by that party: (1) that is a trade secret or commercial or financial in substance and is privileged or confidential; or (2) that includes medical files or similar files, the disclosure of which would constitute a clearly unwarranted invasion of privacy." Vaccine Rule 18(b). **If neither party files a motion for redaction within 14 days, the entire opinion will be posted on the website and available to the public in its current form.** *Id.*

[2] The National Vaccine Injury Compensation Program is set forth in Part 2 of the National Childhood Vaccine Injury Act of 1986, Pub. L. No. 99-660, 100 Stat. 3755, codified as amended, 42 U.S.C. §§ 300aa-10 to 34 (2012) (hereinafter "Vaccine Act" or "the Act"). Hereinafter, individual section references will be to 42 U.S.C. § 300aa of the Act.

[3] Hereinafter, A.C.W. is referred as A.W. for the purposes of this decision.

(ECF No. 1). Based on a full review of the evidence and testimony presented, I find petitioners, on behalf of A.W. is entitled to compensation.[4]

I. Procedural History

Petitioners, on behalf of A.W. filed their claim in the Vaccine Program on December 15, 2015. Petition (ECF No. 1). The petitioner filed medical records and an expert report by Dr. Marcel Kinsbourne, M.D.[5] by compact disc. (ECF No. 1). The undersigned held an initial status conference on February 3, 2016. *See* Order (ECF No. 7). On March 14, 2016, respondent filed a status report stating that he wanted to obtain an expert report and submit a Rule 4(c) report. Respondent ("Resp.") Status Report (ECF No. 8).

On May 16, 2016, respondent filed his Rule 4(c) report, recommending against compensation. Resp. Report at 6. Respondent stated that A.W. did not meet the specific diagnostic criteria for acute transverse myelitis. Resp. Report at 9. Respondent stated that "there was no evidence of inflammation within A.W.'s spinal cord on her MRI, CSF analysis or other laboratory tests." *Id.* Therefore, respondent concluded, "even if Dr. Kinsbourne's report and theory is found to satisfy petitioner's burden under *Althen* prong 1, it cannot be relied upon to meet *Althen* prongs 2 and 3." *Id.* The same day, respondent filed an expert report from Dr. Soe S. Mar, M.D.[6], a pediatric neurologist. Resp. Ex. A (ECF No. 13). Respondent also filed medical literature Dr. Mar referenced in her report. Medical Literature (ECF Nos. 14-15).

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[4] Pursuant to Section 300aa-13(a)(1), in order to reach my conclusion, I have considered the entire record including all of the medical records, statements, expert reports, and medical literature submitted by the parties. This opinion discusses the elements of the record I found most relevant to the outcome.

[5] Dr. Marcel Kinsbourne is a pediatric neurologist, and as seen in his curriculum vitae ("CV"), he received his medical degree in England and has been licensed to practice medicine in North Carolina since 1967. Pet. Ex. 14 at 1-2. He has held a variety of academic positions over the course of his career, teaching and researching subjects including neurology, psychology, pediatrics and occupational therapy. *Id.* at 2-3. Relevant to this case, his clinical experience includes serving as a senior staff physician in Ontario, Canada from 1974-80 and as a clinical associate in neurology at Massachusetts General Hospital from 1981-91. *Id.* He also was a lecturer on neurology at Harvard University for the same time period. *Id.* He has published hundreds of articles on various neurological issues and currently serves on the board of numerous editorial boards of medical literature publications. *Id.* at 3. Dr. Kinsbourne has served as an expert in many other vaccine cases. Tr. 93. Respondent noted that Dr. Kinsbourne has not been in clinical practice since 1992. Tr. 110. However, Dr. Kinsbourne has remained in teaching positions in the field of neuroscience. *Id.* at 111. Petitioner offered Dr. Kinsbourne as an expert in this case in the field of neurology and I admitted him as an expert in the field of neurology. Tr. 113.

[6] Dr. Soe S. Mar is a pediatric neurologist and is currently the Residency Program Director of the Pediatric Neurology Residency Training Program at the Washington University School of Medicine in St. Louis, Missouri. Resp. Ex. I at 1-2. Dr. Mar currently treats children with demyelinating disease. Tr. 129. She also received her medical degree in the United Kingdom and completed her pediatric residency at the Albert Einstein College of Medicine in 2005. *Id.* She has served a pediatric neurologist since 2005 at the St. Louis Children's Hospital and has served as the medical director for the Pediatric onset Multiple Sclerosis, Other Demyelinating Diseases and autoimmune Encephalitis Center. *Id.* at 1-2. She currently serves as an ad hoc reviewer for multiple medical journals, including Pediatric Neurology and the Journal of Pediatrics. *Id.* at 4. Dr. Mar has published many articles on pediatric neurology topics. *Id.* at 7-11. Respondent offered Dr. Mar as an expert in the field of pediatric neurology and I admitted her as an expert in the field of pediatric neurology. Tr. 130.

On May 25, 2016, the undersigned held a Rule 5 status conference. Order (ECF No. 16). During the status conference, I discussed the expert reports submitted by both parties. Respondent's counsel asserted that the issue of whether A.W. suffered transverse myelitis or transverse myopathy was a significant issue, because if there was no inflammation of A.W.'s spinal cord, then Dr. Kinsbourne's theory would not apply. Order at 2. I ordered petitioner to file a supplemental expert report addressing A.W.'s diagnosis based on the MRI readings and lab reports, the likelihood of the diagnosis of transverse myelitis compared to transverse myopathy (and explain transverse myopathy), as well as to supply additional evidence of homology between Gardasil and the central nervous system to support the theory of molecular mimicry. *Id.*

Petitioner filed a supplemental report written by Dr. Kinsbourne on May 17, 2018. Petitioner's Exhibit ("Pet. Ex.") 22 (ECF No. 49). Additionally, petitioner filed a report by Dr. Lawrence Steinman, M.D.,[7] a neurologist. Pet. Ex. 24 (ECF No. 49). Respondent filed a responsive supplemental report by Dr. Neil D. Romberg[8] and supporting medical literature on January 27, 2017. Respondent's Exhibit ("Resp. Ex.") D (ECF No. 33); Resp. Exs. F1-F12 (ECF Nos. 34-35). Respondent also filed a responsive supplemental report by Dr. Soe S. Mar on February 9, 2017. Resp. Ex. G (ECF No. 36).

After reviewing the additional filings of both parties, the undersigned held another status conference on March 23, 2017. During this status conference, I stated that both Dr. Kinsbourne and Dr. Steinman addressed the questions posed after the last status conference and my preliminary view was that petitioners have satisfied *Althen* prong one. Order at 1 (ECF No. 38). Specifically, I stated that both the experts persuasively explained why they each accepted A.W.'s treating physicians' diagnosis of transverse myelitis. *Id.* at 2. I also noted that A.W.'s treating physician, Dr. Mark Gorman, considered the association of transverse myelitis to the Gardasil vaccine. *Id.* Further, I stated, "petitioners will likely be able to establish a diagnosis of transverse myelitis and that Dr. Steinman has provided reasonable evidence of homology to support a theory of molecular mimicry." *Id.* I ordered the parties to attempt to resolve this case informally, and if that could not be done, then to file a joint status report requesting a hearing. *Id.* at 3.

[7] Dr. Lawrence Steinman obtained his medical degree from Harvard Medical School, where he completed a fellowship in chemical neurobiology. He completed a residency in pediatrics and neurology at Stanford University. Pet. Ex. 25 at 1. He joined the faculty of Stanford in 1980, where he presently serves as the George A. Zimmerman Professor of Neurological Sciences, Neurology, Genetics and Pediatrics. *Id.*; Tr. 60. Dr. Steinman chaired the Immunology Department at Stanford for ten years. Tr. 61. Dr. Steinman has published extensively in peer-reviewed journals on topics including neuroimmunology and GBS. Pet. Ex. 25. He has demonstrated expertise in both a wide variety of central nervous system diseases (multiple sclerosis in particular) and immunologic issues. Tr. 61. Petitioner offered him as an expert in the fields of neurology and immunology and I admitted him as an expert in the same fields without objection from respondent. Tr. 61-2.

[8] Dr. Neil D. Romberg is board certified as an allergist and as a clinical immunologist and is currently an attending physician in immunology at Children's Hospital in Philadelphia, Pennsylvania. Resp. Ex. E at 1; Tr. 187-88. He graduated Pennsylvania State College Medicine in 2004 and completed a pediatric residency at the New York University School of Medicine in 2008. Dr. Romberg was an Allergy and Clinical Immunology Fellow at Yale University from 2008-2011. Resp. Ex. E at 1. He currently serves as an ad-hoc reviewer for three medical journals, including the Journal of Allergy and Clinical Immunology. *Id.* at 2. Respondent offered Dr. Romberg as an expert in allergy and immunology and I admitted him as an expert in the same fields. Tr. 188.

On May 24, 2017, respondent filed a status report stating that he was opposed to engaging in settlement discussions and the parties will identify mutually-agreeable dates for an entitlement hearing. Resp. Status Rept. (ECF No. 40). A hearing order was entered on July 18, 2017, setting an entitlement hearing for July 31, 2018-August 1, 2018. Hearing Order (ECF No. 45). Both parties briefed the case prior to the hearing. Pet. Prehearing Submission (ECF No. 56); Resp. Prehearing Submissions (ECF No. 61).

An entitlement hearing was held on July 31, 2018 in Washington, D.C. Petitioner, Heidi White and A.W. offered fact testimony. Petitioner presented expert testimony from Dr. Lawrence Steinman in person and Dr. Kinsbourne via videoconference. Respondent presented expert testimony from Dr. Soe Mar and Dr. Neil Romberg. The parties submitted post-hearing briefs addressing key issues raised during the entitlement hearing. *See* Pet. Post-Hearing Brief (ECF No. 92); Resp. Post-Hearing Brief (ECF No. 97); and Pet. Post Hearing Response (ECF No. 98).

This matter is now ripe for adjudication.

II. Legal Standard

The Vaccine Act was established to compensate vaccine-related injuries and deaths. § 300aa-10(a). "Congress designed the Vaccine Program to supplement the state law civil tort system as a simple, fair and expeditious means for compensating vaccine-related injured persons. The Program was established to award 'vaccine-injured persons quickly, easily, and with certainty and generosity.'" *Rooks v. Sec'y of Health & Human Servs.,* 35 Fed. Cl. 1, 7 (1996) (quoting H.R. No. 908 at 3, *reprinted in* 1986 U.S.C.C.A.N. at 6287, 6344).

A petitioner bears the burden of establishing his or her entitlement to compensation from the Vaccine Program. There are two avenues to compensation. The first requires the petitioner to demonstrate a Table injury but that is not alleged in the present case. The second avenue requires the petitioner to prove that a vaccine listed on the Vaccine Table was the cause-in-fact of the injury.

To prove causation-in-fact, the petitioner must "show by preponderant evidence that the vaccination brought about the injury by providing 1) a medical theory connecting the vaccination and injury; 2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and 3) a showing of proximate temporal relationship between vaccination and injury." *Althen v. Sec'y of Health & Human Servs.,* 418 F. 3d 1274, 1278 (Fed. Cir. 2005). There must be preponderant evidence for each *Althen* prong. *Caves v. Sec'y of Health & Human Servs.*, 100 Fed. Cl. 119, 132 (2011), *aff. per curiam*, 463 Fed. Appx. 932 (Fed. Cir. 2012)

The preponderance of the evidence standard requires demonstrating that it is "more likely than not" that the vaccine caused the injury. *Moberly v. Sec'y of Health & Human Servs.,* 592 F.3d 1315, 1322 n.2 (Fed. Cir. 2010). Proof of medical certainty is not required. *Bunting v. Sec'y of Health & Human Servs.*, 931 F.2d 867, 873 (Fed. Cir. 1991). A petitioner must demonstrate that the vaccine was "not only [a] but for cause of the injury but also a substantial factor in bringing about the injury." *Moberly*, 592 F.3d at 1321 (quoting *Shyface v. Sec'y of*

Health & Human Servs., 135 F.3d 1344, 1352-53 (Fed. Cir. 1999); *Pafford v. Sec'y of Health and Human Servs.*, 451 F.3d 1352, 1355 (Fed. Cir. 2006). Causation is determined on a case-by-case basis, with "no hard and fast *per se* scientific or medical rules." *Knudsen v. Sec'y of Health & Human Servs.*, 35 F.3d 543, 548 (Fed. Cir. 1994). A fact-finder may rely upon "circumstantial evidence" which is consistent with the "system created by Congress, in which close calls regarding causation are resolved in favor of injured claimants." *Althen*, 418 F. 3d at 1280.

A petitioner often presents expert testimony in support of his or her claim. *Lampe v. Sec'y of Health & Human Servs.,* 219 F.3d 1357, 1361 (Fed. Cir. 2000). Expert testimony in the Vaccine Program is usually evaluated according to the factors set forth in *Daubert v. Merrell Dow Pharm., Inc.*, 509 U.S. 579, 594-96 (1993); *see also Cedillo*, 617 F.3d at 1339 (citing *Terran v. Sec'y of Health & Human Servs.,* 195 F.3d 1302, 1316 (Fed. Cir. 1999). A special master may use the *Daubert* framework to evaluate the reliability of expert testimony, but expert testimony need not meet each *Daubert* factor to be reliable. *Boatmon v. Sec'y of Health & Human Servs.*, 941 F.3d 1351 (Fed. Cir. 2019). The *Daubert* factors are "meant to be helpful, not definitive," and all factors " 'do not…necessarily apply even in every instance in which the reliability of scientific testimony is challenged.' " *Boatmon*, 941 F. 3d at 1359 (citing *Kumho Tire Co. v. Carmichael*, 526 U.S. 137, 151, 119 S. Ct. 1167, 143 L.Ed.2d 238 (1999). Thus, for Vaccine Act claims, a "special master is entitled to require some indicia of reliability to support the assertion of the expert witness." *Moberly* at 1324. 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.,* 219 F.3d 1339, 1347 (Fed. Cir. 2010) (citing *Lampe*, 219 F.3d 1357 at 1362).

Once a petitioner has proven causation by preponderant evidence, the burden shifts to respondent to show by a preponderance of the evidence that the injury is due to factors unrelated to the administration of the vaccine. *Deribeaux v. Sec'y of Health & Human Servs.,* 717 F.3d 1363, 1367 (Fed. Cir. 2013) (citing § 13(a)(1)(B)). Respondent has the burden of demonstrating that "a factor unrelated to the vaccination is the more likely or principal cause of injury alleged. Such a showing establishes that the factor unrelated, not the vaccination, was 'principally responsible' for the injury. If the evidence or alternative cause is seen in equipoise, then the government has failed in its burden of persuasion and compensation must be awarded." *Knudsen*, 35 F.3d at 551.

III. Summary of Relevant Facts

On January 7, 2013, A.W. had her eleven-year old well visit with Dr. Jennifer Jones. Pet. Ex. 9 at 26-29. At this visit, A.W.'s physical exam was normal. *Id.* Aside from expressing concern of occasional feelings of dizziness while running during gym class, Dr. Jones described A.W. as a "healthy child," with normal growth and development. *Id.* at 29. A.W. also received her first HPV vaccine, as well as, a Tetanus-Diphtheria-Pertussis ("Tdap") and meningococcal vaccine. *Id.* at 30; Pet. Ex. 2 at 1. A.W. returned to her pediatrician's office on March 29, 2013 for her second HPV vaccination. *Id.* at 32. On July 30, 2013, A.W. received her third HPV vaccination. *Id.* at 33.

On August 26, 2013, A.W. began her first day of seventh grade. Tr. 8; Pet. Ex. 3 at 1. Mrs. White testified that A.W. was very athletic and active and into gymnastics, tennis and basketball. Tr. 8. She explained that when A.W. returned from her first day of seventh grade, A.W. told her, "it was the best school day she ever had, [the] best first day of school she had ever had." Tr. 10. That evening, A.W. played basketball with her brother, took a shower and went to read a book on her bed while waiting for dinner. *Id.* Mrs. White stated, "suddenly [A.W.] screamed out in pain." Tr. 11. A.W. testified that it "was the worst pain" she had ever felt and described it as "really sharp" in her "upper back." Tr. 43. Her parents gave her a heating pad and Advil, initially thinking A.W. had a muscle spasm or pinched nerve. Tr. 11, 44. After dinner, A.W. began to complain about her arms feeling weird. Tr. 11. A.W. testified that her arms felt "floaty" and that when she raised her arms above her head "they would just fall." Tr. 44. A.W. took another shower to reduce the pain in her back. *Id.* A.W. explained that when she went to get clothes, she could not open her drawers and called her father for assistance. *Id.* At that point, A.W.'s father drove her to the emergency department at Exeter Hospital. Tr. 13.

A.W. arrived at the emergency department ("ED") of Exeter Hospital at 11:20 PM EST the same day. Pet. Ex. 3 at 1. By the time she arrived at the hospital, A.W.'s weakness had spread to her feet and she had difficulty walking. *Id.* A physical exam in the ED showed A.W. had altered sensation to light touch on the right and left torso, bilateral arms and legs. *Id.* at 2. A.W. was unable to grip and demonstrated weak hip and knee flexion, weak wrist flexion and her fingers were held flexed. *Id.* at 2-3. A CT scan of A.W.'s cervical and thoracic spine were ordered. *Id.* at 4. The attending physician, Dr. Heidi Blake, stated, "This is an 11 year-old with symptoms suggestive of incomplete cord level C5-6. There is no history of fever, rash, bite or trauma. Onset with acute pain is concerning for transverse myelitis." *Id.* at 4. Dr. Blake contacted Boston Children's Hospital ("BCH") and arranged A.W.'s transfer by ambulance to BCH. *Id.*

A.W. was admitted to the Intensive Care Unit ("ICU") at BCH on August 27, 2013. Pet. Ex. 4 at 604. When she arrived at BCH, A.W. demonstrated decreased sensation on the left side of her face compared to the right; she had decreased strength bilaterally in her triceps and grip strength; demonstrated bilateral weakness in the lower extremities; and she had to use her right hand to lift her left hand to her nose. *Id.* at 602. The attending physician in the ICU, Dr. Amy Sanderson, assessed A.W. with a "serious condition," and ordered an MRI of A.W.'s spine to assess for "an abnormality that could explain the patient's symptoms." *Id.* A.W. had a neurology consult with Dr. Rejean Guerriero, a pediatric neurology resident on August 27, 2013 at 12:26 pm. *Id.* at 651. He noted that A.W.'s "legs are held in paretic fashion. Unable to asses pronator drift or fine motor movements." A physical exam revealed she had "decreased pinprick from T2 down on the back, decreased T7 down on the front. Decreased sensation on flank and back compared with front and periumbilical area. *Id.* at 652. Decreased sensation in UE and LE to pinprick and temp, left greater a greater extent than right in diffuse pattern. Intact proprioception in LE." *Id.* Dr. Guerriero reviewed A.W.'s MRI and stated, "An MRI of the cervical and thoracic spine was obtained that reveals an anterior cord T2 hyperintensity with very mild cord swelling, and no enhancement would be consistent with transverse myelitis." *Id.* at 653. He wrote, "Her exam this morning appears to be worsening a bit raising concern that she has greater deficits than early changes on the MRI reveal." *Id.* Dr. Mark Libenson, the ICU attending neurologist concurred with Dr. Guerriero's assessment of A.W. and wrote, "The

clinical presentation is most consistent with transverse myelitis, beginning with back pain followed by extremity paresthesia. She appears to have advanced since her early morning exam now with near complete weakness of the RLE and little to no movement in the ankle….Agree with plan above for high dose steroids, LP,(lumbar puncture) brain MRI, ID (presumably infectious disease) and serological testing." *Id.* at 654. A.W. was started on high dose methylprednisolone[9] for a five-day course. *Id.* at 610.

On August 29, 2013, A.W. was transferred out of the ICU to the pediatric floor. *Id.* at 611. While in the hospital, A.W. was tested for various infections, including Epstein-Bar Virus ("EBV"), adenovirus, serum titers for Lyme, enterovirus and West Nile Virus. *Id.* All viral studies were negative. *Id.* Additionally, serum studies for auto-immune conditions were performed and the findings were "unremarkable." *Id.* at 611. A.W.'s IgG was mildly elevated but her IgM and IgA were normal. *Id.* On September 1, 2013, A.W. was evaluated by Dr. Peter Tzu-Shin, neurologist, who noted that A.W.'s CSF was "clean," making an infectious etiology very unlikely, but he opined that an "autoimmune process remains quite possible." *Id.* at 383. He also noted that her ANA and SS-B have returned negative. *Id.* He stated, "11 year-old with clinical and imaging findings most consistent with transverse myelitis," and recommended a repeat MRI, continue steroid and plasmapheresis if A.W. did not significantly improve. *Id.* at 384. After the five-day course of IV steroids, she began an oral course of steroids. *Id.* She had some improvement in her lower extremity strength and sensation, but her arms remained "significantly affected." *Id.*

On August 30, 2013, A.W. was seen by Dr. Mark Gorman, Director of Pediatric Neuroimmunology at Boston Children's Hospital, who assumed management of her care from that point forward. Pet. Ex. 4 at 647. He reviewed her history of present illness and noted, "[A.W.] received Gardasil #3 on 7/30/13. She had moderate local pain with injections #1 and #2 but no other symptoms. No recent illnesses or travel." Dr. Gorman examined A.W. and observed that she was experiencing significant distal weakness compared to proximal and it was greater on the right side. *Id.* at 648. He noted she had decreased sensation to cold temperatures in all limbs and absent vibration sensation in her toes and ankles with markedly decrease in her knees and fingers. *Id.* In his assessment and recommendations, Dr. Gorman wrote:

> 11 year-old girl with sudden onset of back pain followed by motor and sensory changes affecting all four limbs peaking at about 12-18 hours from onset. History also suggests bladder and bowl dysfunction…Differential includes inflammatory transverse myelitis, ischemic spinal cord infarct, and fibrocartiagenous embolism….I think inflammatory TM most likely diagnosis.

Id. at 649. Dr. Gorman recommended a repeat MRI with contrast, stating, "If clear signs of ischemia, this would alter management. If no signs of ischemia, would presume inflammatory TM even if still no contrast enhancement especially as treated with steroids." *Id.* He also

[9] Methylprednisolone is a synthetic glucocorticoid derived from progesterone used in replacement therapy for adrenocortical insufficiency and as an anti-inflammatory and immunosuppressant in a wide variety of disorders; administered orally. *Dorland's Illustrated Medical Dictionary* 32nd ed. (2012) (hereinafter "*Dorland's*") at 1154. *Dorland's* at 1154.

ordered additional labs to test for mycoplasma IgM and IgG, West Nile virus, anticardiolipin antibodies and beta 2 glycoprotein antibodies. *Id.* He also recommended that if A.W. does not have marked improvement she should undergo five cycles of plasmapheresis.[10] Beginning on September 5, 2013, A.W. was treated with plasmapheresis and it ended on September 13, 2013. *Id.* at 611.

A.W. underwent an additional MRI on August 31, 2013. *Id.* at 259-60. This MRI showed a "contiguous T2 prolongation within the cervical cord that has enlarged in both size and signal intensity, extending from C4-T1." *Id.* at 259. The impression was, "Interval evolution of T2 signal abnormalities of the spinal cord from C4-T11, without associated enhancement. Most likely represents transverse myelitis." *Id.* at 260. According to the discharge document, "This study showed the evolution of her lesion, but there were no findings consistent with infarction." *Id.* at 611.

Through her hospital course, A.W. slowly improved. *See* Pet. Ex. 4 at 339, 388, 391, 611. A.W. also participated in physical therapy while in the hospital. *Id.* at 521-93, 611. A.W. made steady improvement in her lower extremity strength, however, had slower improvement in her distal upper extremity strength and dexterity. *Id.* at 351, 339, 387, 611. An EMG/nerve conduction study was performed on September 13, 2013. *Id.* at 214. The right median and ulnar motor studies demonstrated reduced amplitudes; the right peroneal F response was absent; tibial H reflex was absent; and the concentric needle examination demonstrated no voluntary motor units in the right first dorsal interosseous with occasional positive sharp waves at the right biceps. *Id.* The conclusion of the study was an "abnormal study," with electrophysiologic evidence suggestive of a mild to moderate motor neuronopathy or motor neuropathy affecting the upper extremities. *Id.* This finding was "consistent with [A.W.'s] known diagnosis of transverse myelitis," and there was no evidence to suggest concurrent peripheral neuropathy. *Id.*

A.W. was discharged from BCH on September 16, 2013 with a diagnosis of transverse myelitis and she was to follow up with Dr. Mark Gorman. *Id.* at 613. She was also prescribed a steroid tapering plan over a five-week period. *Id.* at 611. On the day A.W. was discharged, she had "full strength in her left side and right lower extremity. She had mild weakness in her right upper extremity and notable weakness in her distal right upper extremity." *Id.* The discharge document stated that she had an MRI scan with diffusion sequence that did not find any signs of infarction. *Id.* It also noted that testing was performed for adenovirus, Lyme disease, CMV, Epstein-Bar virus, mycoplasma, enterovirus and West Nile virus which were all negative. *Id.*

On September 24, 2013, A.W. had her first follow-up appointment since being discharged from BCH with Dr. Gorman. *Id.* at 196. At this visit, A.W. reported she continued to experience tingling in her fingertips and that the bottom of her feet and toes were numb. *Id.* A.W. reported that she "continued to have altered sensation on the left side of her back." *Id.* Additionally, A.W. explained that she was unable to dress herself and required significant assistance with activities of daily living ("ADLs"). *Id.* A physical exam showed A.W. had decreased strength in her right triceps and bicep, decreased right wrist extension; decreased

[10] Plasmapheresis is the removal of plasma from withdrawn blood, with retransfusion of the formed elements into the donor; generally, type-specific fresh frozen plasma or albumin is used to replace the withdrawn plasma. *Dorland's* at 1456.

finger extension and abduction bilaterally; and leg strength 5/5 throughout. *Id.* at 197. Further, A.W. demonstrated decreased sensation to vibration in her toes bilaterally and decreased joint position sensation. *Id.* A.W. had "significantly decreased temperature sensation in the left leg," and "decreased sensation to light touch in the right upper extremity, right abdomen, and left lower back to approximately T6." *Id.*

Dr. Gorman described A.W. as "an 11-year old young woman with active transverse myelitis." *Id.* Dr. Gorman noted A.W.'s upper extremity limitations to be, "…significant enough to recommend additional immune therapy." *Id.* A.W. was prescribed IVIG as an outpatient with a total of 2gm/kg over a two-day course. *Id.*

On October 1, 2013, A.W. had the first of two IVIG treatments for her [diagnosis] of transverse myelitis. *Id.* at 146. She had her second treatment on October 2, 2013. *Id.* A.W. had another appointment with Dr. Gorman on October 9, 2013. *Id.* at 93. He noted that approximately four days after the IVIG treatment, A.W. began to notice improvement in the strength of her fingers. *Id.* A.W. was able to extend and abduct her fingers. *Id.* Upon a physical exam, A.W. demonstrated decreased muscle tone in the distal arms bilaterally. *Id.* at 94. She again had decreased sensation to temperature in the left leg up to the T6 level. *Id.* Dr. Gorman wrote, "[A.W.] is a 12-year old girl with acute transverse myelitis now six weeks ago. She has made dramatic improvements and continues to improve in her hands and fingers….At this point in time I did not recommend any further immunotherapy as she has received intensive treatments and this is most likely to be a monophasic condition." *Id.* Dr. Gorman ordered a repeat MRI "six months from onset," unless other concerns arise sooner. *Id.* at 95.

On November 18, 2013, A.W. had a repeat MRI on her cervical and thoracic spine. *Id.* at 55. The MRI revealed a, "circumscribed T2 signal abnormality seen within the cervical spinal cord extending from C5-C7, consistent with cystic myelomalacia evolved from the previous area of demyelination. Previously this area of signal abnormality was more patchy and ill-defined, now it is chronic appearing and well defined." *Id.* at 55. The impression was, "Evolution of the previously seen patchy signal abnormality within the lower cervical spinal cord, now defined, chronic and encephalomalacic[11] in appearance. Signal abnormality within the cervical spinal cord from C2-C5-6, not apparent on the prior examination suggestive of additional cord involvement." No associated enhancement was observed. *Id.* at 56.

On November 20, 2013, A.W. had another appointment with Dr. Gorman. *Id.* at 40. At this appointment, A.W.'s mother reported that A.W. was limping and having trouble initiating voiding two days prior to the appointment. *Id.* A.W. reported intermittent muscle tightening/cramping throughout the day and that her arms, legs and hands clench unprovoked. *Id.* A physical exam of A.W. showed she had mildly increased bilateral ankle tone, continued decreased finger extension and abduction bilaterally and her sensation to light touch was in-tact. *Id.* at 41. Additionally, A.W. was able to sense minimal cold in the left foot, which was an improvement. *Id.*

Dr. Gorman reviewed the MRI from November 18, 2013. He observed that, "There was new signal abnormality in the cervical spine. However, there is no enhancement and currently

[11] Encephalomalacia is the softening of the brain, especially that caused by an infarct. *Dorland's* at 613.

no changes in her exam, so we do not feel that this is an acute change, but rather something that had evolved over the course of her illness though difficult to time precisely. More concerning is the original lesion which is now encephalomalacic in appearance." *Id.* at 42. Dr. Gorman explained that this means that "…it is unlikely that [A.W.] will regain 100% function and is likely to have permanent deficits, though it is difficult to know to what extent." *Id.*

On December 18, 2013, A.W. met with Dr. Marc Cendrom, urologist, for urinary incontinence. Pet. Ex. 8 at 227. Dr. Cendrom noted, "Since the onset of the transverse myelitis, [A.W.] reports that she has a very mild incontinence during the daytime…" *Id.* After a physical exam and a review of system, he opined that A.W. may be experiencing bladder spasms, as she had reported arm spasms. *Id.* He recommended she start a mild anticholinergic. *Id.* A.W. had two follow-up appointments with Dr. Cendrom on March 3, 2014 and July 18, 2014. Pet. Ex. 8 at 85, 156-57.

A.W. had a repeat MRI on February 3, 2014. Pet. Ex. 8 at 207. The cervical MRI found, "…the T2 hyperintensity involving the cervical cord from approximately C5-C7, level, measuring approximately 1.6 cm in length. The maximal transverse dimension is 0.6 cm (measured at the C5 level)." *Id.* There was no evidence of abnormal enhancement with intravenous infusion of contrast. *Id.* at 208. The impression of the MRI was, "No interval change in the appearance of the spinal cord since the previous exam dated 11/18/2013. There remains focal T2 hyperintensity involving the cervical cord extending from C5-C7 with ill-defined T2 prolongation extending superiorly to the level of C2, unchanged." *Id.* Dr. Gorman requested that A.W.'s mother be notified that the "MRI was stable," on February 4, 2014. *Id.* at 203. On February 5, 2014, the MRI results were reported to A.W.'s mother. *Id.* at 202. At that time, Mrs. White reported that A.W. was experiencing increased headaches and her temperature regulation was off. *Id.*

On February 12, 2014, A.W. had a follow-up appointment with Dr. Gorman. *Id.* at 189. Dr. Gorman noted that A.W. was having "a variety of bothersome symptoms referable to the prior myelitis…" *Id.* These symptoms included headaches that began in December, heat intolerance, hand spasms, pruritus, left leg myoclonus, allodynia, and fatigue. *Id.* at 189-190. After a physical exam, he stated that "A.W. is a 12-year old girl with acute transverse myelitis. She has made dramatic improvement since the peak of her illness. Although there [have] been some fluctuations in her symptoms over the past [three] months and her MRI has evolved, overall I think this is still a monophasic, albeit severe, myelitis." *Id.* at 191. He recommended she begin gabapentin. *Id.* He also recommended she continue physical and occupational therapy. *Id.*

A.W. continued to have follow-up appointments with Dr. Gorman and repeat MRIs in 2014. *See* Pet. Ex. 8 at 69-71, 97-99. Dr. Gorman continued to treat A.W. for "acute transverse myelitis," noting that she has made dramatic improvements since the peak of her illness, but still suffered from scattered weakness and sensory symptoms. *Id.* at 70. He noted that the MRI from November 18, 2013, showed "signal abnormality within the cervical spinal cord from C2-C5-6, not apparent on the prior examination suggestive of additional cord involvement," but he "felt that the apparently new involvement from C2 to C6 likely had appeared closer to the onset of her

myelitis rather than reflecting an acute change proximate to the follow-up MRI." *Id.* at 69. Dr. Gorman noted that her MRIs since November 18, 2013 did not reflect any changes. *Id.* at 70.

On August 27, 2014, A.W. had an appointment with Dr. Donald Bae, orthopedist, for a follow-up evaluation. Pet. Ex. 8 at 61. A.W. reported persistent weakness in her right triceps and dysesthetic type symptoms on the dorsal aspect of her right hand that A.W. described as "burning, tingling and itching." *Id.* She demonstrated decreased strength in her right triceps and active wrist extension and radial deviation. *Id.* at 61. A.W. had active wrist extension and good digital flexors and extensors in her right upper extremity. *Id.* An examination of her knee and lower leg revealed some mild medial joint line tenderness mostly over her MDL, but was negative for apprehension and patellar grind sign. *Id.* An EMG/nerve conduction study was ordered. *Id.*

A.W. continued to have appointments with Dr. Gorman and at the BCH Orthopedic clinic from 2014 through 2018. *See* Pet. Exs. 20, 30 and 38.

Notably, on January 20, 2016, A.W. had a follow-up appointment with Dr. Gorman. Pet. Ex. 20 at 1. He recounted her history and noted that A.W. has "recovered significantly but has residual scattered weakness, sensory changes and pain." *Id.* Her physical exam showed A.W. had decreased muscle tone in the distal arms bilaterally and mild atrophy in the hands, left more than the right. *Id.* at 2. A.W. demonstrated some deficits in her ability to extend her fingers in her hands and had decreased sensation to vibration in her big toes bilaterally. *Id.* Dr. Gorman reviewed the MRI from January 11, 2016 and noted, "Stable appearance of myelomalacia involving the lower cervical cord. No new signal abnormality or abnormal enhancement in the spinal cord to suggest active or interval inflammation/demyelination." Dr. Gorman reiterated that A.W. has a history of transverse myelitis with an onset of August 2013. *Id.* at 3. He explained that A.W. still experiences scattered weakness, sensory symptoms (numbness and allodynia) and mild headaches. *Id.* A follow-up appointment was scheduled for six-months later.

A.W. had another MRI of the cervicothoracic spine on January 12, 2017. Pet. Ex. 30 at 7-8. This MRI revealed that A.W.'s spinal cord, "remains notable for high T2, nearly fluid signal intensity at C4-C7." *Id.* at 8. The high T2 signal begins at the right C4, involves the central cord and dorsal columns at C5, and extends to the left at C6-C7, unchanged since December 2014. *Id.* The impression was, "Stable pattern of myelomalacia involving the lower cervical cord. No new signal abnormality or abnormal enhancement in the spinal cord to suggest active or interval inflammation/demyelination." Additionally, mild, partially visualized thoracolumbar S-shaped scoliosis was observed. *Id.*

At a follow-up appointment with Dr. Gorman on January 25, 2017, he explained that he did not have any concerns for a relapse of myelitis. *Id.* at 11. During the physical exam, A.W. had a positive Lhermitte's sign.[12] *Id.* at 10. She demonstrated brisk reflexes at the biceps

[12] Lhermitte's sign is the sudden development of transient, electric-like shocks spreading down the body when the patient flexes the head forward; seen mainly in multiple sclerosis but also in compression and other disorders of the cervical cord. *Dorland's* at 1713.

bilaterally, triceps bilaterally and in the knees bilaterally. *Id.* She had right ankle clonus with stretching and her toes were mute on the left and up on the right. *Id.* He once again noted her "dramatic improvement since the peak of her illness," and stated that she still experienced "scattered weakness and sensory symptoms." *Id.* He asked that she follow-up in two weeks with an update on her headaches and discussed an option to increase gabapentin. *Id.*

On May 24, 2017, A.W. had another appointment with Dr. Bae. Pet. Ex. 30 at 17. A.W. reported that since her last appointment with him, her triceps strength has improved, but that she experiences "persistent tremulousness and sensations of spasms in her hands." *Id.* The physical exam revealed that A.W.'s triceps strength on the right was weak and an "obvious ulnar subluxing extensor tendons to the long and ring finger on the left hand," was observed. *Id.* Additionally, mild tremulousness was appreciated. *Id.* Dr. Bae, A.W. and Mrs. White discussed surgical intervention for stabilization of the tendon. *Id.* Dr. Bae explained the nature, risks and benefits of surgical intervention and the family decided to proceed with scheduling the tendon stabilization. *Id.* at 18.

A.W. had a follow-up appointment with Dr. Gorman and Dr. Grace Gombolay, a pediatric neuroimmunology fellow, on July 26, 2017. *Id.* at 21. Since A.W.'s last visit with Dr. Gorman in January, she reported twitches in both hands, with the left being worse than the right. *Id.* Dr. Gombolay noted that A.W. still experienced sensory symptoms (including numbness and allodynia) and scattered weakness. *Id.* at 23. Dr. Gombolay's physical exam findings were essentially the same as the findings from January. *Id.* Dr. Gombolay explained A.W.'s hand twitches are fasciculations[13] and described them as "sequelae of her transverse myelitis." *Id.* Dr. Gombolay also noted that A.W. was to have tendon tethering surgery the following month. *Id.* at 21.

On August 18, 2017, A.W. underwent a left long and ring finger tendon stabilization. *Id.* at 25. In a January 31, 2018 visit with Dr. Gorman, he noted that the tendon tethering for the fourth digit on her left hand failed, but the third digit on her left hand was intact and a repeat surgery may be considered in the future. Pet. Ex. 30 at 46.

A.W. also underwent a neuropsychological evaluation by Dr. Ferne Pinard, PhD at BCH. *Id.* at 29. Dr. Pinard noted that fatigue continued to be an issue for A.W. *Id.* at 31. She reported that A.W.'s overall cognitive ability is in the high-average range. *Id.* at 34. A.W.'s reasoning, vocabulary knowledge, problem solving for structured tasks and memory skills were well developed and although A.W. exhibited mild anxiety, there were no significant concerns about A.W.'s social, emotional or behavioral functioning. *Id.* However, A.W. demonstrated issues with focusing and sustaining attention. *Id.* at 35. Dr. Pinard described A.W.'s profile as "consistent with her neurological history. Research indicates that in addition to fine-motor problems, children diagnosed with Transverse Myelitis also exhibit difficulties in attention, and memory and to a lesser extent, processing speed and verbal fluency." *Id.*

On August 8, 2018, Dr. Gorman had a follow-up appointment with A.W. Pet. Ex. 38 at 102. He noted that since her last visit in January 2018, A.W. was "overall about the same," but

[13] A small local contraction of muscles, visible through the skin, representing a spontaneous discharge of a number of fibers innervated by a single motor nerve filament. *Dorland's* at 682.

A.W. continued to have issues with painful locking of her fingers in her left hand and her right knee locking, fatigue and random jolt-like-pain. *Id.* Her physical exam findings were consistent with the previous exam. *Id.* at 103. Dr. Gorman noted that an MRI from August 3, 2018 showed "stable myelomalacia involving the cervical cord from C4 through C6. No new lesions are seen." *Id.* at 104. Dr. Gorman, again, concluded his appointment report, stating that A.W. has a history of transverse myelitis with an onset of August 2013. *Id.* He stated that "Now that she is five years out from her presentation, and the risk of recurrence is very low, I do not think she needs surveillance imaging any longer unless she develops new symptoms or signs." *Id.*

IV. Analysis

A. Petitioner's Diagnosis

The first issue to be resolved is A.W.'s diagnosis. The respondent disputed petitioner's diagnosis of acute transverse myelitis. *See* Pet. Prehearing Brief at 1 (ECF No. 56); Resp. Prehearing Brief at 2 (ECF No. 61).

Petitioners alleged that A.W. suffered acute transverse myelitis as a result of receiving the third dose of HPV vaccine on July 30, 2013. Petition at Preamble. Petitioners stated that A.W. was diagnosed with acute transverse myelitis by Dr. Mark Gorman, the "Director of the Pediatric Neuroimmunology Program," at Boston Children's Hospital. Pet. Prehearing at 3. Additionally, petitioner asserted that Dr. Gorman is board certified by the American Board of Psychiatry and Neurology with Special Qualification in Child Neurology. *Id.* at 3. Petitioner stated Dr. Gorman's diagnosis of acute transverse myelitis from September 2013 was reaffirmed in the many outpatient visits he had with A.W. following her hospitalization. *Id.* at 4. Petitioner argued that respondent's experts' make post-hoc challenges to Dr. Gorman's diagnosis, which are speculative and should be given little weight. *Id.*

Respondent acknowledged A.W.'s diagnosis of acute transverse myelitis by Dr. Gorman but asserted that "the clinical record is inconsistent with the diagnostic criteria for acute transverse myelitis." Resp. Prehearing Brief at 2. Respondent argued that A.W.'s condition is "more precisely classified as acute idiopathic transverse myelitis without evidence of inflammation." *Id.* Specifically, respondent argued that the term "acute inflammatory transverse myelitis or ATM is the proper term only when the presence of inflammation in the spinal cord has been confirmed." Resp. Post-Hearing Brief at 12 (ECF No. 97). Respondent's expert also raised the issue of whether A.W. may have add acute flaccid myelitis.

Both parties' experts provided reports, medical literature and testified on the issue of A.W.'s diagnosis.

1. Acute Transverse Myelitis (ATM)

The medical literature submitted by both parties that focused on the characteristics of acute transverse myelitis ("ATM"), including clinical signs and symptoms to base a diagnosis of ATM were essentially consistent.

Transverse myelitis is defined as a "focal inflammatory disorder of the spinal cord and exists on a spectrum of neuroinflammatory conditions characterized by abrupt neurologic deficits associated with inflammation, demyelination and axonal damage." Resp. Ex. C-6 at 1.[14] The article by Kerr and Ayetey[15] defines acute transverse myelitis as a, "process affecting a restricted area of the spinal cord." Pet. Ex. 28-4 at 2. The article continues, stating that acute transverse myelitis, "is characterized clinically by acutely or subacutely developing symptoms and signs of neurological dysfunction in motor, sensory and autonomic nerve and nerve tracts of the spinal cord. There is often a clearly defined rostral border of sensory dysfunction and a spinal [MRI] and lumbar puncture shows evidence of acute inflammation." *Id.* at 2-3. The article by Sellner et al.,[16] submitted by the respondent, states that "the diagnosis of acute transverse myelitis syndromes is based on the clinical symptoms with evidence of inflammation within the spinal cord such as cerebrospinal fluid (CSF) abnormalities or lesions visible on MRIs." Resp. Ex. F-04 at 1.

Acute clinical characteristics include sensory loss or numbness in limbs, weakness, urinary dysfunction and pain in the initial phase of ATM. Pet. Ex.27-3 at 3[17]; Pet. Ex. 28-4 at 2; Resp. Ex. F-04. In an analysis of 47 cases of children under the age of 18 diagnosed with ATM, twenty-three children described sensory complaints of burning, tingling or electric shock sensations and twenty-seven described disquieting numbness. Pet. Ex. 27-3 at 3. The article stated that "the mean time from the onset of acute symptoms to functional nadir was about two days in these children." *Id.* at 3.

2. Respondent's Experts' Opinions Regarding A.W.'s Diagnosis

Respondent's experts disagreed with A.W.'s diagnosis of ATM and offered alternative diagnoses. Dr. Romberg largely deferred to Dr. Soe Mar regarding A.W.'s diagnosis. Resp. Post-Hearing Brief at 13. The respondent's experts' opinions regarding A.W.'s diagnosis of ATM were consistent with one another.

Dr. Mar stated that A.W. did not meet the criteria for ATM, as there was no evidence of inflammation within the spinal cord. Resp. Ex. A at 3. Dr. Mar continued, stating that A.W. "did not have any cells in her CSF, elevated IgG index or gadolinium enhancement," which would presumably be evidence of inflammation. *Id.* Dr. Mar referenced the Transverse Myelitis Consortium Working Group's ("TMCWG") proposed diagnostic criteria for idiopathic acute transverse myelitis, which provides:

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[14] Kaplin et al., *IL-6 induces regionally selective spinal cord injury in patients with neuroinflammatory disorder transverse myelitis,* 115 J. Clin. Invest. 2731-2741 (2005) [Resp. Ex. C-6].

[15] Douglas A. Kerr & Harold Ayetey, *Immunopathogenesis of acute transverse myelitis,* 15 Curr. Opinion. Neurol. 339-347 (2002) [Pet. Ex. 28-4].

[16] J. Sellner et al., *Diagnosis workup of patients with acute transverse myelitis: spectrum of clinical presentation, neuroimaging and laboratory findings,* 47 Spinal Cord 312-317 (2009) [Resp. Ex. F-04].

[17] F.S. Pidcock et al., *Acute transverse myelitis in childhood,* 68 Neurology, 1474-1480 (2007) [Pet. Ex. 27-3].

"Development of sensory, motor or autonomic dysfunction attributable to the spinal cord; bilateral signs and/or symptoms (though not symmetric); clearly defined sensory level; exclusion of extra-axial compressive etiology by neuroimaging (MRI or myelography; CT of spine adequate); inflammation within the spinal cord demonstrated by CSF pleocytosis or elevated IgG index *or* gadolinium enhancement. If none of the inflammatory criteria is met at symptom onset, repeat MRI and lumbar puncture evaluation between 2 and 7 days following symptom onset meet criteria; and progression to nadir between 4 hours and 21 days following the onset of symptoms."

Resp. Ex. A. at 4; *see also* Resp. Ex. C-01.[18]

The purpose of the TMCWG's proposed criteria was to distinguish between idiopathic acute transverse myelitis from ATM secondary to a known underlying disease. Resp. Ex. C-01 at 1. In her second report, Dr. Mar emphasized that "inflammatory markers for transverse myelitis, for which there is a consensus in the medical/neurological scientific community, are inflammatory cells in CSF, elevated IgG or gadolinium enhancement." She said, "one of these markers must be present, prior to making a definitive diagnosis of transverse myelitis. None of these were present in [A.W.'s] history." Resp. Ex. G at 1. Dr. Mar opined that A.W.'s clinical findings do not fulfill the TMCWG's criteria for idiopathic acute transverse myelitis, but are "more consistent with "acute transverse myelopathy," or " 'possible acute transverse myelitis.' " Resp. Ex. A at 10.

At the hearing, consistent with her reports, Dr. Mar continued to question A.W.'s diagnosis of acute transverse myelitis. Tr. 131-84. Dr. Mar testified that she "disagreed that [A.W.] had inflammatory transverse myelitis," as she did not see any evidence of inflammation through the inflammatory markers required by the TMCWG's proposed criteria. Tr. 137. Dr. Mar testified that A.W.'s condition began with severe acute back pain which progressed rapidly into her arms, followed by her legs within a few hours. *Id.* The lumbar puncture revealed, "normal cells, normal protein, normal glucose, and negative IgG index[19]…no evidence of any inflammatory components." *Id.* She explained that in her experience, in a case like A.W.'s with severe rapid acute progression, she would have expected inflammatory markers to be present. Tr. 139.Dr. Mar testified that the lack of inflammatory markers in A.W.'s lumbar puncture was "inconsistent," with the diagnosis of inflammatory acute transverse myelitis, according to the TMCWG's criteria. *Id.*

Dr. Mar further questioned A.W.'s diagnosis of ATM because A.W.'s initial MRI did not have evidence of enhancement. Tr. 139. Instead, Dr. Mar stated that A.W.'s initial MRI taken on August 27th showed the central cord hyperintensity from C4 to T1 as primarily affecting the gray matter, which was more consistent with acute flaccid myelitis or a stroke. Tr. 140-41; *see also* Pet. Ex. 4 at 710. She explained that demyelination generally is a disease of the white matter and in A.W.'s case, the MRI noted involvement of gray matter. Tr. 142. She opined, "it would be very unusual" for inflammatory ATM to mainly involve the gray matter. Tr. 143. Dr.

[18] Transverse Myelitis Working Group, *Proposed diagnostic criteria and nosology of acute transverse myelitis,* 59 Neurology, 499-505 (2002) [Resp. Ex. C-01].

[19] A.W.'s IgG was mildly elevated and mild swelling of the cord was observed on the MRI. Pet. Ex. 4 at 611, 653.

Mar acknowledged that the MRI taken three months later, on November 18, 2013, revealed a more clearly-defined T2 signal abnormality seen in the cervical spinal cord extending from C5-C7, consistent with cystic myelomalacia "evolved from the previous area of demyelination." Tr. 153; Pet. Ex. 4 at 55.

Additionally, Dr. Mar stated that A.W.'s symptoms of weakness was "quite different" from ATM cases she had seen. Tr. 143. She testified that in cases of regular ATM, spasticity in the lower extremities is more present than in A.W.'s case. *Id.* Dr. Mar explained that in cases of ATM where inflammation causes the transverse myelitis, children are left with leg weakness. *Id.* Typically, in ATM when the cord is inflamed, the proximal muscles are more affected than the distal muscles. Tr. 145. Dr. Mar testified that on physical exams A.W.'s hand muscles were weak compared to her proximal muscles, which is unusual. *Id.*; Pet. Ex. 4 at 651. Dr. Mar stated that the notation in the neurology consult while A.W. was in the ICU stating, "Intact proprioception[20] in lower extremities," is unusual because proprioception is supplied by the dorsal part of the spinal cord, and when inflammation is occurring, this area would be very affected. Tr. 145. Dr. Mar opined that this sensory finding was more consistent with a stroke affecting the anterior spinal artery area sparing the posterior part. Tr. 146.

Dr. Mar also theorized that A.W. may have suffered from acute flaccid myelitis, which she acknowledged was not well known until 2014. Tr. 161, 228. She explained that A.W.'s anterior horn cell of the spinal cord appeared to be permanently affected, which is consistent with acute flaccid myelitis. Tr. 161. Additionally, Dr. Mar explained, "given the fact that [A.W.] has got very patchy distribution of distal muscles in different areas, with a reduced tone distally, makes me worried-in combination with a spinal cord injury [where the] the horn cell was permanently involved," it may be an early acute flaccid myelitis case. Tr. 161-62. Dr. Mar testified that she could not prove or disprove a possible diagnosis of acute flaccid myelitis. Tr. 162.

In both her reports and testimony, Dr. Mar acknowledged that she did not question Dr. Gorman's clinical judgment and she would have treated A.W. the same way at her hospital in St. Louis. Tr. 133; Resp. Ex. G at 3. She testified that she would treat children as if there were inflammatory components, even if none were present, because some of the tests results take too long to be returned. Tr. 133-34. On cross-examination, Dr. Mar was asked if she agreed with Dr. Gorman's diagnosis of A.W. of "inflammatory transverse myelitis," Dr. Mar stated that she disagreed with that diagnosis because "[Dr. Gorman] never used the term 'inflammatory transverse myelitis.' He used the term 'acute transverse myelitis,' as clinicians generally do." Tr. 167. However, when Dr. Mar was directed to Dr. Gorman's record dated August 30, 2013, which stated, "I think inflammatory [transverse myelitis] most likely diagnosis," Dr. Mar conceded Dr. Gorman considered inflammatory transverse myelitis as the diagnosis "at the time," and stated that she would not have questioned his diagnosis. Tr. 169.

At the end of Dr. Mar's testimony, she reiterated that her alternative diagnosis would be "probable idiopathic transverse myelitis," due to the lack of the TMCWG's inflammation criteria. Tr. 171.

[20] Proprioceptor is the sensory nerve terminals found in muscles, tendons and joint capsules, which give information concerning movements and position of the body. *Dorland's* at 1528.

While Dr. Romberg largely deferred to Dr. Mar's assessment of A.W.'s condition for the respondent, in his report and testimony, he opined that, "a non-compressive transverse myelopathy (ATM without inflammation) may best fit the features of [A.W.'s] neurological disease…" Resp. Ex. D at 5.

3. Petitioner's Experts' Opinions Regarding A.W.'s Diagnosis

Petitioner's experts, Drs. Steinman and Kinsbourne agreed with A.W.'s treating physicians' diagnosis of acute transverse myelitis. *See* Pet. Exs. 13, 24, 27; Tr. 64, 114.

In Dr. Kinsbourne's first report, he stated, "[A.W.] suffered acute transverse myelitis, which was diagnosed and treated with some success as an autoimmune disorder. Its course was monophasic, with residual neurological impairments." Pet. Ex. 13 at 3. In his supplemental report, Dr. Kinsbourne directly addressed some of the issues Dr. Mar raised in her report, specifically the reliance on the TMCWG's inflammatory criteria to diagnosis ATM. Pet. Ex. 27 at 2. Dr. Kinsbourne wrote, "Inflammatory markers are not a mainstay of the diagnosis of transverse myelitis. They are quite variable when they appear, if they appear at all." *Id.* He noted that in A.W.'s case, the repeat MRI did not enhance, and she did not have a repeat lumbar puncture within the week, as the TMCWG recommends if inflammatory markers are not present in the first diagnostic tests. *Id.* He stated, "it is quite common for inflammatory markers to appear in the cerebrospinal fluid after a delay, but we simply did not know whether they did in [A.W.'s] case. *Id.* Dr. Kinsbourne also referenced the Pidcock et al., study, which analyzed forty-seven cases of children diagnosed with ATM who met the criteria established by the - TCMWG. *Id.* at 2; Pet. Ex. 27-3. Out of the forty-seven cases reviewed, MRIs were obtained in 38 of the cases which showed T2 signal abnormalities at the cervical level in half of the cases. Pet. Ex. 27-3 at 3. Gadolinium infusion demonstrated lesion enhancement on T1-weighted images in seventy-four percent of cases. *Id.* at 3. Additionally, an elevated white blood cell count was found in only half of the cases with MRIs and positive IgG index was found in less than five percent. *Id.*

Dr. Kinsbourne also referenced A.W.'s ICU medical record from August 30, 2013, which reads, "*neuro:* MRI of spine showed *C4-T1 inflammation within white and gray matter,* concerning for transverse myelitis." Pet. Ex. 27 at 2; Pet. Ex. 4 at 321 (original emphasis). He observed that this note was proceeded by a list of negative outcomes of multiple inflammatory tests for inflammation and yet, the negative laboratory tests did not cause the treating physicians to change their diagnosis or suspend anti-inflammatory treatment. Pet. Ex. 27 at 2.

Testifying by teleconference, Dr. Kinsbourne reiterated his opinion that A.W. was diagnosed correctly with ATM. Tr. 114. He stated that the basis for his opinion was chiefly the clinical presentation of A.W.'s neurological disorder and the MRI findings on her spinal cord. *Id.* Dr. Kinsbourne testified that A.W.'s clinical presentation itself justified immediately beginning immune-modulating treatment, like plasma exchange and IVIG. Tr. 114-15. He stated, "So the fact that the child was diagnosed as having an inflammatory condition," and substances that are known to reduce inflammation were used successfully was a practical validation of the diagnosis. Tr. 115.

Dr. Kinsbourne testified that diagnostic criteria for ATM established by the TMCWG is helpful for clinical research and trials and has to be restrictive to compare and contrast results. Tr. 115-17. He referred to two articles which showed how frequently the inflammatory markers were found in cases of ATM, the Pidcock article discussed above and an article by Brauna et al.[21] Tr. 117. The Brauna article analyzed forty-five cases of patients that fulfilled the TMCWG's diagnostic criteria for possible or definite ATM. Pet. Ex. 32-02 at 4. The study found that of this group, 48 percent met the TMCWG's criteria for definite ATM and 53 percent for possible ATM. In the total group 64 percent of patients had a spinal MRI showing lesions in the T2 sequence. *Id.* Gadolinium enhancement was only present in the MRIs of 56 percent of cases. *Id.* Dr. Kinsbourne stated that the Brauna study made the following finding:

> "Of the 24 patients who fulfilled the criteria for definite ATM, two presented positive MRI, pleocytosis and positive IgG index; five presented positive MRI and pleocytosis; one presented positive MRI and elevated IgG index; one presented pleocytosis and elevated IgG index; seven presented positive MRI only; five presented pleocytosis only; and three presented positive IgG index only."

Pet. Ex. 32-02 at 3; Tr. 123.

The study noted that five patients progressed to multiple sclerosis, three being from the "possible ATM group" and two from the definite ATM group. *Id.* The article stated that the TMCWG's diagnostic criteria was established to "help select homogenous groups of patients in order to facilitate clinical research in idiopathic ATM." *Id.* at 4. The article also stated, "…even when applying the restrictive criteria of the Working Group, a considerable proportion of patients with definite or possible ATM may progress to MS." *Id.* Dr. Kinsbourne testified that he agreed that the proposed TMCWG's criteria only requires a listing of one [inflammatory marker], but he stated, "That is not for clinical treatment guidance…it's for assembling a coherent group for multi-clinic research." Tr. 124.

Dr. Steinman also agreed with A.W.'s treating physicians' diagnosis of ATM. Pet. Ex. 24 at 6; Tr. 62. In Dr. Steinman's report, he stated, "Based on the records, the diagnosis here was clearly acute transverse myelitis." Pet. Ex. 24 at 6. He disagreed with Dr. Mar's assessment that A.W.'s did not have inflammatory ATM. *Id.* Dr. Steinman observed that the A.W.'s board certified neurologists intervened early in the course of A.W.'s illness with three major interventions to suppress inflammation and would not have proceeded with those interventions had her transverse myelitis not been inflammatory. *Id.* at 7. He stated that the intervention with high-dose corticosteroids intravenously for five days, as well as a course of plasmapheresis and intravenous immunoglobulin would likely mask the evolution of an inflammatory response in the course of A.W.'s illness. *Id.*

Dr. Steinman's testimony was consistent with his reports. He stated that it was his opinion that A.W. suffered from ATM. Tr. 64. He noted that none of A.W.'s treating physicians

[21] J. Brauna et al., *Idiopathic acute transverse myelitis: a clinical study and prognostic markers in 45 cases,* 12 Multiple Sclerosis, 169-171 (2006) [Pet. Ex. 32-02].

dissented in A.W.'s diagnosis of ATM. Tr.65. Dr. Steinman testified that A.W. presented with "a devastating spinal cord syndrome with inability to walk, sphincter problems, weakness in the arms," the doctors wanted to avoid further life-threatening emergency….they did exactly what I would do, they did the tests and knowing what the test results were, they started anyway with corticosteroids to prevent the further progression of this disease. Tr. 66-67.

Dr. Steinman conceded that A.W.'s initial MRI did not show gadolinium enhancement and that there was no elevated protein or pleocytosis in the CSF as may be typical in ATM. Tr. 72, 78. However, he observed that the doctors at Children's Hospital unequivocally called A.W.'s condition inflammatory transverse myelitis and definitively treated it as if it were an inflammatory disease, even in the absence of the gadolinium enhancement on the MRI. *Id.* Additionally, he testified that once steroids are started, a "well-known immunosuppressive regimen," further testing may be affected. Tr. 67. He also explained that perhaps the lumbar puncture test was done "too early." *Id.* In his report, he stated, "The early spinal fluid results may have reflected the reality that the "spill-over" of inflammation into the spinal fluid had not yet occurred. Pet. Ex. 24 at 6. Dr. Steinman testified that in some minority of cases, the inflammatory cells may not be present in the spinal fluid or that the MRI may not be enhancing. *Id.*

Dr. Steinman explained that A.W.'s treating physician, Dr. Gorman, was looking for evidence for other causes and did not find any. Tr. 217-18. Dr. Steinman testified that the MRI did not reveal any evidence of a tumor and the treating physicians were able to rule out a vascular cause of the lesion. Tr. 73. He noted that Children's Hospital performed other tests to rule out noninflammatory causes. Tr. 217. Both the radiologist and Dr. Gorman concluded that the MRI was consistent with inflammatory myelitis. Tr. 217; *see also* Pet. Ex. 4 at 649.

Dr. Steinman also responded to Dr. Mar's assertion that A.W. condition may better be described as acute flaccid myelitis attacking the anterior horn cells, due to A.W.'s residual flaccidity in the triceps. Tr. 215-16. He explained that there are patients that have transverse myelitis and recovered but have residual flaccidity. *Id.* He stated, "In transverse myelitis, there aren't distinct boundaries between the posterior, anterior and central parts of the cord." Tr. 216. With reference to "all of the discussion about anterior horn cells and that remarkable flaccidity of [A.W.'s] triceps," he concluded that " [this] is seen in inflammatory transverse myelitis." *Id.* He also agreed that acute flaccid myelitis was not well known in 2013. When questioned about Dr. Mar's observations that A.W. had more distal weakness compared to proximal weakness and A.W. was experiencing residual weakness in her hands more than her legs, which Dr. Mar asserted was more consistent with acute flaccid myelitis, Dr. Steinman stated that transverse myelitis is not confined to a specific system, it goes into "various motor and sensory systems." Tr. 230. He explained that A.W. clearly had sensory and motor symptoms, which is suggestive of a broader area affected such as in transverse myelitis and not as in conditions secondary to specific viruses like enterovirus or perhaps even D68 that are highly specific to certain cells. *Id.*

Dr. Steinman also discussed Dr. Mar's statements that the gray matter involvement noted on the MRI from August 27th was more consistent with acute flaccid myelitis. He testified that you can have gray matter involvement in transverse myelitis, MS, acute flaccid myelitis or polio myelitis. Tr. 227. He noted, however, there was degeneration in the corticospinal tracts (white

matter motor pathway). *Id.* He explained that the boundaries in transverse myelitis are not as clear (as Dr. Mar was describing). *Id.*

Dr. Steinman discussed the TMCWG's proposed criteria of ATM and opined that the criteria was not meant for clinical practice, but rather for clinical research. Tr. 70, 73. Dr. Steinman stated that TMCWG's stated goal of the proposed criteria was to "differentiate individuals into idiopathic and disease-associated categories, both for the purposes of longitudinal natural history studies as well as for eventual recruitment into therapeutic clinical trials." Resp. Ex. C-01 at 4. The paper also states, "The proposed criteria may be perceived as restrictive, we believe the use of these criteria will lead to the identification of more homogenous groups of individuals *for clinical studies.*" *Id.* (emphasis added). He noted that in this case, A.W. was treated with corticosteroids early which would have made it difficult for her to meet the proposed criteria. Tr. 217.

Dr. Steinman reiterated his belief that A.W. suffered an inflammatory traverse myelitis, stating that the most poignant fact supporting his opinion is that A.W. got much better because of the treatment she received. Tr. 80. He stated, "…but I don't think given the steroids, the plasmapheresis and the IVIG would have made a tumor better, would have made an arteriovenous malformation better." *Id.*

4. Discussion of A.W.'s Diagnosis of ATM

The Vaccine Act provides that Special Masters are to consider any medical diagnosis contained in the record. §300aa-13(b)(1). A special master must weigh and evaluate opposing expert opinions, medical and scientific evidence and the evidentiary record in deciding whether petitioners' have met their burden of proof. *Id.* The function of a special master is not to 'diagnose' vaccine-related injuries, but instead to determine based on the evidence as a whole and the totality of the case, whether it has been shown by a preponderance of the evidence that a vaccine caused the petitioner's injury. *Lombardi v. Sec. of Health & Human Servs.*, 656 F.3d 1343, 1351 (citing *Andreu*, 569 F.3d at 1382) (Fed. Cir. 2011). In *Capizzano*, the Federal Circuit provided additional guidance as how special masters should weigh evidence, placing emphasis on the statements of treating doctors. 440 F.3d at 1320 (Fed. Cir. 2006). The Federal Circuit stated, "*Althen III* explained that 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' shows that the vaccination was the reason for the injury.'" *Capizzano* at 1326 (quoting *Althen*, F. 3d at 1280).

Additionally, medical records are generally considered trustworthy. *Cucuras v. Sec'y of Health & Human Servs.*, 993 F. 2d at 1525, 1528 (Fed. Cir. 1993). Where medical records are clear, consistent and complete, they should be afforded substantial weight. *Lowrie v. Sec'y of Health & Human Servs.*, No. 03-1585V, 2005 WL 6117475 (Fed. Cl. Spec. Mstr., Dec. 12, 2005). Medical records may be outweighed by testimony that is given later in time that is "consistent, clear, cogent, and compelling." *Camery v. Sec'y of Health & Human Servs.,* 42 Fed. Cl. at 381, 391 (1998).

If there is a dispute as to the nature of the petitioner's injury, the special master may opine on the nature of the petitioner's injury." *Contreras v. Sec'y of Health & Human Servs.,* 844 F. 3d 1363, 1368 (Fed. Cir. 2017) (citing *Hibbard v. Sec'y of Health & Human Servs.,* 686 F. 3d 1355 (Fed. Cir. 2012); see also *Broekelschen v. Sec'y of Health & Human Servs.,* 618, F.3d 1339 at 1346 (Fed. Cir. 2010). In *Broeklschen,* the Federal Circuit stated that it was appropriate for the special master to first determine which injury is best supported by the evidence presented in the record before applying the *Althen* test. *Broekelschen* at 1346.

In this case, the parties are disputing the nature of A.W.'s injury. Petitioner argued that A.W.'s diagnosis, made by her treating physicians, of inflammatory acute transverse myelitis, is correct. Pet. Prehearing Brief at 3-6. Respondent argued that it is more likely that A.W. suffered transverse myelopathy or idiopathic transverse myelitis, which are not inflammatory in nature. Resp. Post-Hearing Brief at 12-13.

More specifically, the parties primarily disputed whether A.W.'s diagnosis of ATM is supported even when she did not have positive findings of inflammation in the diagnostic tests as required in the TMCWG's proposed diagnostic criteria for ATM, but met the remaining criterion. The parties debated whether A.W. showed sufficient signs of inflammation and how the TMCWG's proposed diagnostic criteria is used in clinical practice compared to its use in clinical research trials. The respondent, through Dr. Mar, posits that the term, "acute transverse myelitis is the proper term only when the presence of inflammation in the spinal cord has been confirmed." Resp. Post-Hearing Brief at 12. She argued that the TMCWG's proposed criteria for ATM required that inflammation within the spinal cord be demonstrated by CSF pleocytosis, elevated IgG or gadolinium enhancement on an MRI and that A.W.'s clinical testing did not demonstrate any of these markers. Tr. 137-39. Dr. Mar also suggested other possible causes for A.W.'s condition, including acute flaccid myelitis or a possible spinal cord-stroke.

The petitioner argued that A.W.'s primary treating physician, Dr. Gorman, a pediatric neurologist with "impeccable credentials," practicing pediatric neuroimmunology at a major children's hospital, diagnosed petitioner with acute transverse myelitis. The petitioner's experts agreed with Dr. Gorman's diagnosis and the medical records support the diagnosis. Pet. Prehearing Brief at 3. Further, petitioner argued, through Drs. Steinman and Kinsbourne, that the ATM criteria proposed by the TMCWG, was meant for use in clinical research and does not necessarily translate to clinical practice. Tr. 70-73;115-17. Finally, petitioner argued that there is no evidence to support respondent's alternative diagnosis of acute flaccid myelitis or a spinal-cord stroke.

A.W.'s substantial medical records provide support for the diagnosis of ATM and Drs. Steinman and Kinsbourne's opinions relating to A.W.'s diagnosis of inflammatory transverse myelitis. Further, A.W.'s diagnosis and disease course are consistent with the medical literature about inflammatory acute transverse myelitis.

On August 27, 2013, A.W. was transferred to Boston Children's Hospital from Exeter Hospital. Pet. Ex. 4 at 651. A.W. arrived at approximately 3:00 am EST. Pet. Ex. 4 at 600. At approximately noon on August 27, 2013, A.W. had a neurology consultation while in the ICU with Dr. Mark Libenson and Dr. Rejean Guerriero, a pediatric neurology resident. *Id.* Dr.

Guerriero noted that A.W.'s MRI of the cervical and thoracic spine "revealed an anterior cord T2 hyperintensity with very mild cord swelling, and no enhancement that would be consistent with transverse myelitis….It is difficult to tell whether there is a demyelinating process in addition to the likely inflammation….Her exam this morning appears to be worsening a bit raising concern that she has greater clinical deficits than early changes on the MRI reveal." *Id.* at 653. Dr. Libenson stated that he agreed with Dr. Guerriero's assessment and stated, "the clinical presentation is most consistent with transverse myelitis…She appears to have advanced since her early morning exam now with near complete weakness…Agree with plan above for high-dose steroids, LP, brain MRI, ID and serological testing." *Id.* at 654. A.W. was started on methylprednisolone that day. *Id.*

On August 29, 2013, Dr. Kristin Castillo examined A.W. while she was in the ICU. Pet. Ex. 4 at 327-29. Dr. Castillo reviewed A.W.s' MRI and wrote, "Given spinal imaging with C4-T1 *inflammation*, concern for transverse myelitis; although imaging not suggestive of infarct, this is a possibility." *Id.* at 328 (emphasis added). A.W. saw Dr. Guerriero again on August 29, 2013. *Id.* at 391. He noted that A.W. was a previously healthy 11-year old who presents with weakness and decreased sensation in her arms and legs and "imaging findings consistent with transverse myelitis." *Id.* at 392. He also noted that her "exam progressed over the first 24 hours which is typical for transverse myelitis." *Id.* Dr. Guerriero wrote, "given the history of the recent Gardasil vaccine, we will need to report this to CDC," and he recommended that the case be further discussed with Dr. Gorman. *Id.*

On August 30, 2013, A.W. was examined by Dr. Gorman. Pet. Ex. 4 at 648. After performing an exam, Dr. Gorman noted, "Progression of symptoms, improvement with steroids, occurrence less than 30 days from vaccination, [family history] of autoimmunity, and personal [history] of autoantibodies all support diagnosis of *inflammatory transverse myelitis." Id.* at 649 (emphasis added). He also considered whether her condition was related to a spinal cord stroke and wrote, "Traditional ischemic infarct unlikely based on tempo of onset and distribution of deficits not fitting anterior spinal artery." *Id.* He then wrote, "Therefore, I think *inflammatory* transverse myelitis most likely diagnosis." *Id.* (emphasis added). Dr. Gorman made the following recommendations, "1) Repeat spine MRI with contrast and Diffusion Weighted Imaging. If clear signs of ischemia, this would alter management. If no signs of ischemia, would presume *inflammatory transverse myelitis even if still no contrast enhancement especially as treated with steroids." Id.* at 649 (emphasis added).

A.W.'s discharge summary diagnosis was acute transverse myelitis. Pet. Ex. 4 at 610. The discharge summary provided a summary of A.W.'s stay in the ICU, which noted, "MRI of spine showed *C4-T1 inflammation in white and gray matter,* concerning for transverse myelitis. Patient was started on *high dose methylprednisone* on the morning of 8/27 for 5-day course." *Id* (original emphasis). The discharge documentation also included a summary of A.W.'s stay on the pediatric neurology floor. *Id.* at 611. It provided that a second MRI scan was performed with diffusion and that "this study showed the evolution of her lesion but there were no findings consistent with infarction." *Id.* Infectious disease testing for adenovirus, Lyme disease, CMV, EBV, mycoplasma, enterovirus and West Nile virus were negative. *Id.*

After A.W. was discharged from the hospital, she was followed by Dr. Gorman to the present time. He never changed A.W.'s diagnosis from acute transverse myelitis. *See* Pet. Ex. 4 at 40, 96, 146; Pet. Ex. 8 at 67-71, 97-99, 189, 203; Pet. Ex. 20 at 3, 11; Pet. Ex. 30 at 23; and Pet. Ex. 38 at 102-04.

The medical records are notable in that not only Dr. Gorman identified the inflammatory nature of A.W.'s condition, but so did other medical professionals that treated her at BCH including the neuro-radiologist. Dr. Guerriero first noted that A.W.'s first MRI at BCH revealed, "an anterior cord T2 hyperintensity with mild cord swelling." Pet. Ex. 4 at 653. He also stated that it was difficult to tell at that time whether there was a demyelinating process "*in addition to the likely inflammation*." *Id* (emphasis added). Dr. Guerriero and Dr. Libenson, the attending neurologist, were concerned about A.W.'s worsening condition and started her on high-dose steroids immediately. *Id.* at 653-54. Dr. Guerriero identified mild cord swelling, even though there was no enhancement on the MRI. In that same record he referred to this as "likely inflammation." Dr. Libenson agreed with Dr. Guerriero's assessment, stating, "The clinical presentation is most consistent with transverse myelitis." *Id.* at 654. On August 30, 2013, Dr. Castillo also noted that the MRI showed C4-T1 inflammation. *Id.* at 323.

Further, the medical records reject the diagnosis of a vascular cause or stroke of the spinal cord. Early on the treating physicians considered whether A.W. had an anterior cord stroke and ordered diffusion weighted imaging of the spine specifically to look for evidence of an infarct. Pet. Ex. 4 at 653. Neurologist Dr. Peter Tasi wrote on August 31, 2013 that A.W.'s "loss of posterior columns bilaterally R greater than left with loss of strength right greater than left and toe extensor on right [are]findings which make an anterior spinal infarction much less likely." *Id.* at 387. Dr. Gorman noted, "Traditional ischemic infarct unlikely based on tempo of onset and distribution of deficits not fitting anterior spinal artery….no clear signs of cord or adjacent vertebral body ischemia/infarct on MRI and improvement this early would be somewhat unusual." *Id.* at 649. Her discharge summary stated that, "As further neurologic workup, after arrival on the floor, she underwent another MRI scan with diffusion sequences to look for sign of infarct. The study showed the evolution of her lesion but there were no findings consistent with infarction." *Id.* at 611.

From the beginning of A.W.'s stay at BCH, all of the medical professionals consistently noted that A.W.'s signs and symptoms were consistent with inflammatory acute transverse myelitis and treated her as such.

The respondent, through Dr. Mar, insisted that in order for a diagnosis of ATM to be valid, inflammatory markers can only be demonstrated by certain diagnostic tests specified by the TMCWG. Tr. 133-139; Resp. Ex. A; Resp. Post-Hearing Brief at 12. Dr. Mar focused on the TMCWG's requirement that inflammation within the spinal cord must be demonstrated by CSF pleocytosis, elevated IgG index or a gadolinium enhancement. *Id.;* Resp. Ex. A at 3. The respondent stated that "the normal CSF results and the lack of gadolinium enhancement on A.W.'s initial MRI were inconsistent with the diagnosis of ATM." Resp. Post-Hearing Brief at 13. However, as discussed above, A.W.'s treating physicians identified inflammation in the imaging, despite the lack of enhancement. *See* Pet. Ex. 4 at 321, 323, 610, and 653. Further, consistent with Dr. Steinman's theory that the immediate treatment of high-dose steroids may

have actually masked inflammatory markers in a follow-up MRI, Dr. Gorman noted, "If no signs of ischemia, would presume inflammatory transverse myelitis *even if still no contrast enhancement especially as treated with steroids."* Tr. 217-18; Pet. Ex. 4 at 649 (emphasis added). When Dr. Gorman made this recommendation and wrote this note, A.W. had been on high dose steroids for three days.

Additionally, the medical literature submitted by both parties support A.W.'s diagnosis of acute transverse myelitis. Most relevant to this case is an article by Deiva et al.[22], the most recent article, which reviewed cases of children diagnosed with idiopathic acute transverse myelitis using the TMCWG's criteria. Resp. Ex. H-01. The study noted, "The utility of the TMCWG definitions in younger children can be limited in practice due to challenges including defining a clear sensory level and the requirement of gadolinium-enhancing scans and lumbar punctures." *Id.* at 1. The study reviewed MRI findings of children with definite and probable acute transverse myelitis and found that cervical or cervico-thoracic lesions were less frequently positive for gadolinium enhancement. *Id.* at 4.

The Pidcock et al., article reported on the clinical characteristics, diagnostic test characteristics and sensory characteristics of patients under the age of 18 diagnosed with acute transverse myelitis. Pet. Ex. 27-3. It found that the mean time from the onset of acute symptoms to functional nadir was about two days in the children. *Id.* Ninety-one percent of the patients described sensory loss or numbness in the initial phase; eighty-nine percent reported weakness; eighty-five percent reported urinary dysfunction; and seventy-five percent reported pain. Significantly, eighty-nine percent were bed bound/wheel chair bound or required assisted ventilation during the initial phase of ATM. *Id.* Further the study noted that in the patients where sensory and motor characteristics were collected, sixty percent had positive sensory complaints of burning, tingling or electric shock sensations, disquieting numbness was present in seventy-one percent of patients and a combination of both sensory characteristics were present in ten patients. *Id.* at 3. At follow-up, fifty-four percent of patients were still experiencing positive sensory dysesthesias and seventy-five reported numbness. *Id.* Additionally, the study noted that impaired bladder control is the most common long-term neurologic deficit following ATM. *Id.* at 6. MRIs were examined in thirty-eight cases and found that T2 signal abnormalities were identified at the cervical level in fifty percent of the cases. *Id.* As discussed during the hearing, gadolinium infusion demonstrated lesion enhancement on T1-weight images in seventy-four percent of cases, meaning that twenty-six percent of MRIs of the ATM patients studied did not enhance. *Id.* at 3. Further, CSF WBC and protein were normal in thirty-one patients. *Id.* at 3.

The article by J. Sellner et al., reviewed 63 cases of patients who had been discharged with a diagnosis of acute transverse myelitis and compared the diagnostic and clinical findings with the TMCWG's proposed diagnostic criteria of ATM. Resp. Ex. F-04 at 5. It found, "The frequency of detectable spinal cord MRI lesions was high (90.4%), but contrast enhancement was not always present (60.3%)." *Id.* The study also noted that, "Abnormal CSF findings were less frequent than evidence for MRI lesions during workup…Normal WBC counts were detected in CSF in about 50% of patients…" *Id.*

[22] Kumaran Deiva, et al., *Acute idiopathic transverse myelitis in children: Early predictors of relapse and disability*, 84 Neurology, 341-349 (2015) [Resp. Ex. H-01].

All or most of the symptoms described in the Pidcock study were present in A.W. Additionally, A.W.'s initial MRI showed a T2 signal abnormality of the spinal cord from C4-T11. Pet. Ex. 4 at 262. A.W.'s initial symptoms were paresthesia and weakness in her lower extremities that followed extreme pain. Pet. Ex. 4 at 600. She described numbness and tingling in her lower extremities. *Id.* at 485. Additionally, A.W. described associated tingling in her arms, which spread to her hands and followed by weakness in her hands. *Id.* at 604. By the time A.W. arrived at Exeter Hospital, she was unable to walk. Pet. Ex. 3 at 1. Her symptoms progressed while in the ICU of BCH until she was started on high-dose steroids. Pet. Ex. 4 at 652-53. While A.W. was at BCH she experienced urinary dysfunction and then her urinary dysfunction continued after her discharge. *See* Pet. Ex. 4 at 612; Pet. Ex. 8 at 69, 145.

The Kaplin et al.[23] article, which studied patients who met the TMCWG's proposed diagnostic criteria, found that while white matter changes, demyelination and axonal injury is prominent in postinfectious myelitis, involvement of the central compartment of the cord, gray matter or neurons is also prominent in some [transverse myelitis] cases, a "finding that supports the view that in TM both gray and white matter compartments may be equally affected." Resp. Ex. F-05 at 2. This article supports Dr. Steinman's statements that acute transverse myelitis is not confined to white matter and therefore, the radiologist's finding of "central cord hyperintensity center in the gray matter," on the initial MRI is not as significant as Dr. Mar posits. Further, A.W.'s medical records indicate that the inflammation was not limited to the gray matter. *See* Pet. Ex. 4 at 321, 610.

As discussed above, A.W.'s treating physicians diagnosed her with inflammatory acute transverse myelitis after running extensive diagnostic tests. Despite the lack of enhancement on the MRI or CSF levels in the spinal fluid, A.W.'s treating physicians recognized her condition as inflammatory and commenced an anti-inflammatory regime. Dr. Steinman was able to provide an explanation as to why certain inflammatory markers would not be present on repeat MRIs, which was also recognized by A.W.'s treating physician, Dr. Gorman. Further, the alternative diagnoses, such as acute flaccid myelitis or a spinal cord stroke proposed by Dr. Mar and the respondent were not supported by the medical records. Finally, the medical literature submitted shows that symptoms and clinical presentation of acute transverse myelitis varies and that while applying the TMCWG's proposed criteria is useful for defining clear cases for study groups, it is overly rigid for application in clinical practice. In fact, Dr. Mar acknowledged in both her report and testimony that she would have treated A.W. the same way if she had presented at her hospital. Tr. 133; Resp. Ex. G at 3.

After reviewing the medical records, the medical literature, the expert reports and testimony from the experts, I find that petitioner has shown by a preponderance of the evidence that A.W. suffered acute transverse myelitis which was inflammatory in nature as diagnosed and treated by her physicians at Boston Children's Hospital.

B. *Althen* Analysis

1. *Althen* Prong One

[23] Adam I. Kaplin et al., *Diagnosis and Management of Acute Myelopathies,* 11 The Neurologist 2-18 (2005) [Resp. Ex. F-05].

a. Legal Standard

Under *Althen* prong one, the causation theory must relate to the injury alleged. Thus, a petitioner must provide a "reputable" medical or scientific explanation, demonstrating that the vaccine received *can cause* the type of injury alleged. *Pafford*, 451 F.3d at 1355-56. The 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). It must only be "legally probable, not medically or scientifically certain." *Id.* at 549. However, the theory still must be based on a "sound and reliable medical or scientific explanation." *Knudsen* at 548. The Federal Circuit explained in *Althen* that "while [that petitioner's claim] involves the possible link between [tetanus toxoid] vaccination and central nervous system injury, *a sequence hitherto unproven in medicine*, the purpose of the Vaccine Act's preponderance standard is to allow the finding of causation in a field *bereft of complete and direct proof of how vaccines affect the human body." Althen*, 418 F.3d at 1280 (emphasis added).

b. Expert Opinions on the Theory of Causation

Petitioners, through Dr. Steinman, proposed a theory of molecular mimicry to explain how the HPV vaccine may cause inflammatory transverse myelitis. Pet. Ex. 24 at 7; Tr. 63. He testified that the Gardasil vaccine includes four versions of the L1 protein that is combined with an alum adjuvant to illicit a strong immunological response. Tr. 63. Dr. Steinman stated that the immune response to the Gardasil vaccine has been shown to be forty times stronger than to the natural infection. *Id.*

Dr. Steinman explained that when proteins are made there are common architectural structures and that these structures repeat in nature, including in foreign antigens. Tr. 82; Pet. Ex. 24 at 8. The foreign antigens have structural motifs that are similar to myelin proteins, which insulate the nerves. Tr. 82. Such similarity creates the potential for molecular mimicry in which T cells, recognizing overlapping amino acid strings in the self peptides and in the vaccine antigens, are provoked to cross react and attack the body tissues that contain the self-antigen-which in the case of ATM can be either myelin or MOG. *Id.*

Dr. Steinman explained that there are three known antigenic triggers for inflammatory transverse myelitis. *Id.* One antigen is the Aquaporin-4, which gives rise to neuromyelitis optica. *Id.* Dr. Steinman noted that the medical records show that A.W. tested negative for the Aquaporin-4 antibody and she did not develop neuromyelitis optica. *Id.*; *see also* Pet. Ex. 4 at 98. He stated that the other known two proteins in the CNS that are attacked in ATM are the myelin basic protein and the myelin oligodendrocyte glycoprotein ("MOG"). Pet. Ex. 24 at 7; Tr. 84.

In determining how much overlap is necessary between an amino acid in immunodominant peptides in the area of the central nervous system and a foreign antigen to cause an immune reaction, Dr. Steinman referenced his own research that found a viral peptide with homology of just five amino acids out of twelve with a self-peptide can induce

neuroinflammation with paralysis in experimental animals. Tr. 82; Pet. Ex. 24 at 8. He also stated that these amino acids need not be consecutive. Pet. Ex. 24 at 8.

He explained that the Gardasil vaccine has four antigens, HPV Types 6, 11, 16 and 18. Pet. Ex. 24 at 8. He performed BLAST searches looking for amino acid homologies between the myelin basic protein or MOG and the four HPV strains. *Id.* at 9; Tr. 84. Dr. Steinman testified that he found that the HPV6 and HPV11 antigens fulfilled the criteria for molecular mimicry with myelin basic protein. *Id.* at 84; Pet. Ex. 24 at 10. For MOG, all four components of the Gardasil vaccine met the criteria. *Id.* Dr. Steinman concluded that, "There are abundant molecular mimics between the components of the Gardasil vaccine and two myelin proteins (MOG and myelin basic proteins) that are known to be the subject of immune attack in transverse myelitis. The degree of mimicry was sufficient to cause neuroinflammation, based on the experimental evidence." Pet. Ex. 24 at 15.

Respondent's expert, Dr. Romberg, first argued that there was no evidence that A.W.'s neurological condition was inflammatory in nature. Resp. Ex. D at 4. He then reviewed Dr. Steinman's theory of molecular mimicry and performed his own BLAST search. Resp. Ex. D at 5. He stated that the identified myelin basic protein segment and the MOG protein segments are ubiquitous and "are similar to tens of thousands of other microbial proteins than they are to the HPV L1 proteins." *Id.* Specifically, he offered that the myelin basic protein segment selected by Dr. Steinman, perfectly matched microbial proteins expressed in viruses, bacteria or fungi. *Id.* at 5. Dr. Romberg concluded, based on homology, an immune response targeting the myelin basic protein and MOG protein segments was more likely due to an exposure to "literally tens of thousands of microbes than due to exposure to Gardasil." *Id.* He also concluded that the myelin basic protein and MOG protein segments Dr. Steinman identified are unlikely to be highly immunogenic. *Id.* He continued, stating that if they were highly immunogenic, "we would all be in a constant state of neuro-inflammation because we are exposed to these protein segments through common childhood illness." *Id.* During the hearing, Dr. Romberg testimony was similar to his report. Tr. 202. He stated that while he believed the HPV vaccination was one of the exposures that A.W. had prior to developing her neurological symptoms, it was not the only exposure that has antigen similarity to the myelin basic protein. *Id.* He opined that A.W. was likely exposed to "lots of other antigens from bacteria or fungus or viruses," that she had previously been exposed to or continues to be exposed to that have similar structures to the myelin basic protein which would have been the cause of her neurological condition. *Id.* Dr. Romberg stated that, "…there is no compelling evidence that there is significant homology between HPV L1 and the myelin basic protein that is greater than literally tens of thousands of other proteins that are found in microorganisms that had either previously infected A.W. naturally, or that she carried either on her skin or mucosal surfaces." Tr. 207.

Dr. Romberg agreed with Dr. Steinman that the adjuvant, alum, makes the HPV more effective. Tr. 203. He suggested that the alum makes the immune system take the vaccine seriously. *Id.* While Dr. Romberg testified that lots of natural adjuvants exist in bacteria, viruses and fungi, alum is the only adjuvant used in vaccines administered in the U.S. Tr. 203. The adjuvant alum is meant to provoke the formation of inflammasome, which produces a lot of IL-1, "the fever cytokine." *Id.* He testified that alum is added to the HPV vaccine because the vaccine

only includes proteins and it does not contain any of "the other stuff that a natural viral infection would produce." Tr. 204.

Dr. Romberg concluded that in order for an inflammatory reaction to damage the brain, it must travel from the deltoid where A.W. received the vaccination, to the central nervous system. Tr. 206. The only plausible way to make this trip, according to Dr. Romberg is through systemic circulation and if that were the case, there would be evidence of inflammation, like fever or tachycardia. Tr. 206. Further, he noted that there was no evidence that the blood-brain barrier was "leaky" at the time it was tested. *Id.* He acknowledged that the lumbar puncture occurred after the initiation of steroids, but he stated that some proteins would have remained in the CSF persistently, even though the cells may go away, and glucose may normalize. Tr. 207.

Dr. Steinman responded to Dr. Romberg's testimony regarding the necessity for a fever for cells to access the brain. Tr. 209. Dr. Steinman explained that certain diseases, like MS, Guillain-Barré, and transverse myelitis, in which diseases he has a particular specialty, are not associated with fever. *Id.* He explained that inflammatory biomarkers are helpful in certain diseases, like rheumatological diseases or Muckle-Wells syndrome, but are not seen in neuroinflammatory diseases like MS or acute transverse myelitis. Tr. 210. He explained that when a cell is activated by encountering an antigen, integrins[24] (Velcro-like materials) are expressed. Tr. 209. There are two chains of an integrin, alpha 4 and beta 1. [The antigen, with the integrins] will get into the brain, whether or not there is a fever, whether or not there is an elevation of C-reactive protein, whether or not there is an elevation of the sed rate. *Id.*

Second, Dr. Steinman discussed Dr. Romberg's theory that A.W.'s neurological disease could have been triggered by another microbe that has sufficient homology with the HPV vaccine and the myelin basic protein. Tr. 210. While he recognized some of the viruses and bacteria Dr. Romberg identified as having a higher level of identity with the myelin basic protein or MOG, there was no evidence that A.W. had one of those entities. Tr. 212. In fact, the record indicates that A.W. was quite healthy and she did not suffer from any infections in the months prior to the onset of her transverse myelitis. Tr. 213. Instead, the record indicates that she received three HPV vaccines and the HPV vaccine has five out of seven amino acids that are homologous to the myelin basic protein. Tr. 212.

He also observed that the naturally active adjuvants that occur in all microbes are not as powerful as the addition of alum to certain vaccines, including the HPV vaccine. Tr. 211. Dr. Steinman cited to the Souayah et al.[25], article which found that the Gardasil vaccine produces a 40-fold increase in HPV antibodies compared with the physiological antibody level triggered by a natural HPV infection. Pet. Ex. 33-01 at 3. He stated that the alum is formulated to the specific HPV antigen that "you want to immunize to," in order to achieve the strong immunogenic effect that is desired when making a vaccine such as Gardasil. Tr. 212. He further observed that it takes three separate immunizations to achieve the strong immunity to the HPV

[24] Integrins are heterodimeric transmembrane (two-chain) receptors that mediate cell-adhesion.

[25] Nizar Souayah et al., *Guillain-Barré syndrome after Gardasil vaccination: Data from Vaccine Adverse Event Reporting System 2006-2009*, 29 Vaccine 886-889 (2011) [Pet. Ex. 33-01].

antigens in the vaccine. *Id.* Dr. Steinman observed that Dr. Romberg never identified a particular antigen/natural adjuvant combination that illicit the same strong effect as the HPV vaccine, as the evidence does not exist. *Id.* at 213. He stated that the evidence does exist for the theory that HPV with an adjuvant specifically tailored to the HPV antigens which have sufficient homology to the myelin basic protein and MOG can trigger neuroinflammation on the third recall response three weeks after the vaccination as occurred in this case. *Id.* Dr. Steinman emphasized that even if there was some evidence that the naturally occurring adjuvants paired with various naturally occurring antigens were as powerful as the alum/HPV antigen combination in Gardasil, there is no evidence that A.W. had one of those infections and in fact the evidence is to the contrary. She was healthy in the months before the onset of her illness and we know that she did receive the third Gardasil vaccine within an immunologically relevant time period before onset.

c. Discussion and Conclusion

As discussed above, I concluded that A.W.'s diagnosis of inflammatory acute transverse myelitis was supported by a preponderance of the evidence. Dr. Steinman opined that the HPV vaccination caused A.W.'s inflammatory acute transverse myelitis. Pet. Ex. 24 at 7; Tr. 62. Dr. Steinman offered a theory of molecular mimicry as the explanation for how the HPV vaccination caused A.W.'s acute transverse myelitis. *Id.*; Tr. 81. I find that the petitioner has provided preponderant evidence that the HPV vaccine can cause acute transverse myelitis via molecular mimicry. Petitioners' theory of causation is supported by sound and reliable scientific evidence.

An article written by Dr. Steinman[26] explains that molecular mimicry works when a foreign antigen shows the immune system stretches of amino acids that look like self….in responding routinely to the foreign antigen, the immune system may become primed to attack the corresponding self-component-myelin. Pet. Ex. 26-13 at 4. Dr. Steinman explained that the homology between the virus and the myelin basic protein need not be extensive. *Id.* at 4; Tr. 82. He noted that research at Stanford which exposed mice to a short stretch of 10 amino acids, only five of which were identical to the myelin basic protein, was able to induce paralysis. *Id.* In his written report, Dr. Steinman noted that in a study published in the Journal of Immunology, 5 of 11 amino acids were identical between the virus and myelin basic protein, and only 3 were consecutive and this was sufficient to activate myelin basic protein clones and induce clinical encephalomyelitis with the viral peptide. Pet. Ex. 24 at 8; Tr. 82. He was then able to demonstrate there were sufficient homologies between the basic myelin protein and two of the HPV L1 strains (HPV 6 and HPV 11) and between MOG and all four HPV antigens in the vaccine. Pet. Ex. 24 at 11; Tr. 84.

Respondent, through Dr. Romberg, argued that by "mere random chance, segments of amino acid homology can exist between two proteins." Resp. Post-Hearing at 7; Tr. 195. Dr. Romberg offered his own BLAST searches, looking across proteins expressed by "fungi, virii and bacteria" to determine whether any of the proteins included in the amino acid sequences that matched the myelin basic proteins identified by Dr. Steinman as having significant homology

[26] Lawrence Steinman, *Autoimmune Disease: misguided assaults on the self produce multiple sclerosis, juvenile diabetes and other chronic illness. Promising therapies are emerging,* Scientific American, 107-114 (1993) [Pet. Ex. 26-13].

with HPV L1 proteins contained in the Gardasil vaccine. Resp. Post-Hearing Brief at 8; Tr.198. Dr. Romberg concluded that there were tens and thousands of proteins expressed by viruses, bacteria, fungi or parasites that were more similar to the myelin basic protein "than the regions which Dr. Steinman identified in the HPV L1 proteins." *Id.* Dr. Romberg postulated that A.W. could have been exposed to one of these viruses, bacteria or fungi that could have resulted in molecular mimicry and caused A.W.'s acute transverse myelitis.

As Dr. Steinman noted, the medical records do not demonstrate that A.W. had exposure to another virus or bacteria at the onset of her condition. Instead, the medical records and the testimony of the witnesses demonstrated that A.W. was healthy prior to the onset of her illness. There were no reports of any illness in the months before the onset of her symptoms. A.W. attended her first day of school and was playing basketball with her brothers the day her symptoms began. Additionally, Dr. Steinman was able to explain, with support from medical literature, how the alum adjuvant specifically combined with the antigens in the HPV vaccine, will cause an immunological reaction that is stronger than the naturally occurring adjuvants in viruses or bacteria Dr. Romberg identified.

The respondent argued that Dr. Steinman did not know for certain the significance of the homology between the proteins in the HPV vaccine and the myelin basic protein. Dr. Steinman acknowledged that the exact segment of the molecule may vary from individual to individual, so one cannot state for certainty that such a reaction occurred in a given patient. Tr. 102. However, Dr. Steinman stated that he conducted his searches specific to the known proteins in the HPV vaccine and the proteins that are "known to be targets of the immune response in transverse myelitis," which provides a sound foundation for the theory of molecular mimicry. *Id.* at 101.

Accordingly, I find that petitioners' have satisfied the requirement of *Althen* prong one by presenting a reputable scientific explanation of how the HPV vaccine could cause acute transverse myelitis.

2. *Althen* Prong Two

a. Legal Standard

Under *Althen* prong two, petitioner must prove "a logical sequence of cause and effect showing that the vaccination was the reason for [her] injury." *Althen*, 418 F.3d at 1278. This prong is sometimes referred to as the "did it cause" test; i.e. in this particular case, did the vaccine(s) cause the alleged injury. *Broekelschen*, 618 F. 3d at 1345 ("Because causation is relative to the injury, a petitioner must provide a reputable medical or scientific explanation that pertains specifically to the petitioner's case"). Temporal association alone is not evidence of causation. *See Grant v. Sec'y of Health & Human Servs.,* 9556 F.2d 1144, 1148 (Fed. Cir. 1992). This sequence of cause and effect is usually supported by facts derived from petitioner's medical records. *ALthen*, 418 F.3d at 1278; *Andreu*, 569 F.3d at 1375-77; *Capizzano*, 440 F.3d at 1326; *Grant*, 956 F.2d at 1148.

b. Discussion and Conclusion

As discussed above, I find that after receiving the third HPV vaccine on July 30, 2013, A.W. manifested the first symptoms of acute transverse myelitis.

Dr. Steinman offered the theory of molecular mimicry to explain how the HPV vaccine A.W. received can cause acute transverse myelitis. Dr. Steinman explained that this theory fit the present case because the administration of the vaccine containing a sufficient homology with the myelin basic protein provoked the onset of acute transverse myelitis within twenty-seven days. Pet. Ex. 24 at 18. Multiple alternate causes were ruled out by A.W.'s treating physicians. *Id.* at 18.

Dr. Steinman observed that prior to A.W. receiving the third HPV vaccination, she was healthy. Tr. 62. A.W. subsequently developed acute transverse myelitis twenty-seven days later. Prior to the onset of A.W.'s symptoms, there was no evidence that A.W. had any viral or bacterial infection. Dr. Steinman noted that A.W. was also treated with steroids, plasmapheresis and IVIG, which are the three major interventions used to suppress inflammation and appeared to respond positively to the treatment. *Id.* at 6, 18.

While the respondent did not affirmatively offer an alternative theory for causation, respondent's experts opined that a variety of causes other than the vaccine could have triggered A.W.'s symptoms of ATM. Dr. Mar opined, without evidence, that A.W. may have suffered from acute flaccid myelitis instead of ATM. *See* Tr. 137-161, 177, 179, 182, 227-229; Resp. Post-Hearing Brief at 13. Respondent's experts focused on the lack of inflammatory markers in A.W.'s CSF and on the MRI as evidence that A.W. was not suffering from ATM, but something else altogether. Dr. Mar stated that at the time A.W.'s spinal tap was performed, "[A.W.] already reached nadir and did not have any progression noted." Tr. 138. However, the medical records contradict Dr. Mar's assertion. When A.W. arrived at BCH in the early morning of August 27, 2013, she was experiencing decreased sensation in her feet, difficulty walking and standing, with decreased strength in her bilateral triceps and grip. Pet. Ex. 4 at 602. A.W. underwent an MRI of her thoracic spine at 4:30 AM and an MRI of her cervical spine at approximately 7:00 AM. *Id.* at 710. A note from 11:00 AM written by Dr. Stefater, stated, "MRI with signs of transverse myelitis C4-T1 and clinical exam *progressing with decreased strength at right ankle and hand movement."* Pet. Ex. 4 at 605 (emphasis added). Around 12:30 PM on August 27, 2013, A.W. was examined by Dr. Guerriero, a neurology resident, who noted that, "Her exam this morning appears to be worsening a bit raising concern that she has greater clinical deficits than early changes in the MRI reveal." *Id.* at 653. The attending neurologist, Dr. Libenson noted, "[A.W's condition] appears to have advanced since her early morning exam now with near complete weakness of the RLE and little to no movement at the ankle, right toe equivocal, left is down. She has little movement in her hands….Agree with plan for high dose steroids." *Id.* at 654. It is apparent from the medical records that A.W.'s symptoms were progressing while she was at BCH and had yet to reach the nadir of her illness when the initial MRIs were performed. Instead, the record supports Dr. Steinman's assertion that the MRI and lumbar puncture were performed early in the disease process and she had not yet reached the nadir when her physicians intervened. Tr. 73. Further, the medical records demonstrate that

A.W.'s symptoms and clinical signs were consistent with acute transverse myelitis that was described in the medical literature submitted by both parties.

Dr. Romberg opined that perhaps A.W. had been exposed to some other type of antigen that has sufficient homologies with the myelin basic protein. Resp. Ex. D at 5. He stated, "An immune response targeting and identifying MBP and MOG protein segments would more likely be due to an exposure to literally tens of thousands of microbes than due to an exposure to Gardasil." *Id.* Once again, the medical records show that A.W. was not experiencing an infection from another virus or antigen and had not experienced any illness in the months before the onset of her symptoms. A.W. was tested extensively for various viruses, all which came back negative. *See* Pet. Ex. 4 at 684, 686, 690. For example, Dr. Romberg identified adenovirus as one possible microbe that could have been the cause of A.W.'s symptoms, however, the records clearly state that A.W. was negative for adenovirus. Pet. Ex. 4 at 326. Dr. Romberg's theory that A.W. was exposed to any of the microbes he identified in his BLAST search is purely speculative.

The onset of A.W.'s symptoms and the progression of those symptoms, along with the appearance of a longitudinally extensive spinal cord lesion, which her treating physicians diagnosed as acute transverse myelitis is consistent with petitioners' theory that the "homologies between the components of the Gardasil and myelin proteins in question were sufficient to trigger neuroinflammation." *See* Pet. Ex. 24 at 17. There is no evidence that A.W. was exposed to any other antigen within the relevant time period that would have been likely to generate autoimmunity in the same way. Accordingly, petitioners have demonstrated a logical sequence of cause and effect, satisfying *Althen* prong two.

3. *Althen* prong three

a. Legal Standard

Althen prong three requires establishing a "proximate temporal relationship" between the vaccination and the injury alleged. *Althen* at 1281. That term has 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." *de Bazan v. Sec'y of Health & Human Servs.*, 539 F.3d 1347, 1352 (Fed. Cir. 2008). The explanation for what is medically acceptable timeframe must also coincide with the theory of how the relevant vaccine can cause an injury (*Althen* prong one). *Id.* at 1352.

b. Discussion and Conclusion

Petitioners argued that there was an acceptable temporal relationship between A.W.'s third HPV vaccination on July 30, 2013 and the onset of the first symptoms of ATM, twenty-seven days later. Pet. Prehearing Brief at 8. Dr. Steinman stated, "The timing is typical of a response to a vaccine, a neuroinflammatory response, whether it's ADEM, Guillain-Barré, acute transverse myelitis." Tr. 88. Dr. Kinsbourne agreed that the onset of A.W.'s ATM twenty-seven days after her third Gardasil vaccination falls well within the time frame of what is considered a

medically reasonable time for the triggering of an immune-mediated neurological injury between five and 42 days. Pet. Ex. 13 at 6. Respondent did not offer any contrary evidence on timing.

Accordingly, petitioners have demonstrated by preponderant evidence that A.W.'s onset of symptoms of ATM was within a medically appropriate timeframe following the third HPV vaccine on July 30, 2013.

V. Conclusion

After a careful review of the entire record, I find that petitioners have established by a preponderance of the evidence that following the third HPV vaccine administered on July 30, 2013, A.W. developed acute inflammatory transverse myelitis.

Petitioners presented evidence that A.W. was a completely healthy seventh-grader prior to the onset of severe pain, which was diagnosed as acute inflammatory transverse myelitis following a complete consideration of A.W.'s symptoms, disease history and a review of MRIs and lab tests. Petitioners' experts, Drs. Steinman and Kinsbourne presented evidence that strongly supports A.W.'s treating physicians' diagnosis of acute inflammatory transverse myelitis. Dr. Steinman presented a theory of molecular mimicry, which he supported by demonstrating BLAST search evidence of several significant homologies with the Gardasil vaccine that could give rise to neuroinflammation.

While Dr. Mar did not dispute that she would have treated A.W. in a similar manner as the treating physicians did at BCH, she retrospectively hypothesized that A.W. could have suffered from acute flaccid myelitis, which was unknown until 2014, instead of acute inflammatory transverse myelitis. Significantly, A.W. has continued to treat with Dr. Gorman at Boston's Children Hospital to the present time and he has maintained the diagnosis of acute inflammatory transverse myelitis. Dr. Steinman concurred with A.W.'s treating physicians' diagnosis and treatment. He believed that she had broad damage which crossed boundaries of grey and white matter in the spinal cord, which does occur in acute inflammatory transverse myelitis. A.W. was tested for possible infectious causes of here symptoms and all were ruled out, as well as, an ischemic stroke.

Given the diagnosis and Dr. Steinman's explanation of molecular mimicry and uncontested evidence of timing, I find that petitioners established each *Althen* prong by preponderant of evidence and, accordingly, petitioners are entitled to compensation. A separate damages order will be issued.

IT IS SO ORDERED.

s/Thomas L. Gowen
Thomas L. Gowen
Special Master