In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

No. 11-693V

(to be published)

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OLIVIA BENDER,	*	
	*	
	*	Filed: October 6, 2017
Petitioner,	*	
	*	Decision; Transverse Myelitis
v.	*	("TM"); Meningococcal Vaccine;
	*	Hepatitis A ("Hep A") Vaccine;
SECRETARY OF HEALTH AND	*	Medically Acceptable Timeframe;
HUMAN SERVICES,	*	Althen Prong Three.
	*	
Respondent.	*	
	*	
* *		

Bruce William Slane, Law Office of Bruce W. Slane, P.C., White Plains, NY, for Petitioner.

Lara Englund, U.S. Dep't of Justice, Washington, DC, for Respondent.

DECISION DENYING ENTITLEMENT[1]

On October 19, 2011, Olivia Bender filed this action seeking compensation under the National Vaccine Injury Compensation Program (the "Vaccine Program"[2]). Petition ("Pet.") (ECF No. 1). Petitioner alleges that she developed transverse myelitis ("TM") as a result of the meningococcal and Hepatitis A ("Hep A") vaccines she received on May 29, 2009. Pet. at 1. An entitlement hearing was held in Washington, DC, on February 9-10, 2017.

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[1] This decision will be posted on the United States Court of Federal Claims' website in accordance with the E-Government Act of 2002, 44 U.S.C. § 3501 (2012). **This means the decision 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 ruling's inclusion of certain kinds of confidential information. Specifically, under Vaccine Rule 18(b), each party has fourteen (14) days within which to request redaction "of any information furnished by that party: (1) that is a trade secret or commercial or financial in substance and is privileged or confidential; or (2) that includes medical files or similar files, the disclosure of which would constitute a clearly unwarranted invasion of privacy." Vaccine Rule 18(b). Otherwise, the entire decision will be available in its current form. *Id.*

[2] The Vaccine Program comprises Part 2 of the National Childhood Vaccine Injury Act of 1986, Pub. L. No. 99-660, 100 Stat. 3755 (codified as amended at 42 U.S.C. § 300aa-10 through 34 (2012)) (hereinafter "Vaccine Act" or "the Act"). All subsequent references to sections of the Vaccine Act shall be to the pertinent subparagraph of 42 U.S.C. § 300aa.

After considering the record as a whole, and for the reasons explained below, I find that Petitioner has failed to carry her burden in establishing causation, and therefore her request for entitlement is DENIED. Petitioner relies too heavily on the absence of evidence of alternative causes to establish that the vaccines she received caused her TM, while offering a theory that is mechanistically deficient. She also has not adequately demonstrated that the six-week period between vaccination and onset is medically acceptable.

I. Factual Background

On May 29, 2009, Olivia Bender received the Hep A and meningococcal (marketed as "Menactra") vaccines after a physical examination. She was fourteen years old and had no prior health problems. Ex. 8 at 4, 6. There is no record evidence of any reaction to either of these vaccines in the intervening period before the incident that caused Ms. Bender to seek medical treatment, and neither Petitioner nor the other fact witnesses testifying in this action have offered testimony suggesting that any symptoms were occurring during this period despite the absence of corroborative proof.[3]

While on a trip to the western half of the United States, on July 10, 2009 (42 days after vaccination), upon disembarking from the bus that was transporting her, Ms. Bender experienced a sudden loss of sensation in her legs, causing her to collapse onto the pavement into a sitting posture. Ex. 1 at 2. She was immediately taken to the nearest hospital - Kingman Regional Medical Center ("KRMC") in Kingman, Arizona, where a variety of tests and lab work was performed, including CT scans of Petitioner's spine (cervical, thoracic, and lumbar regions); a urinalysis; and a complete blood count ("CBC"). *Id.* at 4-8.

On examination, Petitioner had no sensation below her umbilicus and no reflexes in her lower extremities. Ex. 1 at 2-5. The results of the evaluation were otherwise largely unremarkable, except the CT scans showed mild spinal stenosis, mild scoliosis, and mild disc bulging. *Id.* at 6-11. The CBC showed elevated white blood cell count and decreased lymphocytes, i.e.

[3] Certain medical records could be read to suggest some of Petitioner's symptoms may have begun in the 24-hour period before she first sought medical care. Specifically, some records indicate that Petitioner informed certain initial treaters that she had experienced mild lower back discomfort after "go-kart riding" the day before her fall, and that she noticed back pain again the next day prior to disembarking from the tour bus. Ex. 15 at 86. At hearing, however, Ms. Bender testified that she had merely been a passenger in a bumpy jeep ride over rough terrain, and that she had experienced some subsequent back pain due to the rough ride but that it had not persisted. Transcript ("Tr.") at 10-11. Although Respondent has attempted to suggest that this initial pain may have been related to Ms. Bender's subsequent and more obvious TM symptoms, I cannot ascertain from the medical record whether there is in fact any relationship between the two.

leukocytosis.[4] *Id.* at 6. There was no evidence of nerve damage, but the immediate treater's impression was that the Petitioner was experiencing a spinal cord compression. *Id.* at 13.

In order to receive more specialized treatment and diagnosis (since KRMC did not have the medical equipment required to perform an MRI), Ms. Bender was transferred to Sunrise Hospital in Las Vegas, Nevada ("Sunrise") for a neurologic consult. *See generally* Ex. 15; Tr. at 14. Treaters performed MRIs on July 10 and 14, 2009. Ex. 15 at 78, 89, 148,151. The results of the first MRI (on the cervical spine) were mostly normal, except the thoracic spine MRI showed an abnormal T2 signal at the T11-12 levels, and "enhancement[5] within the remainder of the cord," suggesting to the radiologist performing the MRI the presence of an "acute transverse myelitis." *Id.* at 146. The second, July 14th MRI, performed with and without contrast, now showed "abnormal signal *throughout* the distal spinal cord," and extension of the lesions from T8-T12 levels. *Id.* at 81 (emphasis added). The impression of Petitioner's treaters, given her "acute loss of neurologic function," coupled with a lack of evidence of any other obvious spine pathology and the location of lesions, was TM. *Id.* at 88.

Other testing performed on Ms. Bender was somewhat inconclusive. One such result from the CBC measured the segmental neutrophils ("SEGS"), which was slightly high - usually indicating that the patient is experiencing stress or pain. Tr. at 173.[6] Serology for *Mycoplasma pneumoniae* IgM and IgG antibodies[7] were reported as positive, but PCR[8] testing for *Mycoplasma* DNA was negative. Ex. 15 at 122, 127, 133. However, an aspect of that lab report was later discovered by Petitioner to be in error - Petitioner's mycoplasma IgM titers were in fact negative, but had been incorrectly flagged by the lab report as positive. *Id.*, Tr. at 56.[9] Ms. Bender's doctors

[4] Leukocytosis is defined as the transient increase in the number of leukocytes in the blood, and can occur after strenuous exercise, or pathologically accompanying hemorrhage, fever, infection, or inflammation. *Dorland's Illustrated Medical Dictionary* 1028 (32nd ed. 2012) (hereinafter "*Dorland's*").

[5] MRIs often involve the injection into the blood of a contrasting agent, such as gadolinium, intended to increase (or "enhance") the signal of certain types of lesions visible to the radiologist performing the imaging. Active or newer lesions are more likely to enhance than preexisting or older lesions, because the contrasting agent is able to enter the brain via an existing breach in the blood-brain barrier; once that barrier is repaired, and the contrast cannot reach the brain, lesions do not appear enhanced. *See W.C. v. Sec'y of Health & Human Servs.,* 100 Fed. Cl. 440, 444 (2011).

[6] Dr. Chen commented on this CBC SEGS test result, noting that it could also point towards a preexisting bacterial infection, but could not be relied upon as evidence of an existing viral illness absent other abnormal test results. Tr. at 174-75.

[7] Mycoplasma pneumoniae is a genus of bacteria that causes inapparent/subclinical infections or mild respiratory tract disease. *Dorland's* at 1217. The presence of IgM antibodies suggests a recent infection, while IgG antibodies indicate a prior infection that may have been resolved for years. Tr. at 56.

[8] PCR stands for polymerase chain reaction, which is a "type of rapid nucleic acid amplification of specific DNA or RNA sequences, allowing small quantities of short sequences to be analyzed without cloning." *Dorland's* at 1601.

[9] Ms. Bender's IgG titers were, however, correctly read as positive for a prior mycoplasma infection sometime in her childhood, although the precise timing of the prior infection cannot be identified. Tr. at 69.

nevertheless initially relied upon the false IgM reading, diagnosing her with TM secondary to a mycoplasma infection and treating her with azithromycin.[10] *Id*. at 60-61. The doctors at Sunrise seem also to have been including in their initial differential diagnosis an autoimmune etiology, requesting that Ms. Bender receive a neurology referral to help evaluate this possibility. *Id*. at 60.

At Sunrise, Petitioner underwent treatment with IVIG[11] and steroids but showed no improvement in her condition. On July 20, 2009, Ms. Bender was transferred for rehabilitation. The transfer diagnosis was "transverse myelitis secondary to mycoplasma infection." *Id.* at 15. Thereafter she received treatment at a facility closer to her home - Blythedale Children's Hospital in Valhalla, New York - remaining there through early September. Her diagnosis of TM secondary to mycoplasma infection was affirmed (without recognition of the error in the mycoplasma testing discovered by Petitioner). *See generally* Ex. 11.

Ms. Bender was discharged from Blythedale on September 4, 2009, after learning how to manage her own care. On November 6, 2009, petitioner underwent spinal MRIs as well as an MRA of her spinal canal. *Id.* at 5-6. The MRIs showed T2 signal intensity changes in the spinal cord from T5 to T8-9. The MRA showed no vascular abnormalities and no evidence of thrombosis (which had been suspected by an intervening specialist). *Id.*

On December 16, 2009, Ms. Bender saw Douglas Kerr, M.D., a neurologist at Johns Hopkins University, for a consultation after being referred by Dr. Kirshblum. Ex. 13 at 1.[12] Based on her "very rapid onset," Dr. Kerr theorized that the cause of her condition might be a fibrocartilaginous embolism rather than TM, but he noted that the management of her condition would be the same, whatever the cause. *Id.* at 2. Dr. Kerr referred her to the Kennedy Krieger Institute for therapy. *Id.* The records from this visit with Dr. Kerr do not mention the vaccines received prior to onset of Ms. Bender's condition or propose they were causal of her TM.

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[10] Azithromycin is used to treat bacterial infections. *Dorland's* at 187. Here, it was used to treat the mycoplasma pneumoniae infection that it originally seemed Ms. Bender had at the time.

[11] IVIG is a treatment for immunodeficiency disorders made of immune globulin and administered through the veins. *Dorland's* at 785.

[12] In addition to being one of Ms. Bender's treaters, Dr. Kerr was a co-author of an item of medical literature submitted by Petitioner. Graber JJ, *et al., Interleukin-17 in transverse myelitis and multiple sclerosis*. J Neuroimmunology, 196:124-32 (2008), filed as Ex. 30, Tab 8 (ECF No. 104). Dr. Kerr is recognized as having specialized expertise in the study of TM. https://www.the-asci.org/controllers/asci/AsciProfileController.php?pid=500563 (last visited September 18, 2017) (noting that "Dr. Kerr has established the Johns Hopkins Transverse Myelitis Center which is the only such center in the entire world"). Dr. Kerr has offered opinions on behalf of petitioners in other Vaccine Program cases. *See, e.g., Flores v. Sec'y of Health & Human Servs.*, No. 10-489V, 2013 WL 5587390, at *6 (Fed. Cl. Spec. Mstr. Sept. 12, 2013), *mot. for review den'd*, 115 Fed. Cl. 157 (2014), *aff'd*, 586 F. App'x 588 (Fed. Cir. 2014).

At Kennedy Krieger's International Center for Spinal Cord Injury, Petitioner has received treatment from Glendaliz Bosques, M.D. Ex. 7 at 127-34, 25-31; *see also* Ex. 18. On August 6, 2010, Dr. Bosques stated that petitioner was diagnosed with a T8 ASIA A spinal cord injury (meaning that she has no motor or sensory function below the T8 vertebra). Ex. 7 at 29, Ex. 11 at 115-16. No subsequent treaters have, however, associated her TM with the vaccinations she received seven weeks before her immediate and first alarming symptom – although there is also no evidence that such treaters were aware of the mistaken mycoplasma infection test result.

II. Fact Witnesses and Expert Opinions

Petitioner presented three fact witnesses at hearing as well as two experts. Respondent also offered two experts.

A. *Fact Witnesses*

Three fact witnesses - Petitioner and her parents, Drew and Diane Bender – testified at hearing, addressing Petitioner's current condition as well as the circumstances of her initial TM presentation in 2009. Tr. at 5-29. They each offered short testimony regarding their recollection that Olivia had no prior health conditions before her TM diagnosis—including no symptoms of an infection, consistent with her negative IgM results. Tr. at 7-8, 19-20, 25-26. They also testified that on her trip, Olivia had not performed any activities that could have caused her back trauma. Tr. 10-11.

Olivia Bender provided additional details about the first symptom that precipitated emergency treatment. That day, she was travelling with her group by bus to a new location, but when she began to get off the bus at a rest stop, she felt her legs were "all pins and needles and tingly." Tr. at 13. As she proceeded off the bus, she recalled the feeling getting worse so she abruptly sat down. It was at that time that she realized she had no sensation in her legs, as she could not feel the heat of the pavement through her clothes despite the temperature being over 100 degrees. *Id*. After attempts by one of the adult supervisors of the trip to get Ms. Bender to stand, she was carried back onto the bus to go to the hospital. *Id*. Her testimony about her subsequent treatment was otherwise consistent with the medical records previously discussed.

B. *Petitioner's Experts*

1. Dr. Vera Byers

The first of Petitioner's two experts, Vera Byers, M.D., provided an immunological opinion that the Menactra or the Hep A vaccines caused Ms. Bender's TM. Dr. Byers prepared two expert

reports (although only one was submitted as an exhibit) and testified at hearing.[13] *See* Report, dated Oct. 3, 2016, filed as Ex. 30 ("Byers Rep."); Tr. 29-163.

Dr. Byers attended the University of California, Los Angeles for her bachelor's degree, her masters in protein chemistry, and her Ph.D. in immunology. Tr. at 30; Byers CV, filed as Ex. 31 (ECF No. 102), at 3. Before entering medical school, Dr. Byers completed two fellowships: one in protein chemistry at Abbott Labs in Chicago, Illinois, followed by a fellowship in clinical and tumor immunology at the University of California, San Francisco ("UCSF"). Byers CV at 4; Tr. at 30. She then attended medical school and completed a three-year residency at UCSF, before becoming a member of the faculty. Byers CV at 4. Dr. Byers is presently a medical toxicologist and consulting medical director at Immunology Inc. of Incline Village, Nevada, and has frequently served as an expert witness in lawsuits. *Id.* at 1-2. She has throughout her career maintained several positions as an allergist and immunologist performing research and clinical trials in a variety of different areas. Byers CV at 6-7; Tr. at 34-41.

Dr. Byers was careful to state that her opinion drew solely upon her expertise in immunologic matters. Tr. at 42-46. For all matters pertaining to TM itself, she relied on the expert reports of Dr. Chen and his interpretation of Ms. Bender's medical records. Byers Rep. at 5; Tr. at 42.[14]

Dr. Byers opined that Ms. Bender's receipt of the Menactra and Hep A vaccines caused her TM. She defined TM as largely an autoimmune condition characterized by demyelination of the spinal cord. Byers Rep. at 6. Such demyelination can have disparate causes: inflammation propagated by anti-myelin antibodies, and T cells or cytokines attacking the myelin sheath. *Id*. In Dr. Byers's view, the engine of Petitioner's illness was the vaccines' promotion of pro-inflammatory cytokines—particularly IL-6, which is released by T cells. Tr. at 43; Byers Rep. at 6. IL-6 has been found in elevated levels of individuals who experience TM, and also found to mediate spinal cord injury. Byers Rep. at 6; A.I. Kaplin, *et al.*, *IL-6 Induces Regionally Selective Spinal Cord Injury in Patients with the Neuroinflammatory Disorder Transverse Myelitis*, J.

[13] Dr. Byers's first report was filed long after the deadline to submit reports in this case, and without my prior approval. I permitted the report into evidence despite its dilatory character, but informed the parties that I would allow Respondent the opportunity to file a responsive report. *See* Order, dated Oct. 13, 2016 (ECF. No. 105). In addition, due to the looming trial date, plus Petitioner's prior disregard for my orders regarding deadlines for the submission of evidence, I stated that I would not permit the filing of a second report from Dr. Byers; rather, Petitioner would be permitted to address the contents of any final expert report filed by Respondent during the hearing, and (if necessary) file a post-trial written brief in support of Dr. Byers's testimony. *Id*. Petitioner nevertheless commissioned a second expert report from Dr. Byers in violation of my order, referencing it at trial and repeatedly requesting that it be permitted into evidence. Tr. at 44, 65-66. In response (and consistent with my October order), I informed Petitioner that I would allow Dr. Byers to testify to the substance of the report in rebuttal to Respondent's expert testimony, and that Petitioner could reference points from Dr. Byers's unauthorized second report in her post-hearing brief. Petitioner agreed to my proposed concession. *Id.* at 393-94.

[14] Dr. Byers's report does state, however, that she relies in part on Dr. Chen's proposal that certain vaccines, including the meningococcal vaccine, are associated with TM. Byers Rep. at 5.

Clinical Investigation, 115(10):2731-41 (2005), filed as Ex. 30, Tab 12 (ECF No. 104-1) ("Kaplin"). Here, Dr. Byers proposed that "autoreactive antigen specific T cells" were produced outside the central nervous system ("CNS"), but then "homed in" to the CNS and caused production of the IL-6 cytokines sufficient to promote a demyelinating process leading to TM. Byers Rep. at 7; Tr. at 101.

At the outset, Dr. Byers made a significant concession relevant to her theory. She unequivocally agreed that molecular mimicry[15] was not a plausible biologic mechanism at work herein, admitting that she could not identify sufficient homology between antigens from components of the vaccines Ms. Bender received and self-protein structures. Byers Rep. at 7; Tr. at 47 ("I excluded molecular mimicry, because there is no evidence that there is molecular mimicry between the two vaccines and the association with autoimmune reactions"). But Dr. Byers disputed that autoimmunity can *only* be the result of cross-reactivity, mediated by B cells and encouraged by "shared epitopes" (i.e. via molecular mimicry). Byers Rep. at 6. Instead, she maintained that "more recent studies" demonstrated that autoimmunity can be driven by cytokines, which stimulate T and B cells even if an initial cross-reaction due to an autoimmune attack has not occurred. *Id.* at 6. Vaccines, Dr. Byers reasoned, must "provoke protective immune reactions" if they are to have any effectiveness at all. Byers Rep. at 6; Tr. at 94-95. Accordingly, the potency of vaccines generally is enough to cause a pathogenic autoimmune reaction in "an appropriately susceptible host." Byers Rep. at 6; *see also* Tr. at 160 ("I am saying that any vaccine that is immunogenic enough to be approved by the FDA has the ability to cause an autoimmune disease").

In Dr. Byers's view, several immune mechanisms other than direct molecular mimicry could have been involved in the pathogenesis of Ms. Bender's TM. Tr. at 47. First, she discussed the concept of "bystander activation." Tr. at 49-50, 53-54, 59. Dr. Byers defined bystander activation (or what she also termed "polyclonal activation") to occur when "you have cytokines that are released by either an infection or a vaccination which not only activates [the] antigen-specific immune system, but also activates other reactive cells as well, so they . . . can go after their true target, which is actually autologous self-antigens." *Id.* at 53.

To support bystander activation as a plausible mechanism, Dr. Byers pointed to studies suggesting that inflammation caused by receipt of a vaccination can provoke an autoimmune response by releasing cytokines that activate T and B cells that, while usually dormant, attack self after being stimulated by cytokines. *Id.* at 49, 54; K. Murali-Krishna, *et al.*, *Counting Antigen-Specific CD8 T Cells: A Reevaluation of Bystander Activation During Viral Infection*, Immunity, 177–87 (1998), filed as Exhibit 30, Tab 18 (ECF No. 104-1) ("Murali-Krishna"). Murali-Krishna, however, involved wild virus infections rather than vaccination, and Dr. Byers did not offer any medical literature directly involving the propensity of the Hep A or meningococcal vaccines to

[15] Molecular mimicry "simply means that the 3D structure of the antigen that is presented on the surface of the macrophage generates an immune response which cross-reacts with some of the body's own components and therefore it triggers an autoimmune reaction." Tr. at 47.

cause the kind of cytokine-driven inflammatory response that she was proposing could become pathogenic via this mechanism . She nevertheless maintained that because Menactra (the form of meningococcal vaccine at issue) contains a diphtheria toxoid component to increase its "immunogenicity," it would inherently provoke a sufficiently strong immune response to have the effect theorized. Tr. at 153-54.[16]

The other mechanism proposed by Dr. Byers was epitope spreading, defining it as occurring "when the primary antigen [from a vaccine] that is being presented [to the immune system] does not have – cannot find its perfect specific T cells to wipe out, and so therefore more and more cells of less specificity are allowed into the – into the mix." Tr. at 52. Yet (and even though she had already conceded that she could not identify sufficient homology involving the meningococcal vaccine to propose molecular mimicry in this case), Dr. Byers characterized epitope spreading as a kind of molecular mimicry unique to susceptible individuals who cannot muster a proper focused immunologic response to vaccine antigens, resulting in an autoimmune attack instead. Tr. at 52 ("it's just molecular mimicry on a very individual basis"), 53, 60-61 ("in the case of epitope spreading, those highly specific cells that could very rapidly eliminate the infection would not be there, primarily on a genetic basis").

Dr. Byers also offered more general evidence that she purported demonstrated an association between different vaccines and TM. Consistent with arguments first made by Dr. Chen (and as discussed below), she observed that the package insert included with the meningococcal vaccine received by Ms. Bender allowed for the possibility that TM could occur after receipt of the vaccine, and that this constituted some recognition by the vaccine manufacturer that the risk was real. Byers Rep. at 5; Tr. at 89-90 ("the package insert is approved by both the company, it's proposed by the company, and every year, it's re-reviewed by the FDA"). She also referenced the Vaccine Adverse Events Reporting System (VAERS), noting that it recorded instances in which a person receiving the Hep A or meningococcal vaccine reported developing TM thereafter. Byers Rep. at 5; Tr. at 80-81, 89-90, 127 (averring that VAERS reports are somewhat reliable proof of a vaccine's potential harm).[17]

Besides defending the causal role Ms. Bender's vaccines could have played in developing her TM, Dr. Byers argued that the timeframe in which Ms. Bender experienced her first TM symptoms post-vaccination was medically appropriate, despite the fact (as she acknowledged) that Ms. Bender's medical records revealed "no symptoms of any kind of an inflammation until the sudden onset of day 41 or 42 of the [TM]." Tr. at 102. In support, she referred to an article that considered several instances of wide time intervals between onset of TM and a variety of vaccines.

[16] Respondent's immunologist expert, Dr. Forsthuber, agreed that the diphtheria toxoid was included in the vaccine for this purpose (although he did not accept the broader point that the meningococcal vaccine can have the alleged pathogenic effect simply because it contains diphtheria toxoid). Forsthuber Rep. at 5.

[17] VAERS is a national vaccine safety surveillance program co-sponsored by the Centers for Disease Control and Prevention and the Food and Drug Administration, and allows individuals who believe they may have experienced a vaccine reaction to make a report of the incident. *See* https://vaers.hhs.gov/index (last visited August 16, 2017).

Tr. at 77; N. Agmon-Levin, *et al.*, *Transverse Myelitis and Vaccines: A Multi-Analysis*, Lupus 18:1198-1204 (2009), filed as Ex. 30, Tab 1 (ECF No. 104-1) ("Agmon-Levin"). The Agmon-Levin article contained a chart based on case reports of 37 instances of post-vaccination TM, indicating the temporal period between vaccination and onset. Agmon-Levin at 1200. Dr. Byers expressly reproduced the chart in her expert report and discussed it in her trial testimony, noting that for the cases discussed (none of which involved either of the vaccines in question), timing of onset ranged from four days to 27 weeks. Byers Rep. at 4; Tr. at 77.

Based on Agmon-Levin as well as her own expertise, Dr. Byers proposed that four weeks, or 28 days, would typically be the longest period in which she would expect an immune process to result in TM. Byers Rep. at 7. Here, as Dr. Byers conceded, 42 days was somewhat longer than she would expect, but maintained that it did not preclude the possibility that Ms. Bender's TM was vaccine-caused. Tr. at 77. In so doing, she emphasized that she would not place an upper limit on the amount of time that could pass between vaccination and TM, making the representation that (to her knowledge) no Vaccine Program decision had ever held that there was a temporal cut-off when determining if a vaccine had caused injury. *Id.* at 102-03 ("I'm not positive that the vaccine court has to worry about all of this stuff, because there has never been an upper boundary for development of an autoimmune disease"), 149.

Dr. Byers's testimony also touched upon the issue of the false lab result regarding Ms. Bender's IgM levels. She noted that the data from these results plainly revealed a discrepancy between the low IgM titers measured in Ms. Bender's cerebral spinal fluid ("CSF"), and the characterization of those results as high. Tr. at 46, 56-58. In order to double-check the result, Dr. Byers called the lab that had performed the CSF study, and obtained their confirmation that the positive indicator was in error. *Id*. Dr. Byers described the significance of this finding, stating that had the IgM been positive, it would have indicated the existence of a prior recent infection that is known to be linked to TM. Tr. at 62. Thus, the absence of such evidence increased the likelihood that Ms. Bender's TM did not originate in infection. *Id.*

At the same time, Dr. Byers gave little weight to the implications of the positive IgG antibodies screen. She referenced several studies that showed that 70 percent of all young people were positive for IgG, which was usually linked back to a long-resolved infection, the evidence of which could stay in the body for years - thereby diminishing the possibility that some other prior infection had occurred close enough in time to have caused Ms. Bender's TM. Tr. at 64, 70. Indeed, Dr. Byers stressed her overall view that because no other immediate possible explanation existed for Ms. Bender's TM, the only logical conclusion was that it was caused by the vaccines she had received approximately six weeks before. *Id.* at 138.

2. Dr. Chone Ken Chen

Petitioner's second expert was a pediatric neurologist, Dr. Chone Ken Chen. Dr. Chen submitted two expert reports in this case and testified at hearing. *See* First Report, dated Aug. 28, 2014, filed as Ex. 25 ("Chen Rep."); Responsive Rep., dated June 5, 2015, filed on February 10, 2016 as Ex. 23 ("Chen Responsive Rep.")[18]; Tr. at 163-236.

Dr. Chen obtained his bachelor's degree and medical degree from Boston University. Chen CV, filed as Ex. 24 (ECF No. 96); Tr. at 164-66. He completed a residency and internship in Pediatrics at Mount Sinai Medical Center in Manhattan and Queens, New York, followed by a residency and fellowship in neurology at New York University in Manhattan, New York. Chen CV at 2. Throughout his career, Dr. Chen has worked in various hospitals in the areas of adult and pediatric neurology, but is currently a pediatric neurologist with the Department of Pediatrics at New York University Downtown Hospital in Manhattan, New York. *Id*. at 1. In that role, Dr. Chen sees many patients, estimating that over his career he has treated hundreds of children and adults with neurological injuries. Chen Rep. at 1. Respondent pointed to an occasion when Dr. Chen's testimony was excluded, but it was not in the context of a vaccine case. Tr. at 200.

In his initial report, Dr. Chen reviewed Ms. Bender's medical records from the time of her initial presentation to KRMC, admitting that she was "asymptomatic of any respiratory or neurological disorders" for 40 days after vaccination. Chen Rep. at 2. He thereafter noted there was scientific support linking certain vaccines to autoimmune and/or demyelinating conditions, and that the manufacturer of the meningococcal vaccine Petitioner received had acknowledged in the relevant package inserts that it could be related to TM. *Id.* at 5, Ex. 25, Tab 22. He proposed that interaction of "multiple vaccine components" that Ms. Bender received in May 2009 was to blame for her TM. Chen Rep. at 6-8. He also suggested that in his reading of the medical records, because there was a "total lack of clinical change" in Petitioner's condition after her initial presentation, the autoimmune process that had resulted in her TM likely began "one to two weeks prior" to her collapse upon leaving the tour bus. *Id.* at 9.

Dr. Chen's 46-page supplemental report was designated as responsive to Respondent's initial expert report from Dr. Timothy Lotze (discussed below). In reacting to Dr. Lotze's review of Ms. Bender's medical history, Dr. Chen stressed that the progressive evolution of lesions on Petitioner's spinal cord (as revealed in the MRIs performed in July 2009 and thereafter) suggested to him that the autoimmune processes that produced those lesions had to have begun before she first sought medical intervention on July 10th – and therefore her onset was likely closer in time to the vaccinations at issue than 42 days. Chen Responsive Rep. at 4-6. He reached this conclusion

[18] Dr. Chen's responsive report was originally filed within a compilation of exhibits and documents submitted by compact disc on August 17, 2015, but subsequently refiled after current counsel's appearance in the case.

despite the total lack of symptoms prior to the falling-down incident that impelled Petitioner to seek treatment. *Id.* at 9.[19] In his view, the initial lesions observed by MRI in July 2009 were "already quite advanced in development," meaning that the process resulting in her TM likely began far earlier. *Id.* at 11.

Beyond the above, Dr. Chen's second report simply expanded (at far greater length) on the same points made in his first – *i.e.,* that the package inserts and marketing materials associated with the meningococcal and Hep A vaccines all disclose TM as a possible reaction (Chen Responsive Rep. at 16-21), and that other vaccines have a similar capacity to cause the same injury (*Id.* at 23-36).[20]

At hearing, Dr. Chen performed a narrative review of Ms. Bender's medical records, attempting to exclude a variety of other possible causes for her TM. Tr. at 186-88. He discussed in detail each of Ms. Bender's negative test results, opining (consistent with Dr. Byers) that because there were no signs of an ongoing infection between the date of her vaccination and onset, the vaccine could be assumed by process of elimination to have caused her TM. *Id.* at 185.

In addition, Dr. Chen reiterated his report's point that after initial evaluation at KRMC, Ms. Bender's TM remained static in terms of severity and development. Tr. at 192. This lack of disease progression indicated to Dr. Chen that the autoimmune process affecting Ms. Bender had to have begun in the days before her admission to the hospital— thus, in his view, shrinking the timeframe between vaccination and onset. *Id.*; First Chen Rep. at 9. He deemed this as possibly meaning that Petitioner "met the 30-day requirement" for presumption under the Vaccine Act, although it is not clear to which portion of the Act he was intending to refer in so proposing. *Id.*[21]

[19] Dr. Chen's responsive report referenced the nonexistent "30-day (statutory) requirement for qualification of presumption of vaccine causation" discussed below. *See* Chen Responsive Rep. at 10.

[20] Dr. Chen also attempted to rebut Dr. Lotze's assertions that the Institute of Medicine ("IOM") had not found sufficient evidence with respect to the vaccines in question to deem them associated with TM, arguing that Dr. Lotze had misinterpreted the language used by the IOM. Chen Responsive Rep. at 12-13. I accept this evidence, and note that IOM evidence is often given credence in the Program. *Garner v. Sec'y of Health & Human Servs.,* No. 15-063, 2017 WL 1713184 (Fed. Cl. Spec. Mstr. Mar. 24, 2017). However, I do not find in this case that this particular kind of evidence is notably probative either way. I also note that *neither* Drs. Lotze nor Chen have immunological expertise – and because both parties have offered qualified immunologists, I have given testimony from non-immunologists on such matters significantly less weight.

[21] It may be that Dr. Chen was advancing the argument that the claim herein is akin to a Table Claim, for which causation is presumed when sufficient evidence is adduced to meet the requirements of particular claims. But TM is *not* included in the injuries specified for either of the vaccines in question – or *any* other vaccine for that matter. In addition (and ignoring for the moment Dr. Byers's incorrect statements that there is effectively no temporal limit for a Program claim to the timeframe between onset and vaccination), there is no requirement - whether set forth in the Act or the decisions of any special master or controlling federal court ruling reviewing such decisions – that a vaccine injury claim establish onset within 30 days of receipt of the vaccine at issue.

Although Dr. Chen mostly attempted to provide an explanation on the course of Ms. Bender's TM, he also proposed an opinion regarding causation (a topic he was somewhat less qualified to opine upon than Dr. Byers). *See generally* Tr. at 200-25. In support, he referenced evidence from VAERS, which he proposed indicated that vaccines akin to what Petitioner had received could result in TM. Chen Rep. at 6; Tr. at 217-18. He also pointed out (consistent with Dr. Byers's arguments) that the package inserts included with the relevant vaccines by their manufacturers acknowledge the possibility of TM as a side effect. *See generally*, Chen Rep. at 8; Chen Responsive Rep. at 23-36; Tr. at 205-06.

C. *Respondent's Experts*

1. Dr. Timothy Lotze

The first of Respondent's experts to testify was Dr. Timothy Lotze, a pediatric neurologist, who submitted a single written report. Report, dated Feb. 12, 2015, filed as Ex. A (ECF No. 67) ("Lotze Rep."); Tr. 238-76.

Dr. Lotze obtained his bachelor's degree from Texas A&M University in College Station, Texas, followed by his medical degree at the University of Texas, San Antonio. Lotze CV, filed as Ex. B (ECF No. 67). Thereafter, he completed two residencies and an internship at The Ohio State University, in Columbus, Ohio, finishing his education with a residency in Child Neurology at Baylor College of Medicine in Waco, Texas. *Id*. at 1. He was then hired as a faculty member at the Baylor College of Medicine, where he is currently employed. *Id*. Through his current role with the College, he treats children, with a special focus on multiple sclerosis and muscular dystrophy. Tr. at 239. Dr. Lotze estimated that he has seen around 150 children with TM. *Id*.

Although Dr. Lotze acknowledged that he lacked specific training or expertise in immunologic matters, he opined that Ms. Bender's TM was not related to either of the vaccinations she received. Tr. at 242. After reviewing all of Ms. Bender's medical records, Dr. Lotze concluded that her TM was instead more likely than not idiopathic. *Id*. He admitted that the IgM reading relied upon initially by treaters was incorrect, but stated that it was still not possible to conclude whether or not Ms. Bender's TM was connected with a prior mycoplasma infection, as the testing for the titers was never performed again in her treatment. Lotze Rep. at 4. Otherwise, Dr. Lotze could not identify a cause of Ms. Bender's TM, nor was he aware of any association between TM and vaccination set forth in any medical or scientific literature. *Id*. In his understanding, because TM is considered to be an autoimmune process, it needs an environmental trigger to cause the inflammation leading to the condition. Tr. at 246. He stated that he would expect a reaction to this trigger within three weeks – sooner than what Ms. Bender experienced. *Id*. at 251.

Dr. Lotze also took issue with Dr. Chen's proposal that the progression of lesions observed from MRIs performed between July 10 and 14, 2009, suggested some kind of subclinical onset occurring before July 9th. On the contrary - Dr. Lotze maintained that the rather significant progression from the time of the first to the second MRI was actually good evidence of how acute and recent the onset of TM was – not that it had to have been ongoing for some time, especially with the absence of other neurologic symptoms pre-dating her acute loss of below-waist sensation on July 9, 2009. Lotze Rep. at 3. In Dr. Lotze's view, onset of TM would not likely occur longer than three to four weeks after an infectious exposure, making a 42-day time interval too long to implicate the vaccines Ms. Bender had received in causing her TM. Tr. at 250-51.

Dr. Lotze rejected Petitioner's contention that the Agmon-Levin article was persuasive evidence of vaccine causation. Tr. at 253. That article, he testified, listed case reports of incidences of TM after vaccination, but he opined that there were other, more likely, explanations for the associations found in the article. *Id*. at 254. For example, one of the case reports Agmon-Levin considered was from a child with an ongoing autoimmune condition *known* to produce TM. *Id*. Another report was from a patient who had received the oral polio vaccine - a live vaccine known to have the potential to cause poliomyelitis, the kind of direct infection that could in turn cause TM. *Id*. at 254-55. These case studies therefore were distinguishable, and did not provide reliable baselines for determining the timeframe for post-vaccination TM.

2. Dr. Thomas Forsthuber

Respondent's second expert was Dr. Thomas Forsthuber, an immunologist. Dr. Forsthuber provided testimony at hearing and produced one expert report in the case. *See* Report, dated Jan. 19, 2017, filed as Ex. C ("Forsthuber Rep."); Tr. at 277-361.

Dr. Forsthuber received his medical degree from the University of Tübingen in Germany and then completed a post-doctoral fellowship in immunology at the University of California, Los Angeles. Tr. at 277; Forsthuber CV, filed as Exhibit D (ECF No. 115). He completed an additional post-doctoral fellowship at Case Western University in Cleveland, Ohio. Forsthuber CV at 2; Tr. at 278. He became a member of the faculty at the University of Texas, San Antonio, and began performing research in immunology and now runs a research lab that does T cell biology work and B cell immunology. *Id*. In addition, Dr. Forsthuber has published over 75 publications (reviews and book chapters) in the areas of T cell immunology and autoimmune diseases. Forsthuber Rep. at 1.

Dr. Forsthuber opined that the vaccines Ms. Bender received played no causal role in the development of her TM. Tr. at 280. He noted (as had Dr. Lotze) that he could identify no literature associating either the meningococcal or Hep A vaccines with TM. Forsthuber Rep. at 5. But his report and testimony particularly took issue with the proposed immunological mechanisms

suggested by Dr. Byers—bystander activation and epitope spreading – arguing that neither was supported by sufficient medical or scientific evidence to provide reliable explanations for how TM could occur after the relevant vaccinations.[22]

First, Dr. Forsthuber discussed whether bystander activation could explain the process by which Ms. Bender developed TM. To do so, he relied on his direct research experience regarding T cells, especially in light of technological advances permitting better understanding of the function of T cells in the immunologic process. Tr. at 286. As Dr. Forsthuber proposed, the researchers first responsible for the theory of bystander activation had been forced to rely on imprecise detection methods, thereby misleading them into believing that nonspecific T cells present at an inflammation site were nevertheless being activated in large numbers and thereby contributing to the ongoing inflammatory process. *Id*. at 284. But more up-to-date technological detection methodologies (in particular, "tetramer staining"[23]) had convinced researchers that "the majority of T cells in an infection are specific for the antigen," meaning that "bystander activation is occurring to a degree, but to a lesser degree." *Id*. at 287; 284-86. Thus, given Dr. Byers's admission that she could not identify homology between any components of the vaccines Ms. Bender had received and self-antigens (and therefore could not offer molecular mimicry as a causative mechanism in this case), the entire concept of bystander activation as possibly explaining the pathogenesis of TM was lacking a key component. Some specific level of T cell activation *caused* by molecular mimicry at the outset of an alleged autoimmune process was required for bystander activation to even occur. *Id*. at 355.[24]

Dr. Forsthuber was also critical of the scientific support offered by Petitioner and her experts regarding bystander activation as a possible autoimmune mechanism. Referencing Dr. Byers's cited article, Murali-Krishna, Dr. Forsthuber noted that in fact the article *confirmed* that the primary antigens responsible for inducing autoimmune responses were highly specific in their targets, undermining the notion that nonspecific immune cells could initiate the same response on their own. Forsthuber Rep. at 16-17; Tr. at 289. Indeed, Murali-Krishna determined that infection mainly impacted the number of specific T cells as opposed to bystanders, meaning bystander

[22] Besides addressing Dr. Byers's contentions, part of Dr. Forsthuber's report was devoted to rebutting several of Dr. Chen's points about causation. *See, e.g.*, Forsthuber Rep. at 6 (attacking Dr. Chen's contention that receipt of multiple vaccines at once could enhance their pathogenic impact). I do not address these aspects of Dr. Forsthuber's opinion at length, however – both because they were largely not raised at hearing, but also because it is the contentions of Petitioner's immunologist expert, Dr. Byers, that form the core of Petitioner's causal theory (and are therefore far more credible than unsupported speculation regarding causality by Dr. Chen).

[23] Tetramer staining involves "a reagent that highly specifically recognized a T cell that is specific for a particular virus…[i]t is really a peptide that these T cells would recognize, and then they have a soluble image C molecule that this peptide is clued into, and then they attach a color to this and now you have a molecule that's very sensitive and recognized not all the T cells, but specifically T cells, for example, that would recognize influenza." Tr. at 285.

[24] In addition, Dr. Forsthuber noted that bystander activation is known to occur most efficiently with CD8 positive T cells - but autoimmune conditions such as TM are posited to be caused by CD4 positive T cells, thus further reducing the likelihood that bystander activation was applicable to this case. Tr. at 288.

activation may be occurring but to a lesser degree – the opposite of Dr. Byers's contention. Forsthuber Rep. at 16; Tr. at 287; Murali-Krishna at 185 ("this study provides definitive evidence that the majority of CD8 T cells responding to a viral infection are antigen-specific"). Thus, although Murali-Krishna observed that nonspecific T cells did aid in destroying other cells in an autoimmune process, they did so only *after* being re-stimulated by an initial infectious virus – thus again underscoring the need for an initial cross-reactive process to have already begun, via molecular mimicry. Tr. at 293.

In response to Dr. Byers's second proposed causal mechanism, epitope spreading, Dr. Forsthuber pointed out he was well qualified to opine on the topic, as he was one of the researchers responsible for initial evaluation of the concept and a co-author of an early article on it. Tr. at 300, *citing* P.V. Lehman, *et al., Spreading of T-Cell Autoimmunity to Cryptic Determinants of an Autoantigen,* 358 Nature 155-57 (July 1992) (Dr. Forsthuber identified as one of three authors). As he described it, epitope spreading occurs when autoimmunity is initiated by a specific set of T cells, those cells precipitate inflammation in a tissue, and the inflammatory process in turn causes the release of additional antigens in that location, ultimately causing a new set of autoimmune T cells to activate, go to the tissue/site of ongoing inflammation, and cause further damage. *Id*. at 302; Forsthuber Rep. at 20. It was accordingly a "continuation" of an already-underway autoimmune process – not its initiation. Tr. at 303.

Dr. Byers's characterization of the concept of epitope spreading, by contrast, was in Dr. Forsthuber's view nothing more than a description of molecular mimicry. Tr. at 303. But because Dr. Byers had already conceded that she could not provide an antigen-specific mechanism to explain TM's alleged vaccine-induced pathogenesis herein, epitope spreading failed as an alternative explanatory mechanism for Ms. Bender's TM because it inherently relied on a molecular mimicry process occurring *first*. *Id.* at 357.

Dr. Forsthuber also challenged Petitioner's overarching theory that cytokines like IL-6 inherently induced by vaccination were central to the pathogenesis of her TM. While he admitted that such cytokines likely did play a role in TM's development or exacerbation, he disagreed that they alone were sufficient to initiate a process resulting in TM. *Id.* at 309. Dr. Forsthuber also rejected Dr. Byers's reliance on Kaplin for such points. Forsthuber Rep. at 17. In his view, Kaplin showed that the cytokine IL-6 was *not* able by itself to instigate a pathologic process leading to TM, and therefore could not be identified as a mechanism of bystander activation, even if vaccination could cause upregulation of such cytokines. *Id.*

At bottom, the question this aspect of Petitioner's theory posed was whether IL-6 (or any cytokines for that matter) could be considered a cause of an autoimmune pathologic process or an "effector mechanism" responsive to T cell action, with Dr. Forsthuber favoring the latter explanation. He maintained that reliable scientific literature more credibly suggested that

autoimmune processes were "antigen-specific," and that any cytokine release subsequently associated with inflammation would be "transient, of low titer, and [would] rarely progress to autoimmune diseases" not already instigated by a direct viral attack. Forsthuber Rep. at 16.

Dr. Forsthuber's testimony also referenced[25] a recent epidemiologic study involving the propensity of a number of vaccines to cause TM - R. Baxter, et al., *Acute Demyelinating Events Following Vaccines: A Case-Centered Analysis*, 63 Clinical Infectious Diseases 1456-61 (2016), filed as Ex. C, Tab 4 (ECF No. 114-5)("Baxter"), Tr. at 321-22.[26] In Baxter, researchers considered all cases of TM (as well as acute disseminated encephalomyelitis ("ADEM")) in the United States that were recorded to have occurred after administration of nearly 64 million vaccine doses, including over 3.4 million Hep A doses and 1.5 million meningococcal vaccine doses comparable or identical to Menactra. Baxter at 1457. This study was case-centered, meaning it compared vaccination of each studied case to vaccination of all matched persons in the study population, looking at two specific exposure intervals of 28 and 42 days after vaccination. *Id*. at 1456. No statistically significant heightened risk of TM could be seen in either 5-28 days following vaccination (as compared to the nine months after), or the longer 2-42 day time period. Dr. Forsthuber admitted that Baxter was not a "randomized study," and therefore could not be cited as definite proof that the vaccines relevant herein could never be associated with TM in the studied time periods, but he otherwise expressed the view that it was reliable and relevant evidence. Tr. at 350-52.

With respect to possible alternative causes, Dr. Forsthuber emphasized Ms. Bender's initial CBC results, which (given the elevated white blood cell counts and decreased lymphocytes) suggested to him some concurrent infectious process could have been to blame for her TM, despite the fact that no other evidence of infectious disease was found. Forsthuber Rep. at 2; Tr. at 329.[27] In so arguing, Dr. Forsthuber maintained that (contrary to Dr. Chen's argument that Ms. Bender's demyelination process had to have been underway for some time prior to her first clinical

[25] I take note of the fact that Dr. Forsthuber is not a statistician or epidemiologist, and therefore his testimony about the reliability of Baxter must be weighed against his lack of specific expertise on such topics. At the same time, however, I note that *no* experts who testified in this matter possessed that kind of specialized knowledge – putting all of them on a level playing field, so to speak, when it came to opining as to the reliability of epidemiologic evidence. In any event, Respondent was free to submit any evidence he felt relevant to Petitioner's claim, including Baxter, and I have duly considered it (although, as with any item of medical or scientific literature, it does not gain credence simply because an expert with different expertise testifies about it).

[26] Baxter was similarly, if briefly, mentioned by Dr. Lotze. *See, e.g.,* Tr. at 248-49.

[27] Dr. Forsthuber also accepted the fact that the reported high IgM titer reading was incorrect, but proposed that the positive IgG reading still allowed for the conclusion that Ms. Bender had experienced a mycoplasma infection closer in time to her initial onset than vaccination (since the short half-life of IgM did not preclude a mycoplasma infection in the two weeks after vaccination). Forsthuber Rep. at 12. This argument is intriguing, but ultimately speculative, absent other corroborative evidence of a prior infection close enough in time to Ms. Bender's initial symptoms to be associated.

manifestation of a neurologic symptom) such test results underscored the extent to which the unknown cause of Petitioner's TM likely occurred close in time to her presentation – not six weeks prior. Forsthuber Rep. at 9.

Finally, Dr. Forsthuber proposed three to four weeks to be a reasonable timeframe for onset of an autoimmune illness like TM. Forsthuber Rep. at 8; Tr. at 313. He based this on his own experience in evaluating the time it takes for an immune response from vaccination generally. *Id*. After the 30th day, however, he would expect the immune response to be dwindling greatly (and thus no longer possess a pathogenic capacity). In response to the Agmon-Levin article, which proposed a potentially longer timeframe for TM's development after several different vaccinations, Dr. Forsthuber (like Dr. Lotze) looked at the individual case examples that were relied upon to create the chart, but found reason in each case to question their scientific reliability (for example, because the subject of a case study had some identified cofactor that might have caused the TM, or because of misdiagnosis). *Id*. at 315-17. He also noted that Agmon-Levin did not involve the relevant vaccines herein. *Id.* at 317.

IV. Procedural Background

After initiating this action (originally assigned to former Special Master Hastings) in October 2011, Petitioner began filing medical records and securing an expert witness, a process that became slow, delaying the progression of the case. Nonetheless, Respondent filed his Rule 4(c) Report on July 25, 2012. For a year thereafter Petitioner looked for an expert but was ultimately unsuccessful. Eventually, Petitioner's attorney chose to withdraw from the case on February 2, 2014.[28] Thereafter, the case was reassigned to me and Petitioner became *pro se*.

After holding a status conference with Petitioner on June 30, 2014, I issued an order directing her to file an expert report in six months. *See* Scheduling Order dated July 1, 2014. Petitioner was able to file her expert report from Dr. Chen early, on September 2, 2014. Over the next year, Respondent filed his expert report from Dr. Lotze, Petitioner sought to retain an expert to provide a supplemental expert opinion, and the parties began informal settlement negotiations.

On December 22, 2015, Petitioner's current attorney entered an appearance in the case. Shortly thereafter, on January 13, 2016, the parties indicated in a joint status report that settlement was not likely to occur, and I scheduled a two-day entitlement hearing for February 9-10, 2017. *See* Joint Status Report, dated Jan. 13, 2016 (ECF No. 81); Prehearing Order, dated Mar. 22, 2016 (ECF No. 86). After the filing of additional expert reports referenced above and medical literature

[28] Former counsel expressed the desire to withdraw a year earlier, on February 3, 2013, but Petitioner's inability to obtain new counsel, a dispute in the request for interim attorney's fees and costs, and a stay in the case due to the 2013 government shutdown further delayed the case's progress.

from both parties, the hearing was held as scheduled. Post-hearing briefs were filed between the second half of April and end of June. This matter is now ripe for a decision.

V. Applicable Law

A. *Petitioner's Overall Burden in Vaccine Program Cases*

To receive compensation in the Vaccine Program, a petitioner must prove either: (1) that he suffered a "Table Injury" – *i.e.*, an injury falling within the Vaccine Injury Table – corresponding to one of the vaccinations in question within a statutorily prescribed period of time or, in the alternative, (2) that his illnesses were actually caused by a vaccine (a "Non-Table Injury"). *See* Sections 13(a)(1)(A), 11(c)(1), and 14(a), as amended by 42 C.F.R. § 100.3; § 11(c)(1)(C)(ii)(I); *see also Moberly v. Sec'y of Health & Human Servs.*, 592 F.3d 1315, 1321 (Fed. Cir. 2010); *Capizzano v. Sec'y of Health & Human Servs.*, 440 F.3d 1317, 1320 (Fed. Cir. 2006).[29] In this case, Petitioner does not assert a Table claim.

For both Table and Non-Table claims, Vaccine Program petitioners bear a "preponderance of the evidence" burden of proof. Section 13(1)(a). That is, a petitioner must offer evidence that leads the "trier of fact to believe that the existence of a fact is more probable than its nonexistence before [he] may find in favor of the party who has the burden to persuade the judge of the fact's existence." *Moberly*, 592 F.3d at 1322 n.2; *see also Snowbank Enter. v. United States*, 6 Cl. Ct. 476, 486 (1984) (mere conjecture or speculation is insufficient under a preponderance standard). Proof of medical certainty is not required. *Bunting v. Sec'y of Health & Human Servs.*, 931 F.2d 867, 873 (Fed. Cir. 1991). In particular, a petitioner must demonstrate that the vaccine was "not only [the] but-for cause of the injury but also a substantial factor in bringing about the injury." *Moberly*, 592 F.3d at 1321 (quoting *Shyface v. Sec'y of Health & Human Servs.*, 165 F.3d 1344, 1352-53 (Fed. Cir. 1999)); *Pafford v. Sec'y of Health & Human Servs*., 451 F.3d 1352, 1355 (Fed. Cir. 2006). A petitioner may not receive a Vaccine Program award based solely on his assertions; rather, the petition must be supported by either medical records or by the opinion of a competent physician. Section 13(a)(1).

In attempting to establish entitlement to a Vaccine Program award of compensation for a Non-Table claim, a petitioner must satisfy all three of the elements established by the Federal Circuit in *Althen v. Sec'y of Health & Human Servs.,* 418 F.3d 1274, 1278 (Fed. Cir. 2005): "(1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause

[29] Decisions of special masters (some of which I reference in this ruling) constitute persuasive but not binding authority. *Hanlon v. Sec'y of Health & Human Servs.*, 40 Fed. Cl. 625, 630 (1998). By contrast, Federal Circuit rulings concerning legal issues are binding on special masters. *Guillory v. Sec'y of Health & Human Servs.*, 59 Fed. Cl. 121, 124 (2003), *aff'd* 104 F. App'x 712 (Fed. Cir. 2004); *see also Spooner v. Sec'y of Health & Human Servs.*, No. 13-159V, 2014 WL 504728, at *7 n.12 (Fed. Cl. Spec. Mstr. Jan. 16, 2014).

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*, 418 F.3d at 1278.

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

Petitioners may satisfy the first *Althen* prong without resort to medical literature, epidemiological studies, demonstration of a specific mechanism, or a generally accepted medical theory. *Andreu v. Sec'y of Health & Human Servs.*, 569 F.3d 1367, 1378-79 (Fed. Cir. 2009) (citing *Capizzano*, 440 F.3d at 1325-26). Special masters, despite their expertise, are not empowered by statute to conclusively resolve what are essentially thorny scientific and medical questions, and thus scientific evidence offered to establish *Althen* prong one is viewed "not through the lens of the laboratorian, but instead from the vantage point of the Vaccine Act's preponderant evidence standard." *Id.* at 1380. Accordingly, special masters must take care not to increase the burden placed on petitioners in offering a scientific theory linking vaccine to injury. *Contreras v. Sec'y of Health & Human Servs.*, 121 Fed. Cl. 230, 245 (2015) ("[p]lausibility . . . in many cases *may* be enough to satisfy *Althen* prong one" (emphasis in original)), *vacated on other grounds*, 844 F.3d 1363 (Fed. Cir. 2017). But this does not negate or reduce a petitioner's ultimate burden to establish his overall entitlement to damages by preponderant evidence. *W.C. v. Sec'y of Health & Human Servs.*, 704 F.3d 1352, 1356 (Fed. Cir. 2013) (citations omitted).[30]

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

[30] Although decisions like *Contreras* suggest that the burden of proof required to satisfy the first *Althen* prong is less stringent than the other two, there is ample contrary authority for the more straightforward proposition that when considering the first prong, the same preponderance standard used overall is also applied when evaluating if a reliable and plausible causal theory has been established. *Broekelschen v. Sec'y of Health & Human Servs*., 618 F.3d 1339, 1350 (Fed. Cir. 2010).

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

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

B. *Law Governing Analysis of Fact Evidence*

The process for making determinations in Vaccine Program cases regarding factual issues begins with consideration of the medical records. Section 11(c)(2). The special master is required to consider "all [] relevant medical and scientific evidence contained in the record," including "any diagnosis, conclusion, medical judgment, or autopsy or coroner's report which is contained in the record regarding the nature, causation, and aggravation of the petitioner's illness, disability, injury, condition, or death," as well as the "results of any diagnostic or evaluative test which are contained in the record and the summaries and conclusions." Section 13(b)(1)(A). The special master is then

required to weigh the evidence presented, including contemporaneous medical records and testimony. *See Burns v. Sec'y of Health & Human Servs*., 3 F.3d 415, 417 (Fed. Cir. 1993) (it is within the special master's discretion to determine whether to afford greater weight to contemporaneous medical records than to other evidence, such as oral testimony surrounding the events in question that was given at a later date, provided that such determination is evidenced by a rational determination).

Medical records that are created contemporaneously with the events they describe are presumed to be accurate and "complete" (i.e., presenting all relevant information on a patient's health problems). *Cucuras*, 993 F.2d at 1528; *Doe/70 v. Sec'y of Health & Human Servs.*, 95 Fed. Cl. 598, 608 (2010) ("[g]iven the inconsistencies between petitioner's testimony and his contemporaneous medical records, the special master's decision to rely on petitioner's medical records was rational and consistent with applicable law"), *aff'd, Rickett v. Sec'y of Health & Human Servs*., 468 F. App'x 952 (Fed. Cir. 2011) (non-precedential opinion). This presumption is based on the linked propositions that (i) sick people visit medical professionals; (ii) sick people honestly report their health problems to those professionals; and (iii) medical professionals record what they are told or observe when examining their patients in as accurate a manner as possible, so that they are aware of enough relevant facts to make appropriate treatment decisions. *Sanchez v. Sec'y of Health & Human Servs.*, No. 11-685V, 2013 WL 1880825, at *2 (Fed. Cl. Spec. Mstr. Apr. 10, 2013); *Cucuras v. Sec'y of Health & Human Servs.*, 26 Cl. Ct. 537, 543 (1992), *aff'd*, 993 F.2d at 1525 (Fed. Cir. 1993) ("[i]t strains reason to conclude that petitioners would fail to accurately report the onset of their daughter's symptoms").

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

However, there are situations in which compelling oral testimony may be more persuasive than written records, such as where records are deemed to be incomplete or inaccurate. *Campbell v. Sec'y of Health & Human Servs*., 69 Fed. Cl. 775, 779 (2006) ("like any norm based upon common sense and experience, this rule should not be treated as an absolute and must yield where the factual predicates for its application are weak or lacking"); *Lowrie*, 2005 WL 6117475, at *19 ("[w]ritten records which are, themselves, inconsistent, should be accorded less deference than

those which are internally consistent") (quoting *Murphy*, 23 Cl. Ct. at 733)). Ultimately, a determination regarding a witness's credibility is needed when determining the weight that such testimony should be afforded. *Andreu*, 569 F.3d at 1379; *Bradley v. Sec'y of Health & Human Servs*., 991 F.2d 1570, 1575 (Fed. Cir. 1993).

When witness testimony is offered to overcome the presumption of accuracy afforded to contemporaneous medical records, such testimony must be "consistent, clear, cogent, and compelling." *Sanchez*, 2013 WL 1880825, at *3 (citing *Blutstein v. Sec'y of Health & Human Servs*., No. 90-2808V, 1998 WL 408611, at *5 (Fed. Cl. Spec. Mstr. June 30, 1998)). In determining the accuracy and completeness of medical records, the Court of Federal Claims has listed four possible explanations for inconsistencies between contemporaneously created medical records and later testimony: (1) a person's failure to recount to the medical professional everything that happened during the relevant time period; (2) the medical professional's failure to document everything reported to her or him; (3) a person's faulty recollection of the events when presenting testimony; or (4) a person's purposeful recounting of symptoms that did not exist. *La Londe v. Sec'y of Health & Human Servs*., 110 Fed. Cl. 184, 203-04 (2013), *aff'd*, 746 F.3d 1334 (Fed. Cir. 2014). In making a determination regarding whether to afford greater weight to contemporaneous medical records or other evidence, such as testimony at hearing, there must be evidence that this decision was the result of a rational determination. *Burns*, 3 F.3d at 417.

C. *Analysis of Expert Testimony*

Establishing a sound and reliable medical theory often requires a petitioner to present expert testimony in support of his claim. *Lampe v. Sec'y of Health & Human Servs*., 219 F.3d 1357, 1361 (Fed. Cir. 2000). Vaccine Program expert testimony is usually evaluated according to the factors for analyzing scientific reliability set forth in *Daubert v. Merrell Dow Pharm., Inc.*, 509 U.S. 579, 594-96 (1993). *See Cedillo v. Sec'y of Health & Human Servs.*, 617 F.3d 1328, 1339 (Fed. Cir. 2010) (citing *Terran v. Sec'y of Health & Human Servs.*, 195 F.3d 1302, 1316 (Fed. Cir. 1999). "The *Daubert* factors for analyzing the reliability of testimony are: (1) whether a theory or technique can be (and has been) tested; (2) whether the theory or technique has been subjected to peer review and publication; (3) whether there is a known or potential rate of error and whether there are standards for controlling the error; and (4) whether the theory or technique enjoys general acceptance within a relevant scientific community." *Terran*, 195 F.3d at 1316 n.2 (citing *Daubert*, 509 U.S. at 592-95).

The *Daubert* factors play a slightly different role in Vaccine Program cases than they do when applied in other federal judicial for a (such as the district courts). *Daubert* factors are usually employed by judges (in the performance of their evidentiary gatekeeper roles) to exclude evidence that is unreliable and/or could confuse a jury. In Vaccine Program cases, by contrast, these factors are used in the *weighing* of the reliability of scientific evidence proffered. *Davis v. Sec'y of Health*

& Human Servs., 94 Fed. Cl. 53, 66-67 (2010) ("uniquely in this Circuit, the *Daubert* factors have been employed also as an acceptable evidentiary-gauging tool with respect to persuasiveness of expert testimony already admitted"). The flexible use of the *Daubert* factors to evaluate the persuasiveness and reliability of expert testimony has routinely been upheld. *See, e.g.*, *Snyder*, 88 Fed. Cl. at 742-45. In this matter (as in numerous other Vaccine Program cases), *Daubert* has not been employed at the threshold, to determine what evidence should be admitted, but instead to determine whether expert testimony offered is reliable and/or persuasive.

Respondent frequently offers one or more experts of his own in order to rebut a petitioner's case. Where both sides offer expert testimony, a special master's decision may be "based on the credibility of the experts and the relative persuasiveness of their competing theories." *Broekelschen v. Sec'y of Health & Human Servs*., 618 F.3d 1339, 1347 (Fed. Cir. 2010) (citing *Lampe*, 219 F.3d at 1362). However, nothing requires the acceptance of an expert's conclusion "connected to existing data only by the *ipse dixit* of the expert," especially if "there is simply too great an analytical gap between the data and the opinion proffered." *Snyder*, 88 Fed. Cl. at 743 (quoting *Gen. Elec. Co. v. Joiner*, 522 U.S. 146 91997)); *see also Isaac v. Sec'y of Health & Human Servs*., No. 08-601V, 2012 WL 3609993, at *17 (Fed. Cl. Spec. Mstr. July 30, 2012), *mot. for review den'd*, 108 Fed. Cl. 743 (2013), *aff'd*, 540 Fed. App'x 999 (Fed. Cir. 2013) (citing *Cedillo*, 617 F.3d at 1339). Weighing the relative persuasiveness of competing expert testimony, based on a particular expert's credibility, is part of the overall reliability analysis to which special masters must subject expert testimony in Vaccine Program cases. *Moberly*, 592 F.3d at 1325-26 ("[a]ssessments as to the reliability of expert testimony often turn on credibility determinations"); *see also Porter v. Sec'y of Health & Human Servs*., 663 F.3d 1242, 1250 (Fed. Cir. 2011) ("this court has unambiguously explained that special masters are expected to consider the credibility of expert witnesses in evaluating petitions for compensation under the Vaccine Act").

D. *Consideration of Medical Literature*

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

ANALYSIS

I. Overview of TM

TM is an autoimmune inflammatory condition causing damage to the spinal cord, which can produce neurological deficits with sensory loss in the extremities. Tr. at 241. It is understood to be mediated by pathogens that cause demyelination. *See* Wolf VL, *et al., Pediatric Acute Transverse Myelitis Overview and Differential Diagnosis*, 27 J. of Child Neurology 11:1426-36 (2012), filed as Ex. A, Tab 1 (ECF No. 67). Acute TM is so characterized because of its abrupt onset of motor and autonomic dysfunction. *Id*. at 1426. Diagnosis of the condition typically comes after inflammation is revealed on a spinal MRI, as well as evidence of inflammation derived from CSF analysis. Tr. at 242.

In the Program, petitioners have successfully established that a number of different vaccines were causally connected to their subsequent development of TM. *Schmidt v. Sec'y of Health & Human Servs.*, No. 07-20V, 2009 WL 5196169 (Fed. Cl. Spec. Mstr. Dec. 17, 2009) (influenza vaccine and TM); *Hargrove v. Sec'y of Health & Human Servs.,* No. 05-0694, 2009 WL 1220986 (Fed. Cl. Spec. Mstr. Apr. 14, 2009) (Diphtheria-tetanus-acellular pertussis vaccine and TM); *Raymo v. Sec'y of Health & Human Servs.,* No. 11-0654V, 2014 WL 1092274 (Fed. Cl. Spec. Mstr. Feb. 24, 2014) (tetanus diphtheria-acellular-pertussis vaccine and TM). No such published decisions, however, involve the two vaccines at issue herein.[31]

II. Petitioner Has Not Carried Her Burden of Proof

I cannot conclude that Petitioner has carried her burden of proof by a preponderance of the evidence. While Petitioner makes a number of persuasive points rebutting Respondent's proposed alternative explanations for her illness, there is insufficient reliable evidence to support the conclusion that the two vaccines she received are *themselves* reasonable explanations for it.

A. *Althen* Prong One

Petitioner's general theory – that a vaccine could cause a demyelinating condition - is consistent with other successful causation theories frequently proposed in Program cases. *See, e.g., Schmidt,* 2009 WL 5196169. And other special masters have ruled that different vaccines can cause an autoimmune process resulting in TM. *Raymo, 2*014 WL 1092274, at *1. While these decisions

[31] I note that Special Master Abell ruled in favor a petitioner who claimed that she developed a peripheral neuropathic autoimmune illness, Guillain-Barré syndrome, featuring aspects of TM, about a month after receiving the meningococcal vaccine. *Whitener v. Sec'y of Health & Human Servs.,* No. 06-0411V, 2009 WL 3007380 (Fed. Cl. Spec. Mstr. Sept. 2, 2009).

do not bind me (and significantly for present purposes, involve different vaccines), I take note of them and their sound analyses.

Petitioner has also proposed mechanisms associated with different autoimmune processes, such as bystander activation. Petitioners need not establish a particular mechanism in order to prevail, but the mechanisms she proposes have often found favor in Vaccine Program cases. *Raymo, 2*014 WL 1092274, at *19-22. Were my decision governed solely by these prior determinations, and without evaluation of any other evidence, Petitioner would have presented a close case that Program precedent suggests would require a decision in her favor on this particular *Althen* prong. *Andreu,* 569 F.3d at 1378.

But there *is* other evidence that must also be factored into my determination. Petitioner's immunologic expert, Dr. Byers, conceded at the outset that the mechanism most frequently offered by Program petitioners to explain how a vaccine might precipitate an autoimmune condition like TM – molecular mimicry – is inapplicable in this case. This concession makes sense from a scientific standpoint, especially with regard to Menactra, a vaccine intended to combat a bacterial rather than viral infection, and the vaccine that Dr. Byers seemed to stress in enunciating her theory. In *Henderson v. Sec'y of Health & Human Servs.,* No. 09-616V, 2012 WL 5194060 (Fed. Cl. Spec. Mstr. Sept. 28, 2012), a claimant attempted to argue that the pneumococcal conjugate vaccine (similar in composition to the meningococcal vaccine[32]) could cause a neurologic injury (ADEM) via molecular mimicry, but that mechanism was rejected by the special master because the vaccine in question contained no proteins or amino acids that could possibly be homologous with like protein/amino acid sequences found in the human central nervous system. *Henderson,* 2012 WL 5194060, at *15. The meningococcal vaccine at issue similarly contains nothing that could potentially cross-react with a self-protein sequence sufficient to initiate an autoimmune process.

Petitioner attempts instead, via Dr. Byers's testimony, to propose two other possible mechanisms, thereby inviting my scrutiny in evaluating if she has been successful in her efforts.[33] But as Dr. Forsthuber persuasively established, the most reliable scientific and medical evidence supports the conclusion that if bystander activation or epitope spreading are to play any contributory role in the pathogenesis of an autoimmune condition like TM, there must *first* be an

[32] Menactra is a sterile solution of meningococcal polysaccharides conjugated to diphtheria toxoid. *Dorland's* at 2016.

[33] Even though it is well understood that a claimant need not establish a biological mechanism in order to meet his burden of proof with respect to the first *Althen* prong, where a claimant offers such evidence and makes it a centerpiece of her causation theory (especially in the absence of other kinds of evidence linking the relevant vaccine to the claimed injury), it is appropriate for the special master to weigh the evidence offered and determine if the claimant has successfully met her self-determined evidentiary goal. *W.C.,* 704 F.3d 1352. Petitioner did not offer any direct evidence associating either of the relevant vaccines to TM.

autoimmune response to a specific antigen presented by a vaccine component that tricks the immune system into that response – in other words, via the mechanism of *molecular mimicry* (absent evidence of a direct infectious process, which is absent herein). Indeed, Dr. Byers herself virtually admitted that either of her proposed mechanisms presupposes molecular mimicry having occurred first. *See, e.g.,* Tr. at 50. Thus, Petitioner's concession that she could not establish molecular mimicry does significant harm to her overall causation theory, since she cannot demonstrate the initiation of an autoimmune process in the first place that might *later* be encouraged by one of her proposed secondary mechanisms.

Petitioner otherwise attempted to argue that the immunologic stimulation that vaccinations generally provide (which inherently encourage cytokine production) could still result in an autoimmune demyelinating condition like TM. Thus, Petitioner's theory was rooted (as Dr. Byers forthrightly acknowledged) in the general proposition that virtually *any* vaccine could be pathogenic and result in TM. *See* Tr. at 160. But she has offered *nothing* in the form of reliable scientific or medical evidence that addresses the specific pathogenicity of the two vaccines in dispute, nor anything connecting *other* vaccines to TM based merely on their recognized pro-inflammatory capacities (as opposed to a cross-reactivity caused by a vaccine component – something Dr. Byers disavows occurred here). And the literature she relies upon does not reliably establish that cytokines *can* instigate an autoimmune process – as opposed to amplify an ongoing autoimmune condition.

The concept that vaccination can promote production of cytokines that have an inflammatory capacity is well-known – and is often pointed to by claimants in attempting to explain a vaccine's causal role in their illness. Sospedra, M., *et al*., *Immunology of Multiple Sclerosis*, Annual Review of Immunology, *23*(1), 683-747 (2005), filed as Ex. C, Tab 17 (ECF No. 114); *Godfrey v. Sec'y of Health & Human Servs.*, No. 10–565V, 2014 WL 3058353, at *19 (Fed. Cl. Spec. Mstr. June 11, 2014), *mot. for review granted on other grounds*, 2014 WL 7474332, (Fed. Cl. Dec. 2, 2014), *on remand*, 2015 WL 10710961 (Fed. Cl. Spec. Mstr. Oct. 27, 2015), *mot. for review den'd*, *slip op.* (Fed. Cl. May 25, 2016). But as I have previously ruled in other cases, claimants cannot transmute scientific evidence exploring how vaccines normally function in the immune system into a reliable and persuasive causation theory that *any* vaccine can be pathogenic without a more specific showing that applies to the circumstances at hand. *Olson v. Sec'y of Health & Human Servs.*, No. 13-439V, 2017 WL 3624085 (Fed. Cl. Spec. Mstr. July 14, 2017), *mot. for review docketed*, (Aug. 14, 2017). It is too far a leap from the valid science establishing what cytokines do generally, or the role they play in encouraging TM (once it has already been initiated by infection or some other trigger), to conclude they are causal of it. *Copenhaver v. Sec'y of Health & Human Servs.*, No. 13-1002V, 2016 WL 3456436 (Fed. Cl. Spec. Mstr. May 31, 2016), *mot. for rev. den'd,* 129 Fed. Cl. 176 (Oct. 5, 2016).

Petitioner's reliance on VAERS data or vaccine package inserts to help establish her causal theory is also greatly misplaced. Because it is a passive reporting system, VAERS database findings that individuals have complained of a supposed adverse effect from a particular vaccine cannot be reasonably interpreted to suggest causation. For this reason, special masters do not typically afford great weight to VAERS data in determining causation. *See Analla v. Sec'y of Health & Human Servs.*, 70 Fed. Cl. 552, 558 (2006) ("the Court [of Federal Claims] uniformly has upheld the Chief Special Master's concerns about the reliability of VAERS data") (*citations omitted*).

Similarly (and as I have previously observed in other cases), vaccine package inserts do not constitute causation evidence meriting significant weight. *Sullivan v. Sec'y of Health & Human Servs.*, No. 10-398, 2015 WL 1404957, at*20 (Fed. Cl. Spec. Mstr. Feb. 13, 2015)("[s]tatements contained in vaccine package inserts do not constitute reliable proof of causation, and cannot be deemed admissions that the vaccines in question have the capacity to harm a particular petitioner in a specific manner"); *see also Werderitsh v. Sec'y of Health & Human Servs.*, No. 99–319V, 2005 WL 3320041, at *8 (Fed. Cl. Spec. Mstr. Nov. 10, 2005) (quoting 21 C.F.R. § 600.80(l) as saying "[a] report or information submitted by a licensed manufacturer ... does not necessarily reflect a conclusion by the licensed manufacturer or FDA that the report or information constitutes an admission that the biological product caused or contributed to an adverse effect").

By contrast, I give *some* weight to the Baxter epidemiologic study offered by Respondent as suggesting no association between the relevant vaccines in this case and TM. Although it is unquestionably the case that Vaccine Program litigants need not offer epidemiologic evidence to prevail, special masters may take note of its existence and consider it when determining if a claimant has met his burden of proof. *Taylor v. Sec'y of Health & Human Servs.*, 108 Fed. Cl. 807, 819–21 (Fed. Cl. 2013) (special master did not err in considering epidemiological evidence); *Andreu*, 569 F.3d at 1379 (a special master may assess epidemiological evidence in "reaching an informed judgment as to whether a particular vaccination likely caused a particular injury").

Here, Respondent offered a very recent, scientifically-reliable retrospective case-centered study that suggests there is no statistically significant association between Menactra and/or Hep A and TM – whether the timeframe is within the 30 days that all experts herein seemed to agree was reasonable for an autoimmune reaction to occur, or the longer, 42-day period at issue. Baxter at 1457. While I take note of Petitioner's general argument that the fact that vaccine injuries are rare means that such epidemiologic evidence cannot conclusively refute a causation theory that is otherwise reliable and/or scientifically plausible, the existence of such evidence only undercuts the conclusion that the relevant vaccines could have caused Petitioner's TM. *Crutchfield v. Sec'y of Health & Human Servs.*, No. 09-0039V, 2014 WL 1665227, at *15 (Fed. Cl. Spec. Mstr. Apr. 7, 2014) ("[i]t is, in fact, *always* true that epidemiologic studies can *never* prove definitively that

Factor A *never* causes Condition B . . . [b]ut it is not the Respondent's burden in this case to prove that it is *impossible* that [the relevant vaccine] can cause [the alleged injury]").

All told, Petitioner's theory of causation relies too heavily on points general to the association between certain vaccines and autoimmune illnesses (more often than not mediated by the inapplicable mechanism of molecular mimicry), *without* offering reliable and persuasive evidence that the vaccines Ms. Bender actually received can cause the specific autoimmune disease she experienced. Her theory has not been established by a preponderance of the evidence.

B. *Althen* Prong Two

Petitioner's showing on the second, "did cause" prong founders in a different manner than her unsuccessful effort to satisfy the first. The evidentiary record largely supports Petitioner's challenges to Respondent's proposed alternative explanations for her TM. Thus, she has successfully established that the IgM levels relied upon by initial treaters as pointing to a mycoplasma infection as the cause of her TM were a false positive. Moreover, other than elevated white blood cell/lymphocyte levels observed by Respondent's experts as possibly suggesting a post-vaccine infectious process, the record contains no other clues as to other alternative causes for her condition.

However, it is virtually black-letter law in the Vaccine Program that evidence of the development of a disease temporally following a vaccination is insufficient on its own to establish causation. *Grant v. Sec'y of Health & Human Servs.*, 956 F.2d 1144, 1148 (Fed. Cir. 1992). Accordingly, merely identifying the vaccine as causal because of its existence as a known, pre-onset occurrence is insufficient to establish causation without corroborative record proof demonstrating the "logical sequence of cause and effect" required. *Id*. As noted above, a wide variety of indirect and circumstantial evidence can support that determination, whether in the form of test results or witness testimony as to an injured party's state at the relevant time.

Such evidence is lacking in this case. Petitioner cannot point to anything in the 42-day period prior to her first symptom that would suggest that a vaccine-caused autoimmune and inflammatory process was in fact underway. She cannot identify record evidence from the time of her treatment – a test result, for example – that would give circumstantial support to her theory. No medical test results shed light on the matter (besides confirming her TM once she sought treatment). And there is no evidence that any treaters (including TM specialists like Dr. Kerr) suspected that the vaccines played any role in her TM (although the existence of the vaccinations was made known at the outset of her treatment). *See, e.g.*, Ex. 15 at 89. The mere fact of injury following vaccination is all that remains, but is not enough of a basis for establishing the "did

cause" *Althen* prong under the circumstances, even in the absence of persuasive alternative explanations.[34]

I also do not find persuasive Petitioner's conclusory suggestions that she was idiosyncratically "susceptible" to an autoimmune attack, thereby rendering the expected immunogenicity of the meningococcal and Hep A vaccines toxic for her. Petitioner did not establish any proof of such susceptibility. It is otherwise circular reasoning to propose that because vaccine injuries are rare, and because a claimant allegedly experienced a post-vaccination injury, that the individual must have somehow been susceptible even if the nature of that susceptibility has not been identified or demonstrated. Even the relaxed evidentiary standards of the Vaccine Program require more than such an assumption, and yet that appears to be the basis for much of Dr. Byers's opinion. *See, e.g.*, Tr. at 76.

My analysis of the sufficiency of Petitioner's prong two showing is also informed by the unpersuasive quality of Dr. Chen's opinion and testimony. Although Dr. Chen's explanation of the medical records had some utility, overall I did not find his testimony (which was conclusory and presented in a confusing manner) helpful to Petitioner in establishing her burden of proof. Dr. Chen also advanced opinions about matters not presently before me that diminished his credibility – for example, the wholly-discredited concept in the Vaccine Program that vaccines cause autism. *See, e.g.*, Chen Rep. at 8-9; Tr. at 225-28. Although my misgivings about the persuasive character of Dr. Chen's opinion are tertiary to my previously-discussed analysis on the substantive merits of Petitioner's claim, they nevertheless are reasonably factored into my ultimate determination. *Porter*, 663 F.3d 1242 at 1250.

Given the above, the evidence best supports the conclusion that Petitioner's TM was idiopathic in origin, as opposed to vaccine-caused.

3. *Althen* Prong Three

Petitioner's evidence supporting the medical acceptability of the 42-day period between vaccination and onset of her TM came largely from Dr. Byers, who in turn relied on some literature (primarily Agmon-Levin) as well as her own opinions based on her individual expertise. With respect to the former, however, Dr. Forsthuber persuasively established that Agmon-Levin (which does not even address either of the two vaccines at issue) was based on individual case reports that careful scrutiny revealed proved far less than contended, and thus lacked sufficient medical reliability to offer reliable timeframes applicable to Ms. Bender's claim. Tr. at 254. I have in other cases noted that Agmon-Levin does not establish medically acceptable timeframes for autoimmune

[34] I note, however, that my *Althen* prong two analysis also relies on my prior finding that Petitioner failed to carry her burden of proof with respect to the first, "can cause" *Althen* prong. In a case where a claimant successfully met that initial burden by establishing a reliable association between the vaccine and alleged injury, the lack of a persuasive alternative explanation for a particular petitioner's illness following vaccination would be far more compelling.

conditions when (as here) applied to vaccines the article does not discuss or disparate injuries. *See, e.g., Garner v. Sec'y of Health & Human Servs.*, No. 15-063V, 2017 WL 1713184, at *16 (Fed. Cl. Mar. 24, 2017), *mot. for review den'd*, 2017 WL 3483352 (Fed. Cl.). Here, even though TM is the relevant injury, the disparate nature of the case studies Agmon-Levin draws from makes it impossible to deem its timeframe conclusions reliable. Petitioner otherwise offered no literature establishing that any vaccine could initiate the upregulation of cytokines for a six-week period sufficient in severity and degree to cause a sudden autoimmune condition like TM.

Dr. Byers's pronouncements on this topic proved even less persuasive than Agmon-Levin. Not only did she acknowledge that the timeframe in question would be somewhat long for an autoimmune process to result in TM, but she offered a particularly expansive reading of Vaccine Program precedent, proclaiming in sweeping fashion that as a matter of law there is no formal "limit" to the amount of time that can pass from vaccination to injury. *See, e.g.*, Tr. at 102-03, 149. This is an overstatement in the extreme. Even if controlling precedent does not prohibit non-Table claims based solely on the measure of the onset timeframe, the *entire purpose* of the third prong is to gauge whether the amount of time that has passed is medically acceptable under the circumstances. Implicit to this is the reasoned view that in any case, *some* amount of time will be too long even for vaccines that have been established as causal of particular illnesses or injuries. Were this not so, this *Althen* prong would be toothless. *See, e.g., Hennessey v. Sec'y of Dep't of Health & Human Servs.*, 91 Fed. Cl. 126, 142 (2010) (rejecting causation theory that "any conceivable timing could qualify as an appropriate temporal relationship" as rendering "*Althen's* third prong a nullity").

Admittedly, 42 days has been deemed reasonably acceptable with respect to the timeframe for *other* vaccines to establish an autoimmune response like TM. *Tompkins v. Sec'y of Health & Human Servs.*, No. 10-261V, 2013 WL 3498652 (Fed. Cl. Spec. Mstr. June 21, 2013). But such a timeframe is more applicable to cases involving the mechanism of molecular mimicry – something Petitioner's own immunologist agreed was inapplicable. Tr. at 47. It has not otherwise been demonstrated that the other mechanism proposed by Petitioner (the upregulation of cytokines that *any* vaccine might encourage) is more than a transient process that is localized to the site of vaccine administration, rather than ongoing with sufficient intensity to result in an autoimmune illness six weeks after vaccination. *Godfrey*, 2015 WL 10710961; *Koehn v. Sec'y of Health & Human Servs.*, 773 F.3d 1239, 1244 (Fed. Cir. 2014). Because Petitioner could not credibly establish that the vaccines she received could cause TM via any of the proposed mechanisms, she has also not established that the autoimmune process resulting in the disease would take as long as it purportedly did.

Dr. Chen advanced the notion that the medical records revealing the state of Petitioner's lesions as of the dates they were first observed on MRI allowed for the conclusion that an autoimmune process was well underway by that time – thus suggesting an onset *before* 42 days,

and therefore closer in time to the date of vaccine administration (and closer to the period all experts agreed was reasonable). But as Dr. Lotze observed, the combination of a total lack of neurologic symptoms before July 9th, coupled with the abrupt onset of TM-associated symptoms, and the evidence of new lesion progression observed over the four-day period in which the MRIs were performed, actually far better supports the conclusion that onset of Ms. Bender's TM occurred no sooner than 42 days post-vaccination. Lotze Rep. at 3. To so conclude is in keeping with both what is understood about the acute nature of TM, as well as the reliable science suggesting that the manifestation of an autoimmune process resulting in TM would occur no more than three to four weeks of an inciting event. Petitioner did not otherwise offer literature supporting Dr. Chen's contention that TM would invariably be characterized by a subclinical onset that would predate obvious symptoms, and has not cited any medical record evidence corroborating his proposed earlier onset.

Ultimately, based upon this record and the expert opinions offered, I cannot conclude that the vaccines Ms. Bender received could acceptably cause the reaction alleged in 42 days, and therefore that Petitioner failed to carry her burden on this *Althen* prong.

CONCLUSION

Ms. Bender and her family have unquestionably suffered greatly as result of the illness she experienced (and continues to struggle with), and they articulately testified to the challenges they face in dealing with it. Their claim reflects a good faith effort to establish a causal theory based on what appeared a potential explanation for her TM. I also commend the Bender family for their effective prosecution of the claim during the period of time they were without counsel. But my personal sympathies for their grit in adjudicating this claim are not a basis for an entitlement decision. Rather, such a decision must be the product of a careful review of the evidence, balancing it against the applicable legal standards based upon its probative weight and overall persuasiveness. Here, that balancing leads me to conclude that Ms. Bender has not carried her burden of proof, and therefore I must DENY entitlement in this case.

In the absence of a timely-filed motion for review (see Appendix B to the Rules of the Court), the Clerk shall enter judgment in accord with this decision.[35]

[35] Pursuant to Vaccine Rule 11(a), the parties may expedite entry of judgment by filing a joint notice renouncing their right to seek review.

IT IS SO ORDERED.

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