

In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

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JACQUELINE S. HUNT,	*	
legal guardian of a minor child,	*	No. 12-232V
ELIJAH MCLEOD,	*	Special Master Christian J. Moran
	*	
Petitioner,	*	Filed: February 23, 2015
	*	
	*	
v.	*	Entitlement; Varicella Vaccine;
	*	Tetanus-Diphtheria Acellular
	*	Pertussis (“Tdap”) Vaccine;
SECRETARY OF HEALTH	*	Pneumococcal Vaccine; Multiple
AND HUMAN SERVICES,	*	Sclerosis; Acute Disseminated
	*	Encephalomyelitis (ADEM);
Respondent.	*	Significant Aggravation; Timing.

* * * * *

Daniel Pfeifer, Pfeifer, Morgan & Stesiak, South Bend, IN, for petitioner;
Tara J. Kilfoyle and Heather L. Pearlman, United States Dep’t of Justice,
Washington, DC, for respondent.

PUBLISHED DECISION DENYING COMPENSATION¹

Elijah McLeod, now age 15 years, suffers from multiple sclerosis. Multiple sclerosis impairs the functioning of the central nervous system, causing the person difficulty with tasks such as walking. The etiology of multiple sclerosis is not known. Scientists generally believe that the body’s immune system, which usually attacks invaders such as viruses and bacteria, aberrantly turns on itself and attacks the host’s central nervous system. What prompts this attack is not known.

¹ The E-Government Act of 2002, Pub. L. No. 107-347, 116 Stat. 2899, 2913 (Dec. 17, 2002), requires that the Court post this decision on its website. Pursuant to Vaccine Rule 18(b), the parties have 14 days to file a motion proposing redaction of medical information or other information described in 42 U.S.C. § 300aa-12(d)(4). Any redactions ordered by the special master will appear in the document posted on the website.

In this case, the basic claim is that vaccinations that Elijah received are responsible for his multiple sclerosis. Recovery is sought via two different causes of action. First, there is a claim that the vaccinations caused Elijah to suffer multiple sclerosis. This new onset theory is premised on an assertion that Elijah had not experienced any symptoms of multiple sclerosis before the vaccinations. As an alternative, the petitioner also alleges that if Elijah were suffering from multiple sclerosis before the vaccinations, then the claim is that the vaccinations significantly aggravated his multiple sclerosis.

Jacqueline S. Hunt, the petitioner,² has presented the opinions of David Mattson. Many of Dr. Mattson's patients suffer from multiple sclerosis and, in fact, Elijah is one of his patients. Dr. Mattson opined that the vaccinations harmed Elijah in either of the two ways described above.

The Secretary disagreed with this opinion and retained Subramanian Sriram. Like Dr. Mattson, Dr. Sriram has experience in treating patients with multiple sclerosis. Dr. Sriram's opinion was that there was not persuasive evidence linking the vaccinations to Elijah's multiple sclerosis. In Dr. Sriram's view, Elijah had problems in his central nervous system prior to the administration of the allegedly causal vaccinations that Dr. Sriram retrospectively recognized as manifestations of multiple sclerosis. Hence, the vaccinations did not cause the multiple sclerosis. Furthermore, the vaccinations did not make the multiple sclerosis worse than it would have been otherwise.

Dr. Sriram's opinion on the viability of the new-onset claim is more persuasive. He accounted for reports of Elijah's problems before vaccination to show that Elijah's multiple sclerosis probably pre-dated the vaccinations. Conversely, Dr. Mattson's attempts to dismiss Elijah's double vision and dominant hand weakness were not persuasive. Thus, Elijah's claim is actually a claim of significant aggravation, not a new onset claim.

Under a significant aggravation theory, a petitioner must establish six elements. Although Dr. Mattson's opinions addressed all six topics, his opinions lacked persuasiveness in several respects. The theory that vaccinations can worsen

² Originally, the named petitioner was Tomika McLeod, Elijah's mother. During this litigation, it was learned that Elijah's legal guardian was his grandmother, Jacqueline S. Hunt. A January 10, 2014 order corrected the caption, designating Ms. Hunt as the petitioner. For simplicity, this decision refers to Ms. Hunt as the petitioner regardless of whether Ms. McLeod or Ms. Hunt was initially the petitioner.

multiple sclerosis is contrary to an unrebutted epidemiologic study on this precise question. Additionally, Dr. Mattson made several assumptions and drew attenuated inferences that weakened the value of his opinion that relevant vaccines can cause multiple sclerosis. If a relevant vaccine could cause multiple sclerosis, then the proposed biologic process would take at least three days. However, Dr. Sriram persuasively showed that the contemporaneously created medical records establish that Elijah was suffering overt neurologic problems within one day of vaccination. This swiftness is inconsistent with the allegation that the vaccinations worsened Elijah's multiple sclerosis.

In short, Ms. Hunt has failed to present a preponderant case that the vaccinations caused Elijah to be worse than he would have been but for the vaccinations. She has shown that Elijah was worse after the vaccinations but she has not shown Elijah was worse because of the vaccinations. Because her proof is lacking, she is not entitled to compensation and the Clerk's Office is directed to enter judgment in accord with this decision.

I. Facts³

Elijah was born in 1999. Exhibit 1 at 1. As a young boy, Elijah did not have any lasting health problems according to the records of his pediatrician. See exhibit 3.

Reports given to his doctors indicate that in the fall of 2010, Elijah started using his right hand more than his left hand. See exhibit 5 at 11 (Dr. El-Zind); exhibit 7 at 1 (Dr. Toper); exhibit 12 at 708 (report to physical therapist on June 22, 2011). Dr. Mattson obtained a history that Elijah suffered a small accident while playing sports, but did not seek any medical attention. Exhibit 10 at 1. Elijah also testified about this injury. Tr. 257-61.

In February 2011, again according to histories provided later, Elijah started having double vision. Exhibit 5 at 11 (Dr. El-Zind); exhibit 7 at 1 (Dr. Toper);

³ These facts are not disputed as the parties' briefs largely track each other. Compare Pet'r's Posthr'g Br. at 1-8 with Resp't's Posthr'g Br. at 3-8. Although Dr. Mattson and Dr. Sriram accept the accuracy of records created contemporaneously with the events the records describe, they reach different conclusions about the significance of some events in Elijah's history. Dr. Mattson's and Dr. Sriram's interpretations are interspersed throughout the narrative.

exhibit 7 at 53 (Dr. Yoon). Elijah did not see a doctor for his vision problem at this time.

The experts differed in their views about Elijah's arm problem and double vision. Dr. Mattson acknowledged that an inability to use one's dominant hand could be a symptom of multiple sclerosis in general. Tr. 105. But, Dr. Mattson did not see the switch in hand-dominance as a manifestation of multiple sclerosis in this particular case because of an alternative explanation: Elijah had a sports injury that may have affected his left hand. Id. at 79-80, 105-06, 245.

Similarly, Dr. Mattson did not give much weight to the later-given reports of double vision because he was "handicapped by not having any evaluations in real time." Tr. 106. In addition, as discussed below, once Elijah's trouble with double vision came to light, an ophthalmologist could not confirm the presence of double vision. Tr. 107, 117. Nevertheless, Dr. Mattson agreed that before the vaccinations, it was likely that Elijah was suffering from subclinical multiple sclerosis. Tr. 119.

In contrast, Dr. Sriram stated that the switch in handedness and complaints of double vision "are telltale signs of some neurologic abnormality." Tr. 179. Dr. Sriram went further and declared that "those were [Elijah's] first events" of multiple sclerosis. Id. at 180.⁴

When Elijah was 12, he received a set of vaccines on April 20, 2011. Specifically, Elijah was administered a dose of the tetanus-diphtheria acellular pertussis ("Tdap"), varicella, and meningococcal vaccines. Exhibit 2 at 1-3.

The next day, Elijah was sick at school. He vomited and felt dizzy and off-balance. Exhibit 4 at 3, 12; see also exhibit 19 (affidavit of Ms. McLeod) ¶ 3. Elijah's mother took him to the emergency room of Memorial Hospital of South Bend. Dr. Kavanaugh attended to Elijah in the emergency room. Elijah told Ms. McLeod about his previous experience of problems with his left arm for the first time because the current tingling sensation on his face was similar to the tingling he had felt in his left arm months earlier. Tr. 259-61. Dr. Kavanaugh noted a

⁴ Dr. Mattson and Dr. Sriram agreed that Elijah could not be diagnosed as suffering from multiple sclerosis based upon a single event, such as an arm injury. Tr. 80-81 (Dr. Mattson suggesting that Elijah's left arm problem might constitute a "clinically isolated syndrome"), 208 (Dr. Sriram stating that the arm problem was Elijah's first event and the April 22, 2011 presentation was the second event).

small area of redness on Elijah's left arm as well as mild tenderness and a bit of warmth. Dr. Kavanaugh also observed some possible slight swelling on the left side of Elijah's face. Dr. Kavanaugh reported that Elijah was oriented to person, place, and time, and appeared to be in no acute distress. Dr. Kavanaugh assessed Elijah as having a localized reaction to a vaccination. Exhibit 4 at 3. Elijah was not admitted to the hospital. See exhibit 19 ¶ 3.

Again, Dr. Mattson and Dr. Sriram drew different conclusions from Elijah's presentation at the emergency room on April 21, 2011. Dr. Mattson averred that Elijah's problems were "really more related to a local injection. . . . [T]here really was nothing indicating any kind of focal neurologic problem at that point." Tr. 26.

Dr. Sriram, by contrast, stated that "some of his symptoms were . . . a local reaction to the injection." But, Dr. Sriram could also see that "some of them were clearly neurological." Tr. 194. The neurological symptoms included dizziness and unsteadiness in walking. From the observation that Elijah's face was swollen, Dr. Sriram reasoned that Elijah's facial muscles were weak and not functioning normally. Tr. 193-94, 238. Dr. Mattson did not controvert Dr. Sriram's basis for concluding that Elijah had weakness in his facial muscles and said that Dr. Sriram's explanation was "certainly a possibility." Tr. 248.

The following day, April 22, 2011, Elijah was still not feeling well enough to return to school. Exhibit 19 ¶ 4. Elijah's grandmother brought him back to the emergency room where Dr. Kavanaugh saw him again. Exhibit 5 at 15. The chief complaint was that Elijah was "'not himself.'" Exhibit 5 at 355. The doctor was concerned about Elijah's poor balance and ordered a CT scan of Elijah's head. Id. The CT scan identified at least two areas of hypodensity in Elijah's brain. Id. at 347.

Dr. Mattson recognized that on April 22, 2011, Elijah "was starting to develop some focal signs or focal symptoms of neurologic dysfunction." Tr. 28. To Dr. Sriram, Elijah's presentation on April 22, 2011, constituted a "second event" for making a diagnosis of multiple sclerosis. The "first event" preceding the April 22, 2011 "second event" was the arm weakness and double vision. Tr. 201-02.

Very late in the evening of April 22, 2011, Elijah was admitted to the pediatric unit of Memorial Hospital. Exhibit 5 at 29. A nurse's assessment stated that Elijah was "'acting like he had a stroke.'" In the neurological history, the nurse recorded that Elijah had had no previous medical history but, tonight, he was

having numbness on the left side of his face. Id. at 375-76. Very early in the morning of April 23, 2011, a doctor ordered an MRI to evaluate the abnormality detected on the CT scan and Elijah's ataxia. Id. at 28.

At approximately 10:00 AM on April 23, 2011, Dr. Samira El-Zind saw Elijah for the first time. (Dr. El-Zind has followed Elijah throughout the course of his illness.) The history Dr. El-Zind obtained is consistent with the history presented above. Dr. El-Zind stated "when I talked to mom later I understood that there was some concern about his hand for the past 7 months [as] he is left handed and he was using the right hand. . . [P]atient also said that he has double vision that was going on for 2 months." Exhibit 5 at 11.⁵ Dr. El-Zind recommended an MRI, a spinal tap, and an MS panel. She stated that she was "concerned about the fact that some of the symptoms [have] been there for a while." Id. at 12.

Dr. El-Zind's impression on April 23, 2011, was that Elijah had "possible acute disseminating encephalomyelitis with [a] post-immunization reaction." Dr. El-Zind came to this conclusion before any of the tests she ordered (an MRI, spinal tap, and MS panel) were conducted. Exhibit 5 at 12. In his testimony, Dr. Mattson discussed that Dr. El-Zind stated, on April 23, 2011, that Elijah may have ADEM. Tr. 30-31. To Dr. Sriram, Dr. El-Zind's conclusion was reasonable based upon her knowledge at that time. When the information about Elijah's later course is added, Dr. El-Zind's "assessment has to change." Tr. 214.

Elijah had an MRI on April 23, 2011. It identified large areas of abnormal signals. Allison Lamont, the radiologist who interpreted the MRI, stated that the abnormalities were "likely related to acute disseminated encephalomyelitis (ADEM), seen in postvaccination settings. A demyelinating process such as multiple sclerosis is felt to be much less likely." Exhibit 5 at 350.⁶

Dr. Mattson mentioned Dr. Lamont's diagnosis without adding much. Tr. 32. Dr. Sriram questioned Dr. Lamont's ability to diagnose ADEM or multiple

⁵ Dr. El-Zind's notes tend to be written in lower case letters only. In this decision, the capitalization is changed without notation.

⁶ The MRI was performed with and without contrast. "On the postcontrast images, variable enhancement is demonstrated." Exhibit 5 at 350. Although the presence of enhanced lesions could provide some information about the age of the lesions, see W.C. v. Sec'y of Health & Human Servs., 704 F.3d 1352, 1354 (Fed. Cir. 2013), the enhancements on Elijah's initial MRI were not discussed extensively. See Tr. 31-32, 178.

sclerosis because those are clinical entities, but she had neither seen Elijah nor obtained his history. Tr. 212-13.

Elijah also had a lumbar puncture on April 23, 2011. The test revealed two or more oligoclonal bands in Elijah's cerebrospinal fluid. The report stated that "oligoclonal bands are present in approximately 95 percent of patients with multiple sclerosis but may also be present in the CSF from patients with... [other diseases]." Exhibit 5 at 339.

Dr. Mattson opined that the presence of oligoclonal bands was consistent with a diagnosis of ADEM. They also "increase the risk of going on to be [multiple sclerosis]." Tr. 34. In contrast, to Dr. Sriram, the presence of oligoclonal bands meant that Elijah already was suffering from multiple sclerosis. Tr. 195.

The doctors prescribed high-dose steroids while Elijah remained in the hospital. While hospitalized, Elijah started physical therapy. His therapist reported that he was "concerned about writing with his left hand – has bad grip on pencil. Left fingers feel big and heavy." Exhibit 5 at 818.

Elijah was discharged on April 29, 2011, and was prescribed prednisone to taper over the next two weeks. At discharge, Elijah's diagnosis "seem[ed] consistent with ADEM; however multiple sclerosis is still in the differential." Exhibit 5 at 4.

At the hearing, Dr. Mattson's testimony about Elijah's status as of his discharge at the end of April 2011 was confusing. Dr. Mattson asserted that with the information available in April 2011, a doctor could not diagnose Elijah as having multiple sclerosis because Elijah, in Dr. Mattson's view, had not experienced two events disseminated in time and space. Tr. 99.⁷ When pressed to say whether Elijah could be diagnosed as suffering from multiple sclerosis in April 2011 based upon all the information known through the date of the hearing, Dr. Mattson seemed to equivocate between saying that Elijah had ADEM, which became multiple sclerosis, and saying that Elijah always had multiple sclerosis. Tr. 100-02.

⁷ Dr. Mattson discounted Elijah's history of a change in hand dominance and double vision for reasons explained in the text above. Dr. Mattson considered Elijah's presentation on April 22, 2011 to be the first manifestation of neurologic symptoms.

Following his April 2011 hospitalization, Elijah's first appointment was with Dr. El-Zind on May 5, 2011. Elijah told her that he was feeling "tingling" in the left side of his face and in his right fingertips. Elijah also reported that he did not use his left arm or hand and he felt fatigued if he was doing too much. Dr. El-Zind reported that Elijah was weaning off of prednisone. She stated that Elijah had "possible ADEM / MS." Dr. El-Zind requested another MRI. Exhibit 6 at 7-8.

Elijah's next appointment was on May 6, 2011, with Ziya Toper, his primary care physician. Dr. Toper's history recited that Elijah had weakness in his left hand for one year and double vision for two months before he was hospitalized. Because of the possibility of ADEM, Dr. Toper referred Elijah to an ophthalmologist. Exhibit 7 at 1-2.

Elijah saw an ophthalmologist, Eric Yoon, on May 13, 2011. Dr. Yoon recorded that Elijah "complains of some double vision intermittently for the past two months. He states that he does not have any[]more double vision." Dr. Yoon gave him a prescription for glasses and recommended a routine examination in one year. Exhibit 7 at 53. Dr. Mattson asserted that the double vision could have resolved by the time Elijah saw the ophthalmologist. Tr. 37.

On May 16, 2011, Elijah had his second MRI. The interpreting radiologist, Pedro A. Miro, compared this MRI to the April 23, 2011 MRI. Dr. Miro did not note any significant enhancement and identified only a small new lesion. Dr. Miro stated "the findings are consistent with the patient's repeated history of acute disseminated encephalomyelitis." Exhibit 9 at 232. Dr. Miro added "[a]s per discussion with Dr. El-Zind[,] the possibility of multiple sclerosis is not excluded." Id. at 233.

Dr. Mattson had a slightly different interpretation of the imaging. He was not convinced that the lesion was new. Tr. 39. But, even if the lesion were new, Dr. Mattson interpreted the two MRIs (one on April 23, 2011, and the other on May 16, 2011) as "consistent with that first wave of inflammatory demyelination." Tr. 39; accord Tr. 143-44.

That day, Dr. El-Zind reviewed the MRI during an appointment with Elijah. She also again recorded a history in which "mom said that the symptoms in his left hand with clumsiness and avoiding to use it in[]spite of being left[]handed [have] been going on for 7 months. Also 2 months before the hospital admi[ss]ion he had blurred vision." Currently, although Elijah's balance has been better, his legs and

feet still tired easily. Dr. El-Zind recommended admitting him to the hospital for another course of IVIG. Exhibit 6 at 5-6.

Elijah stayed in Memorial Hospital from May 16, 2011 to May 21, 2011. Exhibit 9 at 3 (discharge report). Another study of his CSF again revealed oligoclonal bands, “suggesting multiple sclerosis.” Id. During this hospitalization, Dr. El-Zind consulted neurologists at Indiana University Hospital, where Dr. Mattson works. According to an email, Dr. El-Zind told one of Dr. Mattson’s colleagues that Elijah “had a 7 month history of decreased use of the left arm. He was treated with steroids, has oligoclonal bands and positive myelin basic protein and a new lesion on his second MRI.” The email indicates that Dr. El-Zind “is pretty convinced [Elijah] has MS.” Exhibit 10 at 50.

Some records suggest that doctors at Memorial Hospital were thinking that Elijah was suffering from multiple sclerosis in May 2011. For example, the handwritten orders for his discharge state that Elijah was diagnosed with a “MS flair.” Exhibit 9 at 11, 203.

Dr. Mattson saw Elijah at Indiana University Hospital on June 10, 2011. Dr. Mattson’s history did not include Elijah’s report of having double vision. Exhibit 26 at 1; Tr. 146. With that addition, Dr. Mattson obtained a history that was consistent with the information provided above. With respect to Elijah’s trouble with his left arm since the fall of 2010, Elijah told Dr. Mattson that he “chalked this up to [an] injury playing football and never sought medical attention for it and did not tell his mother about it even.” Exhibit 17 at 21. Dr. Mattson was not told that Elijah was having double vision for two months before his hospitalization.

Dr. Mattson stated that he was being consulted “about a postvaccination acute disseminated encephalomyelitis, which raises the possible diagnosis of multiple sclerosis.” Id. In addition to obtaining Elijah’s medical history, Dr. Mattson examined him. Dr. Mattson recorded that Elijah had a decreased sensation to touch in his left arm and leg. Elijah also had difficulty walking.

Dr. Mattson reviewed both of Elijah’s MRIs. Dr. Mattson interpreted the second MRI as showing improvement, such as a lack of enhancement. He was not convinced that the second MRI showed a new lesion, “but even if there were [a new lesion], that [new lesion would] still [] be part of a protracted first event of demyelination in response to his vaccinations.” Id. at 22.

Dr. Mattson considered “the oligoclonal IgG bands in his spinal fluid [to be] consistent with an acute disseminated encephalomyelitis.” But, Dr. Mattson

recognized that the presence of oligoclonal bands “increases the risk that this will go on to be multiple sclerosis.” Dr. Mattson “certainly would give him the benefit of doubt [that] this is a one time postvaccination event.” Id.

For treatment, Dr. Mattson prescribed a medication for headaches and encouraged Elijah to continue his physical therapy. Dr. Mattson also recommended another MRI in September 2011, to check whether the lesions had disappeared. Exhibit 10 at 3.

On June 20, 2011, Elijah saw Dr. El-Zind again. He complained about problems with his equilibrium and pain in various parts of his body. Dr. El-Zind recommended a third MRI. Exhibit 6 at 3-4. The report from that MRI stated that “the number and distribution of the lesions appears stable.” It also stated there were “three new foci of abnormal enhancement.” The radiologist reported that the lesions are “nonspecific but consistent with the expected changes of evolving demyelinating lesions such as can be seen with MS or ADEM.” Exhibit 12 at 251-52. Elijah remained in the hospital for 5 days. Id. at 3. Dr. El-Zind called Dr. Mattson regarding this MRI. On June 20, 2011, Dr. Mattson stated he wanted to see Elijah as soon as possible to start Elijah on Rebif, a medication for pediatric-onset multiple sclerosis. Exhibit 10 at 47.

Elijah had headaches, body aches, and a stomach ache on August 17, 2011. When he went to the emergency room, the doctor recognized that Elijah had problems walking and muscle twitching. Elijah had a fourth MRI on August 18, 2011. This MRI showed a progression of white matter disease with several more lesions. The radiologist interpreted the results as consistent with multiple sclerosis. Exhibit 13 at 3-4.

With a copy of his most recent MRI, Elijah returned to see Dr. Mattson on August 26, 2011. Dr. Mattson stated that “I now feel very comfortable that this has been declared as multiple sclerosis.” Dr. Mattson prescribed Copaxone. Exhibit 17 at 5-6; see also Tr. 117 (Dr. Mattson describing Elijah’s presentation in August 2011 as an “exacerbation of his multiple sclerosis”).

On December 23, 2011, Dr. Mattson saw Elijah for a follow-up. Dr. Mattson stated that Elijah has had a case of pediatric-onset multiple sclerosis for “approximately 8 months duration.” Exhibit 24 at 3. Other follow-up appointments with Dr. Mattson were held on September 4, 2012, and May 14, 2013. Exhibit 43 at 1-3; see also Tr. 97-98 (Dr. Mattson’s estimate that he sees

Elijah every 6 to 12 months). While taking Copaxone, Elijah has done relatively well. He has not had any severe flares of his multiple sclerosis.

II. Procedural History

The petition was filed on April 10, 2012, and was originally assigned to a different special master. Ms. Hunt filed medical records in July 2012. The material included a nine-paragraph affidavit from Dr. Mattson, who averred that Elijah's ADEM and multiple sclerosis were "caused in fact by his vaccinations received on April 20, 2011." Exhibit 18 ¶¶ 7-8.

The Secretary reviewed this material in her report, filed pursuant to Vaccine Rule 4, on August 29, 2012. The Secretary's assessment forecast the issues that remained disputed throughout the litigation. The Secretary argued that Elijah did not suffer from ADEM and that he suffered from only multiple sclerosis. Resp't's Rep. at 10-11. For the multiple sclerosis aspect, the Secretary maintained that Ms. Hunt had not established that any vaccine caused Elijah's multiple sclerosis. The Secretary argued Elijah experienced symptoms of multiple sclerosis before the vaccination. The Secretary noted that it appeared that Dr. Mattson was not aware of these symptoms and characterized Dr. Mattson's affidavit as "conclusory." Finally, in a footnote, the Secretary remarked that Ms. Hunt had not alleged that the vaccinations significantly aggravated Elijah's pre-existing multiple sclerosis.

A few days after the Secretary filed her report, the case was reassigned to the undersigned. A status conference was held later that month. In that status conference, the undersigned suggested that Ms. Hunt file an affidavit regarding damages and obtain a more comprehensive report from Dr. Mattson.

Ms. Hunt filed a two-page report from Dr. Mattson on December 28, 2012. He stated that vaccinations can cause ADEM and once a person experiences an initial episode of ADEM, the person is more vulnerable to having a second attack. After a second attack, "a diagnosis of multiple sclerosis (MS) can be made." Exhibit 26 at 1.

With respect to Elijah's history, Dr. Mattson asserted that he "had no event of inflammatory demyelination prior to the vaccine in question." Dr. Mattson disregarded Elijah's reports of having difficulties with his left hand because Elijah attributed them to a sports injury. In addition, Dr. Mattson appeared not to value reports of double vision because Dr. Mattson had not obtained a similar history from Elijah. Finally, Dr. Mattson asserted that even if Elijah had an episode of

inflammatory demyelination, a vaccine provoked “the second and MS-defining event.” Id. at 2.

The submission of this report and its accompanying literature prompted the Secretary to retain an expert. On March 29, 2013, the Secretary filed a five-page report from Dr. Sriram. Dr. Sriram agreed that Elijah suffers from multiple sclerosis. In his view, Elijah actually was suffering from a previously undiagnosed case of multiple sclerosis before he was vaccinated. In support, Dr. Sriram pointed to the oligoclonal bands detected in Elijah’s cerebrospinal fluid 48 hours after vaccination. Dr. Sriram maintained that the immune system could not generate oligoclonal bands in such a short amount of time as the production of the relevant antibody would take at least five days. As further evidence regarding the onset of Elijah’s multiple sclerosis, Dr. Sriram identified left-hand weakness and double vision as neurological symptoms. Dr. Sriram asserted that the vaccines Elijah received do not cause a worsening in multiple sclerosis. Lastly, Dr. Sriram disagreed with how Dr. Mattson explained the connection between ADEM and multiple sclerosis. Exhibit A.

Ms. Hunt filed a response from Dr. Mattson on June 13, 2013. Dr. Mattson maintained that “ADEM is part of the spectrum of inflammatory demyelinating disease.” ADEM can be “the first event of what becomes a recurring pattern of inflammatory demyelinating events to make a diagnosis of multiple sclerosis.” Exhibit 38 at 1. Dr. Mattson generally indicated that vaccinations can cause ADEM or can exacerbate multiple sclerosis, although Dr. Mattson did not identify the process through which vaccinations can cause or aggravate a demyelinating disease. See id. at 1-2.

Dr. Mattson presented a two-part construct for Elijah’s medical history similar to what he presented in his previous report. Initially, Dr. Mattson maintained that Elijah’s “multifocal demyelination began within a day of the vaccinations,” starting when Elijah had a “febrile response.” Dr. Mattson stated that he “dismissed the prior history of left hand difficulties and vague visual complaints, as not significant enough for the patient to have sought medical attention, and attributable in the case of the left hand symptoms to a sports related injury.” Id.

Alternatively, if Elijah had experienced symptoms of multiple sclerosis before vaccination as Dr. Sriram had asserted, then the events of April 22, 2011 constituted a “second and MS-defining event.” Dr. Mattson opined that the initial pre-vaccination symptoms “may never have led to a recurrent pattern of

inflammatory demyelination to make an MS diagnosis if he had not received the vaccinations in question.” Id. at 2.

In the ensuing status conference, Ms. Hunt acknowledged that Dr. Mattson had overlooked the question of timing. Dr. Mattson had not explained how the vaccinations could cause multiple sclerosis when the cerebral spinal fluid taken from Elijah 48 hours after vaccination contained oligoclonal bands. Hence, Ms. Hunt was ordered to obtain another report from him. In addition, the parties were encouraged to explore settlement. Order, issued July 3, 2013.

In response, Dr. Mattson revised his opinion, at least slightly. Dr. Mattson agreed that the oligoclonal IgG bands were likely present in Elijah before vaccination. The oligoclonal bands are “indicator[s] of ongoing immune dysregulation or hyperactivity in the central nervous system.” Referencing a study on twins with multiple sclerosis, Dr. Mattson asserted that a person could have oligoclonal IgG bands but never have experienced “a clinical event suggestive of inflammatory demyelination.” Exhibit 41 at 1 (citing exhibit 42 (Adrian Williams et al., Multiple sclerosis in twins, 30 *Neurology* 1139 (1980))) at 1143. Dr. Mattson opined that Elijah could have followed such a course. “Had these vaccines not been given, this hyperactivity and predisposition might never have been manifest as the fulminant and devastating ADEM event.” Exhibit 41 at 1.

In a discussion about Dr. Mattson’s opinion, Ms. Hunt stated that she was pursuing a theory that the vaccinations aggravated an asymptomatic condition. The parties also continued their preparation for a hearing and the Secretary was ordered to obtain another report from Dr. Sriram.

Dr. Sriram’s September 3, 2013 report addressed the recent statements from Dr. Mattson. With respect to the significant aggravation theory, which Dr. Mattson had characterized as fueling the fires of inflammation, Dr. Sriram stated that there is “no prospective study which has shown an increase in relapses after vaccinations of any kind.” Exhibit H at 2. Dr. Sriram also questioned the usefulness of the twin study because those authors stated that the “unaffected twins with oligoclonal bands have subclinical MS.” Id. at 3.

After the Secretary filed this report, the undersigned issued an order for the parties to file relatively lengthy briefs before the hearing. This order encouraged Ms. Hunt to confirm with Dr. Mattson that he was opining that the vaccinations significantly aggravated an underlying condition, as opposed to causing the condition. If Ms. Hunt were pursuing a significant aggravation theory, the parties

should present reports from their experts explaining how Elijah would have been but for the vaccination. Order, issued Sep. 24, 2013 at 8-9 (citing Locane v. Sec'y of Health & Human Servs., 685 F.3d 1375, 1381 (Fed. Cir. 2013); Loving v. Sec'y of Health & Human Servs., No. 02-469V, 2009 WL 3094883, at *11-23 (Fed. Cl. Spec. Mstr. July 30, 2009), recons. granted in part on other grounds, 2010 WL 1076124 (Fed. Cl. Spec. Mstr. Mar. 2, 2010); Gruber v. Sec'y of Health & Human Servs., 61 Fed. Cl. 674, 684 (2004)).

On November 25, 2013, Ms. Hunt filed updated medical records and her pretrial brief. Her pretrial brief asserted that she was entitled to compensation through three different avenues: (1) Elijah suffered an encephalopathy as defined in the Vaccine Injury Table, (2) the vaccinations caused Elijah to develop “postvaccinal encephalomyelitis, which went on to be multiple sclerosis,” and (3) the vaccinations significantly aggravated his multiple sclerosis. With respect to the significant aggravation theory, Ms. Hunt did not file another report from Dr. Mattson in which he discussed the expected course of multiple sclerosis. She represented that “if Dr. Mattson were asked whether Elijah would never have developed MS if it were not for the vaccinations, that Dr. Mattson would respond that it is possible that Elijah would have lived his entire life without any development that would trigger MS. But, Dr. Mattson cannot say for sure.” Pet’r’s Prehr’g Br. at 41.

Dr. Sriram discussed Elijah’s anticipated course of multiple sclerosis in a report filed on November 26, 2013. Dr. Sriram stated that the future course of multiple sclerosis cannot be predicted easily. He also said that “[i]t is very unlikely that vaccination alters the natural history of MS.” Exhibit N at 4. The Secretary incorporated Dr. Sriram’s opinion into her pretrial brief, filed on December, 16, 2013. The Secretary addressed each of the three theories of recovery, explaining Ms. Hunt’s position was not persuasive.

After reviewing the parties’ pretrial submissions, the undersigned suggested that they may wish to consider settlement before the forthcoming hearing. Order, issued Dec. 18, 2013. The parties agreed to pursue this possibility. Settlement was again discussed during the January 3, 2014 pretrial conference.

The parties’ efforts to resolve the case informally did not succeed. Thus, a hearing was held on January 9, 2014. As permitted by Vaccine Rule 8(b)(2), Dr. Mattson appeared via videoconferencing. Dr. Mattson was joined at the Indiana videoconferencing facility by an associate attorney, Ms. Hunt, and Elijah. Ms.

Hunt's attorney of record was at the Office of Special Masters in Washington, DC, where Dr. Sriram was.

Following the hearing, the parties submitted briefs. Ms. Hunt filed an initial brief on March 10, 2014, and a reply brief on June 16, 2014.⁸ In between those submissions, the Secretary filed one brief on May 23, 2014. Subsequently, the undersigned again requested that the parties explore settlement. However, the parties could not reach an agreement and submitted the case for adjudication.

As the expert reports and briefs have foreshadowed, two topics require resolution. The first issue concerns Elijah's health just before he was vaccinated. While the experts agree that his immune system was dysregulated, Dr. Mattson and Dr. Sriram draw different implications from the oligoclonal bands. The second issue is whether vaccinations made Elijah's health worse than it would have been but for the vaccinations.

III. Standards for Adjudication

Petitioners are required to establish their cases by a preponderance of the evidence. 42 U.S.C. § 300aa-13(1)(a). The preponderance of the evidence standard requires a "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 v. Sec'y of Health & Human Servs., 592 F.3d 1315, 1322 n.2 (Fed. Cir. 2010) (citations omitted). Proof of medical certainty is not required. Bunting v. Sec'y of Health & Human Servs., 931 F.2d 867, 873 (Fed. Cir. 1991).

Distinguishing between "preponderant evidence" and "medical certainty" is important because a special master should not impose an evidentiary burden that is too high. Andreu v. Sec'y of Health & Human Servs., 569 F.3d 1367, 1379-80 (Fed. Cir. 2009) (reversing special master's decision that petitioners were not entitled to compensation); see also Lampe v. Sec'y of Health & Human Servs., 219 F.3d 1357 (2000); Hodges v. Sec'y of Health & Human Servs., 9 F.3d 958, 961 (Fed. Cir. 1993) (disagreeing with dissenting judge's contention that the special master confused preponderance of the evidence with medical certainty).

⁸ In her initial brief and reply brief, Ms. Hunt did not assert that Elijah suffered an encephalopathy as defined in the regulations associated with the Vaccine Injury Table.

IV. Elijah's Pre-Vaccination Status

The first matter requiring resolution concerns Elijah's health before he received the vaccines on April 20, 2011. The determination on this point controls whether Ms. Hunt may pursue either a claim that the vaccinations caused Elijah a new injury or a claim that the vaccinations significantly aggravated a pre-existing condition.

The Court of Federal Claims has discussed the difference between the two theories of recovery in a case involving parents who maintained that vaccines caused their child's developmental delay. The Secretary argued that the vaccines were not causative because the child had manifested symptoms of a neurologic injury before the vaccinations. The Court explained that the answer to this question was to look for evidence of the disease for which the petitioners were claiming compensation before the vaccination. "If [the child's] neurological . . . symptoms, however defined, were manifested pre-vaccination, then [his] case involves a significant-aggravation claim. . . . If not, then [his] case concerns a new-injury claim." Paluck v. Sec'y of Health & Human Servs., 104 Fed. Cl. 457, 469 (2012) (remanding case), reversing decision after remand, 113 Fed. Cl. 210, 225 (2013), appeal filed, No. 14-5080 (Fed. Cir. Apr. 25, 2014). Accordingly, the question in this case is whether Elijah manifested symptoms of multiple sclerosis before the vaccination.⁹

⁹ In their post-hearing briefs, both parties discussed whether Elijah's pre-vaccination health affects the legal framework. Ms. Hunt argued that "[t]his is not a case where the [special master] must diagnose the injury as a prerequisite to applying the Althen factors." Pet'r's Br., filed Mar. 10, 2014, at 18; accord Pet'r's Reply, filed June 16, 2014, at 1-4. Ms. Hunt's argument is mistaken because the parties do not controvert Elijah's diagnosis, unlike cases in which the diagnosis was disputed and, therefore, became a prerequisite to the Althen analysis. E.g., Lombardi v. Sec'y of Health & Human Servs., 656 F.3d 1343 (Fed. Cir. 2011); Broekelschen v. Sec'y of Health & Human Servs., 618 F.3d 1339 (Fed. Cir. 2010). As discussed in the text below, Ms. Hunt's emphasis on whether the doctors caring for Elijah on April 22, 2011, could have diagnosed him as suffering from multiple sclerosis is misdirected.

The Secretary maintained that it was not necessary "to determine whether Elijah initially suffered from ADEM, which developed into multiple sclerosis, or whether Elijah's symptoms were always attributable to his multiple sclerosis." Resp't's Br., filed May 23, 2014, at 9. Although the Secretary provided several reasons for this assertion, they boil down to the same point --- Ms. Hunt cannot prevail on either the theory that Elijah suffered a new injury or the theory that Elijah's condition was significantly aggravated.

On this narrow question, the parties have relatively little disagreement. They mostly agree about the symptoms of multiple sclerosis and they mostly agree about the symptoms that Elijah experienced.

Multiple sclerosis is a disease in which parts of a person's immune system are presumed to attack the person's central nervous system. The specific component of the central nervous system is myelin, which insulates the axons that conduct electrical impulses throughout the brain and spinal cord. Tr. 13-14, 174. Because myelin is attacked, multiple sclerosis is classified as a demyelinating disease.¹⁰

Symptoms of multiple sclerosis include blurred vision, facial numbness, urinary problems, and mild cognitive impairment. Exhibit 40 (DH Miller et al., Differential diagnosis of suspected multiple sclerosis: a consensus approach, 14(9) *Mul. Scler.* 27 (2008)) at 27-28 (table 3); see also exhibit D (John H. Noseworthy et al., Multiple Sclerosis, 343(13) *The New England Journal of Medicine* 938 (2000)) at 938 (presenting an extensive list of signs and symptoms). Some of these symptoms are similar to the symptoms of other demyelinating diseases. Multiple sclerosis differs from diseases like ADEM because those other demyelinating diseases tend to be considered monophasic.¹¹ Traditionally, to be diagnosed with multiple sclerosis, a person must have "at least two events" "disseminated in time and space." Tr. 34; accord Tr. 71; exhibit 32 (Chris H. Pulman et al., Diagnostic criteria for multiple sclerosis: 2010 revisions to the McDonald criteria, 69 *Ann. Neurol.* 292 (2011)) at 295; exhibit 34 (Anita L. Bellman et al., Challenges in the classification of pediatric multiple sclerosis and future directions, 68 (Supp. 2) *Neurology* 1 (2012)) at 4; exhibit 40 (Miller) at 2. Due to this overlap, Dr. Mattson and Dr. Sriram agreed that a person can have an initial demyelinating episode that doctors may characterize as ADEM. When the person has a second demyelinating episode, the doctors will then diagnose the

¹⁰ Other central nervous system demyelinating diseases include transverse myelitis, optic neuritis, and ADEM. Dr. Mattson and Dr. Sriram disputed the taxonomic relationship between multiple sclerosis and ADEM. Compare Tr. 84, 102 (Dr. Mattson), with Tr. 175-77, 207 (Dr. Sriram).

¹¹ To be more precise, Dr. Mattson asserted that ADEM can rarely have a multiphasic course. Tr. 75. However, Dr. Sriram did not agree. Tr. 173. Because the experts agree that Elijah's current diagnosis is multiple sclerosis, there is no need to explore multiphasic ADEM in more detail.

person as suffering from multiple sclerosis. Tr. 21, 56, 110, and 135 (Dr. Mattson), 175-76, and 228-29 (Dr. Sriram).¹²

Dr. Mattson's and Dr. Sriram's agreement about the features of multiple sclerosis largely, but not entirely, carried over to an evaluation of Elijah's health before vaccination. A very important point of agreement concerns the presence of oligoclonal bands in Elijah's cerebrospinal fluid obtained on April 23, 2011. Exhibit 5 at 339.

Before the hearing, Dr. Sriram interpreted Elijah's oligoclonal bands as inconsistent with a theory that the April 20, 2011 vaccinations caused an immune-mediated reaction in Elijah's central nervous system because the biologic process that creates oligoclonal bands takes several days. Exhibit A at 3. Dr. Mattson was instructed to respond to this specific aspect of Dr. Sriram's report. Orders, issued April 16, 2013 and July 3, 2013. In response, Dr. Mattson indicated that he agreed that Elijah most likely had oligoclonal bands before the vaccination. Exhibit 41. Dr. Mattson repeated this opinion at the hearing. Tr. 83-84, 91, 107. The presence of oligoclonal bands signifies, at least, hyperactivity in the immune system. Tr. 251.

In addition to this sign of a dysregulated immune system, Elijah experienced at least two symptoms that could be manifestations of a problem in his central nervous system before vaccination. First, Elijah developed weakness in his dominant hand, which happened to be his left hand. Exhibit 5 at 11. Second, Elijah experienced episodes of double vision. *Id.* Dr. Sriram asserted that both a switch in handedness and double vision were manifestations of a "neurological abnormality" and were Elijah's "first events." Tr. 179-80. Dr. Mattson disagreed because the left-handed weakness could have been the effect of a sports injury and there was no medical confirmation of the double vision. Tr. 105-07; but see Tr. 148, 245.

The evidence favors a finding that Elijah experienced clinical symptoms of multiple sclerosis before the April 20, 2011 vaccinations. Elijah testified that numbness in his arm was the same as the numbness he felt on the left side of his face one day after vaccination. Tr. 261. In addition, the reason Dr. Mattson gave

¹² During the October 8, 2014 status conference, the undersigned discussed his review of the transcript and recommended that respondent review the accuracy of Dr. Sriram's testimony on page 229 line 16. Order, issued October 9, 2014. Respondent clarified her expert's testimony. Resp't's Status Rep., filed Nov. 7, 2014.

for discounting the report of double vision, the lack of objective verification, is not persuasive. At age 12, Elijah is capable of reporting episodes of double vision accurately. Neither Ms. Hunt nor Dr. Mattson has suggested that Elijah's report was erroneous. They simply argue it was unverified. However, verification is not needed for double vision. Finally, the two symptoms tend to corroborate each other.

Even if these clinical symptoms could be discounted, Dr. Mattson conceded, on cross-examination, that before the vaccinations, Elijah suffered from subclinical multiple sclerosis. Tr. 119. This finding carries medical and legal implications.

The legal consequence of finding that Elijah suffered clinical symptoms of multiple sclerosis and had (undetected) laboratory evidence of multiple sclerosis means that Ms. Hunt may pursue her significant aggravation theory only. Her alternative theory of recovery, the new injury claim, is not tenable. Locane, 685 at 1381 ("Given the Special Master's finding that the illness was present before the vaccine was administered, logically, the vaccine could not have caused the illness."). A complete analysis of the significant aggravation claim is set forth in section V below. As discussed in that section, a critical aspect of that analysis is how Elijah would have progressed but for the vaccinations.

Predicting Elijah's course as of April 19, 2011 (the day before the vaccination) is nearly impossible. By April 19, 2011, Elijah had experienced such problems in his dominant hand that he stopped writing with it for a time, had episodes of double vision, and had abnormal antibodies in his cerebrospinal fluid. A fundamental question is given this constellation of signs and symptoms, would Elijah have experienced more overt episodes associated with demyelination?

For this question, the evidence was sparse and evidence based on more than just opinion was rarer still. A series of examinations reflect refinement in Dr. Mattson's opinion. Initially, Dr. Mattson was asked whether, assuming that Elijah had multiple sclerosis before the vaccinations, could he have "lived a normal life without any further symptoms or complications?" Dr. Mattson responded: "[T]hat's a very likely possibility." Tr. 92-93. On cross-examination, Dr. Mattson was asked: "[W]hat is it about Elijah, in particular, that makes you believe that it's more likely than not that he never would have had a problem?" His response was: "Perhaps the fact that he was young and it's an unusual condition at a younger age." Tr. 117. Because Dr. Mattson's first response was expressed as a "very likely possibility," Dr. Mattson was asked whether there is "a reasonable

probability that Elijah would have had a normal life but for the vaccines?” His answer was solely “Yes.” Tr. 161.

Dr. Sriram’s opinion was that before vaccination, Elijah had displayed symptoms of multiple sclerosis (hand problems and double vision) and Elijah’s deterioration after vaccination constituted a normal course of multiple sclerosis, one that the vaccinations did not affect. See Tr. 196. For the predicted course of multiple sclerosis, Dr. Sriram emphasized that in addition to the oligoclonal bands, Elijah had abnormal vision and abnormal function in his arm. Those clinical features change the expected “long-term course.” Tr. 232.¹³

The predictions about how Elijah would have fared as of April 19, 2011 (before the vaccinations and before he had his MRI) need to be placed in context with predictions that could be made about Elijah as of his condition on April 29, 2011 (when he was discharged). Between April 21, 2011 and April 22, 2011, Elijah felt dizzy and off-balanced, had swelling in his face, and, later, acted like he had a stroke. After a CT and an MRI revealed lesions in his brain, doctors diagnosed him as suffering ADEM. Exhibit 5 at 4 (discharge summary).

Based on an article, Dr. Mattson opined, that in zero to 28 percent of ADEM cases, the individual is later diagnosed with multiple sclerosis. Tr. 35-36 and 74 (citing exhibit 35 (Silvia Tenenbaum et al., Acute disseminated encephalomyelitis, 68 Neurology S23 (2007)) at S31). Tenenbaum, in turn, relies upon four studies in which the rates of multiple sclerosis were reported as 0%, 9.5%, 27%, and 28%. The last study, whose lead author is Yann Mikaeloff and which is reference 39 in the Tenenbaum article, appears in the record as exhibit Q (Yann Mikaeloff et

¹³ The simple presence of oligoclonal bands does not necessarily augur the development of multiple sclerosis. The Williams study on twins suggests that some people can have oligoclonal bands but not any clinical symptoms. Exhibit 42 (Williams) at 1146. Dr. Sriram agreed with this conclusion. Tr. 230. When Dr. Mattson was asked about the significance of the oligoclonal bands, he stated Elijah “could have had those bands forever and never caused a problem. We don’t know.” Tr. 116.

Scientists have relatively little information about whether oligoclonal bands can be useful in predicting the course of multiple sclerosis. One problem is that because spinal taps are invasive procedures, doctors do not perform them without a good reason.

This lack of knowledge contributed to an erroneous argument the Secretary offered. The Secretary pointed out that approximately 90 to 95 percent of people with multiple sclerosis have oligoclonal bands. Resp’t’s Br. filed May 23, 2014 at 27. However, this statistic is not quite on point. The better but unknown piece of information is the percentage of people with positive oligoclonal bands who develop multiple sclerosis.

al., First Episode of Acute CNS Inflammatory Demyelination in Childhood: Prognostic Factors for Multiple Sclerosis and Disability, 144 J Peds 246 (2004)) at 249. Ms. Hunt emphasizes that even if the highest figure is accepted (28 percent), then in more than two-thirds of ADEM cases, the person is not later diagnosed with multiple sclerosis. Pet'r's Br. at 18; Pet'r's Reply at 3, 8, 10.

Dr. Sriram's opinion on this point was not presented well. Although Dr. Mattson had disclosed the zero to 28% range in his reports, Dr. Sriram did not respond to this aspect in his pre-trial disclosures. When the undersigned asked for Dr. Sriram's opinion during the hearing, he stated that 60 percent of people with ADEM go on to suffer a second demyelinating event (thereby satisfying the diagnostic criteria for multiple sclerosis) within five years. The problem was that Dr. Sriram did not cite articles for the basis of his opinion. Tr. 185. In the Secretary's brief, she attempted to fill this gap by citing to the Mikaeloff article. Resp't's Br. at 40 n.17.

Unfortunately, neither expert testified about the Mikaeloff article, making an interpretation of it difficult.¹⁴ When experts do not discuss an article, special masters are not required to decipher its meaning after a party cites it in a post-hearing brief. Moberly v. Sec'y of Health & Human Servs., 85 Fed. Cl. 571, 598 (2009), aff'd, 592 F.3d 1315 (Fed. Cir. 2010).

In any event, even if Dr. Sriram's estimate that 60 percent of children who experience a demyelinating attack have a second event within five years were credited, there would remain a substantial minority of children who do not have a second attack. Ms. Hunt's theory is that absent the vaccination, Elijah would have belonged in the group of children who experienced only a single event. Dr. Mattson averred: If what happened in April were a second event, "then it was triggered in particular by the vaccine and that's led to the fact that he has gone on to have a pattern of reoccurrence. He may never have had another event because, again, people with their first clinical event may never go on to have another event." Tr. 83.

Given the finding that Elijah was suffering from multiple sclerosis before the vaccination, Ms. Hunt may recover compensation by establishing that the

¹⁴ Similarly another article, which the experts did not discuss, estimated that the chance a person who had a clinically isolated syndrome with an abnormal MRI will develop multiple sclerosis in two years at 50 percent. Exhibit C (Alastair Compston et al., Multiple sclerosis, 372 Lancet 1503 (2009)) at 1503.

vaccinations significantly aggravated Elijah's multiple sclerosis. The following section analyzes this cause of action.

V. Significant Aggravation

As confirmed in W.C. v. Sec'y of Health & Human Servs., 704 F.3d 1352, 1357 (Fed. Cir. 2013), the elements of an off-Table significant aggravation case were stated in Loving. There, the Court blended the test from Althen v. Sec'y of Health & Human Servs., 418 F.3d 1274, 1279 (Fed. Cir. 2005), which defines off-Table causation cases, with a test from Whitcotton v. Sec'y of Health & Human Servs., 81 F.3d 1099, 1107 (Fed. Cir. 1996), which concerns on-Table significant aggravation cases. The resulting test has six components. These are:

(1) the person's condition prior to administration of the vaccine, (2) the person's current condition (or the condition following the vaccination if that is also pertinent), (3) whether the person's current condition constitutes a "significant aggravation" of the person's condition prior to vaccination, (4) a medical theory causally connecting such a significantly worsened condition to the vaccination, (5) a logical sequence of cause and effect showing that the vaccination was the reason for the significant aggravation, and (6) a showing of a proximate temporal relationship between the vaccination and the significant aggravation.

Loving, 86 Fed. Cl. at 144. Each element is discussed below.

A. Theory

One way to analyze the six Loving prongs is to start with the fourth prong, which corresponds to the first prong of Althen. Hennessey v. Sec'y of Health & Human Servs., No. 01-190V, 2009 WL 1709053, at *42 (Fed. Cl. Spec. Mstr. May 29, 2009), mot. for rev. denied, 41 Fed. Cl. 126 (2010). This approach brings to the forefront the question of whether the vaccine can cause a significant aggravation.

Through Dr. Mattson, Ms. Hunt advances two theories (molecular mimicry and bystander activation). Dr. Mattson opined that these theories explain how vaccines can cause ADEM and whatever can cause ADEM can also cause multiple

sclerosis. Pet'r's Br. at 25-30. When Dr. Mattson was pressed to explain which of the three vaccines Elijah received harmed him, he focused on the varicella vaccine. Unlike the Tdap and pneumococcal vaccines, the varicella vaccine contains a live attenuated virus. Tr. 119.

Identifying the particular vaccine relevant to a claimed injury is an aspect of petitioner's obligation to "provide a reputable medical or scientific explanation that pertains specifically to the petitioner's case." Broekelschen, 618 F.3d at 1345. Information about the possible harmful side effects of other vaccines may constitute "existing data" from which an expert may extrapolate. See Gen. Elec. Co. v. Joiner, 522 U.S. 136, 146 (1997). Whether this extrapolation is reasonable depends upon many factors, including the extent to which the expert has explained why the vaccines are analogous. See Cedillo v. Sec'y of Health & Human Servs., 617 F.3d 1328, 1339 (Fed. Cir. 2010). Here, a predicate for Dr. Mattson's theory is that some vaccines may cause ADEM. The specific vaccines are the rabies vaccine and the smallpox vaccine. Dr. Sriram seemed to accept the proposition that older form of the rabies vaccine can cause ADEM. See exhibit A (Dr. Sriram's report) at 4; Tr. 171. The accepted basis for the causal connection is that the rabies vaccine contained remnants of neural tissue. Exhibit 34 (Hans-Peter Hartung et al., ADEM: Distinct disease or part of the MS spectrum?, 56 *Neurology* 1257 (2012)) at 1257; Tr. 78.

While Dr. Mattson cited articles linking either rabies vaccine or smallpox vaccine to ADEM, none of these articles linked those vaccines to multiple sclerosis, as Dr. Mattson conceded on cross-examination. Tr. 103. Further, one study looked for articles linking rabies vaccine and multiple sclerosis. These authors found two articles and concluded that both showed "a null association." Exhibit G (Mauricio F. Farez et al., Immunization and risks of multiple sclerosis: systematic review and meta-analysis, 258 *J. Neurology* 1202 (2011)) at 1202. Besides the rabies vaccine and the smallpox vaccine, there appears to be less acceptance that vaccines can cause encephalomyelitis. Tr. 157-58.

As to whether any of the vaccines that Elijah received (the Tdap, varicella, and meningococcal vaccines) can cause multiple sclerosis, the Secretary presented two valuable studies: the articles by Farez and Confavreux. Exhibit E (Christian Confavreux et al., Vaccinations and the risk of relapse in multiple sclerosis, 344(5) *The New England Journal of Medicine* 319 (2001)) at 324 (table 3). These studies support the proposition that the varicella vaccine (Farez) and the Tdap vaccine (Confavreux and Farez) do not affect multiple sclerosis.

The Confavreux researchers studied 643 people with multiple sclerosis who received various vaccines, including the tetanus vaccine. The authors examined whether the participants suffered more relapses of their multiple sclerosis during the two months after vaccination compared with relapses at other times. For combined tetanus vaccines, the relative risk was 0.22 and the 95 percent confidence interval was 0.05-0.99.¹⁵ The authors concluded: “Most vaccinations, especially those against tetanus plus poliomyelitis or diphtheria, were actually associated with a lower risk of relapse, although the difference was not significant.” Id. Dr. Mattson recognized that a relative risk of 0.22 suggests that receipt of the tetanus vaccine actually protected the individual against relapses. Tr. 122. Because the people in the Confavreux study already had multiple sclerosis when they were vaccinated, Elijah closely resembles those participants and the findings from the study provide some information about his case.

The other significant study was by Farez and colleagues. This group looked through various databases to find results of randomized clinical trials and non-randomized studies that examined whether various vaccinations affect the likelihood of developing multiple sclerosis or having a relapse. Exhibit G (Farez) at 1198. The located studies were the basis for a meta-analysis in which the researchers pooled data from the individual studies. Id.; Tr. 122-23, 189.

Pertinent to Elijah’s case, Farez and colleagues analyzed vaccines against tetanus, varicella, diphtheria, diphtheria-tetanus-pertussis, and pertussis.¹⁶ Except for the varicella vaccine, Farez et al. concluded that the vaccines were not associated with a higher risk of developing multiple sclerosis or higher risk of relapse. Exhibit G (Farez) at 1203.

For the varicella vaccine, the Farez researchers identified only one study, which was the Zorzon study. Exhibit G (Farez) at 1201. The Farez group declined to draw a causal connection and cited three studies, including the Confavreux study, as “fail[ing] to establish a link between vaccinations and MS.” Id. Furthermore, Ms. Hunt did not elicit any testimony regarding Zorzon and did not

¹⁵ The information for the combined tetanus vaccine differed from the information for the tetanus vaccine alone. For just the tetanus vaccine, the relative risk was 0.75 with a 95% confidence interval of 0.23-2.46.

¹⁶ The researchers could not find any studies regarding the meningococcal vaccine. Exhibit G (Farez) at 1204.

cite this study in either her posthearing brief or posthearing reply. Consequently, no weight is given to the Zorzon study.

Without Zorzon, the epidemiological evidence is inconsistent with a theory that a vaccination can cause or worsen multiple sclerosis. Ms. Hunt's response is to challenge the value of epidemiological evidence because of the small sample sizes. Pet'r's Br. at 29. In Dr. Mattson's view, vaccines can cause neurologic events so rarely (perhaps at a rate of one case of ADEM per 3 million doses of vaccine) that any epidemiological study would need to involve millions of people.¹⁷ Thus, because the Confavreux study involved fewer than 700 people, the results are not meaningful. Tr. 109-10.

The soundness of Dr. Mattson's criticism is difficult to assess because Dr. Mattson does not have any training in epidemiology. Tr. 131. Likewise, although Dr. Sriram had confidence in the statisticians in Confavreux's group, Dr. Sriram does not have any specialized knowledge about statistics. Tr. 188. For their part, Confavreux and colleagues asserted that their study design was strong because data exposures were collected during the entire period, patients were unaware of hypothesis, and medical records confirmed patient's documentation. They represented that it had a "90 percent power to detect a doubling of the risk of relapse within two months of vaccination." Exhibit E at 325.

The ability of epidemiologic studies to detect an increased incidence of rare events is a recurring question. See Knudsen v. Sec'y of Health & Human Servs., 35 F.3d 543, 550 (Fed. Cir. 1994) (discussing relative infrequency of encephalopathies caused by the diphtheria-tetanus-pertussis vaccine). In the Vaccine Program, petitioners may establish that a vaccine can cause a disease without submitting an epidemiologic study. Capizzano v. Sec'y of Health & Human Servs., 440 F.3d 1317, 1325 (Fed. Cir. 2006). But, the Federal Circuit has

¹⁷ Dr. Mattson's estimate comes from an analysis of a European database that collects reports of adverse events following varicella vaccination. The researchers reported that after 3.3 million doses of varicella vaccine had been distributed over five years, there was one report of ADEM. Exhibit I (Nicolas Golleret et al., Safety profile of live varicella virus vaccine (Oka/Merck): Five-year results of the European Zoster Virus Identification Program (EU VZVIP), 28 Vaccine 5878 (2010)) at 5879-80. However, this report of ADEM after vaccination does not establish that the vaccination caused the ADEM. See Analla v. Sec'y of Health & Human Servs., 70 Fed. Cl. 552, 558 (2006) (noting that the VAERS database may not provide reliable evidence regarding causation).

also ruled that in denying compensation, a special master may rely on epidemiologic studies that cast doubt upon the causal theory asserted. W.C., 704 F.3d at 1361 (citing Confavreux); Grant v. Sec'y of Health & Human Servs., 956 F.2d 1144, 1149 (Fed. Cir. 1992)(“epidemiological studies are probative evidence relevant to causation”).¹⁸

In accord with these precedents, Farez and Confavreux constitute some evidence that contradicts or at least undermines the theory that vaccinations cause or worsen multiple sclerosis. See Bazan v. Sec'y of Health & Human Servs., 539 F.3d 1347, 1353 (Fed. Cir. 2008) (holding that special masters may consider evidence that the government has introduced in determining whether a petitioner has met her burden of proof). But, these epidemiologic studies cannot establish that it is impossible for vaccines to affect multiple sclerosis. Thus, it is necessary to examine the specific theories Dr. Mattson advanced to explain how a vaccination can cause or worsen multiple sclerosis.

To link vaccinations and multiple sclerosis, Dr. Mattson presented two theories. First, Dr. Mattson proposed molecular mimicry. Second, Dr. Mattson offered bystander activation. See Pet'r's Postthr'g Br. at 26.

Molecular mimicry is based upon an assertion that the molecular structure of vaccines resembles (or mimics) the molecular structure of tissue found in the body. Tr. 52 and 60 (Dr. Mattson), 181 (Dr. Sriram agreed with Dr. Mattson's description of molecular mimicry). Researchers have proposed molecular mimicry as a method to explain how infectious agents may cause ADEM, although this theory remains unproven from a scientific standpoint. See exhibit 35 (Tenenbaum) at S32 (“microbial infections”); exhibit 37 (Alex Tselis and Robert P. Lisak, Acute disseminated encephalomyelitis, Clinical Neuroimmunology 147 (2005)) at 153 (“infecting virus or other antigen”); exhibit 34 (Hartung) at 1259 (“[v]iral or bacterial superantigens”). From this foundation, Dr. Mattson

¹⁸ After briefing in Ms. Hunt's case closed, the Federal Circuit issued an opinion critical of the (undersigned) special master's citation to epidemiological studies. Koehn v. Sec'y of Health & Human Servs., 773 F.3d 1239, 1243 (Fed. Cir. 2014). However, Koehn did not overrule W.C. and Grant, which remain binding precedent. South Corp. v. United States, 690 F.2d 1368, 1370 n.2 (Fed. Cir. 1982) (en banc); Johnston v. IVAC Corp., 885 F.2d 1574, 1579 (Fed. Cir. 1989). The continued vitality of the acceptance of epidemiology in W.C. is significant because Ms. Hunt's case and W.C. involved the same studies.

extrapolates from infectious agents to vaccines and from ADEM to multiple sclerosis. Tr. 69 (discussing exhibit 37 (Tselis)), 111.

The obstacle is that there is no basis for finding any similarity between any of the vaccines at issue here and neurologic tissue. Tr. 119-20 (Dr. Mattson). Dr. Sriram questioned the reliability of the molecular mimicry theory. He stated: “The evidence that any of the human autoimmune diseases are based on molecular similarities between an antigen or part of the protein in the central nervous system . . . is still very hypothetical.” Tr. 181. Dr. Sriram explained that scientists have looked for similarities between vaccines and myelin basic protein but not found any similarities. Id. Thus, Dr. Sriram characterized molecular mimicry as “a biological possibility.” Id.

Dr. Sriram’s description fits. Dr. Mattson has provided a theory of what might happen, but he has not presented persuasive evidence that molecular mimicry does happen with the relevant vaccines. Ms. Hunt seems to argue that requiring more supporting evidence from Dr. Mattson would erroneously raise her burden of proof. See Pet’r’s Postthr’g Br. at 30.¹⁹

Ms. Hunt is not correct. Judges at the Court of Federal Claims have explained that special masters do not err when they require petitioners establish the reliability of an expert’s opinion. See La Londe v. Sec’y of Health & Human Servs., 110 Fed. Cl. 184, 201 (2013) (the petitioner’s expert “could not back up his hypothesis with a reliable medical or scientific explanation.... [The special master] quite properly required petitioner to carry her burden to bring forward a reliable medical or scientific explanation”), aff’d, 746 F.3d 1334, 1340 (Fed. Cir. 2014); Langland v. Sec’y of Health & Human Servs., 109 Fed. Cl. 421, 441 (2013) (“the Special Master did not commit a legal error by requiring a sufficiently-detailed explanation of how” a vaccine can cause a disease); Taylor v. Sec’y of Health & Human Servs., 108 Fed. Cl. 807, 819 (2013) (“the mere existence” of expert testimony about a theory “is insufficient to satisfy the burden of showing a ‘persuasive’ medical theory—this theory must also preponderate”). More specifically, an evaluation to see whether a vaccine at issue is structurally similar to relevant human tissue is consistent with the special master’s role in determining whether a petitioner has established the first Althen prong. W.C., 704 F.3d at

¹⁹ Ms. Hunt also argues that Dr. Mattson’s opinion is entitled to deference because he treated Elijah. Pet’r’s Postthr’g Br. at 25-26. This argument is discussed below in section C.

1360; Caves v. Sec’y of Health & Human Servs., 100 Fed. Cl. 119, 135 (2011), aff’d without op., 463 Fed. Appx. 932 (Fed. Cir. 2012).

Ms. Hunt’s evidence regarding molecular mimicry is about the same as evidence in these other cases. Molecular mimicry is plausible as a theory, in the sense that molecular mimicry is consistent with how the immune system responds. But, when the question turns from plausibility to legal probability, Ms. Hunt’s claim falters. She has not established that it is likely that any of the vaccines Elijah received can cause multiple sclerosis via molecular mimicry.

The second theory, bystander activation, actually has less evidentiary support than molecular mimicry. Dr. Mattson briefly mentioned the bystander activation theory in his testimony but did not explain it very well. See Tr. 59-60. Dr. Mattson referred to the Tselis article as describing bystander activation, but his testimony was only two sentences. Tr. 69. The article does not use the term “bystander activation” so additional testimony by Dr. Mattson would have been useful. Additionally, in the portion of the article that appears to be most relevant, the authors present a “possible mechanism.” Exhibit 37 (Tselis) at 153. With the relatively sparse evidentiary support of bystander activation, Ms. Hunt’s arguments about bystander activation are conclusory. Pet’r’s Postthr’g Br. at 26-27; Pet’r’s Reply at 5-6.

In sum, Ms. Hunt has not met her burden of proof to present a theory that explains how a relevant vaccine can cause (or can significantly aggravate) multiple sclerosis. This finding is based upon epidemiologic studies that have looked for a connection between vaccinations and multiple sclerosis and have not found such. This finding is also separately based upon the two theories Dr. Mattson posited, molecular mimicry and bystander activation. Dr. Mattson did not present persuasive evidence that either theory shows that it is more likely than not that the vaccines contribute to multiple sclerosis.

B. Timing

Another aspect of Ms. Hunt’s case that she is required to establish is that the significant aggravation arose in a time in which it is medically acceptable to infer that a vaccine caused the worsening. The appropriate temporal relationship is reflected in the third prong in Althen. 418 F.3d at 1278. After Althen, other Federal Circuit cases have explored dimensions of the timing aspect and Loving, as confirmed by W.C., imported the timing requirement from causation cases into significant aggravation cases.

The Federal Circuit interpreted Althen as permitting a special master to find that an alleged reaction to a vaccine occurred too quickly after the vaccination to support a causal relationship. Bazan, 539 F.3d at 1352. Thus, Bazan stands for the legal proposition that a petitioner must establish the appropriate temporal relationship between the vaccination and the onset of the problem for which the petitioner seeks compensation. This temporal relationship must be neither too soon nor too long. Bazan also demonstrates that the special master does not have to accept the testimony of a treating doctor regarding the appropriate temporal relationship.

The Court of Federal Claims recognized that the third prong of Althen actually contains two parts: the medically acceptable interval and the date on which the symptoms began. Shapiro v. Sec’y of Health & Human Servs., 101 Fed. Cl. 532, 542-43 (2011), recons. denied after remand on other grounds, 105 Fed. Cl. 353 (2012), aff’d without op., 503 Fed. Appx. 952 (Fed. Cir. 2013). In accord with the structure identified in Shapiro, these two aspects are addressed.

1. Medically Acceptable Interval

At hearing, Dr. Mattson offered the opinion that Elijah’s neurologic symptoms began two days after vaccination and that two days is a medically acceptable interval. On direct examination, his testimony on this topic was only a few lines:

Q. Do you believe there is a proximal temporal relationship between the vaccines and Elijah’s injuries?

A. Yes.

Q. Tell the Court, if you would, please, why you believe that.

A. Because it occurred within the three -- I guess the focal signs develop within a couple days of the vaccine -- two days of the vaccine and then, ultimately, develop into a more full-blown stuttering bimodal onset of different areas of inflammation in the brain.

Tr. 62; see also Tr. 92, 115-16. Later, Dr. Mattson identified the Scott article as supporting an incubation period of 2 to 18 days. Tr. 64. Ms. Hunt relies upon Dr.

Mattson's testimony, the Scott article, and the Tenenbaum article. Pet'r's Posthr'g Br. at 36.

When Dr. Scott wrote his article in 1967, the smallpox vaccination was still administered. He reported that children under two years old developed encephalitis after smallpox vaccination in "2 to 18 days." Exhibit 36 (Thomas F. McNair Scott, Postinfectious and Vaccinal Encephalitis, 51(3) Medical Clinics of North America 701 (1967)) at 705 (table 3). However, the incubation period in children older than two years old differed. In the older children, the interval was "8 to 15 days." Id.

On cross-examination, this difference was pointed out to Dr. Mattson. He was asked why the latency period differed, and Dr. Mattson said he did not know. Tr. 156-57. Because Elijah was 12 years old, the Scott article does not support Dr. Mattson's opinion that two days is an acceptable interval.

The remaining article is by Tenenbaum and colleagues. They stated: "Postinfectious forms of ADEM typically begin within 2 to 21 days after an infectious event." Exhibit 35 at S32. Unfortunately, neither Dr. Mattson nor Dr. Sriram was asked about this particular passage.

Dr. Sriram testified more generally about the appropriate medical interval. Dr. Sriram stated that the process by which a vaccination can trigger the immune system to attack myelin in a person's brain would usually take approximately one week. Individual steps in this process include: presenting parts of the vaccine to the regional lymph nodes, recognizing the vaccine as something foreign, producing an appropriate T cell response, amplifying the T cell response through division, crossing the blood brain barrier, (mis)identifying myelin in the brain as a foreign substance, multiplying again, and then attacking the myelin. Tr. 236-37; see also Tr. 192. Dr. Sriram stated that it is "highly unlikely for the kinetics of the time frame of lymphocytes to react, activate, travel through the nervous system, recruit, damage myelin and develop symptoms in a two-day time frame. It's extremely unlikely." Tr. 193; accord exhibit A (Dr. Sriram's report) at 3. In Dr. Sriram's view, the amount of time to develop neurologic deficits is "usually five to seven days." Tr. 193.²⁰

²⁰ As the Secretary noted, several articles are consistent with a latency period of approximately one week. Resp't's Br. at 33. These articles include: exhibit 31 (Til Menge et

On rebuttal, Dr. Mattson was given an opportunity to address Dr. Sriram's opinion that the kinetics of antibody production leading to neurologic problems takes at least five days. Dr. Mattson did not challenge the sequence of steps and he did not challenge that the expected amount of time is at least five days. See Tr. 242-43, 249-50. Instead, Dr. Mattson's opinion was that Elijah's pre-vaccination health decreased the required amount of time. The oligoclonal bands in Elijah's cerebrospinal fluid indicated that his "immune system [was] already primed . . . to take off with him more quickly." Tr. 251.

Dr. Mattson's idea that an individual who was primed to respond to an antigen will respond to a repeated exposure of that antigen more quickly has some merit. A foundation for vaccination is that immunized people will mount an immune response to defend themselves against infectious organisms rapidly and strongly. Although neither expert testified about some of the basic principles of immunology, the undersigned has frequently heard testimony from experts retained by both petitioners and respondents about how the immune system operates. This background provides a basis for considering Dr. Mattson's priming theory. See Lampe, 219 F.3d at 1362 (noting that special masters may use their "accumulated expertise" to resolve cases).

For the priming theory, Dr. Mattson has left unanswered at least two questions. First, the priming theory seems based upon a similarity between the initial antigen and the latter antigen. For example, the measles vaccine primes a person to respond to the measles virus. However, as Dr. Mattson conceded on cross-examination, the initial agent that prompted Elijah to develop oligoclonal bands is not known. Tr. 115-16. Without this knowledge, Dr. Mattson must be assuming that a relevant vaccine was somehow similar to the spark for Elijah's multiple sclerosis and there is no evidence to support this assumption.

Second, even if priming were assumed, Dr. Mattson has not attempted to quantify how quickly a primed immune response would take. If a normal immune

al., Acute Disseminated Encephalomyelitis, 62 Arch Neurol 1673 (2005)) at 1674 (latency of 7 to 14 days); exhibit 29 (Richard T. Johnson et al., Postinfectious Encephalomyelitis, 5(2) Seminars in Neurology 180 (1985)) at 183 (the latency between rabies vaccination and encephalomyelitis was 10 to 41 days); exhibit 37 (Tselis) at 5 (the latency between infection and ADEM is one to three weeks). The Secretary cited these articles as a basis to contradict the latency reported in Tenenbaum, which was 2 to 21 days. Unfortunately, again, neither Dr. Mattson nor Dr. Sriram testified about the latency periods that Menge, Johnson, and Tselis reported.

process takes five days, how fast is a primed immune response? Dr. Mattson did not say. Dr. Sriram stated that in animal models of experimental autoimmune encephalitis, primed animals have been reported to respond in three days. Tr. 193.

Overall, the evidence is mixed and both sides could have presented their positions more thoroughly. In support of Ms. Hunt's assertion that two days is appropriate, she fairly pointed to Dr. Mattson's testimony, the Tenenbaum article, and the general theory that primed individuals respond more quickly. In contrast, the Secretary pointed to the uncontradicted testimony from Dr. Sriram that a normal immune-mediated response takes at least five days, the articles that mentioned a five, seven, or ten day interval, and Dr. Sriram's testimony that primed animals take three days to respond.

This evidentiary record supports a finding that three days is an acceptable temporal relationship in a case where the immune system is primed. Specific reasons include that the majority of the articles indicated the temporal relationship was at least five days. Although Ms. Hunt's reliance upon Tenenbaum's statement about "2 days" is legitimate, the Tenenbaum article provided no basis for the statement. Furthermore, Dr. Sriram has detailed the biologic processes that must occur for a vaccination to lead to an immune-mediated neurologic problem. Dr. Sriram's research on experimental models gives him a foundation for opining on how long immune processes underlying molecular mimicry, such as cell division, take. See Tr. 192-93. Dr. Mattson was not willing to opine how much time is needed for cells to divide. Tr. 250.

From the starting point of five days, the priming theory suggests a faster response. Although Dr. Mattson's explanation about this theory was not strong, it is reasonable to accept that the oligoclonal bands suggest some aberration in Elijah's immune system could contribute to a quicker reaction. Ms. Hunt, as noted above, did not provide any basis for finding that the reaction would be so fast that it would happen in two days. Dr. Sriram's testimony that even primed animals take three days, although based upon articles that were not filed into the record, fills this gap.

2. Onset of Elijah's Acute Neurologic Problem

The second aspect of the temporal relationship prong from Althen concerns when the vaccinee's problems arose. This is another disputed point between the parties. For the reasons explained below, the Secretary's position that Elijah's neurologic problems started the day after vaccination is credited.

Initially, it appeared that the parties were not disputing when Elijah's neurologic problems began. In Dr. Mattson's first substantive report, he stated: "Within a day of vaccination (Tdap, varicella, Meningococcal), associated with a febrile inflammatory response, Elijah McLeod developed symptoms and signs of multifocal inflammation in his white matter (dizziness, bilateral leg weakness, left leg weaker, right eye visual decrease, left face numbness)." Exhibit 26 at 1.

Dr. Sriram did not contest this onset. In his first report, Dr. Sriram wrote: Elijah's "symptoms began within 24 hours after the receipt of the vaccinations." Exhibit A at 2. In this report, Dr. Sriram also asserted that the time for the immune system to generate a response to the vaccine would be at least five days, and, thus, the vaccinations could not have caused the bands of antibodies detected as oligoclonal bands. Id. at 3-4.

Dr. Mattson's next report started to blur different symptoms. Dr. Mattson wrote: "The event in question of multifocal demyelination began within a day of the vaccinations (Tdap, meningococcal conjugate, varicella) in question, with a febrile response and the next day more focal neurological complaints." Exhibit 38 at 1. Dr. Mattson did not identify the complaints that he considered to be "more focal."

More specificity came in Dr. Mattson's final report. He stated: "Elijah McLeod received the vaccinations in question on 4/20/2011, had dizziness and vomiting starting 4/21/2011, developed focal neurologic symptoms and signs starting on 4/22/2013." Exhibit 41. The combination of these two reports suggests that Dr. Mattson considered Elijah's dizziness and vomiting, which he had on April 21, 2011, to be a febrile response to the April 20, 2011 vaccination.

Dr. Mattson's direct testimony about the temporal relationship was thin. He simply said that Elijah's "focal signs develop[ed] within a couple days of the vaccine." Tr. 62. He did not elaborate.

On cross-examination, Dr. Mattson was asked about his earlier reports in which he wrote about Elijah developing problems "within a day of vaccination." Dr. Mattson conceded that his reports did say this, but he said he "was off a day." Tr. 113-14. Dr. Mattson maintained that his second report corrected the first report

in that the second report said that a febrile response began within a day of vaccination. Tr. 114; see also exhibit 38.²¹

Dr. Sriram's testimony was consistent with his reports. Dr. Sriram opined that on April 21, 2011, which is the day following vaccination, Elijah was demonstrating neurologic symptoms. Dr. Sriram point out that Elijah was dizzy, unsteady in his gait, and had fullness in the left side of his face. Tr. 193-94.

The evidence preponderates in favor of finding that Elijah was having neurologic problems on April 21, 2011. In Dr. Mattson's first report, he listed "dizziness" and "left face numbness" as examples of "symptoms and signs of multifocal inflammation in his white matter." Exhibit 26 at 1. While Dr. Mattson attempted to push the onset of neurologic problems ahead to April 22, 2011, on April 21, 2011, Elijah did report he was feeling dizzy and his mother said his face was full. Exhibit 4 at 3.

Ms. Hunt did not present any reason for discounting these problems as manifestations of a neurologic problem. On cross-examination, Dr. Mattson agreed that dizziness and unsteadiness are "nonspecific" neurologic symptoms. Tr. 115. Dr. Sriram explained that a weakness in facial muscles can cause a person to appear to have a swollen face. Tr. 193-94. Dr. Mattson did not seriously challenge Dr. Sriram's explanation, saying it was "certainly a possibility." Tr. 248.

Ms. Hunt's brief emphasizes the symptoms that Elijah experienced on April 22, 2011. See Pet'r's Br. at 36. But, this emphasis is misplaced in that the Secretary does not dispute that the April 22, 2011 problems, like difficulty with balance, were manifestations of a neurologic problem. The issue concerns the symptoms on April 21, 2011, and, on this point, the evidence favors a finding of neurologic problems.

3. Summary

The interval between the April 20, 2011 vaccinations and when Elijah experienced symptoms of his neurologic disease has been a difficulty for Ms. Hunt

²¹ Ms. Hunt argues that the "febrile response was a localized reaction to the vaccinations." Pet'r's Br. at 37. However, in the cited portion of the transcript (page 114), Dr. Mattson does not describe Elijah's fever as part of a localized reaction. Instead, in other places in the transcript, Dr. Mattson equates Elijah's sore arm as part of a localized reaction. Tr. 26, 249.

throughout this litigation. Ultimately, the evidence suggests that an immune-mediated reaction in a person with an intact central nervous system takes at least five days. Because Elijah's central nervous system already contained some antibodies (as detected as oligoclonal bands), he might respond more rapidly. Although Ms. Hunt's proof for this proposition was not especially persuasive, a generous estimate in her favor is that the interval might be as few as three days.

Shortening the interval from five days to three days still does not assist Ms. Hunt. The evidence supports her conclusion that, more likely than not, Elijah developed symptoms of a neurologic disorder within only one day. She has not presented any evidence to show that the necessary steps can occur so quickly. Consequently, Ms. Hunt has failed to meet her burden of proof regarding the appropriate temporal interval.

C. Logical Sequence

For reasons just explained, Ms. Hunt has failed to present a persuasive theory explaining how a vaccine can worsen multiple sclerosis and she has not established that any worsening could occur within one day. Another element of Ms. Hunt's case is to present a logical sequence of cause and effect connecting the vaccinations to either the onset of Elijah's multiple sclerosis or the worsening of Elijah's multiple sclerosis. This element is the second prong of the three-part Althen test and the fifth prong of the six-part Loving test.

Simply as a matter of logic, because Ms. Hunt has not established the general proposition that one of the relevant vaccines can worsen multiple sclerosis, she also cannot establish the specific proposition that one of the vaccines did worsen Elijah's multiple sclerosis. See Veryzer v. Sec'y of Health & Human Servs., 100 Fed. Cl. 344, 352-53 (2011) (describing general causation and specific causation), aff'd without op., 475 Fed. Appx. 765 (Fed. Cir. 2012); Caves, 100 Fed. Cl. at 145 (discussing the logical relationship between Althen prong one and Althen prong two). Similarly, the problems with the temporal interval prevent a conclusion that a vaccine worsened Elijah's multiple sclerosis. Koehn v. Sec'y of Health & Human Servs., 773 F.3d 1239, 1243 (Fed. Cir. 2014) (affirming judgment denying compensation on the ground that petitioner did not establish a proximate temporal relationship). Thus, Ms. Hunt cannot meet her burden on this element.

Nevertheless, additional analysis is merited because Ms. Hunt is relying upon Dr. Mattson, who has assisted in caring for Elijah for many years. The

Federal Circuit has instructed special masters to consider carefully the opinions of treating doctors: “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.’” Capizzano, 440 F.3d at 1326, quoting Althen, 418 F.3d at 1280.

However, in this case the factual bases for deferring to Dr. Mattson simply because he treated Elijah appear to be absent. Dr. Mattson, who specializes in treatment of multiple sclerosis (Tr. 13-14), stated: “We don’t know the cause” of ADEM and multiple sclerosis. Tr. 102. He continued that for ADEM, “we have things that we assume are triggering it. . . . [But], in general we don’t know why because a lot of people have the same triggers that don’t ever end up getting ADEM or MS.” Tr. 102-03.²² The literature also notes that the etiology for multiple sclerosis is unknown. Exhibit D (Noseworthy) at 942 (“the sequence of events that initiates the disease remains largely unknown”); exhibit F (Frank DeStephano et al., Vaccinations and Risk of Central Nervous System Demyelinating Diseases in Adults, 60 Arch Neurology 504 (2003)) at 504 (“Unknown environmental factors, including certain infections, are also suspected to be involved in its pathogenesis”).

When the medical community does not understand what causes a disease, how can a treating doctor offer a reliable opinion about whether a vaccination contributed to the disease’s course? Dr. Mattson was specifically asked whether his first-hand experience as Elijah’s treating doctor gave him an advantage in identifying the cause of Elijah’s multiple sclerosis. Dr. Mattson responded that it did not. Tr. 152.

Dr. Mattson’s forthright assessment that his stature as a treating doctor did not give him special insights into the cause of Elijah’s multiple sclerosis added to his credibility as a witness. He was believable, at times, because he acknowledged

²² Dr. Sriram discussed three different theories for the pathogenesis of multiple sclerosis. Tr. 174-75. He testified that in his patients with multiple sclerosis, “in most of my cases, we do not have a cause.” Tr. 175.

his lack of knowledge. Tr. 23, 102.²³ But the same admissions leads to a finding that the petitioner's proof on this particular prong is lacking.

The admitted lack of knowledge about the causes of multiple sclerosis lies at the heart of the finding that Dr. Mattson was not persuasive in opining that vaccinations can worsen multiple sclerosis. The finding that Dr. Mattson was not persuasive on this specific matter is not intended to be viewed as a depreciation of his abilities as Elijah's doctor. Dr. Mattson has won awards from a statewide multiple sclerosis organization. Exhibit 27 (curriculum vitae) at 2. Additionally, he appeared to express most of his opinions with sincerity.

However, neither a doctor's sincerity nor vaunted experience necessarily makes the expert persuasive. See Doyle v. Sec'y of Health & Human Servs., 92 Fed. Cl. 1, 8 (2010). The doctor's experience in treating the vaccinee is one factor, although a very important factor, in considering the value of the doctor's opinion.

In Bazan, the petitioner presented the opinion of her treating neurologist and Dr. Hansen opined that the tetanus-diphtheria vaccination can cause a demyelinating disease to appear within 11 hours of vaccination. The special master did not credit this testimony for several reasons, including the conflicting testimony from Dr. Sriram, who opined that 10-14 days were required. Bazan, 539 F.3d at 1353. The Federal Circuit held that the special master did not commit an error in determining "that Dr. Sriram's testimony was more credible and probative than that of Dr. Hansen." Id. at 1354.

Bazan illustrates the principle that a special master is not required, as a matter of law, to agree with the testimony of a treating doctor. The example in Bazan limits the Federal Circuit's statement that "treating physicians are likely to be in the best position to determine" whether the vaccine injured the person. Capizzano, 440 F.3d at 1326. Thus, after Capizzano, in all cases, the special master must consider carefully the views of the treating doctor. In some cases, the testimony of a treating doctor may be persuasive. In other cases, the testimony of a treating doctor is not persuasive. See Snyder v. Sec'y of Health &

²³ On the other hand, Dr. Mattson's testimony that he made a simple mistake when he wrote in his first report that Elijah's experienced neurologic problems within a day of vaccination was less believable. His demeanor suggested uneasiness about this opinion. Apart from his demeanor, Dr. Mattson also conceded that Elijah's dizziness and unsteadiness were neurologic problems, albeit "nonspecific" ones. Tr. 115.

Human Servs., 88 Fed. Cl. 706, 745 n.67 (2009) (indicating that testimony from a treating doctor is not sacrosanct and may be rebutted).

Bazan resembles Ms. Hunt's case in several respects. In both cases, the petitioner relied upon the opinion of a doctor who treated the injured person. In both cases, the petitioner asserted a theory that a vaccine adversely affected the recipient's central nervous system. In both cases, the manifestation of this harm occurred within approximately 24 hours. Finally, in both cases, the Secretary relied upon the opinion of Dr. Sriram, who stated, among other points, that the manifestation happened too quickly. Ms. Hunt's attempts to distinguish Bazan (see Pet'r's Reply at 14) were conclusory. The outcome in Bazan supports (but does not require) the same outcome in Ms. Hunt's case.²⁴

For all these reasons, Ms. Hunt has not met her burden of presenting persuasive evidence showing a logical sequence of cause and effect beginning with the April 20, 2011 vaccinations and the course of Elijah's multiple sclerosis. She did not establish the vaccinations either caused or significantly aggravated the multiple sclerosis. This finding is another reason why compensation must be denied to Ms. Hunt.

D. Worsening

The remaining three prongs of the Loving test concerns Elijah's condition. Because of the previous findings, this analysis can be relatively brief.

1. Health before Vaccination

Before his April 20, 2011 vaccinations, Elijah had not suffered any overt problems that were diagnosed. But, he had two symptoms that, retrospectively, could be seen as manifestations of an undiagnosed episode of multiple sclerosis. These were numbness in his dominant (left) hand and double vision. At the time

²⁴ Although the Federal Circuit's legal determinations constitute binding precedent in the Vaccine Program, the determination that the special master was neither arbitrary nor capricious in finding that 11 hours was too quick an interval for a tetanus-diphtheria vaccine to cause a demyelinating disease depended upon the evidentiary record in that case. If there were a different evidentiary record, the outcome might be different because a "special master's task is to make a factual determination of causation based on the evidence in a particular case." Lampe, 219 F.3d 1357, 1366 (Fed. Cir. 2000). But, in weighing the evidence, special masters may use their "accumulated expertise." Lampe, 219 F.3d at 1362 (quoting Hodges v. Sec'y of Health & Human Servs., 9 F.3d 959, 961 (Fed. Cir. 1993))

of his vaccination, his cerebral spinal fluid contained antibodies, although they were not detected as oligoclonal bands until after the vaccination.

2. Health after Vaccination

Following the April 20, 2011 vaccinations, Elijah's health declined. He required hospitalization for seven days during which he was diagnosed as having ADEM. Approximately, six months later, Elijah suffered another attack during which the disease "declared" itself as being multiple sclerosis.

More recently, Elijah has been relatively healthy. Medications appear to be preventing additional attacks.

3. Whether there was a "Significant Aggravation"

Elijah's health has been worse after the April 20, 2011 vaccinations than he was before the vaccinations. But, when the record is viewed as a whole, there is not persuasive evidence that any vaccine caused the worsening.

VI. Conclusion

Elijah suffers from multiple sclerosis. Like anyone suffering from a permanent disease, he deserves sympathy and compassion. Yet, Congress restricted Vaccine Program compensation to people who establish that a vaccine caused or significantly aggravated their illnesses. Ms. Hunt has not established the legal requirements. Thus, her request for compensation must be DENIED.

IT IS SO ORDERED.

s/ Christian J. Moran
Christian J. Moran
Special Master