In the United States Court of Federal Claims
OFFICE OF SPECIAL MASTERS

KEVIN SPARROW and DANIELLE SPARROW, parents and natural guardians, on behalf of L.S.,	*	
Petitioners,	*	No. 18-295V Special Master Christian J. Moran
v.	*	
SECRETARY OF HEALTH AND HUMAN SERVICES,	*	Filed: March 19, 2024
Respondent.	*	

Scott B. Taylor, Urban & Taylor, S.C., Milwaukee, WI, for petitioner;
Rachelle Bishop, United States Dep't of Justice, Washington, D.C., for respondent.

DECISION DENYING COMPENSATION[1]

Kevin and Danielle Sparrow allege that a measles, mumps, and rubella (MMR) vaccine caused their daughter, L.S., to suffer from acute demyelinating encephalomyelitis (ADEM). The Secretary disputes this claim. The parties have presented evidence in support of their positions, including expert opinions, medical literature, testimony. They also argued their positions through briefs.

The Sparrows have not persuasively shown that the MMR vaccine harmed L.S. The basic problem is that the evidence, when considered as a whole, favors an infection as the cause of her initial neurologic problems. The causative virus was not likely to have come from the MMR vaccine. Secondarily, even if a virus

[1] Because this Decision contains a reasoned explanation for the action taken in this case, it must be made publicly accessible and will be posted on the United States Court of Federal Claims' website, and/or at https://www.govinfo.gov/app/collection/uscourts/national/cofc, in accordance with the E-Government Act of 2002. 44 U.S.C. § 3501 note (2018) (Federal Management and Promotion of Electronic Government Services). This means the Decision will be available to anyone with access to the internet. In accordance with Vaccine Rule 18(b), the parties have 14 days to identify and move to redact medical or other information, the disclosure of which would constitute an unwarranted invasion of privacy. Any changes will appear in the document posted on the website.

could be excluded as a potential cause, the Sparrows have not demonstrated how an MMR vaccine can cause ADEM or that it did in L.S.'s case.

I. Medical History

The parties agree that the medical records accurately recount events that took place around the time the medical record was created.[2] However, as discussed below, a challenge is that the doctors writing records about L.S. did not know what caused L.S.'s illness in March 2015. This lack of certainty, in turn, is the foundation for the competing opinions of the parties' experts, neurologist Dr. Lawrence Steinman and pediatric neurologist Dr. Michael Sweeney.

L.S.'s history is divided into periods. For the critical periods, this decision summarizes events in L.S.'s life by citing medical records and, to a lesser extent, Ms. Sparrow's CaringBridge journal.[3] Those summaries are followed by commentaries from Dr. Steinman and Dr. Sweeney because the experts' opinions contextualize L.S.'s signs and symptoms.

A. Birth to Vaccination

L.S. was born on February 28, 2009, after a gestation of approximately 36 weeks. Exhibit 1 (pediatrician's records) at 10; Exhibit 3 (birth certificate). L.S.'s development was delayed, and she received some therapies. Tr. 14-18. The extent of the delays appears not to be significant as the Secretary did not argue that any pre-existing problem caused L.S.'s illness in March 2015.

In any event, shortly before L.S. reached six years old, she saw her pediatrician, Claudia Koch, for a suspected urinary tract infection. Dr. Koch prescribed an antibiotic. During this appointment, L.S. received her first dose of the MMR vaccine. Exhibit 1 at 127-28 (Feb. 6, 2015). L.S. had received her Hib,

[2] This decision draws upon the recitation of facts as the parties have presented in their briefs. The decision often relies upon information from the Secretary's brief because the Secretary's brief is detailed about what happened to L.S.

[3] Ms. Sparrow shared her reflections on her daughter's illness, describing what was happening to L.S., what the medical staff was telling her, and her own feelings. Reading the journal conveys the anxiety Ms. Sparrow felt. However, the journal does not add much to the medical records, which trained professionals created. Thus, the decision cites mostly to the medical records.

pneumococcal, and DTaP vaccines in years prior, and Ms. Sparrow did not recall any adverse reaction. Tr. 39-40.

B. February 28, 2015 through March 4, 2015

1. February 28, 2015: Birthday Party and March 1, 2015: Bowling

L.S. was less energetic and declined to participate in birthday activities on Saturday, February 28, 2015. Exhibit 64 (CaringBridge journal), Exhibit 4 (Ms. Sparrow's affidavit) ¶ 3; Tr. 19, 34. She was also less energetic the next few days. Id.

On Sunday, March 1, 2015, Mr. Sparrow took L.S. bowling. Tr. 19. However, L.S. did not feel well and complained, among other problems, that her neck hurt. Tr. 19-20. Ms. Sparrow worried that pain in a child's neck meant that the child had meningitis. Exhibit 64 (CaringBridge journal) at 4, Tr. 37.

L.S.'s health at the end of February / beginning of March 2015 is a point when Dr. Steinman and Dr. Sweeney begin to differ in how they interpret what was happening to her. For Dr. Steinman, L.S. was starting to manifest symptoms of what was later diagnosed as ADEM. For Dr. Sweeney, L.S. was experiencing a viral infection.

2. March 2, 2015: First Trip to Emergency Room

L.S.'s parents brought her to the emergency room at Children's Hospital of Wisconsin ("CHOW") on Monday, March 2, 2015. Exhibit 2 at 3. This is 24 days after February 6, 2015, the date of vaccination. Ms. Sparrow recounted that L.S. had a headache starting March 1, 2015, and a fever and neck pain. Id.; see also Exhibit 64 (CaringBridge journal) at 4; Tr. 20-21. The doctor in the emergency room stated: "No rash noted." Exhibit 2 at 5. The doctors evaluated L.S. and discharged her with a prescription for an antibiotic.[4]

Although Ms. Sparrow was giving L.S. Tylenol and ibuprofen, L.S. was not improving. Exhibit 64 (CaringBridge journal) at 4; Tr. 20, 36. Ms. Sparrow informed Dr. Koch that L.S.'s symptoms continued later on March 2, 2015. Dr. Koch recommended returning to the emergency room. Exhibit 1 at 134.

[4] During the March 2, 2015 hospitalization, L.S. tested positive for strep. Exhibit 2 at 5, 7. However, doctors later indicated that the test reflected colonization and not disease. Id. at 113, 661.

3. March 2, 2015: Second Trip to Emergency Room

L.S. had a second visit to the emergency room at CHOW on March 2, 2015. Complaints included lethargy, vomiting, fever (101 degrees), headache and neck pain. Exhibit 2 at 42. Her parents reported she did not have congestion, rhinorrhea, or a sore throat but she did have a cough. Id. In the hospital, her axillary temperature was measured at 100.8 degrees and 101.3. Id. at 52 (time was 21:32), 43. Upon physical examination, no rash was noted and the parents denied a rash on review of system. Id. at 42-43. The doctors continued to suspect that she had strep throat, and discharged L.S. again. Id. at 44.

To Dr. Steinman, the fevers that L.S. was experiencing were manifestations of an inflammatory reaction in L.S.'s brain. Tr. 72. Dr. Sweeney disagreed. Dr. Sweeney stated that L.S.'s presentation was consistent with a viral infection. Tr. 192. Dr. Sweeney opined that children of L.S.'s age are frequently ill, perhaps as often as six times per year. He stated that a child attending school in Wisconsin in the winter was likely exposed to many pathogens. Tr. 255.

4. March 4, 2015: Third Trip to Emergency Room (Columbia St. Mary's Hospital)

On March 4, 2015, at approximately 4:00 P.M., L.S.'s parents arrived at the emergency department at Columbia St. Mary's Hospital. Her rectal temperature was 101.5 degrees Fahrenheit. Exhibit 11 at 246. The parents reported a history of nausea and vomiting ("N/V") for two days and L.S. had a blotchy rash encompassing her body. Id. at 247. She also had headaches and weakness. Id. By approximately 6:00 P.M., the doctors were giving L.S. antibiotics intravenously and planning to transport her to CHOW. Id. at 251. She was transferred to CHOW at approximately 7:15 P.M. Id. at 240 (discharge summary). At the time of discharge, L.S.'s rectal temperature was 102.0 degrees. Id. at 241.

While emergency medical personnel were transporting L.S. to CHOW, L.S.'s blood pressure and heart rate dropped. Exhibit 2 at 119. The emergency medical personnel gave her norepinephrine. Exhibit 2 at 119.

L.S. returned to the emergency department at CHOW on March 4, 2015 at approximately 8:09 P.M. Exhibit 2 at 183. An initial history and physical was conducted at approximately 9:00 P.M. by Rainer Gedeit. The history Dr. Gedeit

obtained was more-or-less consistent with that recounted above.[5] At the time of the examination, L.S.'s temperature was 97.3 degrees.[6] She was "uncomfortable," "irritable," "moaning" and "withdrawing to stimuli." Id. at 120. As part of Dr. Gedeit's examination of the skin, he noted: "generalized pinpoint/erythematous rash noted at previous hospital (comes and goes) no rash noted on this examination." Id. Dr. Gedeit was concerned about sepsis and/or meningitis. Id. L.S. was admitted to pediatric intensive care unit. Id. at 120, 183. This hospitalization lasted until April 4, 2015, during which she was periodically in critical care. Id. at 109.

C. March 5, 2015 to April 4, 2015: Hospitalization at CHOW

The medical records associated with this 30-day hospitalization run more than four thousand pages. Exhibit 2, passim. From this extensive documentation, the parties and their experts have identified a few key points. See Exhibit 18 (Dr. Steinman's report) at 4-7, Exhibit C (Dr. Sweeney's report) at 2-3, Pet'rs' Prehear'g Br. at 6-7, Resp't's Pre-hear'g Br. at 3-6.

1. Initial Treatment and Testing

One of the doctors' initial steps was to prescribe acyclovir. Exhibit 2 at 123. Acyclovir is an antiviral that is used to treat the herpes simplex virus (HSV-1). Tr. 74 (Dr. Steinman). Results from other tests showed that L.S. was not infected with herpes. Exhibit 2 at 660, 672-73.

Other early steps included an MRI and a spinal tap, which merit more extended discussions.

2. First MRI

The doctors ordered an MRI, which L.S. underwent on March 5, 2015. The MRI showed asymmetrical long TR hyperintensity and cortical swelling of the bilateral orbitofrontal, bilateral mesial temporal, left cingulate, and bilateral insular

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[5] With respect to routine immunizations, Dr. Gedeit recorded "Immunizations up-to-date per mother (received vaccines in Paris)." Exhibit 2 at 120. However, Ms. Sparrow stated that L.S. did not receive vaccinations in France. Tr. 42.

[6] Around 10:00 P.M., L.S.'s axillary temperature was 98.1 degrees. Exhibit 2 at 2697.

regions without enhancement. Exhibit 2 at 655. The interpreting radiologist, Subramanian Subramanian, found that this pattern was most consistent with an infection caused by HSV-1. Id. Dr. Subramanian also stated that other viral infections and ADEM were possible. Id.

Neither Dr. Steinman nor Dr. Sweeney reviewed the images from the MRI. Tr. 75, 195. Yet, both offered opinions about the diagnostic significance of the first MRI. Dr. Steinman averred that Dr. Subramanian's report was consistent with ADEM. Tr. 76. On the other hand, Dr. Sweeney stated that the MRI was more consistent with a viral etiology. Dr. Sweeney explained that in ADEM, the brain's deep great structures are more often involved and this pattern was not evident in L.S.'s first MRI. Tr. 195-96, 254. But, Dr. Sweeney acknowledged that the MRI does not rule out ADEM absolutely. Tr. 195, 254. Ultimately, Dr. Sweeney stated that the MRI does not help to differentiate L.S.'s neurologic problem as being either viral or autoimmune. Tr. 241.

3. Spinal Tap

L.S. underwent a spinal tap on March 5, 2015. See Exhibit 2 at 115; see also Exhibit 64 at 6; Tr. 24. Testing on her cerebrospinal fluid revealed that her protein was 78, her white blood cell count was 115, and she had oligoclonal bands. Exhibit 2 at 113, 659, 712.

Dr. Steinman stated that the showing of oligoclonal bands supported the diagnosis of ADEM. Tr. 80; see also Tr. 78.

Dr. Sweeney differed. In Dr. Sweeney's opinion, the presence of white blood cells in cerebrospinal fluid is not expected. A count of more than 100 white blood cells would be very unusual for ADEM. Tr. 198. Thus, the testing on L.S.'s cerebrospinal fluid was more consistent with a viral infection. Tr. 243.

Both Dr. Sweeney and Dr. Fujinami disputed Dr. Steinman's opinion regarding oligoclonal bands. Dr. Sweeney stated that most patients with ADEM do not have oligoclonal bands. Tr. 203. Similarly, Dr. Fujinami said that oligoclonal bands can be found in people with a viral encephalitis. Tr. 296, see also Tr. 356.

4. Clinical Picture on March 6-7, 2015

A specialist in pediatric infectious diseases, Kelly Henricksen, evaluated L.S. on March 6, 2015. Dr. Henricksen stated that L.S.'s clinical picture was consistent with HSV-1 encephalitis but other possibilities included other viruses.

Exhibit 2 at 123. Dr. Henricksen's assessment was febrile meningoencephalitis. Id.

Later, a neurologist evaluated L.S. Exhibit 2 at 114. To address L.S.'s seizures, the neurologist started Keppra. The neurologist also ordered tests from the Mayo Clinic for autoimmune encephalopathies but the testing was negative. Exhibit 2 at 2799.

The neurologist also ordered a long-term EEG, which took place from March 6-7, 2015. The EEG showed seizures. Exhibit 2 at 169-70.

On March 7, 2015, a neurologist, Nadir Khan, described L.S. as clinically stable. Exhibit 2 at 194. On the same day, Dr. Henricksen characterized L.S. as "significantly improved" from the previous day. Id. at 188. Dr. Henricksen's view of L.S. appears to be consistent with how Ms. Sparrow described L.S. in the CaringBridge journal. Ms. Sparrow memorialized that L.S. had a small ability to move her arms and legs, L.S. could track people with her eyes, and L.S. was more talkative than she had been while in the hospital, despite being unable to speak clearly. Exhibit 64 at 14, 17-18.

5. Clinical Picture on March 8-9, 2015

March 8, 2015, which was a Sunday, is an important date in how Dr. Sweeney views L.S.'s diagnosis. On this day, Dr. Henricksen stated that L.S. had improved cognitively and with her motor coordination. Exhibit 2 at 189. The CaringBridge journal documented that L.S. woke up early, smiled, laughed, sang, spoke more clearly, and wiggled her fingers and toes as directed. Exhibit 64 at 21, 24. Ms. Sparrow's oral testimony was similar. Ms. Sparrow testified that after the EEG, L.S. was "doing better." Tr. 24.

By March 9, 2015, L.S.'s health declined. Dr. Henricksen stated that L.S. was less responsive, compared with how she was interactive and talking the previous day. Exhibit 2 at 204. Ms. Sparrow's journal memorialized that L.S. spiked a fever and became verbally nonresponsive and weak. Exhibit 64 at 29. Ms. Sparrow also contrasted L.S.'s condition on that day by writing that "Sunday [the previous day] was an amazing day and we thought [L.S.] was on the way up." Id.

A specialist in infectious diseases continued to recommend treatment for HSV-1, although the MRI and PCR testing indicated that L.S. did not have an infection with a herpes simplex virus. Exhibit 2 at 205. This specialist also documented that L.S. had a "blotchy transit rash" on her right lower face.

As brought out during oral testimony, Dr. Sweeney opined that L.S. initially suffered from a viral encephalitis. The progression of her disease indicated to Dr. Sweeney that she developed a post-infectious process, such as an autoimmune reaction, fitting the diagnostic criteria for ADEM. Dr. Sweeney marked March 8, 2015, as the beginning of this second disease. Tr. 225-26.

6. Clinical Picture on March 10-16, 2015

L.S. had multiple events in which her four extremities postured and stiffened on March 10, 2015. Exhibit 2 at 221. L.S. was given a medication to prevent seizures, Dilantin. Exhibit 2 at 115.

The doctors ordered another MRI. See Exhibit 2 at 136. When the neurologist reviewed the results of the MRI, the neurologist stated that L.S.'s condition "could be a progression of viral meningoencephalitis [or] it could also be a worsening of an autoimmune encephalitis." Exhibit 2 at 229 (March 11, 2015). However, the results from the second MRI do not differentiate a viral etiology from an autoimmune etiology. Tr. 214-15, 241. The doctors prescribed a course of steroids, methylprednisolone. Exhibit 2 at 245; see also Tr. 200. L.S. took steroids for five days. See Tr. 227.

According to Dr. Sweeney, steroids can take weeks to improve a person's condition. Tr. 227. The effects of steroids are non-specific. Id.

On March 12, 2015, L.S. was intubated to protect her breathing while undergoing additional MRIs. Exhibit 64 at 30-31. The MRI on orbits was read as normal. Exhibit 2 at 737-38. An MRI on her spine showed lesions in her cervical spine, suggesting a demyelinating process. Id. at 739-41.

On March 13, 2015, a transpyloric feeding tube was inserted. Exhibit 2 at 155. L.S. was still breathing with mechanical assistance. Id. at 164. Ms. Sparrow's journal seems to express some disappointment as she wrote that March 13 "was the first that that [L.S.] could possibly show signs of improvement as it was the third day of being treated with steroids," but there was no improvement. Exhibit 64 at 38.

In contrast, on March 14, 2015, Ms. Sparrow documented: "Today, she is showing some progress. She is looking around seems somewhat responsive to our voices." Exhibit 64 at 39-40. Likewise, on the next day, Ms. Sparrow described L.S. as having taken a "step forward." Exhibit 64 at 42-44.

On March 16, 2015, L.S. was intermittently opening her eyes and looking at her parents. Exhibit 2 at 240. Mr. and Ms. Sparrow informed the doctors that L.S. was verbalizing more but they had not seen any purposeful movements. Id. A physical therapist also recorded that L.S. was more awake and opening her eyes. Exhibit 2 at 278. A specialist in critical care stated that L.S. continued to show very slow improvement in her mental status. Id. at 601. With the slow improvement, L.S. continued her course of steroids, and the critical care specialist recommended adding plasmapheresis. Id. Plasmapheresis is a process by which inflammatory components are removed from a person's blood. Tr. 247, 432-33.

A speech therapist evaluated L.S. on March 17, 2015 at approximately 10:14 A.M. The speech therapist described L.S. as more alert with her eyes open, although she had to be cued to keep her eyes open. L.S. was able to answer yes and no questions by nodding, giving a thumbs-up, squeezing her hand, and verbalizing a response. However, L.S. did not participate in counting to ten, which can be an automatic speech task. Exhibit 2 at 280; see also Tr. 201.

On March 17, 2015, a neurologist ordered plasmapheresis. Exhibit 2 at 290.

7. March 18-25, 2015: Plasmapheresis Treatments

a) Medical Records

The evening of March 17 to March 18, L.S. was fussy and uncomfortable and she received a dose of morphine. Exhibit 2 at 331. When the neurologist examined her, L.S. made eye contact occasionally, followed one simple command, and otherwise did not participate. Id. at 335. The assessment was that post-infectious ADEM was "high on the differential diagnosis although this could still be infectious viral encephalomyelitis with no detected pathogen." Id.

L.S. also received services from a speech therapist and physical therapist. During speech therapy, L.S. responded to yes/no questions with a thumbs-up for yes and an open hand for no inconsistently. Exhibit 2 at 336. L.S. did not label any pictures verbally. Id. In physical therapy, L.S. was described as "calmer today and even smiled a few times." Id. at 300.

In the journal, Ms. Sparrow stated that although L.S. was "pretty bright-eyed," when she awoke, "she looked pretty miserable for the rest of the day." Exhibit 64 at 50. Ms. Sparrow was excited that L.S. was able to take in a few bites of applesauce, demonstrating that L.S. could still swallow on her own.

On March 19, 2015, L.S. received her second treatment of plasmapheresis. Exhibit 2 at 318-19. L.S. was noted to have made "some neurologic improvements" and "now show[ed] emotion/softly crie[d] when doctors approached her, whereas 2 days ago she did not." Id. at 319.

The neurologist, too, found some improvement as L.S. was more awake, made eye contact occasionally, and followed a simple command. However, L.S. remained otherwise nonverbal and did not participate much in the exam. Id. at 330.

L.S. had another EEG on March 20, 2015, and the neurologist eventually determined that it was normal. Exhibit 2 at 182, 363. Upon visiting with L.S., the neurologist stated that L.S. appeared "slightly less fussy today." Id. at 349. Sometimes, to communicate with her parents, L.S. used a thumbs-up and open palm to mean "yes" and "no." Id. A physical therapist stated that L.S. was more awake, smiled more, and sat for a longer amount of time. Id. at 347.

On March 21, 2015, a specialist in pediatrics stated that L.S. was making "very slow but encouraging" improvement in her mental status, range of motion and vocalizations. Exhibit 2 at 360-61. A neurologist agreed, noting that L.S. was looking around more and interacting more with her mom. Id. at 365. Ms. Sparrow's journal entry indicates that L.S. was "regaining some control over her arms & legs but cannot sit, walk, or hold her head up yet. Her speech is very limited but her awareness appears sharp." Exhibit 64 at 68. During the morning of March 21, 2015 L.S. received her third treatment with plasmapheresis. Exhibit 2 at 362.

On March 23, 2015, during speech therapy, L.S. could count to ten independently, say the letters A through J, and label common animals verbally. Exhibit 2 at 374. L.S. also received her fourth plasmapheresis treatment. Id. at 373.

On March 25, 2015, L.S. received her fifth and final treatment with plasmapheresis. Exhibit 2 at 416. She was noted to be more talkative and able to count to six. Id. at 421. Ms. Sparrow journaled that L.S. was "talking more than yesterday, moving more than yesterday, and eating more than yesterday.

Yesterday, we said the same exact thing and the day before we said it too. So I think it's safe to say that we are moving forward." Exhibit 64 at 70.[7]

b) Oral Testimony and Expert Commentary

During the hearing, Ms. Sparrow testified about how plasmapheresis affected L.S. The two retained neurologists, Dr. Steinman and Dr. Sweeney, commented about Ms. Sparrow's testimony. Then, Ms. Sparrow testified again.

Ms. Sparrow averred that L.S.'s condition in the hospital did not change for a very long time, but that the doctors gave L.S. plasmapheresis and she responded immediately. Tr. 25-26; see also Tr. 38.

Having listened to the testimony of Ms. Sparrow, Dr. Steinman asserted that with plasmapheresis, L.S. woke up and was a different person. Tr. 71. He said that the treatment worked "rather spectacularly." Tr. 72.

Dr. Steinman emphasized the significance of L.S.'s improvement on plasmapheresis. He stated that this improvement was very impressive circumstantial evidence that her condition was autoimmune in origin. Tr. 72. Plasmapheresis worked because the treatment knocked out the antibodies that were harming L.S. Tr. 146. On cross-examination, Dr. Steinman went so far as to identify L.S.'s improvement during plasmapheresis as the "best" evidence for an autoimmune process. Tr. 139.

Dr. Sweeney differed. First, Dr. Sweeney questioned the accuracy of Ms. Sparrow's recollection that L.S. acutely changed after plasmapheresis. Tr. 200, 228. Dr. Sweeney pointed out that some medical records indicated that L.S. started to improve before she started plasmapheresis. Tr. 200-01.

Second, Dr. Sweeney disputed whether plasmapheresis can improve someone's health immediately. In connection with this dispute, Dr. Sweeney made two points. Dr. Sweeney pointed out that when L.S., according to Ms. Sparrow's oral testimony, was improving, steroids were still in her system. Thus, the steroids could have been working in tandem with the plasmapheresis. Tr. 229. In addition, the biologic process of plasmapheresis is unlikely to produce a "Eureka!" moment. Tr. 247.

[7] The entry in the CaringBridge journal preceding the March 25, 2015 entry was created on March 21, 2015, so there are no entries for "yesterday . . . and the day before." Exhibit 64 at 65.

After Dr. Sweeney's testimony, Dr. Steinman responded in rebuttal. He agreed that the process of removing inflammatory components through plasmapheresis was likely to take more than one day. But, L.S. improved over two to three days. Tr. 432-33.

Ms. Sparrow was afforded the last spoken word on the topic of plasmapheresis. She stated that on March 18, 2015, L.S. moved from the pediatric intensive care unit to the neurology floor, where she ate some applesauce. Tr. 439. In Ms. Sparrow's recollection, L.S.'s improvement was significant enough that it seemed to be a "miracle." Tr. 440.

8. March 26, 2015 to April 4, 2015: Remaining Treatment and Discharge

After L.S.'s plasmapheresis treatment ended, she remained hospitalized for approximately ten days. These chronological details about her health generally do not affect whether Mr. and Ms. Sparrow are entitled to compensation. None of the experts who testified emphasized treatment records from these ten days.[8] Some information about L.S.'s progress can be found in Ms. Sparrow's journal. Exhibit 64 at 70-89.

L.S. was discharged from the hospital on April 4, 2015. The diagnoses included acute meningoencephalitis, "viral versus autoimmune;" probable ADEM; seizures; dysautonomia; and irregular heartbeat. Exhibit 2 at 112. The plan was for L.S. to continue medications at home; follow up with her primary care physician as well as specialists in neurology, physical medicine and rehabilitation, and cardiology over the next month; and set up outpatient physical and occupational therapy appointments. Id. at 117-18.

9. Opinions about Causation from Treating Doctors around the time of Hospitalization at CHOW.

Occasionally, doctors caring for L.S. while she was in the Children's Hospital of Wisconsin commented about possible causes of her illness. Due to the importance of the views of these professionals, they merit particular evaluation.

One of L.S.'s doctors was Harry Whelen, whom Dr. Sweeney knew by reputation as a good child neurologist (Tr. 223). Dr. Whelen assessed L.S. as

[8] Comments from the treating doctors regarding causation are summarized in Section VI.B.

having monophasic ADEM. Exhibit 2 at 2928. Dr. Steinman pointed to the fact that "board-certified treating doctors . . . called it ADEM" as supportive of Dr. Steinman's opinion that the MMR vaccination caused L.S. to suffer ADEM. Tr. 139. When counsel for Mr. and Ms. Sparrow questioned Dr. Sweeney about Dr. Whelen's record on cross-examination, Dr. Sweeney disclosed that he agreed with the conclusion that L.S. suffered ADEM later in her hospitalization. Tr. 225. But, as discussed above, Dr. Sweeney maintained that L.S.'s initial presentation was due to a viral encephalitis.

Shortly before L.S. was discharged, her parents spoke with an infectious disease specialist, Erika Chou, about the "possibility of MMR [vaccine] causing the ADEM." Exhibit 2 at 558. Dr. Chou responded that causation was "possible but very unlikely that the MMR is what caused this meningoencephalitis." Id. Dr. Chou added that she had "no problem with continuing the MMR series." Id.; see also Tr. 230-31. Ms. Sparrow testified that Dr. Chou was the only doctor to say this. Tr. 53.

About two weeks after Dr. Chou's comments, L.S. saw her regular pediatrician Dr. Koch. Exhibit 1 at 142 (April 16, 2015). Dr. Koch agreed to defer the administration of the second dose of the MMR vaccine. Id.; see also Tr. 54.

D. Second Hospitalization at CHOW

Unfortunately, L.S.'s stay outside of a hospital, which had begun on April 4, 2015, did not last long. On April 5, 2015, L.S. developed a rash on her cheeks that extended to her chest and limbs. L.S. also had neck pain and a fever of 100.4 degrees. Exhibit 2 at 2876. Ms. Sparrow brought L.S. back to the hospital where she was admitted.

A dermatologist stated that L.S.'s rash could have been caused by her ingestion of Dilantin. Exhibit 2 at 2907. While in the hospital, L.S. underwent additional neurologic testing, but the results did not point to any specific etiology. Id. at 2873, 2924-28. At discharge, on April 9, 2015, L.S.'s diagnosis was a rash "likely due to a drug reaction to Dilantin." Id. at 2873.

E. More Recent Health History

In the months after leaving the hospital, L.S. had various follow-up appointments. However, most records of treatment do not inform an assessment of causation. For more details, see Pet'rs' Posthear'g Br. at 12-14; Resp't's Posthear'g Br. at 19-21.

On August 13, 2015, L.S. saw a neurologist, Delphine Sallowm. Dr. Sallowm was familiar with L.S.'s history. She wrote that L.S. "had received [an] MMR vaccination about 3 weeks prior to this presentation making me wonder if it was a trigger factor" for L.S.'s ADEM. Exhibit 2 at 3981. Dr. Sallowm recognized that an "extensive workup did not reveal any pathogen." Id. at 3985.

Ms. Sparrow testified that L.S. had a long road of rehabilitation, including repeating first grade. Tr. 27-29. The school system has provided L.S. with an individualized education plan and L.S. is making progress, although she remains behind her peers. Tr. 29-31. After L.S. was weaned off anti-seizure medications, she has not had more seizures. Tr. 28.

II. Procedural History

Mr. and Ms. Sparrow alleged that the MMR vaccine harmed L.S. Pet., filed Feb. 27, 2018. They filed medical records over the next six months.

The Secretary reviewed this material and recommended that compensation be denied. Resp't's Rep., filed Dec. 20, 2018, at 5-10. The Secretary identified two deficiencies. First, the Secretary maintained that Mr. and Ms. Sparrow did not establish that the MMR vaccine caused any problem in L.S. Second, the Secretary argued that L.S.'s problems did not meet the severity requirement. Id.

To address the argument regarding severity, Ms. Sparrow explained how long L.S. has suffered consequences. Exhibit 16 (affidavit, filed May 20, 2019). This information apparently has satisfied the Secretary as the Secretary has not continued to assert that L.S.'s neurologic problems resolved within six months. See, e.g., Resp't's Prehear'g Br., filed June 18, 2021. Instead, the parties dispute whether the MMR vaccine caused any adverse consequences.

The parties were provided with a set of draft instructions to facilitate obtaining useful reports from experts they might retain to opine on causation. Order, issued July 12, 2019. After both parties commented, a set of final instructions was issued on August 15, 2019.

Mr. and Ms. Sparrow submitted the first report from Dr. Steinman on January 13, 2020. Exhibit 18. Dr. Steinman reviewed L.S.'s history and stated that "the correct diagnosis is ADEM." Id. at 18. To explain how the MMR vaccine can cause ADEM, Dr. Steinman based a theory on molecular mimicry. Id. at 18-22. Dr. Steinman asserted that L.S. developed ADEM "3 weeks after the MMR vaccine." Id. at 22. With respect to an opinion about the logical sequence

of cause and effect between the MMR vaccine and L.S.'s ADEM, Dr. Steinman wrote one paragraph, which did not cite any evidence about L.S. Id. at 23.

In response, the Secretary presented reports from two people. The first is an immunologist, who is not a medical doctor, Robert S. Fujinami. Exhibit A (filed June 2, 2020). Dr. Fujinami generally challenged Dr. Steinman's reliance on molecular mimicry. The Secretary's second expert is a pediatric neurologist, Michael Sweeney. Like Dr. Steinman and unlike Dr. Fujinami, Dr. Sweeney summarized L.S.'s medical records. Exhibit C at 1-3. Dr. Sweeney concluded: "After review of her extensive medical records and clinical course, a viral encephalitis is the most likely etiology for her presentation. ADEM is thought to be less likely." Id. at 5.

Dr. Steinman replied in a supplemental report, filed Aug. 7, 2020. Dr. Steinman maintained that molecular mimicry can explain how MMR vaccine can cause ADEM. Exhibit 42 at 1-2. In reply to Dr. Sweeney's proposed diagnosis of a viral encephalitis, Dr. Steinman stated: "No specific viral encephalitis was ever diagnosed . . . Without a specific diagnosis it is hard to make a strong case for viral encephalitis over the other two alternatives, one being ADEM, the other the vaccine. I would argue that the vaccine anyway could trigger ADEM." Id. at 2-3.

The disagreement regarding molecular mimicry continued as Dr. Fujinami authored another report, which was filed on December 4, 2020. Exhibit E. The Secretary did not submit another report from Dr. Sweeney.

A status conference was held on December 18, 2020. Due to the Secretary's defense against the claim (see Resp't's Status Rep., filed Jan. 19, 2021), the parties were directed to submit briefs. Order, issued Feb. 17, 2021.

Mr. and Ms. Sparrow argued that they were entitled to compensation. Pet'rs' Prehear'g Br., filed April 19, 2021. For diagnosis, Mr. and Ms. Sparrow maintained that they "are able to demonstrate that L.S. satisfies the following diagnostic criteria for ADEM set forth in [Krupp]." Id. at 15. Mr. and Ms. Sparrow also contended that they satisfied the Althen prongs to demonstrate that the MMR vaccine was the cause-in-fact of L.S.'s ADEM. Id. at 19-35. For the medical theory, Mr. and Ms. Sparrow invoked molecular mimicry. Id. at 20-28. Mr. and Ms. Sparrow did not argue that a virus in the MMR vaccine directly caused L.S.'s ADEM. For the logical sequence, Mr. and Ms. Sparrow cited reports from two doctors who treated L.S., as well as Dr. Steinman's opinion. Id. at 28-31. For timing, Mr. and Ms. Sparrow claimed that L.S. developed ADEM

approximately three weeks after the MMR vaccine, and that three weeks fell within an appropriate time frame. Id. at 31-35.

The Secretary challenged the entitlement to compensation. Resp't's Prehear'g Br., filed June 18, 2021. With his brief, the Secretary submitted a report from Dr. Sweeney (Exhibit F). Dr. Sweeney explained why viral encephalitis was an appropriate diagnosis for L.S. Exhibit F at 1-3. The Secretary incorporated this opinion into the arguments against compensation.

As to the unresolved question of diagnosis, the Secretary noted that "Dr. Sweeney opines that L.S.'s diagnosis is more likely viral encephalitis, with ADEM . . . less likely." Id. at 11, citing Exhibit C at 5. Quoting Dr. Sweeney's new report, the Secretary argued that "the most important factor in this is the timing of the febrile illness (March 1-5) and concurrent neurologic symptoms. It makes the most sense to attribute this to the most [sic] trigger. In the case of L.S., this would be the recent/ongoing infection, rather than the vaccine 3 weeks prior." Id. at 12. The Secretary concluded: "L.S.'s condition is thus consistent with a viral encephalitis, and a preponderance of the evidence does not support the diagnosis of ADEM." Id. at 13.

As to causation, the Secretary generally challenged the Sparrows' reliance on Dr. Steinman and molecular mimicry. Id. at 13-16. The Secretary disputed whether the treating doctors implicated the MMR vaccine as a cause for L.S.'s neurologic problems. Id. at 16-17. For timing, the Secretary appeared to assert that L.S.'s neurologic problems started either 21 or 24 days after the vaccination. Id. at 19. However, in the view of the Secretary, the MMR vaccine would cause a neurologic problem within only approximately two weeks. Id. at 18-19.

Mr. and Ms. Sparrow addressed these arguments and continued to assert that they were entitled to compensation. Pet'rs' Prehear'g Reply, filed July 19, 2021.

A review of the briefs suggested that there might be common ground with respect to diagnosis. It appeared that Dr. Steinman and Dr. Sweeney agreed that L.S. suffered from some form of "encephalitis." However, Dr. Steinman and Dr. Sweeney parted company as to the causal mechanism with Dr. Steinman proposing an autoimmune pathway and Dr. Sweeney proposing an unidentified virus. Order, issued Aug. 2, 2021. In the ensuing status conference, the parties agreed with that characterization. Order, issued Aug. 26, 2021.

The August 26, 2021 order also began the process for scheduling a hearing. A mutually convenient set of dates for the hearing was determined to be July 14-15, 2022. Order, issued Sept. 13, 2021.

The hearing was held, as planned, on July 14-15, 2022 in Milwaukee, Wisconsin. Ms. Sparrow and Dr. Steinman testified for the petitioners. The respondent called Dr. Fujinami and Dr. Sweeney.

The oral testimony brought forward three developments that were unexpected. First, Ms. Sparrow disclosed that when L.S. was hospitalized, the Sparrows created blog posts through CaringBridge.org that described the parents' observation of L.S. during this critical time. Second, Dr. Steinman proposed, as an alternate theory, that the attenuated viruses contained in the MMR vaccine caused L.S.'s rash, which was noted early in her hospitalization. For this proposition, Dr. Steinman identified three articles, of which two were filed the morning of the second day of the hearing. See CM/ECF No. 105, Exhibits 60 and 61. The third article was filed after the hearing as Exhibit 62. The third unexpected development was that Dr. Sweeney opined that L.S. met the diagnostic criteria for ADEM, but at a date different from the date Dr. Steinman proposed. Dr. Sweeney testified that L.S.'s initial presentation was a viral infection and she developed a post-infectious or autoimmune process around March 8, 2015.

During the hearing, the Secretary objected to Ms. Sparrow's testimony about the content of the CaringBridge journal. Tr. 426; see also Resp't's Posthear'g Br. at 6 n.2. Nevertheless, Ms. Sparrow was allowed to refer to this document during her rebuttal testimony. She was further directed to provide the entire journal and she did so after the hearing by filing it as Exhibit 64. Concurrently, she averred that the journal entries "were made either contemporaneously to or as near to the time that the events or conversations described occurred, except as otherwise noted." Exhibit 63 (affidavit, dated July 19, 2022) ¶ 4. Ms. Sparrow also attested that the website "does not allow edits." Id. ¶ 3. [9]

A purpose of requiring Ms. Sparrow to submit her journal was to allow the Secretary and Dr. Sweeney an opportunity to review its contents. In a report submitted after the hearing, Dr. Sweeney stated that he "did not appreciate

[9] The Secretary's attorney disputed Ms. Sparrow's statement that entries on CaringBridge are not editable. The Secretary's attorney represented that she, herself, created a CaringBridge account and was able to edit her own posts. Resp't's Posthear'g Br. at 6 n.2. Whether CaringBridge posts can be edited does not affect whether Mr. and Ms. Sparrow have established that L.S. suffered from ADEM at the beginning of her hospitalizations.

significant differences from what was stated in this blog to what was reported in the medical records that were reviewed as a part of [his] initial report." Exhibit I at 2.

The parties eventually were directed to advocate for their positions through briefs. Order, issued March 15, 2023. Mr. and Ms. Sparrow submitted their primary brief on June 13, 2023 and their reply on September 28, 2023. In between, the Secretary submitted his sole brief on September 1, 2023. With this submission of the Reply Brief, the case is ready for adjudication.

III. Standards for Adjudication

Petitioners are required to establish their case 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 & Hum. 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 & Hum. 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 & Hum. 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 & Hum. Servs., 219 F.3d 1357 (Fed. Cir. 2000); Hodges v. Sec'y of Health & Hum. 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).

When pursuing an off-Table injury, a petitioner bears a burden "to show by preponderant evidence that the vaccination brought about [the vaccinee's] injury by providing: (1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of a proximate temporal relationship between vaccination and injury." Althen v. Sec'y of Health & Hum. Servs., 418 F.3d 1274, 1278 (Fed. Cir. 2005).

IV. Diagnosis

The parties agree that in early March 2015, L.S. suffered from a neurologic problem, inflammation in her brain. The medical term for inflammation in the

brain is "encephalitis." The term "encephalitis" does not necessarily explain what caused the inflammation. See Tr. 190 (Dr. Sweeney defining "encephalitis"). As to the cause of L.S.'s inflammation in early March, the parties disagree. On behalf of the petitioners, Dr. Steinman proposes that the encephalitis was the result of an autoimmune process that the MMR vaccine initiated. On the other hand, for the Secretary, Dr. Sweeney maintains that for the early course of her illness, L.S. suffered from an infection with an unknown virus. Dr. Sweeney also states that during her hospitalization, the basis for L.S.'s neurologic problem changed, shifting from a viral cause to a post-infectious (or autoimmune) cause.

Dr. Steinman's and Dr. Sweeney's differing opinions have been disputed throughout the case. When the parties were directed to advocate for their positions before the hearing, they were expected to discuss diagnosis. Order, issued Feb. 17, 2021, at 4. The parties did so. Pet'rs' Prehear'g Br. at 14-18; Resp't's Prehear'g Br. at 10-13. After the hearing, the parties repeated this process. Order, issued Mar. 15, 2023, at ¶ II.

The Secretary's position remained consistent with Dr. Sweeney's opinion even as Dr. Sweeney's opinion evolved. Before the hearing, the Secretary argued, "a preponderance of the evidence does not support the diagnosis of ADEM." Resp't's Prehear'g Br. at 13. After the hearing, the Secretary stated, "The parties do not dispute that L.S. ultimately satisfied the diagnostic criteria for ADEM." Resp't's Posthear'g Br. at 23.[10] Yet, a critical question is the cause of L.S.'s initial hospitalization.

Determining the etiology of the initial encephalitis is challenging. The parties did not identify any diagnostic criteria that are useful in distinguishing viral encephalitis from autoimmune encephalitis. See Pet'rs' Posthear'g Br. at 25; Resp't's Posthear'g Br. at 23-24. Dr. Sweeney testified that the diagnostic criteria for ADEM and viral encephalitis have "lots of overlap." Tr. 191. L.S.'s signs and symptoms from early March were generally consistent with both a viral

[10] Dr. Sweeney should have disclosed his opinion that L.S. suffered from ADEM, starting around March 8, 2015, in a report submitted in advance of the hearing. See Simanski v. Sec'y of Health & Human Servs., 671 F.3d 1368, 1382 (Fed. Cir. 2012). This late revelation of Dr. Sweeney's opinion appears not to have prejudiced the Sparrows because Dr. Sweeney's acknowledgement that L.S. suffered from ADEM starting around March 8, 2015 reduces the degree of difference between Dr. Steinman and him. Furthermore, Mr. and Ms. Sparrow did not object to the testimony, and they did not move to strike the testimony. Thus, his testimony remains in the record and has been considered. Nevertheless, Dr. Sweeney should be more forthcoming about his opinions in future reports. See Tr. 262-63.

encephalitis and an autoimmune encephalitis. Thus, some evidence supports the diagnosis of either viral encephalitis or autoimmune encephalitis. The presence of conflicting evidence does not prevent special masters from finding facts. See Doe 11 v. Sec'y of Health & Hum. Servs., 601 F.3d 1349, 1355 (Fed. Cir. 2010). For an example in which a special master weighed evidence regarding whether a child-vaccinee suffered from a viral encephalitis or ADEM, see Carter v. Sec'y of Health & Hum. Servs., No. 04-1400V, 2007 WL 415185, at *14-19 (Fed. Cl. Spec. Mstr. Jan. 19, 2007).

The better and stronger evidence favors a diagnosis of viral encephalitis in early March. On this point, the Secretary advocated more persuasively. The Secretary identified multiple pieces of evidence that tend to align more with a viral encephalitis than an autoimmune encephalitis. See Resp't's Posthear'g Br. at 46-48.

Perhaps the strongest reason for rejecting Dr. Steinman's autoimmune etiology concerns L.S.'s response to plasmapheresis. As mentioned previously, when asked about the "best" evidence to support his opinion, Dr. Steinman selected L.S.'s improvement after starting plasmapheresis, as Ms. Sparrow described. Tr. 139. Dr. Steinman stated that the plasmapheresis "worked rather spectacularly" and described L.S.'s improvement as "an awakening." Tr. 72, 123.

However, Ms. Sparrow's oral testimony does not comport with the documents created while L.S. was hospitalized--- both the medical records and the CaringBridge journal. The evidence regarding L.S.'s course in the days before, during, and after her five doses of plasmapheresis is detailed above. See Section I.C.6-7. In short, before L.S. started plasmapheresis, she was showing some improvements, although she was not entirely better. See, e.g., Exhibit 2 at 601; Exhibit 64 at 39-40. After L.S. started plasmapheresis, she continued to improve, although, again, the improvements were not absolute. See, e.g., Exhibit 2 at 360-61 (a note from March 21, 2015 documenting "very slow but encouraging" improvement).

In light of this unchallenged evidence, Dr. Steinman's assumption that L.S. made a very impressive improvement on plasmapheresis was unwarranted. When an expert assumes facts not supported by the evidence, a special master may reject the expert's opinion. Burns v. Sec'y of Health & Hum. Servs., 3 F.3d 415, 417 (Fed. Cir. 1993).

It stands to reason that if evidence the expert identifies as the "best" evidence supporting his opinion does not, in fact, support his opinion, then the

remainder of his opinion is necessarily weaker. The Secretary highlighted Dr. Steinman's assumption about L.S.'s response to plasmapheresis and the lack of evidentiary support for it. Resp't's Posthear'g Br. at 11 n.4, 43-44. Given the primacy of plasmapheresis in Dr. Steinman's opinion (see Pet'rs' Posthear'g Br. at 14-19, 32), some response from Mr. and Ms. Sparrow might have been expected. However, their reply does not use the term "plasmapheresis" at all.

Beyond plasmapheresis, the Secretary pointed to other evidence that is more consistent with a viral infection, as opposed to an autoimmune pathway. This evidence included, but is not limited to the following:

L.S. had a pain in her neck when she went to the emergency room at CHOW on March 2, 2015 (first visit that day). Exhibit 2 at 3. [11] She also had a fever. Id. This combination suggests that L.S. had a viral infection. See Tr. 192 (Dr. Sweeney: "lymphadenopathy in the neck would be seen with somebody who's fighting a localized infection").

Although Ms. Sparrow gave L.S. two medications (Tylenol and ibuprofen), the fever persisted and was detected when L.S. returned to the CHOW emergency room later on March 2, 2015. Exhibit 2 at 42-43, 52; Exhibit 64 (CaringBridge journal) at 4; Tr. 20, 36. According to Dr. Sweeney, "when children are sick with ongoing infections no matter what antipyretics we give, they still maintain fevers." Tr. 193.

When L.S. went to the emergency room at Columbia St. Mary's, L.S. presented in a way consistent with an infection. Her heart rate was between 130 and 140 beats per minute, and her blood pressure was 116/67. Exhibit 11 at 244, 250. L.S. also had a fever and a blotchy rash. Id. at 246-47. The doctor at Columbia, who transferred L.S. to the intensive care unit at CHOW, was concerned that L.S. was septic. Exhibit 11 at 261. So, too, the doctor who received L.S. at CHOW was concerned about sepsis. Exhibit 2 at 120.

This set of information tends to support a finding that L.S. had a viral illness. Dr. Sweeney explained: "That set of vital signs is concerning for a septic child. So when a child has—becomes kind of vasodilated because of systemic infection and inflammation their diastolic blood pressure tends to drop." Tr. 194. Dr. Sweeney referred to L.S.'s sepsis as supporting an infectious origin to her problems. Tr.

[11] At this early date in what eventually became a prolonged course, the doctor in the emergency room suspected that L.S. had strep throat. Exhibit 2 at 5, 7. However, she was only colonized with, but infected with, the strep bacteria. Id. at 113, 661.

197, 225; see also Tr. 206 (noting distinguishing viral sepsis from bacterial sepsis is difficult). Dr. Steinman, on the other hand, did not comment on how a septic presentation was consistent with an autoimmune pathway.

The results from the complete blood count on blood drawn at Columbia St. Mary's also favor an infectious process. Her white blood count was 21,000 with 83% neutrophils and 5.4% lymphocytes. Exhibit 11 at 259-60. These data show systemic inflammation and are not consistent with ADEM. Tr. 194 (Dr. Sweeney).

The results from the spinal tap at CHOW also tend to align with a finding of an infectious etiology early in L.S.'s disease course. The spinal tap revealed: 2 red blood cells, 115 white blood cells, 78 protein, and 84 glucose. Exhibit 2 at 659. The finding of 115 white blood cells in the spinal fluid tends to suggest that L.S. was not suffering from ADEM. Tr. 198 (Dr. Sweeney: "it is very unusual in . . . ADEM to see a white blood count greater than 100"). Moreover, the composition of the white blood cells divided as follows: 24% neutrophils, 45% lymphocytes, and 31% monocytes. Exhibit 2 at 659. According to Dr. Sweeney, cases of ADEM typically present with 80-90 percent lymphocytes. Tr. 198. Thus, the lower percentage meant that "something acutely infectious [is] happening." Tr. 199. Dr. Sweeney expounded on the basis for his opinion, stating "I was taught by all of my mentors that if you don't have a lymphocytic predominance in your . . . spinal fluid[,] then you should be looking for acute infection." Tr. 243. Dr. Steinman generally agreed with this point, although Dr. Steinman added some qualifications. Tr. 430-32.

When L.S.'s treating doctors searched for an acute infection, they did not discover any infectious organism. See Tr. 211 (Dr. Sweeney acknowledging that negative testing ruled out herpes simplex virus as the cause of L.S.'s neurologic problem); Tr. 220 (Dr. Sweeney acknowledging that testing for viruses such as Epstein-Barr virus and CMV were negative). Dr. Sweeney could not identify any tests that he would have wanted the doctors treating L.S. to perform. Tr. 221. As such, Dr. Sweeney could not identify the virus that underlies his opinion that L.S.'s encephalitis was induced by a virus. Tr. 221; see also Exhibit C at 4.

Dr. Sweeney's inability to specify a particular virus, in turn, constitutes one of the arguments that Mr. and Ms. Sparrow often raised against the finding of a viral encephalitis. See Pet'rs' Prehear'g Br. at 30; Pet'rs' Posthear'g Br. at 24-29; Pet'rs' Posthear'g Reply at 1-7. Dr. Steinman, too, similarly argued that the Government should not be allowed to claim a virus caused L.S.'s neurologic problems without identifying the virus. Exhibit 42 at 3 (citing Torday v. Sec'y of

Health & Hum. Servs., No. 07-372V, 2011 WL 2680687 (Fed. Cl. Spec. Mstr. April 7, 2011); Tr. 73.

This argument misses its mark. Federal Circuit precedent establishes that "a 'viral infection' can be an alternative causation, even though the viral infection is not in the particular case specifically identified by type or name." Knudsen v. Sec'y of Health & Hum. Servs., 35 Fed. Cl. 543, 549 (Fed. Cir. 1994).[12] In accordance with Knudsen, in non-binding opinions, the Court of Federal Claims has found that special masters were not arbitrary in finding an unnamed virus to be the cause of a vaccinee's illness. See, e.g., Raybuck v. Sec'y of Health & Hum. Servs., 98 Fed. Cl. 713, 718-19 (2011) (ruling that a special master was not arbitrary in crediting the opinion of the Secretary's expert that a virus (and not the flu vaccine) caused a rash and stating that the Secretary did not have to prove which virus); Morris v. Sec'y of Health & Hum. Servs., 57 Fed. Cl. 383, 389-90 (2003) (ruling that a special master was not arbitrary in finding a virus caused the vaccinee's transverse myelitis).

Doctors, when treating patients with neurologic illnesses, cannot always identify a virus that might have caused their patient's disease. This lack of identification happens because, in part, not all viruses have been identified. Tr. 73, 203-04, 218. This lack of clarity does not prevent doctors from surmising that a virus has caused a neurologic problem. Tr. 205.

L.S. demonstrates how treating doctors can--and do--suggest a virus caused a neurologic problem even when testing for multiple viruses has come up empty. For example, the specialist in infectious diseases, Dr. Henricksen, stated that L.S. had a form of encephalitis, and causes could include viruses other than HSV-1. Exhibit 2 at 123 (Mar. 6, 20215). Later, after much testing for viruses was negative, the neurology resident Dr. Serena Thompson stated that L.S.'s condition "could be a progression of viral meningoencephalitis [or] it could also be a worsening of an autoimmune encephalitis." Id. at 229 (Mar. 11, 2015).

[12] Mr. and Ms. Sparrow fail to engage with Knudsen. They assert, "Dr. Sweeney's opinion does not meet the standard under . . . the Federal Circuit's holding in Knudsen." Pet'rs' Posthear'g Reply at 2. They make this assertion without stating why Dr. Sweeney's opinion is incompatible with Knudsen.

In short, a preponderance of the evidence supports a finding that L.S. suffered a viral infection that caused her encephalitis in early March 2015.[13] To be clear, this finding reflects an evaluation of the record as a whole, which includes multiple discrete pieces of evidence. None of the individual items of evidence are dispositive by themselves. However, when taken together, the individual items support a finding that the Secretary has presented sufficiently weighty evidence to show on a more likely than not basis that L.S. suffered a viral infection causing her encephalitis.

A person with viral encephalitis can develop a post-infectious or autoimmune process, known as ADEM. Tr. 240 (Dr. Sweeney), 434 (Dr. Steinman). Dr. Sweeney orally testified that L.S.'s course shifted from an infectious etiology to a post-infectious etiology around March 8-9, 2015. Tr. 226, 256, 261. Despite being disclosed late, Dr. Sweeney's opinion that L.S.'s initial presentation was due to a viral encephalitis is persuasive for the reasons given above.

Dr. Sweeney's opinion that after March 8 or March 9, L.S. suffered from ADEM is in harmony with opinions from doctors who treated her. For example, when Dr. Whelan saw L.S. on April 6, 2015, which is during another hospitalization at CHOW, he stated L.S.'s condition "is still Monophasic ADEM." Exhibit 2 at 2928; accord Tr. 223-24. Similarly, another pediatric neurologist, Delphin Sallowm, stated on August 13, 2015 that L.S.'s "diagnosis is ADEM." Exhibit 2 at 3985. Dr. Sweeney agreed that that ADEM was an appropriate diagnosis at the time of those diagnoses. Tr. 224-25.

V. Althen Prong I

Dr. Steinman offered two theories to explain how the MMR vaccine may have caused L.S.'s ADEM. The first theory is that a live measles, mumps, or rubella virus within the MMR vaccine caused L.S.'s viral encephalitis, which in turn led to her ADEM. The second theory is that the MMR vaccine caused ADEM via molecular mimicry. Whether the Sparrows are advancing the first theory is questionable; nevertheless, both theories are discussed.

[13] Because the evidence preponderates in favor of this finding, allocating a burden of proof is not required. If the burden of proof were on the Secretary, the Secretary has met his burden.

A. The MMR Viruses Causing Viral Encephalitis

The finding that a virus that Dr. Sweeney could not identify caused L.S.'s initial encephalitis does not absolutely determine the outcome of the case. Arguably, Mr. and Ms. Sparrow might still be entitled to compensation because, during the hearing, Dr. Steinman stated that the virus that caused L.S.'s illness was contained in the MMR vaccine, i.e., that the measles, mumps, or rubella virus caused her illness. Tr. 69, 140. This argument has both procedural and substantive infirmities.

As a matter of procedure, whether Mr. and Ms. Sparrow are asserting this method of recovery appears unclear. To start, Dr. Steinman's disclosure of an opinion that a measles, mumps, or rubella virus can cause ADEM was slight. In the context of discussing the lack of identification of a virus, Dr. Steinman wrote "the vaccine anyway could trigger ADEM." Exhibit 42 at 3. In their memoranda before the hearing, Mr. and Ms. Sparrow did not assert a theory based upon the viruses contained in the vaccine. See Pet'rs' Prehear'g Br. at 19-28; Pet'rs' Prehear'g Reply at 7-9. Nevertheless, Dr. Steinman opined "the trigger here for ADEM was a live virus vaccine with three live virus components." Tr. 69. Due, in part, to this unexpected nature of this opinion, the parties were directed to brief this issue. See Order, issued Mar. 15, 2023, ¶ III.C. (noting this theory received relatively little testimony).

Mr. and Ms. Sparrow did not present any argument regarding any causal contribution from the measles, mumps, or rubella virus in their primary brief. See Pet'rs' Posthear'g Br. Therefore, the Secretary called out this omission. Resp't's Posthear'g Br. at 46-47 n.12 ("Petitioners abandon this argument in their Brief"). But, Mr. and Ms. Sparrow maintain that they have not abandoned the argument. Pet'rs' Posthear'g Reply at 7-8.

Under these circumstances, Mr. and Ms. Sparrow might fairly be found to have waived any argument based upon the measles, mumps, or rubella virus from the vaccine harming L.S. See Vaccine Rule 8(f). Usually, arguments that are made for the first time in a reply are considered waived. SmithKline Beecham, Corp. v. Apotex Corp., 439 F.3d 1312, 1320 (Fed. Cir. 2006); Ironclad/EEI v. United States, 78 Fed. Cl. 351, 358 (2007). This preference would seem to be stronger when the moving party was specifically ordered to present an argument on the topic.

In any event, the substance of Dr. Steinman's opinion that a live virus from the MMR vaccine caused L.S.'s ADEM lacks sufficient weight to be credited. Dr.

Steinman appears to have mentioned this idea in a few sentences of his oral testimony, which spanned more than 120 pages. See Tr. 69, 140-42. Dr. Steinman did not present any evidence that L.S.'s presentation suggested that she was infected with the virus that causes measles, the virus that causes mumps, or the virus that causes rubella. Dr. Sweeney's unrebutted testimony was that L.S.'s presentation did not match his understanding of any of those three diseases, although Dr. Sweeney pointed out the limits of his knowledge. See Tr. 199-200. Thus, because a direct viral infection appears incompatible with L.S.'s symptoms, Dr. Steinman is left with an autoimmune pathway. This is simply a variation of his molecular mimicry theory. Tr. 144.

B. The MMR Vaccine Causing ADEM

For the reasons explained in Section IV above, preponderant evidence shows that a virus caused L.S.'s initial neurologic symptoms. This finding conflicts with Dr. Steinman's assertion that the MMR vaccine caused L.S. to suffer ADEM by her birthday on February 28, 2015. See Tr. 100. Thus, evaluating whether the MMR vaccine can cause ADEM is not essential to resolving whether Mr. and Ms. Sparrow are entitled to compensation. However, this additional analysis is undertaken to demonstrate that all material has been considered.

The evidence regarding whether the MMR vaccine can cause ADEM falls into three categories. These are: (1) epidemiologic studies, (2) the package insert, and (3) the experts' opinions regarding molecular mimicry.

1. Epidemiology

For a lengthy discussion of the value of epidemiologic studies in the Vaccine Program, see Tullio v. Sec'y of Health & Hum. Servs., No. 15-51V, 2019 WL 7580149, at *5-8 (Fed. Cl. Spec. Mstr. Dec. 19, 2019), mot. for rev. denied, 149 Fed. Cl. 448, 475 (2020). Dr. Steinman and Dr. Fujinami differed as to whether epidemiology supports the proposition that the MMR vaccine can rarely cause ADEM.

a) Overview of Evidence

Dr. Steinman cited a 1982 article by Fenichel.[14] Exhibit 18 at 22. Although Dr. Steinman wrote about this article, he did not testify about it during the hearing. The article was not mentioned in any of the Sparrows' briefs.

Fenichel reviewed several epidemiologic studies. Fenichel at 119. For the measles vaccine, Fenichel states that the Centers for Disease Control conducted two surveillance studies with the first covering January 1965 to February 1967 and the second covering 1963 through 1971. Id. at 124. For the earlier study, all of the health problems reported after vaccination "could be explained by a chance relationship between the onset of symptoms and the time of immunization." Id.

The latter study concerned an eight-year period in which 51 million doses of the measles vaccine were administered. Fenichel at 124. Fenichel reported that:

> 59 children had onset of symptoms [of neurologic disease] between 1 and 15 days with the major cluster between 6 and 15 days. The incidence of encephalopathy after immunization was 1.16 per 1,000,000 doses. In comparison, the background incidence of encephalitis not related to immunization is generally 2 to 3 per 1,000,000 children of similar age.

Id.

Fenichel's assessment of this data appears mixed. Fenichel wrote: "While a cause-and-effect relationship between measles immunization and encephalopathy cannot be established from passive surveillance of cases reported to the CDC, the clustering of cases in the second week after immunization is worrisome." Dr. Steinman quoted this passage. Exhibit 18 at 22.

The next article was written by L. Bennetto and published in 2004. Bennetto was filed as Exhibit 39 and Exhibit A-1. Bennetto and the co-author wrote:

> the non-neural measles, mumps, and rubella vaccinations are most commonly associated with post–vaccination encephalomyelitis. The incidence is 1-2 per million for live measles vaccinations. This is somewhat

[14] Bibliographic information for the articles cited in this decision is found in the appendix.

> less than the 1 in 1000 incidence of post-infectious encephalomyelitis following measles virus infection. They may reasonably conclude that while both a cause and a prevention of ADEM, on balance vaccination dramatically reduces the incidence of ADEM.

Bennetto at i24. However, as Dr. Fujinami pointed out, the "information . . . can't be substantiated" because the article provides no source for this statistic. Tr. 304.

Huynh and colleagues also reviewed the literature, looking to see whether various vaccinations may have precipitated ADEM. They emphasized the difference between a temporal relationship and a causal relationship: "that encephalomyelitis or ADEM – or any other adverse event – that follows administration of an inactivated component or live vaccine may be temporally *associated with*, but is not necessarily *the result of*, administration of a vaccine." Huynh at 1317 (emphasis in original). This group reported "The most common vaccinations associated with ADEM are the non-neural measles, mumps and rubella vaccines. The incidence of 1–2 per million for live measles vaccine is less than the reported 1 in 1000 incidence of post-infectious ADEM following infection with the measles." Huynh at 1317. For this datum, Huynh cited the article by Bennetto, which is reference 1 in the Huynh article.

Even if the information from Bennetto is accurate, the basis for concluding that the live measles vaccine caused the ensuing ADEM is unclear. According to Huynh, the incidence of ADEM is approximately 10 cases per million. Huyhn at 1315 (stating that the annual incidence is 0.8 per one hundred thousand); Tr. 299. Thus, an incidence of 2 cases of ADEM after one million measles vaccinations would be a lower incident rate than the background rate. Tr. 299-300.

The Institute of Medicine also looked at whether vaccines can cause encephalitis. According to an article by Maglione (discussed next), the IOM found the evidence inadequate to accept or to reject a causal relationship between the MMR vaccine and ADEM. Maglione at 89; see also Tr. 303. However, the underlying IOM study is not evidence.

The source of information about the 2012 IOM report is a report written by Maglione and colleagues. These people, apparently, worked for the Southern California Evidence-based Practice Center, which received a contract from the Agency for Healthcare Research and Quality. Maglione at iii. The Agency expects this evidence will inform the health care system as a whole and improve health care quality. Id. at iv. The Maglione group summarized the findings of the IOM and looked for additional studies. Tr. 303.

In 2014, Maglione and colleagues reported that they found "no additional trials." Maglione at 89. They also found four postmarketing studies, but none of those postmarketing studies investigated ADEM. Id. at 91-94 (Table 21).

In 2014, an article by Chang-hui Xiong and others was published. Xiong and colleagues investigated the epidemiological characteristics of ADEM in Nanchang, China. Xiong at 111. They identified people admitted to second-level and third-level hospitals from 2008 to 2010. They found 47 ADEM patients. Id. The average annual incidence was approximately 0.3 cases per 100,000 (3 cases per million). Id. The researchers found that "In the 2 months before the onset of ADEM, 15 patients presented with a preceding infection, but none of the patients received a vaccination." Id. They concluded that "There was no evidence of an association between increased number of vaccines administered and number of cases of ADEM in Nanchang, China." Id. at 5; accord Tr. 306-07.

The next epidemiologic article was published in 2016. Roger Baxter and others used the Vaccine Safety Datalink to search for cases of ADEM and transverse myelitis reported after vaccination. Baxter at pdf 1.[15] "The Vaccine Safety Datalink (VSD) is a collaboration between the Centers for Disease Control and Prevention's (CDC) Immunization Safety Office and several integrated healthcare systems across the United States. These health systems provide essentially all healthcare services and capture data from outpatient department visits, emergency department visits, and hospitalizations. The VSD has data on >9 million subjects annually, including 2.1 million children and 7.2 million adults." Id. at 3. Researchers looked for development of ADEM within 5-28 days and within 2-42 days after vaccinations. Id. at 4. During the study, more than 1.5 million doses of MMR vaccine were administered. Id. at 9 (Table 1). The adjusted odds ratio was 5. Id. at 11 (Table 3). But, the 95% confidence interval was broad, spanning from 0.6 to 29.9. Id. at 11 (Table 3). Baxter and colleagues concluded that the risk of developing ADEM after MMR vaccine was smaller than 1.16 cases per million doses. Id. at 6. There was relatively little testimony about Baxter. Tr. 302.

Another epidemiologic study was written by Yong Chen and others and published in 2018. Chen at 3733.[16] Chen and colleagues "conducted a nested case–control study between January 2011 and December 2015" with four controls

[15] The Secretary submitted a manuscript version of the Baxter article. Therefore, this decision does not cite to page numbers as published in a journal.

[16] In the transcript, "Chen" is spelled as "Chyen." Tr. 300.

per case." Id. Researchers determined if a person with ADEM had received a vaccination within the previous 14 days, 30 days, 60 days, 90 days, or 180 days. Id. at 3734. "No increase in the risk of ADEM was observed for vaccination against . . . measles, mumps [and] rubella." Id. at 3735; accord Tr. 305.

The final epidemiologic study was written by a group of Australians who explored whether childhood vaccines are associated with ADEM. Martin at 2578. They searched for children under 7 years old who were admitted to tertiary-care hospitals in Victoria, Australia from 2000 to 2015. Id. They found 46 cases of ADEM within these parameters. After identifying these cases, researchers determined whether the participants had received a vaccination in two "evidence-based and biologically plausible [risk intervals] for ADEM. . . . A narrow RI of 5–28 days and an exploratory, broad RI of 2–42 days post-vaccination." Id. at 2580; accord Tr. 308. Three patients had received a type of the measles-mumps-rubella vaccine (Priorix) in the 5-28 day risk interval. Martin at 2582. The researchers concluded that these incidents did not constitute "a statistically significant increased risk of ADEM post-vaccination in children aged under 7 years." Id.; accord Tr. 308. However, the researchers recognized that "due to the rarity of ADEM, there remain limitations and potential biases, including low case numbers, retrospective case ascertainment and long study length predisposing to altered patterns in diagnosis and management." Id. at 2583.

b) Assessment

Overall, the parties did not emphasize the epidemiologic evidence. Before the hearing, the parties' discussion of articles was relatively short. See Pet'rs' Prehear'g Br. at 36 (arguing that petitioners do not need to present epidemiologic evidence to prevail); Resp't's Prehear'g Br. at 22 (arguing that special masters may consider epidemiologic evidence) and at 24-29 (providing a sentence on various articles). Similarly, the oral testimony was relatively succinct without many details of epidemiology. For example, the experts did not explain "odds ratio."

To the extent that the epidemiologic evidence merits consideration, the epidemiologic evidence tends to undermine the claim that MMR vaccine can cause ADEM. After 2010, four studies (Xiong, Baxter, Chen, and Martin) have not detected an increased incidence of ADEM after MMR vaccination. These studies carry more weight than the Fenichel article and Huynh article, which are older and do not contain original research. Although Xiong, Baxter, Chen, and Martin can be credited, the overall value is limited because the researchers studied relatively few people with ADEM. In other words, the epidemiologic articles do not definitively allow a conclusion that the MMR vaccine does not cause ADEM. See

Tr. 92-94 (Dr. Steinman's acknowledging that epidemiologic studies generally show the MMR vaccine to be safe but contending L.S.'s experience is a rare case). Thus, other types of evidence should be considered.

2. Package Insert

Dr. Steinman and the Sparrows maintain that the package insert supports the claim that the MMR vaccine can cause ADEM. See Exhibit 18 at 22; Pet'rs' Prehear'g Br. at 23. In his oral testimony, Dr. Steinman said that the package insert states that the MMR vaccine "can cause ADEM." Tr. 68, 117. Dr. Steinman also made a more nuanced statement, stating that the package insert says "that ADEM has been seen with MMR." Tr. 93. On cross-examination, Dr. Steinman conceded that the package insert "didn't say [the MMR vaccine] caused ADEM." Tr. 135.

A package insert for a vaccination contains various sections. See Cottingham v. Sec'y of Health & Hum. Servs., No. 15-1291V, 2021 WL 347020, at *24-25 (Fed. Cl. Spec. Mstr. Jan. 7, 2021), mot. for rev. denied, 159 Fed.Cl. 328 (2022), aff'd No. 2022-1737, 2023 WL 7545047 (Fed. Cir. Nov. 14, 2023). Under the heading "adverse reactions," the package insert for the MMR vaccine states: "The following adverse reactions are listed in decreasing order of severity, without regard to causality . . . acute disseminated encephalomyelitis (ADEM)." Exhibit 25 at 6-8; accord Tr. 297-98.[17]

The package insert also contains two paragraphs of interest. The package insert states:

> Encephalitis and encephalopathy have been reported approximately once for every 3 million doses of M-M-R II or measles-, mumps-, and rubella-containing vaccine administered since licensure of these vaccines.
>
> The risk of serious neurological disorders following live measles virus vaccine administration remains less than the risk of encephalitis and encephalopathy following infection with wild-type measles (1 per 1000 reported cases).{58, 59}.

[17] Dr. Steinman opined that the Federal Drug Administration does not have the "job" to determine whether a vaccine causes an adverse side effect. Tr. 136. The basis for this opinion is not readily apparent.

Exhibit 25 at 7.

The first paragraph, which concerns incidence of encephalitis and encephalopathies after MMR vaccine, is not followed by a citation. The second paragraph, which concerns the incidence of encephalitis and encephalopathies after MMR infection, is followed by two citations. Reference 58 is the Bennetto article and reference 59 is the Fenichel article. Even if it were inferred that the Bennetto article and Fenichel article were intended to support the prior paragraph, then the support remains questionable. As discussed above, neither Bennetto nor Fenichel source their assertions. In any event, the incidence of ADEM after MMR vaccine (once per three million doses) appears to be lower than the background incidence of ADEM as reported in Huynh. See Tr. 298, 389.

To the extent that Dr. Steinman is interpreting the package insert to say that MMR vaccine causes ADEM, Dr. Steinman is not staying true to the evidence. The relevant portion of the package insert expressly states that its recitation of conditions is made "without regard for causality." A more accurate interpretation is that MMR vaccinations have preceded some cases of ADEM. The existence of examples in which an onset of ADEM occurred after an MMR vaccination is not doubted---L.S.'s case presents an example. But, the question is whether Dr. Steinman has presented a reliable theory to explain how the MMR vaccine can cause ADEM.

3. Opinions regarding Molecular Mimicry

To provide a causal mechanism by which the MMR vaccine can cause ADEM, Dr. Steinman relies upon molecular mimicry. Exhibit 18 at 10; Tr. 113. As a foundation for analyzing this theory, the appellate precedents on molecular mimicry are reviewed in section a) below. Next, Dr. Steinman's methodology and the critiques of it by Dr. Fujinami are summarized.[18] The final aspect to this section explains why Dr. Steinman's opinion does not rise to a preponderant level.

a) Appellate Precedents regarding Molecular Mimicry

Because special masters are often called upon to evaluate the persuasiveness of the theory of molecular mimicry, the Court of Federal Claims and the Court of Appeals for the Federal Circuit have considered molecular mimicry in their appellate role. In December 2019, the undersigned identified the leading

[18] Dr. Sweeney said very little about causation. See Exhibit C; Tr. 207-09 (discussing value of case reports).

precedents as W.C. v. Sec'y of Health & Hum. Servs., 704 F.3d 1352 (Fed. Cir. 2013), and Caves v. Sec'y of Dep't. of Health & Hum. Servs., 100 Fed. Cl. 119 (2011), aff'd sub nom., 463 F. App'x 932 (Fed. Cir. 2012). Tullio v. Sec'y of Health & Hum. Servs., No. 15-51V, 2019 WL 7580149, at *12-14 (Fed. Cl. Spec. Mstr. Dec. 19, 2019), mot. for rev. denied, 149 Fed. Cl. 448 (2020). While Tullio describes those cases in more detail, their essence appears to be that although molecular mimicry is accepted in some contexts, special masters may properly require some empirical evidence to show that a particular vaccine can cause a particular disease.

In the next approximately four years, appellate authorities reviewing decisions involving molecular mimicry have generally endorsed the approach of looking for some evidence that persuasively shows that a portion of a vaccine resembles a portion of human tissue, which contributes to causing the disease, and that the immune system will respond to the relevant amino acid sequence.[19] Chronologically, the list of more recent appellate cases begins with the opinion in Tullio, which denied the motion for review. 149 Fed. Cl. 448, 467-68 (2020).

Another example in which the Court of Federal Claims held that the special master did not elevate the petitioner's burden of proof in the context of evaluating the theory of molecular mimicry is Morgan v. Sec'y of Health & Hum. Servs., 148 Fed. Cl. 454, 476-77 (2020), aff'd in non-precedential opinion, 850 F. App'x 775 (Fed. Cir. 2021). In Morgan, the Chief Special Master found that petitioner had not presented persuasive evidence about a relevant antibody. Id. at 477. The Chief Special Master also noted that the articles about the relevant disease do not list the wild flu virus as potentially causing the disease. Id. When examining this analysis, the Court of Federal Claims concluded: "the Chief Special Master did not raise the burden of causation in this case; petitioner simply failed to meet it." Id.

The Federal Circuit also evaluated the Chief Special Master's approach in Morgan. The Federal Circuit concluded: "We discern no error in the special master's causation analysis." 850 F. App'x 775, 784 (Fed. Cir. 2021).

Most other recent appellate cases follow this path. See, e.g., Dennington v. Sec'y of Health & Hum. Servs., 167 Fed. Cl. 640, 653-56 (2023) (finding the special master did not err in rejecting theory of molecular mimicry where petitioner did not specifically link vaccine and injury), appeal docketed, No. 24-

[19] The term "homology" is used when discussing molecular mimicry. "Homology" is defined as "the quality of being homologous; the morphological identity of corresponding parts; structural similarity due to descent from a common form." *Dorland's* at 868.

1214 (Fed. Cir. Dec. 1, 2023); Duncan v. Sec'y of Health & Hum. Servs., 153 Fed. Cl. 642, 661 (2021) (finding the special master did not err in rejecting a bare assertion of molecular mimicry); Caredio v. Sec'y of Health & Hum. Servs., No. 17-79V, 2021 WL 6058835, at *11 (Fed. Cl. Dec. 3, 2021) (indicating that a special master did not err in requiring more than homology and citing Tullio); Yalacki v. Sec'y of Health & Hum. Servs., 146 Fed. Cl. 80, 91-92 (2019) (ruling that special master did not err in looking for reliable evidence to support molecular mimicry as a theory); but see Patton v. Sec'y of Health & Hum. Servs., 157 Fed. Cl. 159, 169 (2021) (finding that a special master erred in requiring petitioner submit a study to establish medical theory causally connecting flu vaccine to brachial neuritis).

b) Summary of Evidence

(1) Dr. Steinman

Dr. Steinman's methodology followed a path that he has frequently put forward. See, e.g., Trollinger v. Sec'y of Health & Hum. Servs., No. 16-473V, 2023 WL 2521912 (Fed. Cl. Feb. 17, 2023), mot. for rev. denied, 167 Fed. Cl. 127 (2023); Pierson v. Sec'y of Health & Hum. Servs., No. 17-1136V, 2022 WL 322836 (Fed. Cl. Jan. 19, 2022); Tullio v. Sec'y of Health & Hum. Servs., No. 15-51V, 2019 WL 7580149 (Fed. Cl. Dec. 19, 2019), aff'd, 149 Fed. Cl. 448 (2020).

The basic idea is that the vaccine contains sequences of amino acids that cause a person's immune system to attack host tissue that consists of similar sequences of amino acids. The attacked tissue should be implicated in a relevant disease's pathology.

By way of background, Dr. Steinman relied upon the vaccine's package insert to determine the components of the MMR vaccine. Exhibit 18 at 9, citing Exhibit 25; Tr. 85. Dr. Steinman identified myelin oligodendrocyte glycoprotein ("MOG") and myelin basic protein ("MBP") as "two nervous system proteins known to be targeted in ADEM." Exhibit 18 at 18, citing Exhibits 35-36, Tr. 85, 113-14.

Dr. Steinman assessed the similarity of these substances. The first part of this process was that Dr. Steinman accessed a database, the Basic Local Alignment Search Tool ("BLAST"). He entered various combinations. Tr. 85, 117, 125. In his report, Dr. Steinman disclosed that he compared the rubella virus with myelin basic protein and the hemagglutinin component of the measles virus strain found in

the vaccine with myelin oligodendrocyte glycoprotein. Exhibit 18 at 15-18.[20] The database calculates an expected (or E) value, which Dr. Steinman presented in screen captures as part of his report. Exhibit 18 at 15-18; Tr. 118.

Dr. Steinman compared the degree of similarity of strings of amino acids. Based upon experiments to which Dr. Steinman contributed in the 1990's, Dr. Steinman asserted that a match of five amino acids in a string of twelve amino acids can be sufficient to induce an autoimmune response. Exhibit 18 at 12; Tr. 85-89, 104-05, 113-14, 155-59. The results of the presented BLAST searches that Dr. Steinman presented meet a criterion of having 5/12 similarity. Although Dr. Steinman acknowledged that some homologies carry no effect, he maintained that he was not responsible for proving that any homology he identified through computer searches was biologically meaningful. Tr. 120.

As a final step for presenting a molecular mimicry theory, Dr. Steinman used a second publicly available database, the immune epitope database ("IEDB"). The IEDB "catalogs experimental data on antibody and T cell epitopes studied in humans, non-human primates, and other animal species in the context of infectious disease, allergy, autoimmunity, and transplantation." Exhibit 18 at 19. Dr. Steinman stated that the relevant strings of amino acids have been reported in the IEDB. Id. at 20-21; see also Tr. 87-89, 129-31.

Dr. Steinman closed his report's section regarding molecular mimicry by discussing testing. He stated that he could not test L.S. for antibodies to either MOG or myelin basic protein because of the therapies that she received. Exhibit 18 at 22; see also Tr. 406. He further explained that even if specimens were available, additional research "would require someone to fund a research lab with credentials to do such assays, and would require ethical review by the host institution." Exhibit 18 at 22; see also Tr. 127-32, 401.

(2) Dr. Sweeney and Dr. Fujinami

Primarily through Dr. Fujinami, the Secretary challenged Dr. Steinman's reliance on molecular mimicry as a way to explain how the MMR vaccine can cause ADEM. Dr. Fujinami, who co-wrote one of the foundational articles about molecular mimicry in 1983, accepted that molecular mimicry is accepted as a

[20] On cross-examination, Dr. Steinman testified that he conducted other searches. However, these other searches were not productive, and Dr. Steinman discarded them. Tr. 125-26.

scientific concept, such as connecting an infection with strep bacteria and heart disease. Tr. 311. Nevertheless, Dr. Fujinami rejected molecular mimicry in the context of an MMR vaccine potentially causing ADEM for various reasons.

Dr. Fujinami asserted that a cross-reaction between a microbe and host tissue might occur but only when an infection or an adjuvant drives a strong immune response. Tr. 312; see also Exhibit A at 4-5. Because the MMR vaccine contains attenuated viruses, the viruses do not replicate well and, therefore, the immune response is less robust than with a natural infection. Tr. 313-14. Instead, Dr. Fujinami theorized that the introduction of similar sequences of amino acids in the context of a weak immune response could protect the recipient. Exhibit A at 4-5, Tr. 319-20, 333-35. Articles about this theory use the term "altered peptide ligand." See, e.g., Brocke; Gaur; Ruiz.

Dr. Fujinami's focus on strong immune responses continued as he discussed Dr. Steinman's assertion that a 5/12 similarity of amino acids could be sufficient. In Dr. Fujinami's view, this ratio could be acceptable in the context of powerful adjuvants.[21] Tr. 329-31. Dr. Fujinami opined that relevant experiments on mice could be completed in about three to four months and would cost hundreds of thousands of dollars. Tr. 385-86.

Dr. Sweeney's main contribution to the controversy regarding whether molecular mimicry can explain how the MMR vaccine can cause ADEM was to question whether the pathogenesis of ADEM involves either the two proteins that Dr. Steinman tested, MOG and MBP. Tr. 207.

c) Steps of Dr. Steinman's Theory

Dr. Steinman's theory involves a series of steps. These are each reviewed below.

Step 1: Identification of Vaccine Components

To start, Dr. Steinman identified components of the measles-mumps-rubella vaccine. Exhibit 18 at 9. For example, for the measles component, the MMR vaccine contains "a more attenuated line of measles virus, derived from Enders'

[21] An example of a powerful adjuvant is complete Freund's adjuvant, which contains killed bacteria, oil, and an emulsifying agent. Tr. 320-21, 343. Incomplete Freund's adjuvant does not contain the killed bacteria. Id. The MMR vaccine does not contain complete Freund's adjuvant or incomplete Freund's adjuvant. Tr. 95.

attenuated Edmonston strain and propagated in chick embryo cell culture." Id.; accord Exhibit 25 (package insert). According to Dr. Steinman, although the viruses are attenuated, weakened viruses can be a basis for molecular mimicry. Tr. 144.

The Secretary did not significantly challenge this step. At most, Dr. Fujinami testified that when he entered the amino acid sequences of the Edmonston strain into the IEDB, no results were produced. Tr. 355. This point seems to pertain to the usefulness of the IEDB, rather than Dr. Steinman's selecting the Edmonston strain as a basis of comparison. Thus, Dr. Steinman's identification of components of the vaccine is reliable and persuasive.

Step 2: Identification of Host Tissue

Dr. Steinman identified two proteins, MBP and MOG, as involved in the pathogenesis of ADEM. Tr. 85. Dr. Sweeney did relatively little to challenge this assertion. Tr. 207. The Secretary also did not contest this point. See Resp't's Posthear'g Br. at 30. Thus, this portion of Dr. Steinman's opinion is reliable and persuasive.

Step 3: Consulting BLAST

Dr. Steinman determined the degree of homology between components of the MMR vaccine and either MBP or MBP through BLAST. Exhibit 18 at 14-19 The Secretary did not challenge this methodology significantly. That is to say, compared to other cases, the Secretary presented relatively little evidence that Dr. Steinman's search through BLAST was mistaken. At best, the Secretary attempted to undermine Dr. Steinman's opinion on cross-examination. See Tr. 117 (discussing disclaimer from website), 119 (discussing E value for Blast searches). Despite some able questioning from counsel, there was relatively little evidence that BLAST was an improper tool.[22]

Step 4: Filtering to a Level of 5 out of 12

[22] In other cases, the Secretary has introduced opinions, supported by articles, that BLAST was not appropriate. See Trollinger, 2023 WL 2521912, at *17 (summarizing an opinion from an expert the government retained) & at *28 (special master's assessment) (Fed. Cl. Spec. Mstr. Feb. 17, 2023), mot. for rev. denied, 167 Fed. Cl. 127 (2023); A.T. v. Sec'y of Health & Hum. Servs., No. 16-393V, 2021 WL 6495241, at *11 (summarizing a report from a government's expert) and at *24-25 (special master's assessment of the evidence) (Fed. Cl. Spec. Mstr. Dec. 17, 2021). However, the Sparrow case does not contain this type of evidence.

Dr. Steinman testified that a similarity of 5 amino acids out of 12 could be sufficient to cause an autoimmune disease. Tr. 88, 114. The basis for this criterion was three experiments, generally referred to as the Gautum articles. The three articles share multiple authors, and the three articles report similar experiments with some variations. Tr. 127, 149. For sake of simplicity, only the earliest published article is summarized.

By way of background, before Gautum and colleagues began their experiments, scientists knew that the first 11 amino acids that formed myelin basic protein were involved in creating a disease known as experimental autoimmune encephalomyelitis ("EAE") in genetically engineered mice. Tr. 149, 325, Gautum (Exhibit 32) at 605. Gautum refers to this sequence of 11 amino acids as "Ac1-11." See Tr. 150. When this series of 11 amino acids was injected into mice in the presence of complete Freund's adjuvant, the mice developed EAE. Exhibit 32 at 606.

The Gautum researchers, who included Dr. Steinman, attempted to determine whether the exact sequence of 11 amino acids was required or whether variations among the 11 amino acids could still induce EAE. Exhibit 32 at 605. Researchers substituted one amino acid, alanine, in different positions along the chain from 1 to 11.

Dr. Steinman pointed to results in Table 1. Tr. 104-05. A critical point is comparing the second row and the third row.

Table 1. *Induction of EAE by Alanine-substituted Peptides*

Groups	Percent incidence	Mean clinical scores	Day of onset
Ac1-11	87 (27/31)	3.8	12.4
Ac3.4.5.6	80 (20/25)*	3.05	14
Ac3.5.6.10	15.7 (3/18)	0.51	15.75
Ac3.5.6	0	0	0

Both the second row and the third row show that the native amino acid remains the same in spots 3, 5, and 6. Row two differs from row three in that the

fourth native protein in row 2 is in spot 4 and the fourth native protein is in spot 10. Tr. 150. The change decreased the incidence of disease from 80 percent to 15.7 percent. Based upon this papers and others, Dr. Steinman acknowledged that a change in one amino acid could make a big difference. Tr. 155.[23] Thus 5 amino acids out of 12 work sometimes but not always. See Tr. 176.

Dr. Fujinami agreed that 5 amino acids out of 12 could work. Tr. 387. However, Dr. Fujinami also opined that antigens with homology with host tissues lead to autoimmune disease only in the context of a robust immune response. Otherwise, a homologous substance, such as an altered peptide ligand, is likely to be protective. See Tr. 333.

Dr. Steinman recognized that, as a theoretical matter, he could test his hypothesis that the specific sequences of amino acids he identified can cause a disease like EAE in mice. Tr. 177-78. There might be practicable obstacles to overcome but an experiment is "doable." Tr. 178.

Step 5: Consulting the IEDB

To tighten up his opinion, Dr. Steinman consulted the IEDB. Tr. 130. Although Dr. Steinman described this step as strengthening his opinion, the process was presented too vaguely to add much weight to Dr. Steinman's overall opinion. Dr. Steinman's first report states that a sequence from the rubella virus was reported as positive in "standard proliferation assays done in humans." Exhibit 18 at 20. A second sequence was also reported to have "positive assays in various platforms." Id. at 21.

On direct examination, Dr. Steinman testified briefly about the IEDB. Tr. 87, 91. He stated that the IEDB shows whether any researcher "report[ed] that region." Tr. 87. On cross-examination, Dr. Steinman stated that an appearance in the IEDB means that "somebody looked at it." Tr. 130.

From this evidence, it is difficult to see how the presence of an epitope in a database advances the proposition that a particular sequence of amino acids either leads to an immune response or leads to ADEM. The presence of an epitope in the IEDB might be consistent with those assertions. But, without a showing about

[23] At transcript page 155, Dr. Steinman is being asked about an article by Chen (Exhibit A-2).

how other researchers used the particular sequence of amino acids, there is a gap in Dr. Steinman's reasoning.

d) Overall Assessment

Overall, Dr. Steinman has presented an interesting hypothesis. However, Mr. and Ms. Sparrow have not established that Dr. Steinman's hypothesis is a theory persuasive enough to meet their burden in the Vaccine Program. A critical aspect is the lack of testing. Testability and the lack of testing are factors a special master may consider in assessing the value of an expert's opinion. Terran v. Sec'y of Health & Hum. Servs., 195 F.3d 1302, 1316 (citing Daubert v. Merrell Dow Pharmaceuticals, Inc., 509 U.S. 579 (1993)).

The Gautum papers illustrate the usefulness of testing a hypothesis that certain sequences of amino acids can lead to autoimmune disease. As explained above, in Gautum, a change in one amino acid out of 11 changed the incidence of EAE from 80% to 15.7%. Exhibit 32 at 607.

Dr. Steinman acknowledged that 5 out of 12 amino acids does not break tolerance every time. Tr. 121. Dr. Steinman has not provided any sound and reliable basis for evaluating whether the sequence of amino acids he identified in his BLAST query can stimulate the production of either T cells or B cells that would attack MOG or MBP. Special masters are not required to accept every assertion from an expert. Cedillo v. Sec'y of Health & Hum. Servs., 617 F.4d 1328, 1435 (Fed. Cir. 2010).

If the Gautum-like experiments were conducted using the sequences of amino acids that Dr. Steinman identified and if the results were positive for inducing a disease, then Mr. and Ms. Sparrow would have a stronger argument concerning the persuasiveness of Dr. Steinman's opinion that molecular mimicry explains how the MMR vaccine can cause ADEM. The Gautum-like experiments would not make petitioners' claim certain because of the differences between EAE in mice and ADEM in humans. However, petitioners do not need to present their cases with certainty.

The usefulness of testing is also shown in articles regarding altered peptide ligands. The concept behind altered peptide ligands resembles the concept underlying molecular mimicry. Tr. 319. Scientists have identified certain sequences of amino acids that cause disease in people or in animals, at least in the presence of powerful stimulators of the immune system, such as complete Freund's adjuvant. These sequences are known as "disease inducing peptides." Tr. 319.

For example, Dr. Fujinami credited Dr. Steinman as identifying a significant stretch of amino acids in the myelin basic protein found in mice. Tr. 325. Researchers modify the disease inducing peptides by changing the sequence of amino acids to create an altered peptide ligand. Tr. 319. The goal is to introduce the altered peptide ligand to prevent the development of the disease.

A group of researchers including Dr. Steinman hoped that they had discovered an altered peptide ligand that would ameliorate multiple sclerosis. Tr. 95-96, 107-08; see also Exhibits 43-44; Brocke; Gaur; Ruiz. In short, the researchers found that the injection of a certain sequence of amino acids in the context of complete Freund's adjuvant prevented mice from developing EAE. Tr. 324-26; Barnett.[24] However, when researchers, including Dr. Steinman, attempted a similar process in people with multiple sclerosis, the participants experienced some adverse reactions from which they recovered. Nevertheless, the experiments were stopped. Tr. 95-97, 157, 339-42.

A lesson to draw from this attempt to create a medical product that would help people is that what looks promising on paper does not always work in real life. See Tr. 108 (Dr. Steinman: "in homo sapiens is veritas"). As Dr. Steinman stated, "it's not easy being a medical scientist," and despite a promising foundation, medical research can "backfire[]." Tr. 97, 155. While the process for governmental approval of pharmaceutical products for use in humans requires a higher degree of confidence in the efficacy and safety of the product, see 21 U.S.C. § 355 (New Drugs), the basic point remains: some degree of testing can be needed to show the reliability of an idea. Terran, 195 F.3d at 1316.

When Dr. Steinman's theory is measured against the Daubert factors, Dr. Steinman's theory cannot be credited. To review, the Supreme Court identified a non-exclusive set of factors trial courts could use to assess the reliability of an expert's opinion. This list includes:

Whether the technique or theory in question can be, and has been tested;

Whether it has been subjected to publication and peer review; and

[24] With his first expert report (Exhibit 18), Dr. Steinman filed an article by Dr. Fujinami (Exhibit 30). Dr. Fujinami discussed this article at the hearing, and was asked about the Barnett study, which is reference 10 in his article. The Barnett study was not filed as a separate exhibit.

> Whether it has attracted widespread acceptance within a relevant scientific community.

Daubert, 509 U.S. at 592-95.[25]

Dr. Steinman's theory that the presentation of certain sequences of amino acids can induce neurologic disease can be tested, at least in animals. However, Dr. Steinman presented no evidence that this testing has been done.

The general theory of molecular mimicry appears in peer-reviewed articles. However, the Federal Circuit stated that special masters are not required to accept a simple invocation of molecular mimicry as satisfying Althen prong one. W.C., 704 F.3d at 1360. If, in accordance with W.C., "molecular mimicry" specifically refers to a theory by which components of the MMR vaccine can cause neurologic injuries, then Dr. Steinman has not identified any instances of peer-review.

The absence of commentary in peer-reviewed journals suggest that the theory that the MMR vaccine can cause neurologic injuries suggests that the theory does not have "widespread acceptance." The Sparrows have not presented any persuasive evidence that the relevant medical community agrees that the MMR vaccine can rarely cause neurologic injuries. Thus, the Sparrows have not presented preponderant evidence, and have not met their burden under Althen prong 1.

Because the Sparrows' case is resolved based upon the first Althen prong, further evaluation of the remaining prongs is not necessary. When special masters can resolve a case a based upon one issue, they do not necessarily need to address all issues. See, e.g., Hibbard v. Sec'y of Health & Hum. Servs., 698 F.3d 1355, 1365 (Fed. Cir. 2012); Holmes v. Sec'y of Health & Hum. Servs., 115 Fed. Cl. 469, 488 (2014); Vaughan v. Sec'y of Health & Hum. Servs., 107 Fed. Cl. 212, 222 (2012). However, if the Sparrows had presented a persuasive theory causally connecting the MMR vaccine and ADEM under Althen prong 1, they cannot establish a logical sequence of cause and effect in Althen prong 2. A discussion of Althen prong 2 follows.

[25] Two other items seem not to fit the theory of molecular mimicry. These are its known or potential error rate, and the existence and maintenance of standards controlling its operation.

VI. Althen Prong II

A. Law / Elements

Pursuant to Althen, a petitioner must establish "a logical sequence of cause and effect showing that the vaccination was the reason for the injury." Althen, 418 F.3d at 1278. A petitioner does not need to present "epidemiologic studies, rechallenge, the presence of pathological markers or genetic disposition, or general acceptance in the scientific or medical communities to establish a logical sequence of cause and effect" to satisfy this prong, but may rely on circumstantial evidence and reliable medical opinions. Capizzano v. Sec'y of Health & Hum. Servs., 440 F.3d 1317, 1325-26 (Fed. Cir. 2006).

B. Opinions of Treating Doctors

The Federal Circuit has instructed special masters to carefully consider the views of treating doctors. Capizzano, 440 F.3d at 1326. The Sparrows note that one of L.S.'s treating doctors, neurologist Delphin Sallowm, opined that L.S. had ADEM, and considered the vaccine as a possible trigger. Pet'rs' Posthear'g Br. at 49-51.

Dr. Sallowm saw L.S. on March 18, 2015. Exhibit 2 at 335. In her assessment, Dr. Sallowm wrote: "Post infectious ADEM is high on the deferential diagnosis although this could still be infectious viral Encephalomyelitis with no detected pathogen." Id. She did not remark about the MMR vaccine. Five days later, the topic of the MMR vaccine came up in Dr. Sallowm's visit with the Sparrows. Id. at 391. There was "concern regarding the safety of MMR immunization after this event, which [we] believe to be ADEM, which may or may not have been triggered by an MMR vaccine 3-4 weeks prior to symptom onset." Id. It is not clear from the record whether it was Dr. Sallowm or the Sparrows who raised concern over the vaccine. "Given the risks and benefits, we have concerns that risks outweigh the benefits." Dr. Sallowm suggested that the Sparrows consider "consulting or referring to infectious disease for their expertise regarding immunizing." Id.

Ms. Sparrow asked for Infectious Disease and Neurology's "opinions on continued vaccinations this episode [had] been related to her MMR vaccine." Id. at 449. On April 2, 2015, Dr. Chou recorded that Infectious Disease "feel it is possible but very unlikely that the MMR is what caused this meningoencephalitis. They have no problem with continuing the MMR series, or if mom would prefer they suggest we could just check titers to measures and also varicella and if there is

a good response, hold off on the vaccine." Exhibit 2 at 543. The next day, Dr. Chou stated: "Parents feel that MMR vaccine triggered current episode and do not want to continue with MMR series." Id. at 559.

On April 5, 2015, Dr. Melzer-Lange made note of Dr. Sallowm's concern, writing: "Neurology expressed concern regarding safety of MMR immunization in the future given the question that her ADEM may or may not have been triggered by an MMR vaccination." Exhibit 2 at 2867. This was also recorded by Dr. Chou in L.S.'s discharge summary three days later. Id. at 115. Dr. Chou added: "This was discussed with [Infectious Disease] who felt that current process was highly unlikely to be due to MRR and that there are no contraindications for pt to receive all of her immunizations as she grows up." Id.

Dr. Sallowm reiterated her concern on August 13, 2015. "[L.S.] had received MMR vaccination about 3 weeks prior to this presentation, making me wonder if it was a trigger factor for her what I think [is] autoimmune acute disseminating encephalomyelitis, ADEM. Extensive workup did not reveal any pathogen." Exhibit 2 at 3985. She continued: "In regard to future MMR vaccination, since she developed ADEM about 3 weeks following this vaccine, I rec avoid further MMR vaccines for now as potentially it could have been triggered her ADEM." Id. at 3986.

The Individual Health Plan sent to L.S.'s school also describes her condition as "meningoencephalitis (ADEM) possibly caused by the MMR vaccination." Exhibit 2 at 4000 (dated August 19, 2015). It is unclear who generated the plan, but the school district's nurse reached out to Dr. Sallowm about the plan. Id. at 3999.

On January 7, 2016, Dr. Sallowm repeated her concern: "[L.S.] had received MMR vaccination about 3 weeks prior to this presentation, making me wonder if it was a trigger factor for her [ADEM.]" Exhibit 2 at 4167. Similarly, on May 23, 2016: "She had received MMR vaccination about 3 weeks prior to this presentation, making it possible as a trigger factor for her [ADEM]." Id. at 4559.

C. Discussion

A finding that a petitioner has not met one element of the Althen prongs justifies a denial of compensation. However, even assuming that the Sparrows had proposed a reliable theory of what can happen – a vaccine-triggered autoimmune response resulting in ADEM– they have not presented preponderant evidence that this happened to L.S. As noted above in Section IV, the evidence supports a

finding that L.S.'s condition began as a viral encephalitis rather than an autoimmune encephalitis. Thus, preponderant evidence does not support a finding that the MMR vaccine caused encephalitis in L.S. via an autoimmune process.

L.S.'s medical records contain questions about possible vaccine causation. "[M]edical records and medical opinion testimony are favored in vaccine cases, as treating physicians are likely to be in the best position to determine whether a logical sequence of cause and effect shows that the vaccination was the reason for the injury." Capizzano, 440 F.3d at 1326 (internal quotation marks omitted). However, opinions from treating physicians are not conclusive; "Any such diagnosis, conclusion, judgment, test result, report, or summary shall not be binding on the special master or court." 42 U.S.C. § 300aa–13(b)(1).

"A variety of circumstances bear on a special master's decision with respect to treating physicians' opinions. Among the many circumstances that might be weighed: clarity and context of the treating physician's opinion; nature and duration of the physician's relationship with the vaccinee; the physician's specialty and level of expertise; and the consistency of the treating physician's opinion with the medical record." Isaac v. Sec'y of Health & Hum. Servs., No. 08-601V, 2012 WL 3609993, at *25 (Fed. Cl. Spec. Mstr. July 30, 2012), mot. for rev. denied, 108 Fed. Cl. 743 (2013), aff'd, 540 F. App'x 999 (Fed. Cir. 2013).

Of all L.S.'s treaters, Dr. Sallowm was the only one to opine that the MMR vaccine may have been a trigger. As a neurologist, Dr. Sallowm is certainly qualified to opine on the etiology of ADEM. However, Dr. Sallowm never seemed to move past "wonder[ing] if it was a trigger factor." Exhibit 2 at 3985. She only ever stated that it "may or may not" have caused L.S.'s condition, and advised forgoing the MMR vaccine out of caution. Id. at 3986. A recommendation to explore discontinuing vaccinations is not definitive proof regarding causation. See K.T. v. Sec'y of Health & Hum. Servs., 132 Fed. Cl. 175, 187 (2017).

Dr. Sallowm recommended that the Sparrows also consult Infectious Disease on the question of the MMR vaccine. Exhibit 2 at 391. Infectious Disease "[felt] it is possible but very unlikely that the MMR is what caused this meningoencephalitis," and they "[had] no problem with continuing the MMR series." Exhibit 2 at 543. Infectious Disease was more definitive in their answer than Dr. Sallowm ("possible but very unlikely" as opposed to "may or may not"), which diminishes the probative value of Dr. Sallowm's opinion.

Dr. Sallowm noted that "Extensive workup did not reveal any pathogen," Exhibit 2 at 3985. However, she also acknowledged that L.S. could have

"infectious viral Encephalomyelitis with no detected pathogen." Id. at 335. Her consideration of the vaccine as a trigger was predominantly based on temporality rather than on the lack of an identified pathogen. See id. at 3985-86 (noting that L.S. "received MMR vaccination about 3 weeks prior to this presentation**, making me wonder** if it was a trigger factor since she developed ADEM about 3 weeks following this vaccine," and recommending that L.S. forgo future MMR vaccination "**since** she developed ADEM about 3 weeks following this vaccine") (emphasis added). Suspicions based primarily on temporality are not strong evidence in support of causation. See Orgel-Olson v. Sec'y of Health & Hum. Servs., No. 15-285V, 2022 WL 1598143, at *34 (Fed. Cl. Mar. 11, 2022) (little weight given to providers' "suspicion" of vaccine causation where "suspicion was based largely on temporality" and providers were equivocal). Further, Dr. Sallowm did not explain why she ceased to consider viral encephalomyelitis at all, and instead turned to the question of the MMR vaccine causing ADEM. Her supposition is not sufficiently explained to constitute preponderant evidence of causation. See Doyle v. Sec'y of Health & Hum. Servs., 92 Fed. Cl. 1, (2010) ("Merely conclusory opinions--or ones that are nearly so as unaccompanied by elaboration of critical premises—will not suffice as proof of causation, no matter how vaunted or sincere the offeror"); Fesanco v. Sec'y of Health & Hum. Servs., 99 Fed. Cl. 28, 34 (2011) (notation that provider was "suspicious" that injury may be related to vaccine was not an affirmative medical opinion of causation).

In sum, preponderant evidence supports that L.S. had viral encephalomyelitis, and so the Sparrows' theory of molecular mimicry cannot explain her condition. Dr. Sallowm's questions over the MMR vaccine, based primarily on temporality, are neither definitive nor explained enough to serve as preponderant proof of causation under Althen prong 2.

VII. Conclusion

The Sparrow family deserves both sympathy and admiration for their perseverance through L.S.'s hospitalization. However, the requirements of the Vaccine Act must be satisfied before compensation can be awarded. Here, the Sparrows have not presented sufficient evidence to support their claim that the MMR vaccine harmed L.S. Accordingly, their claim for compensation is DENIED.

The Clerk's Office is instructed to enter judgment in accord with this decision unless a motion for review is filed. Information about filing a motion for review, including the deadline, can be found in the Vaccine Rules, which are available on the website for the Court of Federal Claims.

IT IS SO ORDERED.

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

Appendix: List of Medical Articles Cited[1]

1. L. A. Barnett et al., Virus encoding an encephalitogenic peptide protects mice from experimental allergic encephalomyelitis. 64 J. NEUROIMMUNOL. 163 (1996); reference 10 in Exhibit 30.

2. Roger Baxter et al., Acute Demyelinating Events Following Vaccines: A Case-Centered Analysis. 63 CLIN. INFECT. DIS. 1456 (2016); filed as Exhibit E-1.

3. L. Bennetto & N. Scolding, Inflammatory/Post-Infectious Encephalomyelitis. 75 J. NEUROL. NEUROSURG. PSYCHIATRY i22 (2004); filed as Exhibit 39 and Exhibit A-1.

4. Stefan Brocke et al., Treatment of experimental encephalomyelitis with a peptide analogue of myelin basic protein. 379 NATURE 343 (1996); filed as Exhibit A-2.

5. Yong Chen et al., Vaccines and the risk of acute disseminated encephalomyelitis. 36 VACCINE 3733 (2018); filed as Exhibit A-3.

6. Gerald M. Fenichel, Neurological Complications of Immunization. 12 ANN. NEUROL. 119 (1982); filed as Exhibit 37.

7. Robert S. Fujinami et al., Molecular Mimicry, Bystander Activation, or Viral Persistence: Infections and Autoimmune Disease. 19 CLIN. MICROBIOL. REV. 80 (2006); filed as Exhibit 30.

8. Amitabh Gaur et al., Amelioration of Autoimmune Encephalomyelitis by Myelin Basic Protein Synthetic Peptide-Induced Anergy. 258 SCIENCE 1491 (1992); filed as Exhibit A-6.

9. Anand M. Gautam et al., A Polyalanine Peptide with only Five Native Myelin Basic Protein Residues Induces Autoimmune Encephalomyelitis. 176 J. EXP. MED. 605 (1992); filed as Exhibit 32.

10. Anand M. Gautam et al., Minimum structural requirements for peptide presentation by major histocompatibility complex class II molecules: Implications in induction of autoimmunity. 91 PROC. NATL. ACAD. SCI. USA 797 (1994); filed as Exhibit 33.

11. Anand M. Gautam et al., A Viral Peptide with Limited Homology to a Self Peptide Can Induce Clinical Signs of Experimental Autoimmune Encephalomyelitis. 161 J. IMMUNOL. 60 (1998); filed as Exhibit 34.

[1] All articles have been considered.

12. William Huynh et al., Post-vaccination encephalomyelitis: Literature review and illustrative case. 15 J. CLIN. NEUROSCI. 1315 (2008); filed as Exhibit A-7.

13. Margaret A. Maglione et al., Safety of Vaccines Used for Routine Immunization in the United States. 215 EVIDENCE REPORT/TECHNOLOGY ASSESSMENT (2014); filed as Exhibit E-3.

14. T. J. Martin et al., Acute disseminated encephalomyelitis and routine childhood vaccinations – a self-controlled case series. 25 HUM. VACCIN. IMMUNOTHER. 2578 (2021); filed as Exhibit H-2.

15. Pedro J. Ruiz et al., Microbial Epitopes Act as Altered Peptide Ligands to Prevent Experimental Autoimmune Encephalomyelitis. 189 J. EXP. MED. 1275 (1999); filed as Exhibit A-8.

16. Chang-hui Xiong et al., Epidemiological characteristics of acute disseminated encephalomyelitis in Nanchang, China: a retrospective study. 14 BMC PUBLIC HEALTH 111 (2014); filed as Exhibit H-1.