In the United States Court of Federal Claims

No. 07-448V
(Filed Under Seal: April 7, 2011)
(Reissued: April 29, 2011)

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JANE DOE 93,	*	**Vaccine Program; Influenza Vaccine; Transverse Myelitis: Vaccine Act; Allocation of the Burden of Proof; Preponderance of the Evidence.**
Petitioner,	*	
v.	*	
SECRETARY OF HEALTH AND HUMAN SERVICES,	*	
Respondent.	*	
* *		

Ronald Homer, Sylvia Chin-Caplan, and Amy Fashano, Conway, Homer & Chin-Caplan, P.C., 16 Shawmut St., Boston, MA, for Petitioner.

Glenn MacLeod, United States Department of Justice, Vaccine/Torts Branch, Civil Division, P.O. Box 146, Ben Franklin Station, Washington, D.C., for Respondent.

OPINION AND ORDER

WILLIAMS, Judge.

This matter comes before the Court on Petitioner's motion for review of the Special Master's decision denying her claim that an influenza vaccination caused her to develop transverse myelitis ("TM"), a debilitating condition of the central nervous system.[1] The Special Master found that Petitioner failed to show that the flu vaccine can cause TM because her expert's theory and supporting literature were not persuasive. John Doe 93 v. Sec'y of HHS,

[1] In accordance with Rule 18(b) of Appendix B of the Rules of the United States Court of Federal Claims ("RCFC"), this opinion was filed under seal on April 7, 2011. Each party was afforded 14 days to object to the public disclosure. No objections or proposed redactions having been received, the Court publishes this opinion in toto, errata corrected.

2010 WL 4205677, at *1 (Fed. Cl. Spec. Mstr. Oct. 20, 2010).[2] Because the Special Master impermissibly elevated the burden of proof on the requirement that Petitioner provide a medical theory causally linking the flu vaccine to TM, the Court vacates the decision and remands the case.

Factual Background[3]

Petitioner seeks compensation under the National Childhood Vaccine Injury Act of 1986, 42 U.S.C. §§ 300aa-1 to -34 ("Vaccine Act"), claiming that her October 8, 2004 flu vaccination caused her TM, a rare demyelinating disorder of the central nervous system "in which an immune-mediated process causes neural injury to the spinal cord, resulting in varying degrees of weakness, sensory alterations and autonomic dysfunction."[4] Tornatore Report at 16 (citation omitted). TM can be caused by an autoimmune process or an infectious agent. Doe 93, 2010 WL 4205677, at *2. "Autoimmunity" refers to a process in which the body's immune system, which typically protects against foreign substances, attacks its own tissue. Id.

Petitioner's Medical History

Petitioner was a "more or less healthy" 61-year-old woman when she received the flu vaccine on October 8, 2004. Id. at *1. Shortly thereafter, she began experiencing a wide array of symptoms, including urinary retention. Petitioner had undergone prior flu vaccinations without incident. After her October 8, 2004 vaccination, however, her arm became sore and red. On December 8, 2004 -- two months after her vaccination -- Petitioner was diagnosed with a urinary tract infection ("UTI"). Id. On December 12, 2004, she visited the emergency room ("ER") due to urinary retention. Id. Petitioner also reported experiencing abdominal pain since her vaccination. Id.

In December of 2004, Petitioner saw Dr. Joseph Mobley, a urologist, and Dr. Paul Marsidi regarding her urinary symptoms. Id.; see also Tornatore Report at 2. Both physicians concluded that her symptoms were of unknown etiology but could have neurological underpinnings. Tornatore Report at 2. In February of 2005, Petitioner was diagnosed with degenerative disc disease by Dr. Brad Wright, an orthopedic surgeon, and underwent a vast array of tests, which indicated that she suffered from a problem of the central nervous system. Id. at 2-3. Petitioner also visited a neurosurgeon, Dr. John Campbell, who observed that Petitioner's symptoms worsened in October of 2004. Id. at 3; Bielawski Report at 1; Doe 93, 2010 WL 4205677, at *2. Throughout February and March of 2005, Petitioner underwent another battery

[2] The decision was reissued on October 20, 2010. The Court cites to the redacted version published by Westlaw.

[3] This background is derived from the record developed before the Special Master and his decision.

[4] Unless otherwise noted, citations to the transcript refer to the January 19, 2010 evidentiary hearing before the Special Master.

of tests and saw several different physicians who all concluded that Petitioner suffered from myelopathy of unclear etiology. See, e.g., Tornatore Report at 3, 5; Bielawski Report at 1-2; Doe 93, 2010 WL 4205677, at *2.

On April 6, 2005, Petitioner was evaluated by Dr. Subramaniam Sriram, a neurologist in the Multiple Sclerosis Clinic at Vanderbilt University. Bielawski Report at 2; Tornatore Report at 5. In Petitioner's patient history, Dr. Sriram noted that Petitioner's symptoms began in October of 2004 and that she began experiencing urinary retention three to four weeks after her flu vaccination. Tornatore Report at 5. He further observed that in January or early February of 2005, Petitioner began suffering from weakness of her lower extremities and difficulty in ambulation and gait. Id. After noting that Petitioner's "spinal fluid shows [her myelopathy] is inflammatory in nature with positive oligoclonal bands and [an] elevated IgG index," Dr. Sriram concluded, "[a]t present, my feelings are this is probably questionable postinfectious, postvaccination etiology of an acute ascending myelopathy." Tornatore Report at 6; Doe 93, 2010 WL 4205677, at *2; see also Bielawski Report at 2. Dr. Sriram also considered a paraneoplastic process and Devic's disease. Tornatore Report at 6; Doe 93, 2010 WL 4205677, at *2.

Petitioner's test results for paraneoplastic antibodies were negative, and a cytopathology report of Petitioner's cerebrospinal fluid ("CSF") and neuromyelitis optica ("NMO") antibody screen were negative; the latter test indicated that Petitioner did not suffer from NMO. Bielawski Report at 2; Tornatore Report at 7-8.

Petitioner had several follow-up visits with Dr. Sriram. During her April 20, 2005 visit, Dr. Sriram noted that Petitioner suffered from "inflammatory myelopathy of unknown etiology." Tornatore Report at 9. During her June 22, 2005 visit, Dr. Sriram listed Petitioner's diagnosis as "inflammatory myelopathy of unknown etiology," although he observed that Petitioner "continue[d] to be a possible Devic's disease suspect, although her oligoclonal bands are positive and [also] her NMO screen is negative." Id. at 10. During Petitioner's subsequent visits with Dr. Sriram during the summer of 2005, he again noted that Petitioner's inflammatory myelopathy was of "unknown etiology" and that her troubles began in October of 2004. Id. at 10-11.

On September 13, 2005, Petitioner was admitted to Henry County Medical Center and examined by Dr. Mobley and Dr. Stephanie Dunagen, both of whom listed her diagnosis as myelitis. Id. at 11. That same day, Petitioner also visited a neurologist, Dr. Karl Misulis, who noted that Petitioner had been diagnosed with inflammatory myelitis but that her prior treating physicians had "essentially ruled out infection according to her report. . . ." Id. at 12 (citing Pet'r's Ex. 8 at 5-6). Dr. Misulis ultimately concluded that Petitioner, who was unable to walk, was "permanently and totally disabled" and suffered from "[m]yelopathy/transverse myelitis." Id. at 12-14. To determine the proper course of treatment, Dr. Misulis consulted with Dr. Sriram by telephone.

In the months that followed, Petitioner saw various physicians, including Dr. Mobley, Dr. Sriram, and Dr. Misulis. Dr. Sriram's notes from Petitioner's October 24, 2005 visit state: "DX: Inflammatory myelopathy of unknown etiology . . . . The etiology is not clear whether this could

be? TM,? Devic's disease,, [sic]? postinfectious myelopathy, they all have been entertained but none of them are definitively proven." Id. at 13. In subsequent visits in 2005 and 2006, Dr. Misulis consistently noted that Petitioner had TM. Id. at 14. Petitioner had not significantly improved by December of 2007. Doe 93, 2010 WL 4205677, at *2.

Procedural History

On June 28, 2007, Petitioner filed her petition. In December of 2007, she filed her medical records and an amended petition. On July 30, 2008, Petitioner filed a supplemental affidavit, which stated that Dr. Sriram had told Petitioner that her "recent neurological problems were a result of [her] flu vaccination." Pet'r's Supp. Aff. ¶ 2. "Dr. Sriram explained that there was a compensation fund available to persons injured by vaccines, and that [Petitioner] should find an attorney who dealt with these matters. [Petitioner] asked him if he could provide [her] with the name of a law firm that could assist [her], but he declined . . . because he had previously worked in the Vaccine Program and did not want to be involved." Id. ¶ 3; see also Oral Arg. Tr. 25.[5] Counsel for Petitioner initially planned to subpoena Dr. Sriram for a deposition but ultimately opted not to do so, since subpoenaing him might have disrupted the physician/patient relationship. Oral Arg. Tr. 25. Counsel for Petitioner also spoke to Dr. Sriram and decided that his testimony would not "add anything more than his note." Id. Dr. Sriram ultimately did not testify.

On January 19, 2010, the Special Master conducted an evidentiary hearing at which the parties' experts testified. Dr. Tornatore testified in person and Dr. Bielawski, by telephone. The parties' experts agree that Petitioner suffers from TM and that the temporal relationship between her vaccination and the onset of her TM symptoms supports a finding of causation. However, the experts disagree as to whether the flu vaccine can cause TM and whether Petitioner's flu vaccine actually caused her injury.

Testimony of Petitioner's Expert, Dr. Carlo Tornatore

Dr. Tornatore is a neurologist with extensive expertise and qualifications. A member of the American Neurological Association and the American Academy of Neurology, he has authored 60 to 70 publications, teaches at Georgetown Medical School, conducts clinical trials, and runs the Georgetown Multiple Sclerosis Center, which treats a "fair number" of TM patients. Tr. 8-13, 94. Dr. Tornatore has treated over 100 TM patients but has never treated Petitioner. Id.

Dr. Tornatore opined that "[v]accination as a possible cause of transverse myelitis is recognized." Tr. 41. Furthermore, "the idea that vaccine-related transverse myelitis is a recognized entity is an acceptable theory." Tr. 54. When the Special Master asked pointedly, "Now how about the flu virus? Do neurologists think that the flu virus causes transverse myelitis?," Dr. Tornatore responded, "I think we would all accept that that were the case." Tr. 103. After observing that about five percent of TM cases remain idiopathic, Dr. Tornatore

[5] "Oral Arg. Tr." refers to the transcript of the February 24, 2011 oral argument before this Court.

opined that when idiopathic TM cases occur within four weeks of flu vaccination, they are "probably vaccine-related." Tr. 77-78.

Dr. Tornatore also discussed medical literature indicating that vaccination, including flu vaccination, may cause TM, even where the specific causal mechanism is unknown. Specifically, he referred to Douglas A. Kerr and Harold Ayetey, Immunopathogenesis of Acute Transverse Myelitis, 15(3) Current Opinion in Neurology 339 (2002) ("Immunopathogenesis of ATM"), which discusses postvaccinal acute TM ("ATM") and describes a patient who developed TM two days after receiving the flu vaccine. Tr. 39-42.[6] According to Dr. Tornatore, the authors observe that the "immunopathogenesis of disease-associated ATM is varied" and indicate that molecular mimicry is a possible mechanism by which the vaccine can cause TM. Immunopathogenesis of ATM at 340, 342; see also Tr. 42. As the authors explain:

> Several reports of ATM following vaccination have recently been published. Indeed, it is widely reported in neurology texts that ATM is a postvaccination event. One publication reports a case of post 'flu vaccine myelitis in which a 42-year-old man with a history of bilateral optic neuritis developed ATM 2 days after an influenza vaccination. A separate study reported a 36-year-old individual who developed a progressive and ultimately fatal, inflammatory myelopathy/ polyradiculopathy 9 days after a booster hepatitis B vaccination. . . . However, it should be noted that extensive data continue to show overwhelmingly that vaccinations are safe and are not associated with an increased incidence of neurological complications. Therefore, such case reports must be viewed with caution, as it is entirely possible that two events occurred in close proximity by chance alone.

Immunopathogenesis of ATM at 340-41 (internal citations omitted).[7]

Dr. Tornatore relied on Naoko Nakamura et al., Neurologic Complications Associated with Influenza Vaccination: Two Adult Cases, 42 Internal Med. 191 (2003) ("Neurologic Complications"), to determine that the flu vaccine "may induce an autoimmune process resulting in TM." Tornatore Report at 16-17. This article discusses the case of a 62-year-old man with cirrhosis who began convulsing five days after receipt of a flu vaccination in 2001. Neurologic

[6] At the time of the article's publication, Dr. Kerr served as an assistant professor in the Department of Neurology at the Johns Hopkins University School of Medicine. Immunopathogenesis of ATM at 339 n.a.

[7] According to Dr. Tornatore, a physician publishes a "case report" when a patient presents with an unusual case that should be reported to the medical community to raise awareness and prompt further investigation. Tr. 59-60 (Tornatore); Tr. 122 (Bielawski) (defining a case report as a sampling of one or two individuals). Dr. Tornatore conceded that proving causality on the basis of a case report is "always difficult . . . [but] if there is some biology behind it, then that firms it up . . . [s]o the case report alone doesn't make the causality, but the subsequent science does." Tr. 115.

Complications at 191.[8] He subsequently presented with bladder dysfunction and was eventually diagnosed with acute disseminated encephalomyelitis ("ADEM"). Id. The article also describes the case of a 70-year-old man with rheumatic arthritis and diabetes mellitus who suffered dysuria and paraplegia seven days after receipt of a flu vaccination. Id. at 191-92. The authors state that "both myelitis and GBS-type [Guillian-Barré syndrome] polyneuropathy might occur after vaccination." Id. at 194.

Dr. Tornatore also based his conclusion that Petitioner's TM was postvaccinal on Rohit Bakshi and John C. Mazziotta, Acute Transverse Myelitis after Influenza Vaccination: Magnetic Resonance Imaging Findings, 6 J. Neuroimaging 248 (1996) ("MRI Findings"). There, the authors observe that "ATM has been reported following vaccinations, including hepatitis B, rabies, smallpox, influenza, and rubella." MRI Findings at 248 (internal citations omitted). They further note that "[n]umerous neurological complications . . . have been associated with influenza vaccination" and appear to "develop with a latency that ranges from 1 to 63 days (mean, 16.5 days) after influenza vaccination." Id. (internal citations omitted). The authors state that MRI findings in postvaccinal ATM are not well described. Id. The authors detail the case of a 36-year-old woman experiencing leg weakness, numbness, and urinary retention four weeks after her receipt of the flu vaccine. Id. No antecedent illnesses were identified, the vaccination was otherwise well tolerated, and an extensive lab evaluation for alternative underlying causes was unrevealing. Id. The authors conclude that "[t]his association of ATM following the influenza vaccination does not prove cause and effect. However, because no other known causes of ATM were identified, a postvaccination syndrome was diagnosed by exclusion." Id. at 250.

Dr. Tornatore relied on A.J. Larner and S.F. Farmer, Myelopathy Following Influenza Vaccination in Inflammatory CNS Disorder Treated with Chronic Immunosuppression, 7 Eur. J. of Neurology 731 (2000) ("Myelopathy following Influenza Vaccination"), to support his opinion that "the influenza vaccination administered on October 8, 2004 resulted in the development of an inflammatory myelitis in [Petitioner's] case." Tornatore Report at 19. The authors report that numerous neurological complications, including TM, have been reported following flu vaccination. Myelopathy Following Influenza Vaccination at 731. The authors describe a 42-year-old man who experienced, inter alia, a spinal cord lesion, visual blurring, hand numbness, and difficulty walking after flu vaccination. Id. at 731-32. The authors caution, however, that the rarity of neurological complications following flu vaccination makes it impossible to establish a definitive causal relationship. Id. at 732. They emphasize that the following factors suggest that the patient's neurological deterioration was postvaccinal: (i) the temporal relationship between the two events; (ii) the anatomical concordance of the cord lesion and injection site; and (iii) the absence of prior cord symptoms or signs. Id. at 732-33. The subject patient's differential diagnosis included NMO or Devic's syndrome. Id. at 733.

[8] At the time of the article's publication, Dr. Nakamura was a member of the Department of Neurology at Fujita Health University's School of Medicine. Neurologic Complications at 191.

Dr. Tornatore Opined that Molecular Mimicry is a Biologically Plausible Mechanism by which the Flu Vaccine Can Cause TM

Dr. Tornatore explained the concept of "molecular mimicry" as follows:

> an idea that some protein [the vaccine] in the environment somehow finds its way into your body, and that can be either an infection or a vaccination, and that your body reacts against that protein, which it should. It should try to get rid of any offending proteins that get in, or it might be some other type of chemical. But as it destroys that invading protein as it were, it will then start looking to see if there is any evidence of that protein elsewhere. And the problem is that not infrequently there are other proteins that are normal parts of the body, host proteins as it were, which look very similar, if not identical, to the proteins that are foreign. Well, the immune system cannot tell the two apart. And basically that protein is mimicking at a molecular level what was foreign protein. The immune system starts to attack . . . that protein and you end up with an autoimmune process. And this is an old concept.

Tr. 42.

The Special Master questioned Dr. Tornatore on molecular mimicry as follows:

> Q. Now, on the molecular mimicry theory, what part of the person's body is affected in the flu vaccine-causing transverse myelitis theory?
>
> A. Well, the theory is with molecular mimicry and influenza, if you get vaccinated, the protein goes into the tissue. You have lymphoid cells there, and so they will recognize there is a form of protein. They will then become stimulated, and then as they become stimulated, immune cells circulate. So they immediately enter the bloodstream and start to circulate. Some of them will cross into the brain, and again rarely, because they have been stimulated with this protein, they now find a protein in the spinal cord which looks very similar to what got injected. And now inflammation develops there. So transverse myelitis following a vaccination is inflammation of the spinal cord that resulted from peripheral cells getting into the spinal cord . . . . [T]he protein is probably a protein of myelin we think in the spinal cord . . . the vaccine is causing inflammation of the myelin. The myelin is found on motor nerves, sensory nerves.

Tr. 97-99.

Although Dr. Tornatore admitted that another mechanism may have been responsible for Petitioner's flu vaccination causing her TM, he ultimately concluded that molecular mimicry was the most biologically plausible mechanism. Tr. 67. Dr. Tornature reasoned:

> Dr. Kerr in his review of transverse myelitis discusses that as a mechanism that can cause transverse myelitis, and it's a very reasonable explanation. Even if it's

> not molecular mimicry per se . . . [t]he purpose of the vaccination is to stimulate the immune system . . . What did [Petitioner] end up with? An autoimmune process. So that vaccine triggered an autoimmune process, whether it was by molecular mimicry, which seems like a very probable cause, or whether it was by diffuse stimulation. Ultimately it doesn't matter. They're both biologically plausible mechanisms. Molecular mimicry seems like the most plausible.

Id.

Dr. Tornatore noted that "almost 400 papers . . . have discussed and put forward the idea of molecular mimicry as the pathogenesis for a lot of different autoimmune processes, neurologic and otherwise," and molecular mimicry is "a generally accepted theory for how autoimmunity works." Tr. 43, 46.

The Special Master asked Dr. Tornatore: "Now, if we had in the same room 100 neurologists and we say how many people think that molecular mimicry explains how flu vaccine causes or flu vaccine can cause transverse myelitis through molecular mimicry, how many people would raise their hand?" Tr. 101. Dr. Tornatore quipped, "[i]t depends on who is in the room" and then asserted that if "100 reasonable neurologists" were in the same room, "almost 100 percent" would think that the flu vaccine can cause TM via molecular mimicry. Id.

Dr. Tornatore also referenced Kai Wucherpfennig et al.'s article -- Molecular Mimicry in T Cell-Mediated Autoimmunity: Viral Peptides Activate Human T Cell Clones Specific for Myelin Basic Protein, 80 Cell 695 (1995) ("Viral Peptides") -- which involves flu peptides and explains molecular mimicry; the study on which the article is based, however, did not find that molecular mimicry resulted in demyelination. Tr. 67-68.

Dr. Tornatore also observed that experimental allergic encephalitis ("EAE") is a vaccine that in animals has been shown to cause acute encephalomyelitis via molecular mimicry; however, he noted that EAE is distinguishable from the flu vaccine. Tr. 66. He testified that other animal models demonstrate molecular mimicry but knew of no animal models showing that the flu vaccine causes TM. Tr. 68-69.

Acknowledging that no epidemiological studies demonstrate that the flu vaccine causes TM, Dr. Tornatore opined that epidemiological studies cannot be expected to demonstrate the existence of very rare events, such as the development of postvaccinal TM. To "rule out a very rare event" like postvaccinal TM, a study would have to sample millions of people. Tr. 52-53, 58-59. The purpose of vaccine-related epidemiological studies is to determine whether the risk-benefit ratio warrants administration of the vaccine, "not to determine the absolute causality of the two." Tr. 57. As such, an epidemiological study is the "wrong tool" to determine the causal mechanism of postvaccinal TM. Tr. 58.

Dr. Tornatore's Opinion that Petitioner's Vaccination Caused Her TM

Based on his review of Petitioner's medical records and the relevant medical literature, the temporal association of Petitioner's vaccination and the onset of her TM symptoms, and the fact that some other potential causes of her TM were ultimately ruled out, Dr. Tornatore

concluded that Petitioner's flu vaccination caused her TM. Tr. 47-48, 53-54, 92-93. Dr. Tornatore pointed out that Petitioner's treating physicians repeatedly recorded in her patient history that her symptoms had begun in October of 2004 -- on or around the date of her flu vaccination. In Dr. Tornatore's opinion, Petitioner's symptoms began "well within that time period where one might see an autoimmune process after being exposed to an offending protein." Tr. 47-48.

Although Dr. Tornatore recognized that many physicians described the etiology of Petitioner's TM as unknown or unclear and none definitively concluded that it was postvaccinal, he considered that a treating physician, Dr. Sriram, had noted in a medical record that Petitioner's condition was "probably a questionable postinfectious, postvaccination etiology of an acute ascending myelopathy." Tr. 36. Dr. Tornatore observed that while no blood test or radiologic test could prove or disprove whether Petitioner suffered from postvaccinal TM, testing had ruled out other potential causes of her TM that Dr. Sriram had considered. Tr. 69-73, 83.

Dr. Tornatore also noted that Petitioner's urinary symptoms switched from frequency to retention shortly after vaccination, which relates to the temporal association of the flu vaccine to her symptoms. As Dr. Tornatore explained, "[t]hat temporal relationship is pretty striking and was discussed by at least four different physicians, one of whom, Dr. Sriram, actually made the notation that this change in her bladder happened following the vaccination. So he didn't have to say the vaccine was a point in time to reference, but he did." Tr. 74. Dr. Tornatore testified that the fact that Petitioner suffered a sore, red arm upon vaccination strengthened his opinion that Petitioner's reaction to the vaccine was atypical. Tr. 75-76. Dr. Tornatore opined that, taken together, these two facts bolstered his conclusion that Petitioner's TM is postvaccinal.

In discussing Respondent's suggestion that Petitioner's treating physicians had not eliminated mycoplasma pneumoniae ("MP") as a possible cause of her TM, Dr. Tornatore testified that while MP can cause TM and some people with MP do not manifest symptoms, MP was uncommon that time of year, and most people do experience symptoms. Tr. 232-34. Dr. Tornatore opined that Petitioner's TM was probably not postinfectious because her CSF was negative for infection when Dr. Sriram examined the results of her lumbar puncture in 2005, she suffered no symptoms of antecedent infection, and the lack of neutrophils in her blood cut against a finding of infection. Tr. 34-35, 82.

Testimony of Respondent's Expert, Dr. Martin Bielawski

Respondent's expert, Dr. Martin Bielawski, is a board-certified neurologist and associate clinical professor at Tufts-New England Medical Center. Tr. 120-21. He testified by telephone. Tr. 2. Between five and ten percent of Dr. Bielawski's patients have TM or other neurodemyelinating diseases. Tr. 121. Based on Dr. Bielawski's review of Petitioner's medical records and relevant medical literature, Dr. Bielawski opined that it is possible, but not probable, that the flu vaccine can cause TM, but he does not believe that Petitioner's flu vaccination caused her TM. Tr. 123, 129. Dr. Bielawski continued: "the only aspect tying [Petitioner's] transverse myelitis to the flu vaccine is the fact that she received a flu vaccine around two or three [weeks] before she began experiencing urinary retention." Tr. 123-24.

Dr. Bielawski opined, "[f]rom my review of the literature and my review of this case, I do not believe that flu vaccine causes transverse myelitis. . . . [T]here are no animal models that show the flu vaccine causes transverse myelitis, and there is no epidemiologic study that points to the flu vaccine causing transverse myelitis." Tr. 124. He further asserted, "there isn't any [objective evidence]" that the flu vaccine causes inflammatory myelitis. Tr. 157. He also testified that because the flu virus is not a live viral vaccine, studies indicating that the live virus can cause myelitis do not necessarily mean that the vaccine can cause it. Tr. 159-60.

Dr. Bielawski critiqued the medical literature upon which Dr. Tornatore relied and discussed other medical literature that led him to conclude that it is improbable that the flu vaccine can cause TM. Tr. 129. According to Dr. Bielawski, the medical literature upon which Dr. Tornatore relied often concluded that vaccination resulted in an injury because of the temporal association of the vaccination and the onset of symptoms, or otherwise by exclusion, which does not definitively prove causation. See, e.g., Tr. 145-46. Specifically, Dr. Bielawski cited to Ami Schattner's article Consequence or Coincidence? The Occurrence, Pathogenesis and Significance of Autoimmune Manifestations after Viral Vaccines, 23 Vaccine 3876 (2005) ("Consequence or Coincidence"). Tr. 146-47. Based on a review of Medline records from 1966 to June of 2004 and articles relating to vaccination, Schattner concludes that "[f]or the overwhelming majority of people, vaccines are safe and no evidence linking viral vaccines with . . . multiple sclerosis . . . can be found." Consequence or Coincidence at 3876. The author further observes, "other neurological syndromes involving the CNS [central nervous system] may rarely coexist, or occur independently following influenza vaccination." Id. at 3880. According to Dr. Bielawski, Consequence or Coincidence supports his assertion that the flu vaccine probably cannot cause TM because Schattner found "no serious neurological central nervous system manifestations after viral vaccines." Tr. 147-49.

When asked to estimate the number of cases of postvaccinal TM, Dr. Bielawski testified, "it's got to be extremely small because the epidemiologic articles are all discussing the fact that there are very rare case reports and that the authors all conclude that the vaccine is safe to give to patients." Tr. 221. When discussing how a physician would eliminate the flu vaccine as a potential cause of TM, Dr. Bielawski opined, "it's not something that can be evaluated with any specific tests." Id. Dr. Bielawski admitted that in teaching how to conduct a patient history for TM, he advises medical residents to ask patients about their vaccination history "[b]ecause there have been some reports about vaccines causing transverse myelitis, not necessarily the influenza vaccine but other reports where vaccines have been implicated." Tr. 209-10. Dr. Bielawski further testified that only "a very small number . . . less than 20, maybe less than 10" neurologists in a hypothetical room of 100 reasonable neurologists would agree that the flu vaccine can cause TM. Tr. 207.

Dr. Bielawski's Views on Molecular Mimicry

When asked whether molecular mimicry is a biologically plausible mechanism by which the flu vaccine can cause autoimmune problems, including TM, Dr. Bielawski responded:

> [I]t is a possibility that there are antigens in a flu vaccine that could cause autoimmune problems. But in terms of plausibility, I wouldn't be able to say that a flu vaccine could cause transverse myelitis. There is nothing that indicates in

> the literature that influenza vaccine causes transverse myelitis. So if you ask me is it possible, I wouldn't want to absolutely say no . . . . But is it probable, I would say no.

Tr. 129.

Although Dr. Bielawski conceded that molecular mimicry is one mechanism by which autoimmune-mediated illnesses occur, he saw no objective evidence that molecular mimicry caused Petitioner's TM. Tr. 129-30. When asked whether there was any "proven evidence of molecular mimicry in [Petitioner's] situation," Dr. Bielawski testified, "I think that one can't say that molecular mimicry is the cause of the influenza vaccine producing myelitis because there really haven't been any models to show that." Tr. 174.

Dr. Bielawski testified that if 100 reasonable neurologists were in the same room, "if the question was posed does the flu vaccine cause myelitis via molecular mimicry . . . very few people would raise their hand because we don't know that the flu vaccine causes myelitis. So whether it's molecular mimicry or some other mechanism . . . very few people would raise their hands to that question." Tr. 158.

After testifying that no epidemiological study demonstrates that the flu vaccine can cause TM, Dr. Bielawski primarily focused on three articles, which led him to conclude that the flu vaccine likely does not cause TM. Tr. 124. The first article by Frank DeStefano et al. -- Vaccinations and Risk of Central Nervous System Demyelinating Diseases in Adults, 60 Arch. Neurol. 504 (2003) ("Vaccinations and Risk") -- was based on a study involving 440 patients with multiple sclerosis ("MS") or optic neuritis and 950 patients with no demyelinating disease. According to Dr. Bielawski, the authors concluded from the study that the "influenza vaccine did not cause any form of demyelination." Tr. 124-25. The second article by Christian Confavreux, M.D., et al., Vaccinations and The Risk of Relapse in Multiple Sclerosis, 344 New Eng. J. Med. No. 5 (2001) ("Risk of Relapse"), was a large population case crossover study of MS patients, which found that there was no short-term risk of relapse in MS patients. Tr. 125.

The third article -- A.E. Miller et al., A Multicenter, Randomized, Double-blind, Placebo-controlled Trial of Influenza Immunization in Multiple Sclerosis, 48 Neurology 312 (1997) ("Influenza Immunization in MS") -- involved 104 patients, 49 who received a flu vaccination and 54 who received a placebo. As Dr. Bielawski explained, the Miller study found "no difference in attack rate for disease progression in patients receiving the influenza vaccine versus a placebo." Tr. 125-26. The authors conclude that "[i]nfluenza immunization in MS patients is neither associated with an increased exacerbation rate [of MS symptoms] in the postvaccination period nor a change in disease course over the subsequent 6 months." Influenza Immunization in MS at 312.

In explaining the significance of the MS population not showing postvaccinal relapse, Dr. Bielawski testified:

> [T]he patients with multiple sclerosis are suffering from an autoimmune disease. Their central nervous system has already been affected by an autoimmune-based mechanism. And if an influenza vaccine or any other stimulus to that immune

> system were given, then one might expect that what we considered a primed central nervous system would react and could potentially produce . . . transverse myelitis. But given that the epidemiologic studies don't show this, I think that it's evidence that the influenza vaccine is not a causative agent for transverse myelitis.

Tr. 127-28.

Dr. Bielawski also relied on Thiravat Hemachudha and Sucheep Piyasirisilp's article Neurological Adverse Events Associated with Vaccination, 15(3) Curr. Opin. Neurol. 333 (2002) ("Neurological Adverse Events"). Tr. 149. The authors, who summarized available data regarding postvaccinal neurologic complications, opine that there does not appear to be an increased risk of GBS following flu vaccination but caution that "immunization is not without risk, and adverse events are a further factor to consider." Neurological Adverse Events at 334, 337. Dr. Bielawski interpreted this article as indicating that "there is really no significant adverse central nervous system effect from the flu vaccine." Tr. 149. Dr. Bielawski opined that, taken together, these articles support his assertion that the flu vaccine probably does not cause TM. See, e.g., Tr. 124-28.

Dr. Bielawski agreed that epidemiological studies will not capture "a one in a million event" and '"lack the statistical power to rule out an extremely rare causal relationship, as even a few well-documented case reports may suggest.'" Tr. 149; 176 (quoting Consequence or Coincidence at 3882).

Dr. Bielawski Opined that the Flu Vaccine Did Not Cause Petitioner's TM

Dr. Bielawski agreed that Petitioner suffers from TM. Tr. 162. However, Dr. Bielawski opined, "the flu vaccine did not cause [Petitioner's] transverse myelitis." Tr. 123. He indicated that her vaccination was merely coincidental with the onset of her TM. Tr. 134. Dr. Bielawski elaborated:

> I think that [Petitioner] developed transverse myelitis. She happened to have a vaccine a few weeks before the onset of some of her bladder symptoms. But we don't know what happened two months prior, three months prior in terms of upper respiratory infection symptoms, which she might not have even bothered reporting for example. So I think that just because she had a flu vaccine one cannot say that it's the definite cause of her neurological picture.

Tr. 135. In support of his assertion, Dr. Bielawski pointed out that Petitioner had received the flu vaccine prior to October of 2004, without incident. Tr. 160. However, Dr. Bielawski admitted that because the flu vaccine changes from year to year, the fact that Petitioner had undergone prior vaccinations without incident does not mean that her 2004 vaccination did not cause her TM. Tr. 200.

Dr. Bielawski observed that Petitioner's treating physicians had diagnosed her with TM of unknown etiology and only Dr. Sriram stated that her TM could be postvaccinal. Tr. 144. Dr. Bielawski agreed with Dr. Tornatore that diagnosis by exclusion is an acceptable approach to

determine the actual cause of Petitioner's TM but indicated that Petitioner's treating physicians had not eliminated all other potential causes of her TM. Tr. 132-33, 169. Specifically, Dr. Bielawski noted that MP can cause TM but was not evaluated in Petitioner. Tr. 133-34, 169. Dr. Bielawski conceded that most patients with MP present respiratory systems and that Petitioner did not; however, he countered that Petitioner might have fallen into the minority of individuals who never manifest symptoms. Tr. 169-71. Dr. Bielawski also characterized Petitioner's work-up as incomplete because she was not evaluated for human T-lymphotropic virus -- an infectious disorder and spasticity disease that can cause TM -- but he had not mentioned this in his expert report. Tr. 169, 172.

On the other hand, Dr. Bielawski testified that Petitioner had not been diagnosed with an infection (other than a UTI), a neoplasm, cancer, Devic's disease, or other type of systemic disorder and that Petitioner was antibody-negative for NMO. Tr. 163-65, 168. He agreed with Dr. Tornatore that Petitioner's bacterial, fungal, and viral cultures were negative. Tr. 173.

Dr. Bielawski opined that the temporal relationship between Petitioner's vaccination and the onset of her symptoms was appropriate for proving causation. Tr. 162.

The Special Master's Decision

On October 8, 2010, the Special Master issued a decision denying Petitioner compensation because she failed to show that the flu vaccine can and did cause her TM. In Althen v. Sec'y of HHS, 418 F.3d 1274, 1278 (Fed. Cir. 2005), the Federal Circuit articulated a three-prong test by which a petitioner can establish a prima facie case under the Vaccine Act:

> Concisely stated, [a petitioner's] burden is to show by preponderant evidence that the vaccination brought about her 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. If [a petitioner] satisfies this burden, she is "entitled to recover unless the [[G]overnment] shows, also by a preponderance of evidence, that the injury was in fact caused by factors unrelated to the vaccine."

Althen, 418 F.3d at 1278 (citing Knudsen v. Sec'y of HHS, 35 F.3d 543, 547 (Fed. Cir. 1994) (alteration in original) (citation omitted)).

In the instant case, the Special Master found Prong One to be dispositive. In assessing Althen's Prong One, the Special Master rejected Petitioner's contention that she satisfied Prong One by showing that it is biologically plausible that the flu vaccine can cause TM. Instead, the Special Master accepted Respondent's argument that Petitioner must show reliable scientific evidence demonstrating that a causal relationship likely does in fact exist between the flu vaccine and Petitioner's TM.

The Special Master opined that, "[a] petitioner's presentation of a reliable opinion containing a 'medical theory causally connecting the vaccination and the injury' does not satisfy

the petitioner's burden to present 'preponderant evidence.'" Doe 93, 2010 WL 4205677, at *8. Distinguishing between "reliable" and "preponderant" evidence, the Special Master concluded that he must evaluate both the reliability and persuasiveness of an expert's opinion. Id. at *8-9 (citing Terran v. Sec'y of HHS, 195 F.3d 1302, 1316 (Fed. Cir. 1999)).

Using this analytical construct, the Special Master compared the conflicting expert testimony and the information upon which the experts relied in forming their opinions to determine whether Petitioner had satisfied her burden of proof regarding whether the flu vaccine can cause TM. See, e.g., id. at *11-16. Because the Special Master determined that the experts disagreed on whether the flu vaccine can cause TM, he reviewed "the information on which the experts base[d] their opinions" to "resolve which opinion [was] more persuasive." Id. at *11. The Special Master concluded that the medical literature on which Dr. Tornatore relied did

> not present a persuasive case that flu vaccine can cause transverse myelitis. Dr. Kerr and Dr. Nakamura recognize that a causal connection between flu vaccination and transverse myelitis is possible. But, these authors refrain from concluding that causation has been established.

Id. at *12.

The Special Master found Myelopathy Following Influenza Vaccination to be a "more assertive statement of causation," presumably because that article stated that "[a] number of neurological complications have on occasion been reported following influenza vaccination in healthy individuals, including transverse myelitis." Id. at *13 (discussing Myelopathy Following Influenza Vaccination at 731-33). However, the Special Master concluded that the article provided "weak support" for the conclusion that flu vaccine can cause TM because case reports have little reliability in establishing causation. Id. The Special Master also acknowledged that the Pender textbook states that "[a] wide variety of vaccines have been reported to trigger . . . acute transverse myelitis, including influenza" but discounted the persuasiveness of this evidence because the statement appeared to have been based on case reports. Id. at *14.

The Special Master described Dr. Tornatore's testimony that the Wucherpfennig study supports his assertion that molecular mimicry is a mechanism by which the flu vaccine can cause TM as "reasonable" but appears to have discounted the article's relevance because it dealt with the wild flu virus, not the flu vaccine. Id. The Special Master observed that Petitioner "has not presented any evidence that the flu vaccine has been tested under conditions like the Wucherpfennig study," and "there is no evidence that the portions of the influenza virus that mimicked MBP [myelin protein] are the same portions of the virus used in the influenza vaccine." Id. at *14-15. According to the Special Master, Dr. Tornatore's failure to perform a test to determine whether "the molecular structure of the flu vaccine resembles the molecular structure of parts of myelin" is "another factor against finding" Dr. Tornatore's opinion that the flu vaccine can cause TM to be persuasive. Id. at *15.

The Special Master found that Respondent's expert, Dr. Bielawski, testified that the wild flu virus can cause TM and that the Institute of Medicine ("IOM") has recognized that if the wild virus can cause an injury, the viral vaccine can cause the same injury. Id. at *20. However, the

Special Master found that the IOM's reasoning was based on a presupposition that the patient received a "live viral vaccine" and the flu vaccine is not a live viral vaccine. Id. As such, the Special Master found Petitioner's "extension of the IOM article unpersuasive." Id.

The Special Master observed that the lack of epidemiological studies that investigated whether the flu vaccine causes demyelinating diseases was not fatal to Petitioner's case on Prong One, but Respondent's introduction of studies that "failed to detect any increased incidence of a demyelinating disease after the flu vaccine" weighed against a finding that the flu vaccine can cause TM. Id. at *22-23.

The Special Master concluded that Petitioner had not presented a persuasive medical theory causally connecting the flu vaccine to TM. Because the Special Master apparently found Petitioner's failure to satisfy Prong One dispositive, he only briefly addressed Prongs Two and Three. Id. at *6, 24-25.[9]

In concluding that Petitioner failed to establish that her vaccination did cause her TM, the Special Master reasoned as follows. First, Petitioner's affidavit, in which Petitioner stated that Dr. Sriram told her that her vaccination may have or probably caused her TM and informed her of the existence of the Vaccine Program, lacked credibility because it was created for the purpose of litigation two-and-a-half years after Dr. Sriram treated her. Id. at *24. Second, because Dr. Sriram's medical reports were created contemporaneously and for the purpose of medical treatment, they constitute stronger evidence of his views regarding the cause of Petitioner's TM and indicate that her TM was of unknown etiology. Id. Third, no physician definitively diagnosed Petitioner with postvaccinal TM. Id. Fourth, the Moberly Court refused to find the existence of actual causation based solely upon the fact that a petitioner develops symptoms of the injury within a medically appropriate time period after vaccination, and no other cause for the injury has been identified. Id. at *24-25 (citing Moberly v. Sec'y of HHS, 592 F.3d 1315, 1322 (Fed. Cir. 2010)).

Discussion

Jurisdiction and Standard of Review

Jurisdiction lies in this Court pursuant to 42 U.S.C. § 300aa-12(e). In reviewing a decision rendered by a special master, this Court may: (1) uphold the findings of fact and conclusions of law; (2) set aside any of the findings of fact or conclusions of law "found to be arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law;" or (3) "remand the petition to the special master for further action in accordance with the court's direction." 42 U.S.C. § 300aa-12(e)(2)(A)-(C); Althen, 418 F.3d at 1277-78; Saunders v. Sec'y of HHS, 25 F.3d 1031, 1033 (Fed. Cir. 1994). Findings of fact are reviewed under the "arbitrary and capricious" standard, legal questions are reviewed under the "not in accordance with law" standard, and discretionary rulings are reviewed under the "abuse of discretion" standard.

[9] Only one-and-a-half pages of the opinion were devoted to Prong Two.

Saunders, 25 F.3d at 1033 (quoting Munn v. Sec'y of HHS, 970 F.2d 863, 870 n.10 (Fed. Cir. 1992)).

As the Federal Circuit has recognized, "it is not . . . the role of [a] court [reviewing a special master's decision] to reweigh the factual evidence, or to assess whether the special master correctly evaluated the evidence." Lampe v. Sec'y of HHS, 219 F.3d 1357, 1360 (Fed. Cir. 2000) (citing Munn, 970 F.2d at 871). Nor should this Court "examine the probative value of the evidence or the credibility of the witnesses. These are all matters within the purview of the fact finder." Id.

Elements and Burden of Proof

Under the Vaccine Act, a petitioner may establish causation in two ways. See 42 U.S.C. § 300aa-13(a)(1); Walther v. Sec'y of HHS, 485 F.3d 1146, 1149 (Fed. Cir. 2007); Capizzano v. Sec'y of HHS, 440 F.3d 1317, 1319-20 (Fed. Cir. 2006); Althen, 418 F.3d at 1277-78. Causation is presumed if a petitioner demonstrates, via medical records or expert testimony, that the injury is listed in and meets the requirements of the Vaccine Injury Table, 42 U.S.C. § 300aa-14(a), and shows by a preponderance of the evidence that the injury occurred within the timeframe that the Table provides. Capizzano, 440 F.3d at 1319-20; Munn, 970 F.2d at 865. In a case where the alleged injury is not listed in the Vaccine Injury Table, however, a petitioner must establish causation-in-fact. Walther, 485 F.3d at 1149; Pafford v. Sec'y of HHS, 451 F.3d 1352, 1355 (Fed. Cir. 2006); Shyface v. Sec'y of HHS, 165 F.3d 1344, 1350-51 (Fed. Cir. 1999).

Specifically the Vaccine Act provides:

> Compensation shall be awarded under the Program to a petitioner if the special master or court finds on the record as a whole --
>
> (A) that the petitioner has demonstrated by a preponderance of the evidence the matters required in the petition by section [300aa-11(c)(1)],[10] and
>
> (B) that there is not a preponderance of the evidence that the illness, disability, injury, condition, or death described in the petition is due to factors unrelated to the administration of the vaccine described in the petition.
>
> The special master or court may not make such a finding based on the claims of a petitioner alone, unsubstantiated by medical records or by medical opinion.

42 U.S.C. § 300aa-13(a)(1).

[10] 42 U.S.C.A. § 300aa-11(c)(1) delineates the requirements for the contents of the petition and essentially states that a petition shall contain supporting documentation that the petitioner sustained an injury caused by the vaccine.

"To prove causation, a petitioner in a [non-table] Vaccine Act case must show that the vaccine was 'not only a but-for cause of the injury but also a substantial factor in bringing about the injury.'" Cedillo v. Sec'y of HHS, 617 F.3d 1328, 1338 (Fed. Cir. 2010) (citing Shyface, 165 F.3d at 1352). However, a petitioner is not required to show that the vaccine was the sole or predominant cause of the injury; nor must a petitioner produce particular types of evidence or prove causation as a matter of scientific or medical certainty. Althen, 418 F.3d at 1279; Shyface, 165 F.3d at 1353; Bunting v. Sec'y of HHS, 931 F.2d 867, 873 (Fed. Cir. 1991).

As the Federal Circuit recognized in Knudsen:

> The determination of causation in fact under the Vaccine Act involves ascertaining whether a sequence of cause and effect is "logical" and legally probable, not medically or scientifically certain. Thus, for example, causation can be found in vaccine cases based on epidemiological evidence and the clinical picture regarding the particular child without detailed medical and scientific exposition on the biological mechanisms.
>
> Furthermore, to require identification and proof of specific biological mechanisms would be inconsistent with the purpose and nature of the vaccine compensation program.

35 F.3d at 548-49 (internal citations omitted).

The Special Master Committed Legal Error by Elevating Petitioner's Burden of Proof for Establishing that the Flu Vaccine Can Cause TM

On appeal, Petitioner alleges that the Special Master "inappropriately elevated the standard of proof for a petitioner to prove a prima facie case in the Vaccine Program . . . by requiring scientific proof of the precise mechanism by which [Petitioner's] flu vaccine caused her TM." Pet'r's Mot. for Review at 14. Whether the Special Master misapplied the burden of proof is a legal issue to be reviewed under the "not-in-accordance-with-law" standard of review. See Althen, 418 F.3d at 1277. The law the Court looks to in examining Petitioner's burden of proof is the Vaccine Act as well as the Federal Circuit's seminal decision in Althen and its progeny. The Vaccine Act requires that compensation shall be awarded, if based on the record as a whole, "the petitioner has demonstrated by a preponderance of the evidence the matters required in the petition" -- essentially that the petitioner received a vaccine that caused the claimed injury -- and there is not preponderant evidence indicating that factors unrelated to administration of the vaccine caused the injury. 42 U.S.C. § 300aa-13(a)(1).

Consistent with this statutory mandate, the elements for proving causation of a non-table injury were delineated by the Federal Circuit in Althen as follows:

> [A petitioner's] burden is to show by preponderant evidence that the vaccination brought about her 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.

418 F.3d at 1278.

Here, Petitioner contended that she satisfied Prong One by showing that it is biologically plausible that the flu vaccine can cause TM. In the Special Master's view, however, Petitioner had to demonstrate "on a more likely than not standard, that flu vaccine can cause transverse myelitis" and provide a medical theory that is "both reliable and persuasive." Doe 93, 2010 WL 4205677, at *9, 24.

This articulation of the burden of proof led the Special Master down a path of examining every piece of evidence relied upon by the competing experts to determine whether Petitioner had provided a persuasive medical theory that the flu vaccine likely can cause TM. Imposing this burden on Petitioner was legal error. Althen's Prong One merely requires a petitioner to "provide" a medical "theory" linking the vaccine to the injury. In addressing the requisite showing necessary for "providing" a medical theory linking a vaccine to an injury, courts have interpreted Althen's Prong One to require a biologically plausible medical theory. See, e.g., Andreu, 569 F.3d at 1375 (stating that the petitioner proved causation in part because Dr. Tornatore presented a "biologically plausible" theory establishing that the vaccine can cause the injury); Walther, 485 F.3d at 1148 (stating that "[t]he government conceded that the Td vaccine was a biologically plausible cause of Walther's ADEM"); Pafford, 451 F.3d at 1356 (discussing a special master's finding that it was "biologically plausible" for the vaccinations at issue to cause the injury); Campbell v. Sec'y of HHS, No. 07-465V, at 11 (Mar. 22, 2011).

Whether a medical theory is "biologically plausible" is a far different inquiry than whether a medical theory is legally persuasive based on a preponderance of the evidence. Althen's requirement that a theory linking the vaccine to the injury be biologically plausible does not mean that a petitioner must prove, as the Special Master determined, that it is more likely than not that a vaccine actually can cause the claimed injury. Imposing this heightened evidentiary burden takes a petitioner's burden of providing a medical theory beyond the realm of biological plausibility into the realm of legal probability.

In Doe/11 v. Sec'y of HHS, this Court vacated a special master's decision for similarly overstating a petitioner's burden of proof under Althen's Prong One. 2008 U.S. Claims LEXIS 71, at *29-30 (Fed. Cl. Spec. Mstr. Jan. 31, 2008). The special master in Doe/11 had articulated the burden of proof on Althen's Prong One as follows:

> To prove causation, petitioners must offer a medical theory causally connecting Child Doe/11's receipt of her hepatitis B vaccination and her death. The causal connection must be more likely than not.

Id. (emphasis added) (citing 42 U.S.C. §§ 300aa-11(c)(1)(C)(ii)(I) and (II); Althen, 418 F.3d at 1278; Shyface, 165 F.3d at 1352-53).

This Court disagreed with the special master's articulation of the standard in Doe/11, stating:

> The sections of the Vaccine Act cited by the Special Master in this passage do not support the conclusion that the medical theory must be "more likely than not." Rather, they simply delineate the requirements for the contents of the petition stating that a petition shall contain supporting documentation that the injured party sustained or significantly aggravated an injury caused by the vaccine. . . . So too, the cited passage in Shyface does not require that a medical theory be "more likely than not," but simply that a medical theory be shown.

2008 U.S. Claims LEXIS 395, at *54 n.23 (Fed. Cl. July 31, 2008) (citations omitted). As this Court explained in Doe/11:

> Nothing in the case law requires that the medical theory be "more likely than not."
>
> ***
>
> Indeed, a "theory" intrinsically has yet to be proven and puts forth a hypothesis. A "theory" is defined to be "a hypothetical . . . structure explaining or relating an observed set of facts", "a judgment, conception, proposition or formula . . . formed by speculation or deduction or by abstraction or generalization from facts", or "a working hypothesis given probability by experimental evidence or by factual or conceptual analysis but not conclusively established or accepted as a law." Webster's Third New International Dictionary 2371 (3d ed. 2002).
>
> ***
>
> As such, the Special Master erred in requiring petitioners to demonstrate that . . . their medical theory had to be "more likely than not." Such a requirement finds no support in the Vaccine Act and conflicts with Althen's statement that a "possible link" between a vaccination and injury may still permit a finding of causation even though that "link" involved a "sequence hitherto unproven in medicine." Althen, 418 F.3d at 1280.

Id. at *55-56.

This Court recognizes that subsequent to its decision in Doe/11, the Federal Circuit in Broekelschen v. Sec'y of HHS framed the issue on Althen's Prong One as whether the petitioner "provided proof by a preponderance of the evidence of a medical theory causally connecting the flu [vaccine] to [the injury]." 618 F.3d 1339, 1350 (Fed. Cir. 2010) (emphasis added).

In Broekelschen, there was a dearth of evidence suggesting any link between the flu vaccine and the claimed injury, anterior spinal artery syndrome. Because the petitioner there claimed that he suffered from postvaccinal TM, his expert predominantly proffered evidence

linking the flu vaccine to TM. As the Federal Circuit noted, there "was little said by either party during the hearing and post-trial briefs regarding whether the flu vaccine can cause anterior spinal artery syndrome." Id. at 1350-51. Rather, the focus of the dispute in Broekelschen was whether the petitioner had TM or anterior spinal artery syndrome. Because the "majority of petitioner's evidence was directed at proving the flu vaccine caused transverse myelitis," an injury the petitioner did not have, the Federal Circuit affirmed the finding that due to the "weak medical evidence," the petitioner had not proven by a preponderance of the evidence a medical theory linking the flu vaccine to anterior spinal artery syndrome. Id. at 1351. In Broekelschen, the unquestionable lack of preponderant evidence linking the vaccine to the injury made it unnecessary for the Federal Circuit to elaborate on what constitutes "preponderant evidence" of a "medical theory."[11]

Broekelschen's requirement for preponderant evidence of a medical theory that a vaccine can cause the claimed injury does not nullify or lessen the longstanding interpretation of Althen's "can cause" standard as articulated in Andreu, Walther, and Pafford. In those decisions, the Federal Circuit consistently reiterated that the required showing for a medical theory linking the vaccine to the injury is one of biological plausibility. See, e.g., Andreu, 569 F.3d at 1375; Walther, 485 F.3d at 1147-48; Pafford, 451 F.3d at 1356.

Here, the Special Master imposed a far more exacting burden on Petitioner under Prong One. Recognizing that two qualified experts disagreed on whether the flu vaccine can cause TM, the Special Master looked to the supporting literature to determine which expert's opinion was more persuasive. In this undertaking, the Special Master required conclusive proof in the medical literature linking the flu vaccine to TM. This contravenes Althen's guidance that a "medical theory" under Prong One can be demonstrated by expert testimony alone; neither "confirmation of medical plausibility from the medical community or literature" nor proof of "an injury recognized by the medical plausibility evidence and literature" is required. 418 F.3d at 1279.

Further, in analyzing the literature, the Special Master discounted the probative value of case reports and a statement from the Pender textbook, noting that various vaccines, including the flu vaccine, have been reported to trigger ATM. Specifically, the Special Master remarked that "legal precedents recognize that case reports have little reliability in establishing causation" but failed to cite a single vaccine case. Doe 93, 2010 WL 4205677, at *13. The Court of Federal Claims has recognized that case reports are not "deprived of evidentiary value in support" of a petitioner's medical theory. Campbell v. Sec'y of HHS, 90 Fed. Cl. 369, 385 (2009); see also Campbell, No. 07-465V, at 23-24 (rejecting the special master's dismissal of the petitioner's case reports because they did not prove a biological chain of causation and explaining that they provided limited support for the petitioner's case) (citing Rotoli v. Sec'y of HHS, 89 Fed. Cl. 71,

[11] Although Broekelschen framed the issue as whether there was preponderant evidence to demonstrate Prong One individually, Pafford characterized the Vaccine Act's requirement for preponderant evidence as applying to the petitioner's "cumulative" burden on causation, not to her burden on each individual Althen prong. 451 F.3d at 1355 (stating that the three Althen prongs must "cumulatively show" that the vaccine caused the injury); see also Doe/11, 2008 U.S. Claims LEXIS 395, at *55-56.

86-87 (2009) (finding that petitioner had satisfied Althen's Prong One even though "only a handful" of case reports supported the petitioner's theory of causation)). Similarly, researchers report that "the assessment of possible rare and unforeseen adverse events after vaccination is methodologically particularly difficult, and mandates making use of all available evidence -- from case reports through randomized and clinically controlled trials . . . . " Consequence or Coincidence at 3882 (internal citations omitted).

The Special Master correctly observed that Petitioner's failure to introduce epidemiological studies that definitively demonstrate a causal link between the flu vaccine and TM was "not fatal" to her claim. Doe 93, 2010 WL 4205677, at *22. The Special Master's analysis, however, did not end there. The Special Master went on to conclude:

> To the extent the epidemiological studies have any evidentiary significance, they are in line with the general conclusion that Ms. Doe has failed to present preponderant evidence that the flu vaccine can cause transverse myelitis. These studies have not detected an increased incidence of transverse myelitis among people who received the influenza vaccine. These studies suggest, but do not prove, that the occurrence of transverse myelitis after receiving the influenza vaccine was a coincidence. This suggestion, in turn, is further supported by the relative rarity of case reports noting that flu vaccine preceded the onset of transverse myelitis. If flu vaccine were causing transverse myelitis in very rare cases, then there probably would be more reports associating flu vaccine and transverse myelitis in the literature. This expectation was not met because the record contains fewer than ten such cases. So, on the whole, the epidemiology does not favor finding causation in this case.

Id. at *23 (emphasis added).

In relying on studies that did not detect an increased incidence of TM among people who received the flu vaccine to militate against finding causation, the Special Master again went beyond the requirement to prove "biological plausibility" and required an actual link between the vaccine and injury.[12] The Special Master continued in this endeavor in critiquing literature on which Dr. Tornatore relied, stating:

> Collectively these articles and textbooks do not present a persuasive case that [the] flu vaccine can cause transverse myelitis. Dr. Kerr and Dr. Nakamura recognize that a causal connection between flu vaccination and transverse myelitis is possible. But, these authors refrain from concluding that causation has been established.

[12] The Special Master's conclusion that there "probably" would be more reports associating flu vaccine and TM in the literature if the flu vaccine were causing TM in very rare cases is untenable and contrary to the evidence that epidemiological studies do not capture rare events such as postvaccinal TM. Here, Petitioner's literature recounted several different case reports linking the flu vaccine to TM.

Id. at *12 (emphasis added).[13]

So too, the Special Master characterized the Larner article on which Dr. Tornatore relied as providing "relatively weak support for the proposition that the flu vaccine causes transverse myelitis." Id. at *13 (emphasis added). As the Federal Circuit recognized in Andreu, it is error to require conclusive evidence in the medical literature linking the vaccine to the injury. The Andreu Court explained that requiring epidemiological studies or general acceptance in the scientific or medical communities impermissibly elevates a petitioner's burden and hinders the purpose of the Vaccine Program, in which close calls regarding causation should be resolved in claimants' favor. 569 F.3d at 1376, 1378; see also Althen, 418 F.3d at 1280 (citing Knudsen, 35 F.3d at 549).

Here, the Special Master discounted the persuasiveness of Dr. Tornatore's opinion that the flu vaccine can cause TM, not because it was based on scientifically unreliable methodology or because Dr. Tornatore was unqualified, but instead, because the evidence upon which Dr. Tornatore relied in reaching his conclusion (compared with the evidence on which Dr. Bielawski relied) did not persuasively prove the existence of a direct causal link between the flu vaccine and TM. As such, the Special Master exceeded the proper role of a gatekeeper to exclude scientifically unreliable evidence and instead, rejected as unpersuasive, case reports, textbooks, and articles based on seemingly sound methodology as well as expert testimony from a well-qualified witness whom the Federal Circuit described as having "excellent medical credentials." Andreu, 569 F.3d at 1377 n.4; see generally Daubert v. Merrell Dow Pharmaceuticals, Inc., 509 U.S. 579, 592-95 (1993).

In analyzing Althen's Prong One, the Special Master further concluded that "the technique of differential diagnosis does not constitute persuasive evidence that the flu vaccine can cause transverse myelitis." Doe 93, 2010 WL 4205677, at *19. He reasoned that "the approach of differential diagnosis requires some showing that a putative agent can cause the suspected condition," but the "[e]vidence in this case has not established this predicate." Id. Further, in analyzing differential diagnosis under Althen's Prong One, the Special Master noted that MP is a potential cause of TM, and a finding that Petitioner was not evaluated for MP would be "detrimental" to her case. Id. at *18. There are two problems with this observation. First, this comment implied that because MP can cause TM and because none of Petitioner's treating physicians evaluated her for this infection, Petitioner's case would suffer because she did not truly eliminate all other potential causes of her TM. Such reasoning would require a petitioner to

[13] In finding Dr. Tornatore's citation to the Kerr and Nakamura articles unpersuasive, the Special Master cited nonvaccine cases where courts excluded expert opinions supporting causation because the experts relied on studies or articles that did not go so far as to say a given agent actually caused a particular injury. Doe 93, 2010 WL 4205677, at *13 ("Extending the findings of a written article beyond what the authors stated is not always persuasive.") (citing General Electric Co. v. Joiner, 522 U.S. 136 (1997); Huss v. Gayden, 571 F.3d 442, 459 (5th Cir. 2009); Moore v. Ashland Chemical, Inc., 151 F.3d 269, 278 (5th Cir. 1998) (en banc); Amorgianos v. Nat'l RR Passenger Corp., 137 F. Supp. 2d 147, 187 (E.D.N.Y. 2000)). These non-vaccine decisions have no place in the analysis of Althen's Prong One. The Special Master improperly relied on these cases to accord Dr. Tornatore's opinion less weight.

be evaluated for every potential condition that could have caused her injury or risk a finding that a failure to have done so would be detrimental to her case.

Second, there is no evidence in the record that Petitioner suffered from MP, an infection. No medical records indicate that Petitioner exhibited any symptoms of MP. Petitioner saw over 20 physicians throughout the course of her medical treatment, and not one appears to have determined that Petitioner should be evaluated for MP. Dr. Misulis noted in 2005 that Petitioner's prior treating physicians "had essentially ruled out infection according to her report." Pet'r's Ex. 8 at 5-6. The experts agreed that Petitioner never manifested symptoms typical of MP even though the vast majority of people do. Dr. Tornatore testified that MP was uncommon for that time of year. Dr. Tornatore also opined that Petitioner's TM was probably not postinfectious because her CSF was negative for infection when Dr. Sriram examined the results of her lumbar puncture in 2005, she suffered no symptoms of antecedent infection, and the lack of neutrophils in her blood cut against a finding of infection. Tr. 34-35, 82. Dr. Bielawski testified that Petitioner had not been diagnosed with an infection (other than a UTI), a neoplasm, cancer, Devic's disease, or any other type of systemic disorder and that Petitioner was antibody-negative for NMO. Tr. 163-65, 168. He agreed with Dr. Tornatore that Petitioner's bacterial, fungal, and viral cultures were negative. Tr. 173.

In the absence of record evidence that Petitioner suffered from MP, it would be error for the Special Master to speculate about Ms. Doe's "possible mycoplasma pneumoniae infection" and use that to undercut "the persuasiveness of Dr. Tornatore's use of differential diagnosis." Doe 93, 2010 WL 4205677, at *18.[14] This type of analysis is not supported in the Vaccine Act jurisprudence and should not be used on remand.

The Special Master's Analysis of Althen's Prong Two Was Insufficient

Although the Special Master determined that Petitioner's failure to satisfy Althen's Prong One was "dispositive," he briefly analyzed whether Petitioner satisfied Althen's Prong Two and concluded that Petitioner failed to establish a "logical sequence of cause and effect" linking her flu vaccine to her TM. See, e.g., Doe 93, 2010 WL 4205677, at *6, 24-25.

In addressing Althen's Prong Two, the Special Master did not sufficiently analyze Petitioner's evidence, including her medical records and the expert testimony regarding actual causation. Id. Rather, the Special Master concluded that Petitioner failed to satisfy Althen's Prong Two primarily because her affidavit was less credible than Dr. Sriram's medical reports indicating that Petitioner's TM was of unknown etiology, and that no treating physician definitively diagnosed Petitioner with postvaccinal TM. Id. Petitioner stated in her affidavit:

[14] The Special Master determined that it was not necessary to resolve "how the meager amount of evidence preponderates because the evidence about Ms. Doe's possible mycoplasma pneumoniae infection affects only the persuasiveness of Dr. Tornatore's use of differential diagnosis," and differential diagnosis does not constitute persuasive evidence that the flu vaccine can cause TM. Doe 93, 2010 WL 4205677, at *18.

1. After I started having neurological problems as a result of my flu vaccination in October of 2004, I was referred to Dr. Subramaniam Sriram, a neurologist working in the Multiple Sclerosis Clinic at Vanderbilt University Medical Center.

2. I first saw Dr. Sriram in April of 2005. He told me he thought my recent neurological problems were a result of my flu vaccination. Dr. Sriram noted that I was healthy before my I received my vaccine.

3. Dr. Sriram explained that there was a compensation fund available to persons injured by vaccines, and that I should find an attorney who dealt with these matters. I asked him if he could provide me with the name of a law firm that could assist me, but he declined. Dr. Sriram explained he had previously worked in the Vaccine Program, and did not want to be involved.

Pet'r's Supp. Aff. ¶¶ 1-3.[15]

The Special Master discounted Petitioner's testimony from her affidavit, reasoning:

Ms. Doe cites to her affidavit in which she avers that her treating neurologist, Dr. Sriram, told her to file a claim in the Vaccine Program. Pet'r Br. at 18, citing exhibit 20 at 1. Ms. Doe's second-hand assertion is not strong evidence about Dr. Sriram's views.

Dr. Sriram's opinions are expressed in the reports that he created while he was treating Ms. Doe. Dr. Sriram stated that Ms. Doe's transverse myelitis was of "unknown etiology." Exhibit 9 at 55. As a medical record created to promote Ms. Doe's treatment, this statement by Dr. Sriram is presumed to set forth Dr. Sriram's view accurately. Cucuras v. Sec'y of Health & Human Servs., 993 F.2d 1515, 1528 (Fed. Cir. 1993). Ms. Doe's affidavit, which was created two and a half years after Dr. Sriram treated her, does not rebut the presumed accuracy of Dr. Sriram's report. Ms. Doe may have misheard, misunderstood, or innocently erred in remembering her conversation with Dr. Sriram. Between the two pieces of evidence that are relevant to Dr. Sriram's views, Dr. Sriram's statement and Ms. Doe's affidavit, the stronger evidence about Dr. Sriram's views is his own statement. Therefore, Dr. Sriram's statement that Ms. Doe's transverse myelitis was of "unknown etiology" will be credited.

Doe 93, 2010 WL 4205677, at *24 (emphasis added).

The Special Master did not sufficiently address a third "piece of evidence . . . relevant to Dr. Sriram's views" -- Dr. Sriram's medical record recounting Petitioner's initial visit in which he listed vaccination as a possible cause of her TM. Pet'r's Ex. 9 at 106-08. As the Special

[15] The Special Master recognized that Dr. Sriram has testified for Respondent in vaccine cases. Doe 93, 2010 WL 4205677, at *24 n.13.

Master recited in the factual background, Dr. Sriram recorded in Petitioner's history: "At present my feelings are this is probably a questionable postinfectious, postvaccination etiology of an acute ascending myelopathy." Doe 93, 2010 WL 4205677, at *2, 17. This entry was in a detailed medical record dated April 6, 2005, which also took the form of a letter to another physician, Dr. Paul Moots, with a copy to Dr. Michael Edgeworth, of the Department of Neurology at Vanderbilt University Medical Center. Pet'r's Ex. 9 at 106-08. Although Dr. Sriram (in later medical notes) did not repeat his notation about a possible postvaccinal etiology and referred to Petitioner's TM as being of "unknown etiology," this does not mean -- as the Special Master seems to have inferred -- that Dr. Sriram disavowed his initial note that Petitioner's TM was "probably questionable . . . postvaccination etiology." Doe 93, 2010 WL 4205677, at *2, 17 (citing Pet'r's Ex. 9 at 108).

The Special Master implied that Dr. Sriram may have changed his original perception of postvaccination etiology "[a]fter additional testing," but further testing could not have illuminated whether Petitioner's TM was caused by her vaccine, because, as both experts acknowledged, in their experience there is no test that can determine whether the flu vaccine causes TM. Tr. 70-71, 121.[16] Further testing only ruled out other possible conditions that Dr. Sriram had suspected, such as a paraneoplastic process and Devic's disease.

To the extent that the Special Master concluded that Dr. Sriram's diagnosis was definitively that Petitioner's TM was of unknown etiology, he did so without sufficiently explaining the import of the April 6, 2005 medical record and letter, reflecting the possible postvaccinal etiology. As the Court in Campbell recently recognized:

> Any expectation that treating physicians will record the precise biological theories behind their belief that a patient's condition was caused by a particular trigger is discordant with the reality of medical treatment. Doctors are and must be concerned with treating patients, not with articulating the precise biological theories upon which they base their diagnoses.

Campbell, No. 07-465V, at 22. Dr. Tornatore similarly explained that the treatment of TM would be the same regardless of its cause. Tr. 72.

As is recounted in detail above, the Special Master imposed an overly onerous burden of proof on Petitioner under Althen's Prong One. Because the evidence on Prongs One and Two overlap, the Special Master's errors in analyzing Prong One appear to have tainted his analysis of

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[16] The Special Master's reference to "additional testing" is as follows:

> Dr. Sriram's diagnosis on April 6, 2005 included "questionable postinfectious, post vaccination etiology of acute ascending myelopathy." Exhibit 9 at 108. After additional testing, Dr. Sriram stated that Ms. Doe had an "inflammatory myelopathy" of "unknown etiology." Exhibit 9 at 55 (report dated Oct. 24, 2005). Thus, Ms. Doe's argument stretches beyond what the facts support.

Doe 93, 2010 WL 4205677, at *17 (emphasis added) (footnote omitted).

Prong Two. Cf. Rotoli, 89 Fed. Cl. at 82. This circumstance combined with the Special Master's insufficient analysis of Prong Two warrants a redetermination of this prong on remand.

Conclusion

1. The decision of the Special Master is **VACATED** and **REMANDED** for a redetermination of causation. On remand, the Special Master shall reassess whether Petitioner met Althen's Prongs One and Two and whether she is entitled to compensation, consistent with the legal principles articulated in this opinion.[17] In remanding this matter, the Court does not dictate any particular determination on causation.

2. Petitioner's Motion to Supplement the Underlying Record is **DENIED**. [18]

3. Pursuant to the Vaccine Act, the remand proceedings shall be completed within 90 days of the date of this decision. 42 U.S.C. § 300aa-12(e)(2); Vaccine Rule 28.

The Clerk shall not disclose this decision publicly for 14 days.

s/Mary Ellen Coster Williams
MARY ELLEN COSTER WILLIAMS
Judge

[17] On remand, the Special Master shall consider the pertinent and well-reasoned recent decision in Campbell v. Sec'y of HHS, No. 07-465V (Mar. 22, 2011).

[18] On March 7, 2011, Petitioner moved this Court to supplement the record developed before the Special Master by taking judicial notice of the fact "that the trivalent influenza vaccination contains, inter alia, strains of the influenza A virus," referenced in Petitioner's proposed Exhibit 28 -- a short excerpt from a 2004 IOM article entitled "Immunization Safety Review: Influenza Vaccines and Neurological Complications." Pet'r's Mot. to Supp. at 1-2. Although this Court does not deem it appropriate to amplify the Special Master's record on appeal, it notes that on remand the Special Master may amplify the record and clarify or reconsider any pertinent conclusions based upon this evidence.