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

No. 06-148V
Filed: July 28, 2011

SANDRA MYER, as next friend of JUSTIN MYER, Petitioner,	)	TO BE PUBLISHED
v.	)	Entitlement; causation-in-fact; Hepatitis B vaccination; Autoimmune encephalitis; Differential diagnosis; Treating physician opinion
SECRETARY OF HEALTH AND HUMAN SERVICES, Respondent.	)	

Brian R. Arnold, Brian R. Arnold & Associates, Dallas, TX, for Petitioner.
Glenn A. MacLeod, U.S. Dep't of Justice, Washington, D.C., for Respondent.

Lord, Special Master.

RULING ON ENTITLEMENT[1]

I. INTRODUCTION AND SUMMARY

The facts underlying this case are not in dispute. Petitioner Sandra Myer filed a petition under the National Childhood Vaccine Injury Act ("Vaccine Act" or "Act"), alleging her son, Justin Myer, suffered an encephalopathy that was caused in fact by a Hepatitis B ("Hep B") vaccination he received in October 2002.[2] In May 2003, Justin began to experience neurological symptoms, including headache and double vision,

[1] The undersigned intends to post this decision on the United States Court of Federal Claims's website, in accordance with the E-Government Act of 2002, Pub. L. No. 107-347, § 205, 116 Stat. 2899, 2913 (codified as amended at 44 U.S.C. § 3501 note (2006)). As provided by Vaccine Rule 18(b), each party has 14 days within which to request redaction "of any information furnished by that party (1) that is trade secret or commercial or financial information and is privileged or confidential, or (2) that are medical files and similar files the disclosure of which would constitute a clearly unwarranted invasion of privacy." Vaccine Rule 18(b). Otherwise, the entire ruling will be available to the public. Id.

[2] The National Vaccine Injury Compensation Program comprises Part 2 of the National Childhood Vaccine Injury Act of 1986, Pub L. No. 99-660, 100 Stat. 3755, codified as amended, 42 U.S.C. §§ 300aa-10 et seq. (2006). Hereinafter, individual section references will be to 42 U.S.C. § 300aa of the Vaccine Act.

which were later diagnosed as autoimmune encephalitis. Over the next several months, Justin's condition continued to deteriorate, and he was hospitalized. In November 2003, Justin fell into a coma, and he remained in that state until his death, on April 27, 2008. Petitioner contends that Justin's condition was caused by his Hep B vaccination, which triggered an autoimmune reaction that eventually led to Justin's death.[3]

Petitioner's case is supported by the testimony of his treating neurologist, Eugene C. Lai, M.D., Ph.D. Dr. Lai cared for Justin from August 2003 to February 2004. During that time, Dr. Lai performed an extensive workup to determine the cause of Justin's condition, and he ruled out many etiologies in a differential diagnosis. Ultimately, Dr. Lai concluded that Justin suffered from autoimmune encephalitis secondary to his Hep B vaccination. Dr. Lai's opinion rested heavily on his personal observation of Justin, the clinical course of Justin's disease, and the absence of any other cause. While Dr. Lai recognized that the medical literature associated the Hep B vaccine with encephalitis occurring within three months or less of vaccination, he opined that seven months was a reasonable time for an autoimmune disease to develop. Given the extremely unusual nature of Justin's illness, Dr. Lai concluded that in Justin's case the only medically reasonable cause of the autoimmune encephalitis was the Hep B vaccination.

Respondent countered Petitioner's allegations with expert testimony that no medical literature has linked a Hep B vaccination, or any vaccination, with an encephalitis with a presentation similar to Justin's. Respondent's expert opined that a reaction first manifesting six months after vaccination falls well outside the medically accepted time frame for vaccine causation.

The experts agreed that Justin suffered from encephalitis, and that Justin's symptoms were complex and puzzling. Dr. Lai's opinion was based on a rigorous differential diagnosis of Justin, and I find his analysis and conclusion to be persuasive. Considered from this vantage, Petitioner has made a prima facie showing under the Vaccine Act. See Althen v. Sec'y of Dep't of Health & Human Servs., 418 F.3d 1274 (Fed. Cir. 2005). Respondent has not demonstrated by a preponderance that an alternative factor was a substantial cause of Justin's disorder. Accordingly, I find that Petitioner is entitled to compensation.

II. FACTUAL BACKGROUND

A. Petitioner's Case

Petitioner alleged that Justin suffered autoimmune encephalitis as a consequence of his Hep B vaccinations. Justin received his Hep B vaccinations on

[3] Ms. Myer was appointed guardian of Justin's person and estate while he was incapacitated, but it does not appear that this appointment survives death. Pet'r Ex. 36. Ms. Myer must file documentation showing that she is entitled to bring this suit on behalf of Justin's estate.

April 25, 2002, May 29, 2002, and October 25, 2002. Pet'r Ex. 26 at 1. The experts agreed that the first symptoms of Justin's condition likely manifested in May 2003. Pet'r Ex. 42 at 1; Resp't Ex. D at 1. In May 2003, Justin developed a chronic headache. Pet'r Ex. 5 at 38. In June 2003, Justin developed vision problems, including diplopia and blurry vision. Pet'r Ex. 5 at 38; Pet'r Ex. 4 at 3.[4] From May to August 2003, Justin saw a variety of doctors to determine the cause of his headaches and vision problems. In August 2003, Justin was first evaluated by Dr. Lai.

1. Dr. Eugene Lai

Dr. Lai is a neurologist at Methodist Hospital (Baylor Medical Center) and a professor at Baylor College of Medicine. Tr. at 13. Methodist Hospital is a tertiary care facility, and it accepts "all the tough cases that local . . . hospitals would not be able to diagnose or take care of . . . ." Tr. at 22-23. Dr. Lai has over 20 years of experience treating encephalitis and encephalopathies. Tr. at 46. Dr. Lai was Justin's treating physician from August 2003 to February 2004. Tr. at 13.

In his expert reports and his testimony at hearing, Dr. Lai opined that Justin suffered from autoimmune encephalitis. He did not determine the cause of Justin's condition at the outset. After he performed an extensive workup, Dr. Lai determined that Justin was suffering from autoimmune encephalitis that was caused by his Hep B vaccination. Dr. Lai opined that Justin's vaccine injury led to his death. Tr. at 22.

a. Dr. Lai's Treatment of Justin

When Dr. Lai first saw Justin in August 2003, Justin complained of lethargy, memory loss, and some incontinence. Pet'r Ex. 5 at 1, 38. Justin reported that he started having headaches with high blood pressure in May 2003. Id. at 38. Justin reported he developed diplopia, hand tremors, and memory problems in June 2003. Id.; see Pet'r Ex. 4 at 3-8; Pet'r Ex. 7 at 1; Pet'r Ex. 9 at 2. Dr. Lai noted that Justin had history of headaches ten years prior, which were suspected to be caused by hydrocephalus. Pet'r Ex. 5 at 49-50.[5] Justin had a shunt placed in his head to help relieve pressure. The experts in this proceeding agreed that that shunt was not a cause of Justin's encephalitis. Tr. at 51-52; Tr. 147-48.

Dr. Lai admitted Justin to the hospital for neurological evaluation and IV therapy on August 29, 2003, with a diagnosis of presumptive encephalitis. Pet'r Ex. 5 at 49-50. In his admission note, Dr. Lai suspected "a subacute encephalitis with a possible viral etiology or may be fungal, otherwise, we would need to consider more unusual

[4] Diplopia is the perception of two images of the same object, sometimes referred to as double vision. Dorland's Illustrated Medical Dictionary (31st ed. 2007) at 532.

[5] Hydrocephalus is a condition caused by the accumulation of cerebrospinal fluid ("CSF") in the skull, and it can result in increased CSF pressure. Dorland's at 890. In adults, the condition can cause dementia. Id.

etiologies such as vasculitis, sarcoidosis, or some other inflammatory or auto-immune process or possibly malignancy." Id. at 39. Justin was discharged on September 8, 2003, with diagnoses of "encephalitis, probably autoimmune in etiology and hypertension." Id. at 49-50.

Justin was readmitted to the hospital on September 19, 2003, for increased lethargy, memory loss, and incontinence. Id. at 4. He remained hospitalized until November 15, 2003. Id.

Dr. Lai performed an exhaustive neurological and medical workup, including magnetic resonance imaging ("MRI") scans of the brain, electroencephalograms ("EEGs"), and lumbar punctures. Initially, he could not find a specific etiology. Tr. at 18; Pet'r Ex. 29; see Pet'r Ex. 5 at 4. Dr. Lai consulted with doctors from pulmonary, general surgery, nephrology, vascular surgery, infectious diseases, interventional radiology, and gastroenterology. Pet'r Ex. 5 at 4.

Dr. Lai felt the workup and test results were consistent with an autoimmune disorder. Tr. at 18-19; Pet'r Ex. 29. Dr. Lai explained that his conclusion was based on observed changes in Justin's EEGs and MRIs between August and November 2003, along with increased white blood cells in the cerebrospinal fluid ("CSF"), abnormalities in immunoglobulin G ("IgG") production, and oligoclonal bands in the CSF. Tr. at 19.[6] The testing also indicated that "there was no infectious, neoplastic, or other systemic cause of [Justin's] fulminant neurological abnormalities." Pet'r Ex. 29. Dr. Lai summarized his diagnosis by saying, "[W]e went through a very extensive evaluation to rule out infection . . .; also maybe inflammation of the blood vessels; . . . multiple sclerosis; a condition related to cancer; . . . Creutzfeldt-Jakob disease. All these ha[d] been eliminated, so at that time, . . . I reasoned that, . . . it is . . . most probably related to [the Hep B vaccination]." Tr. at 20.

Justin was discharged from the hospital on November 15, 2003, with a diagnosis of autoimmune encephalitis. Pet'r Ex. 5 at 4. On discharge, Justin was minimally responsive to sensory stimuli and unresponsive to verbal stimuli. Id. at 5. Over the next few weeks, Justin seemed to improve neurologically, with brief spells of being alert and somewhat responsive. Id. at 11. On December 1, 2003, Justin was readmitted to the hospital under Dr. Lai's care to treat pneumonia. Id. at 11, 14. On admission, Justin was "essentially unresponsive to all stimuli." Id. at 12. During his hospital stay, Justin was in a minimally conscious state, and he had frequent myoclonic jerks. Id. at 14.[7] Justin was discharged on December 15, 2003, in a minimally responsive state. Id. at 15. He was readmitted on January 26, 2004. Id. at 34. Justin was discharged on February 2, 2004, with severe brain damage, and Dr. Lai felt the prognosis for

[6] Justin's MRIs initially were normal, then they showed diffuse changes, and then the diffusion resolved leaving brain atrophy. Pet'r Ex. 5 at 36, 41, 77, 86. Justin's EEGs were diffusely slow with no epileptiform activity. Id. at 20, 102-04.

[7] Myoclonic jerks are shocklike contractions of a muscle or muscles, restricted to discrete areas of the body. Dorland's at 1241.

meaningful recovery of cerebral function was poor. Id. at 35. Justin was to remain under care at home, and Dr. Lai did not treat Justin further.

b. Dr. Lai's Opinion

Dr. Lai's opinion rested on the fact that, in his experience and expertise, he could not find any other explanation for what caused Justin's autoimmune encephalitis. Tr. at 46. The opinion was grounded on his first hand observation of Justin's clinical course. Tr. at 24-26. Dr. Lai testified that when he first saw Justin in August 2003, Justin was able to walk into his office and ask questions. Tr. at 26. One month later, Justin was semi-comatose and unable to respond to simple commands. Id. By February 2004, Justin was totally unresponsive and totally care dependent. Id. Dr. Lai stated, "I took care of him from August of 2003, all the way to the beginning of February" 2004. Tr. at 24. During part of that period, Dr. Lai saw Justin every day. Tr. at 24-25. "I know how his disease progressed and how he changed from a perfectly healthy young man to, you know, a person with vegetative state." Tr. at 25. Dr. Lai relied on his extensive experience "dealing with people with -- day in and day out with encephalopathy . . . there's several other diagnosis [sic] that we entertained regarding encephalopathy which are more common that we see every day, but his case [was] so unusual, so different that in my mind at least, there is no other possibility." Id.

Dr. Lai testified that Justin's Hep B vaccine caused the autoimmune reaction through a process like molecular mimicry. Tr. at 47-48. To show that the Hep B vaccine can cause autoimmune encephalitis, Dr. Lai relied on an article presenting eight patients who suffered encephalitis within 10 weeks of Hep B vaccination. Tr. at 31; A. Tourbah et al., Encephalitis after Hepatitis B Vaccination, Neurology 1999;53;396 (Pet'r Ex. 34 at 1).[8] He also relied on case reports of autoimmune disorders and encephalitis following Hep B vaccination, although he conceded that the reports did not establish a causative link. Tr. at 31-34. Dr. Lai opined that the Hep B vaccine, like all viral vaccines, can cause an autoimmune reaction, and an autoimmune reaction can attack the brain and result in encephalitis. Tr. at 41.

Dr. Lai stated that the timing of onset was medically appropriate. Using multiple sclerosis as an example, Dr. Lai opined that following the first flare-up of an autoimmune condition, some people will get progressively worse, others will get better permanently, while others will get better only to have more flare-ups years later. Tr. at 21. Dr. Lai testified that the immune system is complex, and it is not fully understood

[8] The Tourbah et al. article reported "the clinical and MRI features of eight patients with an inflammatory and demyelinating disease of the [central nervous system] occurring less than 10 weeks after [Hep B] vaccination, to discuss the similarities and differences between this encephalitis and ADEM or MS." Pet'r Ex. 34 at 2. The article noted that the "postvaccinal period during which symptoms of neurologic disease might be considered to be associated with the effects of vaccination is clearly arbitrary. A period of 2 to 3 months after vaccination was cited by the Viral Hepatitis Prevent Board, a World Health Organization Collaborating Centre . . . ." Id. Another study on influenza and multiple sclerosis considered a post-vaccinal delay of up to six months. Id.

why an immunological reaction affecting the nervous system presents in differing manners and at different times. Tr. at 21, 42. Dr. Lai concluded that even if most people react to a vaccine within a few months, it is possible that a few would react several months later; "the timing I don't think is a critical issue here." Tr. at 21. Dr. Lai explained that "this is a very rare, unusual situation, that people sometimes may not even be able to recognize it." Tr. at 28.

Dr. Lai conceded that the literature on which he relied documented cases of autoimmune reactions occurring within just two to three months of Hep B vaccination. Tr. at 30-31. Dr. Lai explained that, in Justin's case, the approximately seven month interval between vaccination and onset was reasonable. Tr. at 31. Dr. Lai also conceded that an IOM study "found no evidence of unequivocal link between [Hep B vaccination] and autoimmune manifestations." Tr. at 31-32.

Dr. Lai explained why he ruled out some other possible conditions. He testified that Justin did not suffer from a demyelinating disorder, because MRI did not show evidence of damage specifically to myelin and Justin's brain damage involved both gray and white matter. Tr. at 49-50.[9] Dr. Lai also explained why he had ruled out Creutzfeldt-Jakob disease ("CJD") and other prion diseases. Tr. at 37.[10] Dr. Lai seriously considered CJD in his differential diagnosis because the neuro-imaging showed some abnormalities with the basal ganglia, consistent with CJD. Tr. at 38; see Pet'r Ex. 5 at 4 (Dr. Lai noted that serial MRI results were possibly consistent with prion disease).[11] He testified that a repeat MRI showed that the abnormality had resolved, which was inconsistent. Tr. at 39. If Justin had CJD, the noted abnormality would be expected to worsen, not to improve. Id. Another marker of CJD is the presence of elevated 14-3-3 protein levels in the CSF. Dr. Lai explained that the 14-3-3 protein is a brain protein, so whenever brain cells are damaged, small amounts of the protein will be spilled out to the spinal fluids. Tr. at 40. Dr. Lai testified that Justin's 14-3-3 levels "show[ed] a slight abnormality, which is not unusual in a person with brain damage of the types that Mr. Myer is having . . . ." Id. Because other tests indicated Justin did not have CJD, Dr. Lai discounted Justin's slightly elevated 14-3-3 protein level and ruled out CJD. Tr. at 37-41.

---

[9] Myelin is the protective covering that surrounds a nerve cell. Dorland's at 1237. Demyelination is the destruction of myelin. Id. at 493. The white matter of the brain is composed of mostly myelinated nerve fibers. Id. at 1819. Gray matter is composed of unmyelinated nerve fibers and supportive tissue. Id.

[10] CJD is a prion disease. A "prion" is a proteninaceous infectious substance, and is a particle that is smaller than a virus. Tr. at 151. The particles are passed from person to person and they can cause diseases. Id. The incubation period of prion diseases can be decades. Id. Mad cow disease, or bovine encephalitis, is one commonly known type of prion disease. Id.

[11] The basal ganglia is a set of gray matter structures in the brain (includes striatum, caudate, and putamen). Dorland's at 1315. Respondent's expert testified that damage to the basal ganglia is the hallmark of CJD. Tr. at 155; see also Resp't Ex. G-3 at 7.

In a supplemental expert report, Dr. Lai addressed the testimony of Respondent's expert, Arthur Safran, M.D. Dr. Safran argued that Justin suffered from variant CJD, a type of CJD recently described in the medical literature. Dr. Lai stated that he had cared for at least ten CJD patients and that he knew how to diagnose the condition. Pet'r Ex. 53 at 2. He stated that he had "not treated a variant CJD patient because it is the rarest of the rare diseases one can think of," with only "3 confirmed cases in the United States in the last 15 years." Id. Using the diagnostic criteria in one of Respondent's exhibits, Dr. Lai asserted that Justin's CSF studies were inconsistent with variant CJD. Id. at 3. Dr. Lai reaffirmed his opinion that Justin suffered from autoimmune encephalitis due to Hep B vaccination. Id.

2. Dr. Paul Gerstenberg and Dr. Irma Dailey

Irma Vargas Dailey, D.O., was Justin's general practitioner until she retired in 2007. Petitioner filed a letter from Dr. Dailey indicating that Justin's headaches started in "April of 2003 or perhaps earlier." Pet'r Ex. 33. Dr. Dailey did not testify at hearing.

Paul Gerstenberg, D.O., was a family practitioner who was Justin's general doctor. He began treating Justin in September 2007. Tr. at 80. Dr. Gerstenberg testified for Petitioner at hearing.

When Dr. Gerstenberg began treating Justin, he thought Dr. Lai's diagnosis seemed unusual. After reviewing the case record, Dr. Gerstenberg concluded that Dr. Lai's diagnosis was correct. Tr. at 87. He testified that there was "no other medical or other explanation for Justin's rapid decline, other than the autoimmune reaction." Tr. at 69. He stated that "lots of other diagnoses . . . were considered in the differential." Id. He stated that Dr. Lai's diagnosis was supported by the radiologist, the laboratory reports, and the other consulting physicians involved with the case. Tr. at 70. He conceded that Justin did not experience a classic, typical autoimmune reaction to vaccination, but in light of the absence of any other explanation, the diagnosis fit. Tr. at 88-89.

Dr. Gerstenberg had some concerns about the timing of Justin's reaction. "[T]he question I have as well is: Is the time close enough to his immunization series? Although it's not the classical typical case that's recorded in the literature, it -- in light of absence of any other explanation, it does fit with the immune system as Dr. Lai addressed . . . ." Tr. at 89. "[I]n Justin's case, I believe that even though it's not within the two months or the four weeks also alluded to here [in the article], it still follows that this is possibly an autoimmune reaction to the hep B vaccine." Tr. at 93.

B. Respondent's Case: Dr. Arthur Safran

Dr. Safran is an expert neurologist who has been practicing for 47 years. Tr. at 133, 135. He works at two hospitals in Boston, Massachusetts, and he is an assistant professor of clinical neurology at the Tufts New England Medical Center. Tr. at 133.

Dr. Safran agreed that Justin's headaches likely were the first symptom of his illness. Tr. at 147-48.

Dr. Safran opined that Justin's illness was not related to the Hep B vaccination. Dr. Safran did not think that Justin's condition was consistent with a vaccine injury because of "the atypicality of the presentation with basal ganglia degeneration and a prolonged course . . . and the absence of any description in the medical literature of the illness." Tr. at 156. Dr. Safran described Justin's illness as progressive, not acute. Tr. at 139-40. Dr. Safran testified that Justin likely suffered from CJD, and not autoimmune encephalitis. Tr. at 140-42. Dr. Safran clarified that his "opinion doesn't rest on an alternative diagnosis, but I think [CJD] is a good one." Tr. at 156.

Dr. Safran recognized that some scattered case reports associated Hep B vaccination with encephalitis, but he testified that they were not significant statistically. Tr. at 139. He opined that "There's a background level of every illness, and . . . one needs to show that there is an increased incidence in association with a particular event. That's not the case with progressive encephalitis particularly." Id. Dr. Safran opined that no case report of progressive encephalitis related to any vaccine has ever been reported in the medical literature. Tr. at 135. Dr. Safran conceded that Dr. Lai described Justin's condition as fulminant (acute), but he thought that description was inaccurate in the context of a possible post-vaccinal encephalitic process. Tr. at 177.

Dr. Safran also testified that a reaction occurring six-plus months after vaccination would be well outside of the usual accepted range for vaccine reactions. Tr. at 136. Dr. Safran testified that most people would limit the appropriate timing for an autoimmune adverse reaction to the Hep B vaccine to two to three months. Tr. at 143-44. Dr. Safran stated that he was unpersuaded by the case reports, however, and he did not accept that the Hep B vaccine had a causal relationship with either acute or progressive encephalopathy, irrespective of the time of onset. Tr. at 145-46. He further testified that molecular mimicry was not a reasonable explanation in Justin's case. Tr. at 169. Dr. Safran explained why Justin's condition was not consistent with a vaccine-caused reaction, and why it was inconsistent with autoimmune encephalitis. Tr. at 142-43.

In his expert reports, he opined that post-vaccinal complications generally are demyelinative in nature. Resp't Ex. A at 3, 5. Dr. Safran stated that slowly progressive encephalitic conditions are rare. Id. at 3. In his expert reports, he suggested that all the disorders listed in Adams and Victor's Principles of Neurology as part of a differential diagnosis of progressive encephalitis more likely were causes of Justin's disorder. Id. at 3.[12] Dr. Safran stated that the diagnosis by exclusion of autoimmune encephalitis "will certainly not stand up to scrutiny as being established beyond medical certainty and in the absence of any similar case in the medical or neurologic literature in relation to hepatitis B vaccine . . . ." Id. at 9. He also opined that the appropriate diagnosis was encephalitis of unknown cause. Id.

[12] Allan H. Ropper & Martin A. Samuels, Adams and Victor's Principles of Neurology 1261-62 (9th ed. 2009)

Dr. Safran testified that in most types of encephalitis, brain damage principally manifests in the white matter, and not in the gray matter. Tr. at 140-41. Dr. Safran testified that he was most familiar with autoimmune encephalitis in the context of acute disseminated encephalomyelitis ("ADEM"). Tr. at 141-42. In ADEM, the body develops antibodies that cause the immune system to attack the brain. Tr. at 141. ADEM is an acute or subacute disease, and it causes changes in the white matter of the brain. Tr. at 142. Dr. Safran explained that after ADEM manifests, it reaches its maximum in one to two weeks. Id.

Dr. Safran testified that there's no evidence that antibodies were attacking Justin's brain. Tr. at 136. The only abnormal antibodies were immunoglobulin banding in the spinal fluid, and this finding was consistent with most inflammatory illnesses. Tr. at 136, 178-79. He testified that MRIs showed that Justin did not have any white matter damage consistent with a demyelinating disorder like ADEM. Tr. at 145-46. Dr. Safran opined that the presentation of Justin's condition was more consistent with a progressive disorder than an acute disorder like ADEM. Tr. at 142-43.

Dr. Safran testified that the medical records indicated that Justin suffered from an unusual symptom: myoclonus. Myoclonus is a jerking movement, and it is an uncommon manifestation for most neurologic conditions. Tr. at 136. He also testified that Justin's MRIs showed damage to the gray matter of the basal ganglia. Tr. at 140-41. The presence of myoclonus and damage to the basal ganglia led Dr. Safran to suspect that Justin suffered from CJD. Tr. at 148-50, 178. He noted that prion diseases like CJD can have an incubation period of decades. Tr. at 150-51; see Resp't Ex. G-3 at 3 (incubation period for CJD can be up to 30 years).

Dr. Safran testified that Justin likely had CJD. Tr. at 148-51. Dr. Safran explained that Dr. Lai may have ruled out CJD because, in the past, CJD was largely confined to older people. Tr. at 156. However, recent literature has described "variant CJD," which occurs in younger patients and has a more progressive course. Tr. at 148-49. Dr. Safran testified that Dr. Lai ruled out the classic form of CJD, but opined that Justin's condition was more consistent with variant CJD. Tr. at 173-74. Although the treating physician generally is in a better position to make a diagnosis, Dr. Safran felt the benefit of hindsight and the recent research into variant CJD made his assessment more reliable than Dr. Lai's. Tr. at 156.

Dr. Safran testified about the clinical features and diagnostic criteria of CJD and variant CJD. Dr. Safran relied on the diagnostic criteria used by the World Health Organization to argue that Justin had CJD. Tr. at 154.[13] Those criteria are 1) progressive dementia, 2) at least two of the following symptoms: myoclonus, visual or cerebellar disturbance, pyramidal/extrapyrimidal dysfunction, akinetic mutism, 3) a typical EEG or a positive 14-3-3 spinal fluid assay with a clinical duration to death less

[13] Dr. Safran actually relied on a publication called UpToDate (June 3, 2010), which used the WHO definition. See Resp't Ex. G-3 at 12.

than two years, and 4) routine investigation should not suggest an alternative diagnosis. Resp't Ex. G-3 at 12; Tr. at 151-53.[14] Abnormalities in the putamen and caudate (part of the basal ganglia) are commonly observed in MRIs. Resp't Ex. G-3 at 7. An elevated 14-3-3 protein in the spinal fluid occurs in most patients with CJD, although it can be caused by other encephalitides. Resp't Ex. G-3 at 10; see Tr. at 149.

Dr. Safran testified that the symptoms and diagnostic criteria of variant CJD are similar to CJD, but variant CJD typically occurs at a younger age, has a less rapid progression of illness, and has some differences in clinical presentation and course. Tr. at 148-50, 173-74; Resp't Ex. G-2 at 4. The literature addressed some of the differences between CJD and variant CJD. CSF studies are rarely helpful in diagnosing variant CJD -- the CSF does not show elevated cell counts and, unlike in CJD, the 14-3-3 protein is a less sensitive marker, occurring in under one-half of all patients. Resp't Ex. G-2 at 5-6. Additionally, EEG changes are not always seen in variant CJD. Tr. at 174.

Dr. Safran testified that Justin's condition was consistent with the diagnostic criteria for CJD because: 1) Justin suffered from progressive dementia; 2) he experienced myoclonus, cerebellar disturbance, and extrapyramidal dysfunction (as shown by basal ganglia degeneration on his MRI); and 3) he had a positive 14-3-3 protein spinal fluid assay. Tr. at 152-53. Dr. Safran opined that "gradual progressive degeneration of his basal ganglia . . . is the hallmark of CJD." Tr. at 155. Dr. Safran opined that Justin's EEG abnormalities were not consistent with CJD but were consistent with variant CJD. Tr. at 173-74. He also opined that the duration of Justin's clinical course was more consistent with variant CJD. Tr. at 148-50.

C. Post-Hearing Medical Literature

Following the hearing, both parties submitted additional medical literature, and Petitioner filed a supplemental expert report from Dr. Lai.

In his report, Dr. Lai asserted that encephalitis is a rare, but real, complication of vaccination. Pet'r Ex. 53 at 1.[15] He cited two articles analyzing encephalitis following small pox vaccination prior to 1968, and a CDC Morbidity and Mortality Weekly Report that reported that cerebrospinal fluid abnormality accounted for 0.5% of all adverse events from 1991 to 2003, and encephalopathy for 0.2%.

[14] Pyramidal/extrapyramidal dysfunction means motor activity dysfunction. Dorland's at 1882, 1975. Akinetic mutism is a state where a person can make no spontaneous movement or sound. Id. at 1233.

[15] In the report, Dr. Lai stated that encephalitis is rare because it only affects patients with a certain predisposed genetic variant of their immune system, and he cites to "appendix 5." Pet'r Ex. 53 at 1. The filing does not contain an appendix 5. The statement otherwise is not substantiated by the record or filed literature, and I do not rely on it.

Dr. Lai also referenced several articles to rebut Dr. Safran's testimony that "there has never been a case of progressive encephalitis in the literature related to any vaccine." Pet'r Ex. 53 at 1-2. Dr. Lai cited to two articles documenting several cases of progressive encephalitis following vaccination with amyloid-β peptide, an experimental Alzheimer's vaccination. Dr. Lai also cited a 1983 case report of a patient who developed encephalitis five months after a rabies vaccination.

Respondent filed a chapter on prion disease from Merritt's Neurology (Lewis P. Roland ed., 11th ed. 2005) (Resp't Ex. F-1) and two articles about CJD and variant CJD (Resp't Ex. G-2; Resp't Ex. G-3).

Merritt's Neurology described CJD and new variant CJD. Clinical features of CJD include the gradual onset of dementia, memory loss that progresses rapidly, weakness and stiffness of limbs, tremors, and myoclonus. Resp't Ex. F-1 at 4. In CJD, routine blood counts, blood chemistries, and CSF tests are usually within normal limits, but the CSF is usually positive for 14-3-3 protein. Id. For variant CJD, symptoms start before age 40, and "clinical manifestations include[] behavioral changes, sensory complaints and ataxia. Myoclonic jerks and the characteristic EEG abnormalities [are] not seen," and the 14-3-3 protein is found in about one-third of patients. Id. at 6.

III. DISCUSSION

A. Petitioner's Burden of Proof

Petitioners seeking to establish causation in fact must show by a preponderance of the evidence that but for vaccination they would not have been injured, and that vaccination was a substantial factor in bringing about the injury. Cedillo v. Sec'y of Dep't of Health & Human Servs., 617 F.3d 1328, 1338 (Fed. Cir. 2010); Shyface v. Sec'y of Dep't of Health & Human Servs., 165 F.3d 1344, 1352 (Fed. Cir. 1999).[16] Proof of actual causation must be supported by a sound and reliable "medical or scientific explanation that pertains specifically to the petitioner's case, although the explanation need only be 'legally probable, not medically or scientifically certain.'" Moberly v. Sec'y of Dep't of Health & Human Servs., 592 F.3d 1315, 1322 (Fed. Cir. 2010) (quoting Knudsen v. Sec'y of Dep't of Health & Human Servs., 35 F.3d 543, 548-49 (Fed. Cir. 1994)); see also Grant v. Sec'y of Dep't of Health & Human Servs. 956 F.2d 1144, 1148 (Fed. Cir.1992) (medical theory must support actual cause).

Causation is determined on a case-by-case basis, with "no hard and fast per se scientific or medical rules." Knudsen, 35 F.3d at 548. A petitioner may use circumstantial evidence to prove the case, and "close calls" regarding causation must be resolved in favor of the petitioner. Althen, 418 F.3d at 1280. Evidence should be viewed under the preponderance standard as it is understood in civil courts and "not

[16] Petitioner alleged this was a "Table" injury, but does not allege that the injury satisfies any of the legal criteria of a Table injury. See 42 C.F.R. § 100.3. Because the injury patently is not a Table injury, I construe Petitioner's claim as one of causation in fact.

through the lens of the laboratorian." Andreu v. Sec'y of Dep't of Health & Human Servs., 569 F.3d 1367, 1380 (Fed. Cir. 2009).

Petitioner can show that the vaccination brought about his 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, 418 F.3d at 1278.

A special master can find that a petitioner has established causation in fact based solely on a treating physician's opinion that a vaccination was causally linked to the vaccinee's injury if the special master finds the opinion to be both reliable and persuasive. Moberly, 592 F.3d at 1324-25; Andreu, 569 F.3d at 1375-76. Evidence used to satisfy one prong of Althen can overlap to satisfy another prong. Cappizzano v. Sec'y of Dep't of Health & Human Servs., 440 F.3d 1317, 1326 (Fed. Cir. 2006).

In evaluating whether a petitioner has presented a legally probable medical theory, "the special master is entitled to require some indicia of reliability to support the assertion of the expert witness." Cedillo, 617 F.3d at 1339 n.3 (collecting cases). A special master is not required to rely on a speculative opinion that "'is connected to existing data only by the ipse dixit of the expert.'" Snyder v. Sec'y of Health & Human Servs., 88 Fed. Cl. 706, 745 n.66 (2009) (quoting Gen. Elec. Co. v. Joiner, 522 U.S. 136, 146 (1997)); accord, e.g., Cedillo, 617 F.3d at 1339 n.3.

If Petitioner succeeds in establishing a prima facie case of causation, the burden then shifts to Respondent to prove alternative causation by a preponderance of the evidence. Althen, 418 F.3d at 1278. If Petitioner fails to establish a prima facie case of causation, however, the burden does not shift. Doe 11 v. Sec'y of Dep't of Health & Human Servs., 601 F.3d 1359, 1357-58 (Fed. Cir. 2010); see Cedillo, 617 F.3d at 1335 (citing Walther v. Sec'y of Dep't of Health & Human Servs., 485 F.3d 1146, 1151 (Fed. Cir. 2007)).

Respondent may offer evidence of an alternative theory of causation to show that a petitioner has not satisfied an element of her prima facie case. Doe 11, 601 F.3d at 1358. When a petitioner bases her case in part on the absence of alternative causes, it is proper for the special master to consider evidence of alternative causes that is presented by Respondent in evaluating whether the petitioner has met her burden of proof. Id.

B. Analysis

1. Differential Diagnosis

Dr. Lai is an expert in neurology with more than 20 years of experience treating encephalitis and encephalopathies, Tr. at 46; he is well qualified to opine in this case. His testimony is based on extensive medical knowledge as well as treatment of patients

with rare and difficult to diagnose neurological disorders. See Tr. at 22-23, 44-46. His opinion was that the only reasonable explanation for Justin's condition was a reaction to his Hep B vaccination; no other neurological disorder or condition could explain his condition.

The foundation of Dr. Lai's opinion was that Justin experienced a very unusual reaction; "this is a very rare, unusual situation, that people sometimes may not even be able to recognize it." Tr. at 28. Dr. Lai performed an exhaustive workup, and he ruled out numerous alternative etiologies. Tr. at 46; Pet'r Ex. 53 at 2. Dr. Lai recognized that Justin's clinical course differed from that described in the literature, but opined that a Hep B vaccine induced autoimmune reaction was the only medically reasonable explanation for Justin's illness. Tr. at 21.

Dr. Lai's opinion clearly rests on differential diagnosis, a useful tool in the medical profession to decide what treatment should be offered to a patient. As a legal matter, especially in establishing causation, the utility of differential diagnosis is less clear. See, e.g., Ruggerio v. Warner-Lambert Co., 424 F.3d 249, 254 (2d Cir. 2005) (stating that the "district judge has broad discretion in determining whether in a given case a differential diagnosis is enough by itself to support a causation opinion"). The Federal Circuit has recognized that a petitioner may present "evidence eliminating other potential causes to help carry the burden on causation and may find it necessary to do so when the other evidence on causation is insufficient to make out a prima facie case . . . ." Walther, 485 F.3d at 1151. A simplistic elimination of other causes, however, does not necessarily mean that a remaining factor actually caused the condition. See Moberly, 592 F.3d at 1323.

Thus, when a differential diagnosis is conducted by treating physicians and/or experts utilizing rigorous medical protocols, the result, if consistent with the other established facts, may point to probable causation. On the other hand, when a non-treater opines on a diagnosis based simply on the perceived absence of other causes for the patient's condition, I am less inclined to rely on that testimony to find causation absent other indicia of reliability. This approach -- neither accepting nor rejecting differential diagnosis as such, but evaluating the strength of the diagnosis based on the particular facts of the case -- seems reasonable and in accordance with the policy of the Vaccine Act.

In the present setting, the determination regarding causation does not emerge from strict analysis of the Althen factors. See de Bazan v. Sec'y of Dep't of Health & Human Servs., 539 F.3d 1347, 1353 n.3 (Fed. Cir. 2008) (noting that the Federal Circuit has "held that a petitioner may instead rule out possible alternative causes to prove causation-in-fact when evidence as to the Althen requirements is insufficient" (emphasis in original)). Dr. Lai's opinion does not derive its persuasiveness because of the strength of his theory of molecular mimicry, for which, in this case, there is less evidence than in some other cases. The strength of Dr. Lai's presentation under prong two, however, outweighs the weaknesses of the theory under prong one and, to the same extent, prong three. Cappizzano, 440 F.3d at 1326. There is little direct medical

evidence that vaccination can cause a devastating encephalopathy to occur after a period of seven months. The reason to credit Dr. Lai's testimony is that, as a practicing specialist with direct knowledge of what occurred in this case, he believes that vaccination is the most likely explanation, and so testified. On this record, I find no reason to reject his testimony or second-guess his medical investigation of Justin's case, which was thorough and well-documented. For these reasons, I rely on his opinion that Justin's encephalopathy was more likely than not caused by his Hep B vaccination.

2. The Althen Factors

a. Prongs One and Three

Petitioner's theory is that the Hep B vaccine can cause a reaction that manifests as autoimmune encephalitis seven months post-vaccination. Dr. Safran testified that Dr. Lai's theory was not plausible because the literature did not document any cases of autoimmune encephalitis associated with vaccination with a seven month incubation period. Dr. Safran conceded that the literature described a few case reports of post-vaccinal acute autoimmune encephalitis, but he was "not frankly willing to accept that there's a causal relationship." Tr. at 145-46. He testified that the scattered case reports were not significant statistically. Tr. at 139. Dr. Safran testified that most people considering an association between a Hep B vaccine and an autoimmune disorder would limit an appropriate timing to within two or three months. Tr. at 143-44.

Dr. Safran's argument is not without merit. The law, however, does not require confirmation in the medical literature to establish a plausible theory of vaccine causation. See Cedillo, 617 F.3d at 1339. If a plausible theory can be constructed based on existing scientific knowledge, it is no answer, under the Vaccine Act, that the theory is unproven or undocumented in the medical literature. The Vaccine Program exists to award or deny compensation in an area devoid of scientific knowledge. Althen, 418 F.3d at 1280. I therefore examine Dr. Lai's opinion to see whether it is plausible and reliable in this case, knowing that it does not prove with scientific certainty an association between autoimmune encephalitis and Hep B vaccination. See Hocraffer v. Sec'y of Dep't of Health & Human Servs., 63 Fed. Cl. 765, 778-79 (2005).

Dr. Lai explained that, in Justin's case, the approximately seven month interval between vaccination and onset was medically appropriate. Tr. at 31. Dr. Lai conceded that the filed literature described patients with autoimmune reactions occurring only within two to three months of Hep B vaccination. Tr. at 30-31. Dr. Lai testified that the immune system is complex, and it is not fully understood why an immunological reaction affecting the nervous system presents in different ways and at different times. Tr. at 21, 42. Based on his experience with other autoimmune disorders, Dr. Lai concluded that even if most people react to a vaccine within a few months, some patients may react several months later. Tr. at 21.

On its face, Dr. Lai's theory is plausible. The premises of Dr. Lai's theory are: 1) Hep B vaccine can cause autoimmune encephalitis, 2) autoimmune disorders can take months to years to develop, and 3) the Hep B vaccine could cause an atypical presentation of autoimmune encephalitis. From these premises, Dr. Lai concludes that Justin's Hep B vaccination likely caused an autoimmune encephalitis that first manifested seven months post-vaccination. Dr. Lai's conclusion is based on science and reliable inferences therefrom. Absent persuasive refutation from Respondent, I accept his testimony in satisfaction of Althen prong one. In addition, I find that Dr. Lai's application of the theory to Justin satisfies Althen prong three.

The question is whether the relationship between vaccine and injury is probable, not certain. Dr. Safran's opinion sets the bar too high; clinical confirmation of Petitioner's theory is not required. Andreu, 569 F.3d at 1378; see Resp't Ex. A at 9 (Dr. Safran described Dr. Lai's diagnosis as not "established beyond medical certainty"). The pertinent standards are not those of the medical scientist. The Vaccine Program requires neither epidemiological evidence nor identification of a specific biological mechanism to explain vaccine injury. All that is required is a plausible, reliable explanation.

That studies have failed to uncover more instances of the phenomenon Dr. Lai described does not invalidate his opinion. If Justin's disease was as rare as Dr. Lai believed it to be, it certainly could avoid detection by the medical community. In these circumstances, it is appropriate to defer to Petitioner's expert and treating physician, recognizing that the Vaccine Act allows for a finding of causation in a field bereft of direct proof, and that the applicable case law instructs a special master to err if necessary on the side of petitioners. Since Dr. Safran has not negated the plausibility of Dr. Lai's theory, Petitioner has carried the burden under Althen prong one. See Andreu, 569 F.3d at 1378 (stating that a theory "hitherto unproven in medicine," or one supported by a paucity of medical literature can satisfy the standard of causation (quoting Althen, 418 F.3d at 1280)).

b. Althen Prong Two

The second prong of Althen requires a petitioner to prove "'a logical sequence of cause and effect show[ing] that the vaccination was the reason for the injury.'" Andreu, 569 F.3d at 1374 (quoting Althen). The sequence of cause and effect must be "'logical' and legally probable, not medically or scientifically certain." Knudsen, 35 F.3d at 548-49. Under prong two of Althen, petitioners are not required to show "epidemiologic studies, rechallenge, the presence of pathologic markers or genetic disposition, or general acceptance in the scientific or medical communities to establish a logical sequence of cause and effect . . . ." Capizzano, 440 F.3d at 1325. Instead, circumstantial evidence and reliable medical opinions may be sufficient to satisfy the second Althen factor. Capizzano, 440 F.3d at 1325-26; Andreu, 569 F.3d at 1375-77 (treating physician testimony).

Dr. Lai was Justin's treating neurologist. Dr. Lai stated that:

> I took care of him from August of 2003, all the way to the beginning of February 2003 [sic]. There was a period I see [sic] him every day. I know how his disease progressed and how he changed from a perfectly healthy young man to, you know, a person with vegetative state. And, you know, . . . [I have] experience dealing with people with -- day in and day out with encephalopathy . . . there's several other diagnosis [sic] that we entertained regarding encephalopathy which are more common that we see every day, but his case so [sic] unusual, so different that in my mind at least, there is no other possibility.

Tr. at 24-25.

As discussed above, a sufficiently rigorous differential diagnosis can support a finding of causation under the Vaccine Act. See de Bazan, 539 F.3d at 1353 n.3; Hocraffer, 63 Fed. Cl. at 777, 779. Here, Dr. Lai performed an exhaustive workup to determine the cause of Justin's illness. Dr. Lai testified that he ruled out every other possibility before concluding the Hep B vaccine caused Justin's illness. The medical records confirm that Dr. Lai's conclusion resulted from a rigorous and methodical differential diagnosis. I am satisfied that the Dr. Lai's conclusion was sound and reliable.

Dr. Safran contended that recent research developments made it more likely that Justin suffered from a newer form of CJD, called variant CJD. Dr. Safran examined the features of Justin's condition and explained why he thought Dr. Lai erroneously ruled out CJD.

Dr. Lai testified, and the medical records corroborate, that he seriously considered CJD and prion disease as an etiology of Justin's condition. Dr. Lai explained that the CSF results, the changes in the neuro-imaging, as well as other abnormalities, were inconsistent with CJD. The recent research on variant CJD did not alter his opinion. Dr. Lai stated that he has experience treating and diagnosing CJD, and as Justin's treating physician his "medical opinion [was] that [Justin] suffered from an autoimmune encephalitis due to Hep[] B vaccination." Pet'r Ex. 53 at 3.

I am persuaded by Dr. Lai's rigorous analysis of Justin's condition and his unequivocal testimony that Justin's condition was caused by his Hep B vaccination. It is clear that he considered the alternative factor proposed by Respondent and rejected it for reasons that find objective confirmation in the medical record. I find that Petitioner has satisfied her legal burden of demonstrating a logical sequence of cause and effect under prong two of Althen. See Andreu, 569 F.3d at 1375-76.

3. Evidence of an Alternative Cause

Once the petitioner has met the initial burden of proof, "the burden shifts to the government to prove '[by] a preponderance of the evidence that the petitioner's injury is

due to a factor unrelated to the . . . vaccine.'" de Bazan, 539 F.3d at 1352 (citations omitted).

Dr. Safran's testimony was reliable. His opinion, although somewhat tentative, see Tr. at 164, patently represented the view of a medical expert both knowledgeable and experienced. His opinion was logical and the facts on which he relied were consistent with the medical record.

Nevertheless, I conclude that Respondent has not established by a preponderance of the evidence that Justin's condition was caused by CJD. Although the record indicated that Justin's illness was somewhat consistent with CJD, that disorder remains a theoretical possibility, not a likely cause. I am persuaded by Dr. Lai's analysis that CJD was not the actual cause of Justin's illness. Dr. Lai's opinion is bolstered by the fact that he treated Justin for several months during his illness and had first-hand knowledge of Justin's condition.

In the end, the record consists of two sound and reliable expert opinions pitted against each other. On this record, it is not possible to ascertain with assurance what happened to cause Justin's condition. Under such circumstances, the Act permits an award of compensation where it is found, as here, that vaccine causation is more likely than not, by a bare preponderance of the evidence.

IV. CONCLUSION

Petitioner has satisfied the legal requirements for proving that Justin's October 25, 2002, Hep B vaccination was a legal cause of his autoimmune encephalitis, and subsequent death. Respondent has not overcome Petitioner's evidence by proving an alternative cause. Therefore, I find that Petitioner has established entitlement to compensation under the Vaccine Act. This case shall proceed to the damages phase.

IT IS SO ORDERED.

s/ Dee Lord
Dee Lord
Special Master