In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

Filed: September 20, 2021

ARON BERAKI	*	PUBLISHED
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Petitioner,	*	No. 17-243V
	*	
v.	*	Special Master Nora Beth Dorsey
	*	
SECRETARY OF HEALTH AND HUMAN SERVICES,	*	Ruling on Entitlement; Causation-in-Fact; Hepatitis B Vaccine; Bell's Palsy.
	*	
Respondent.	*	
	*	

Richard Gage, Richard Gage, P.C., Cheyenne, WY, for petitioner.
Adriana Ruth Teitel, U.S. Department of Justice, Washington, DC, for respondent.

RULING ON ENTITLEMENT[1]

I. INTRODUCTION

On February 21, 2017, Aron Beraki ("petitioner") filed a petition for compensation under the National Vaccine Injury Compensation Program ("Vaccine Act" or "the Program"), 42 U.S.C. § 300aa-10 et seq. (2012).[2] Petitioner alleges that he suffered from Bell's palsy as the result of a hepatitis B vaccination he received on October 2, 2014. Petition at 1 (ECF No. 1).

[1] The undersigned intends to post this Ruling on the United States Court of Federal Claims' website. **This means the Ruling will be available to anyone with access to the internet.** In accordance with Vaccine Rule 18(b), petitioner has 14 days to identify and move to redact medical or other information, the disclosure of which would constitute an unwarranted invasion of privacy. If, upon review, the undersigned agrees that the identified material fits within this definition, the undersigned will redact such material from public access. Because this Ruling contains a reasoned explanation for the action in this case, undersigned is required to post it on the United States Court of Federal Claims' website in accordance with the E-Government Act of 2002. 44 U.S.C. § 3501 note (2012) (Federal Management and Promotion of Electronic Government Services).

[2] The National Vaccine Injury Compensation Program is set forth in 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 to -34 (2012). All citations in this Ruling to individual sections of the Vaccine Act are to 42 U.S.C. § 300aa.

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After carefully analyzing and weighing the evidence in accordance with the applicable legal standards, the undersigned finds that petitioner has provided preponderant evidence that the hepatitis B vaccine he received caused him to develop Bell's palsy, which satisfies his burden of proof under Althen v. Secretary of Health & Human Services, 418 F.3d 1274, 1280 (Fed. Cir. 2005). Accordingly, petitioner is entitled to compensation.

II. PROCEDURAL HISTORY

Petitioner filed medical records in support of his petition from March 21, 2017 through June 26, 2017. Petitioner's Exhibits ("Pet. Exs.") 1-8. On July 31, petitioner filed a Statement of Completion, stating that all relevant medical records had been filed. Statement of Completion, filed July 31, 2017 (ECF No. 10). However, on September 28, 2017, respondent filed a status report, identifying and requesting a number of outstanding records, as well as a copy of petitioner's social security disability application and related file. Respondent's ("Resp.") Status Report ("Rept."), filed Sept. 28, 2017 (ECF No. 11). Petitioner filed medical records and an affidavit regarding his records on December 27, 2017. Pet. Exs. 9-10. Petitioner filed his second Statement of Completion on February 13, 2018. Statement of Completion, filed Feb. 13, 2018 (ECF No. 16).

Subsequently, on March 30, 2018, respondent filed a Rule 4(c) Report in which he concluded that petitioner had not established evidence of "six months of residual symptoms associated with his alleged vaccine injury of Bell's palsy." Resp. Rept. at 9 (ECF No. 17). Respondent also asserted that petitioner had not established a causal association between his vaccination and his alleged injury. Id. In addition, respondent identified additional outstanding records and documents needed. See id. Petitioner filed additional records over the next six months, and his third Statement of Completion on September 28, 2018. Pet. Exs. 11-14; Statement of Completion, filed Sept. 28, 2018 (ECF No. 25).

On February 22, 2019, petitioner filed an amended petition, alleging that "his Bell's Palsy and subsequent related issues were caused by his October 2, 2014 Hepatitis B vaccine." Amended ("Am.") Petition at 1 (ECF No. 29). Thereafter, the parties filed their respective expert reports and supporting medical literature. Pet. Exs. 15-40; Resp. Exs. A-D.

Petitioner filed a Motion for Ruling on the Record on November 17, 2020, and then filed his supporting memorandum on January 19, 2021. Pet. Motion for Ruling on the Record ("Pet. Mot."), filed Nov. 17, 2020 (ECF No. 55); Pet. Memorandum ("Memo."), filed Jan. 19, 2021 (ECF No. 57). Respondent filed medical literature and a Response to the Motion for Ruling on the Record on April 19, 2021. Resp. Ex. F; Resp. Response to Pet. Mot. ("Resp. Response"), filed Apr. 19, 2021 (ECF No. 66).[3] Petitioner filed his Reply on May 21, 2021. Pet. Reply to Resp. Response ("Pet. Reply"), filed May 21, 2021 (ECF No. 69).

This matter is now ripe for adjudication.

[3] Petitioner requested the ruling on the record in lieu of a hearing. Respondent did not object, and agreed that it was appropriate for the undersigned to resolve this case by a ruling on the record. See Resp. Response at 1 n.1.

III. ISSUES TO BE DECIDED

The parties agree that the petitioner was diagnosed with Bell's palsy, and thus, they do not dispute diagnosis. However, they dispute causation. Respondent argued that petitioner failed to show by preponderant evidence that the hepatitis B vaccination administered on October 2, 2014 caused petitioner's Bell's palsy. Resp. Response at 12. Therefore, respondent asserts that petitioner is not entitled to compensation under the Vaccine Act. Id.

IV. MEDICAL TERMINOLOGY

Bell's palsy is a peripheral nerve disease involving the facial nerve (seventh cranial nerve)[4] which affects "facial functions and appearance." Pet. Ex. 26 at 1.[5] The clinical presentation of Bell's palsy is characterized by "weak eyebrow lifting, incomplete eye closure, drooping mouth corner, dry eye, loss of taste sensitivity, hyperacusis[6] and ear pain." Id. There are a number of causes for facial nerve palsy, including idiopathic (referred to as Bell's palsy), infection, congenital, trauma, tumors, and others. Id. Bell's palsy refers to those cases where the cause is unknown, and alternative causes have been excluded. Id.

V. FACTUAL SUMMARY

A. Summary of Relevant Facts

The facts are not in dispute. Petitioner, a pharmacist, was 46 years of age when he received his third hepatitis B vaccination,[7] on October 2, 2014, in his left arm. Pet. Ex. 1 at 6. Petitioner's chiropractic records establish that pre-vaccination, he had a history of low back pain, but his medical history is non-contributory as it relates to his Bell's palsy. See generally Pet. Ex. 2.

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[4] Bell's palsy may involve other nerves as well. See A. Greco et al., Bell's Palsy and Autoimmunity, 12 Autoimmunity Rev. 323 (2012). Greco et al. states that, "[i]t has been proposed that Bell's palsy is in fact a polyneuropathy, as the facial paralysis may be associated with involvement of other cranial nerves." Pet. Ex. 19 at 4.

[5] Yang Zhao et al., Advances in Diagnosis and Non-Surgical Treatment of Bell's Palsy, 10 J. Otology 7 (2015).

[6] Hyperacusis is exceptionally acute hearing, the hearing threshold being unusually low. Hyperacusis, Dorland's Online Med. Dictionary, https://www.dorlandsonline.com/dorland/definition?id=23650 (last visited Aug. 25, 2021). It may or may not be accompanied by pain. Id.

[7] The hepatitis B vaccine is given in a series of three doses on a zero, one-month, and six-month schedule. See Pet. Ex. 41 at 2. Petitioner received the ENGERIX-B vaccine. Pet. Ex. 1 at 6.

On October 6, 2014, petitioner presented to neurologist Dr. Shahbuddin Mukardamwala, with weakness of the left side of his face. Pet. Ex. 3 at 1. Petitioner reported that he had received the hepatitis B vaccine the prior Thursday (October 2, 2014), and that the following day, Friday (October 3, 2014), he had a severe headache involving the left postauricular[8] area. Id. By Saturday (October 4, 2014), petitioner was unable to close his left eye and he had numbness of the left side of his face. Id. He sought treatment at a local emergency room, where he was noted to have neuropathic pain. Pet. Ex. 7 at 2. Petitioner denied having any urinary tract infection, upper respiratory infection, fever, or recent travel. Pet. Ex. 3 at 1. Dr. Mukardamwala's physical exam revealed that petitioner was unable to wrinkle the left side of his forehead, that he had left eye closure weakness, and left nasolabial flattening. Id. Dr. Mukardamwala diagnosed petitioner with "left peripheral seventh nerve palsy, likely idiopathic" and prescribed prednisone, Valtrex,[9] Vitamin B12, and pain medication. Id. at 2.

Petitioner presented to Dr. Mukardamwala on October 13, 2014, with worsening of his left postauricular pain. Pet. Ex. 3 at 3. MRI of the brain performed on October 14, 2014 did not show any acute intracranial process. Pet. Ex. 5 at 15. Petitioner was advised to discontinue Valtrex. Pet. Ex. 3 at 3. To address the pain, petitioner underwent an occipital nerve block on October 17, 2014. Id. at 4.

On January 5, 2015, petitioner saw Dr. Mukardamwala for follow-up, and he complained of panic attacks and night terrors. Pet. Ex. 3 at 7. His Bell's palsy had improved—he had a symmetric smile and symmetric forehead wrinkling. Id. He was prescribed Paxil 20 mg to be taken twice daily for anxiety and melatonin at night for sleep. Id. Petitioner returned on February 24, 2015, with complaints of "left facial tightness and facial spasms." Id. at 8. Warm compresses and methocarbamol[10] were prescribed for facial tightness and spasms, and his dose of Paxil was decreased. Id. Petitioner was also referred to psychiatry. Id.

Dr. Salah Qureshi, a psychiatrist, saw petitioner on March 11, 2015. Pet. Ex. 6 at 1. Petitioner reported facial pain, anxiety, and depression. Id. at 4. Dr. Qureshi prescribed Effexor.[11] Id. at 5. Dr. Qureshi continued to see and treat petitioner over a period of several

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[8] The postauricular area is behind or posterior to the auricle, the exterior portion of the ear. Dorland's Illustrated Medical Dictionary 1479 (33d ed. 2020).

[9] Valtrex (valacyclovir) is an antiviral medication used to treat infections with herpes zoster (shingles), herpes simplex genitalis (genital herpes), and herpes labialis (cold sores). Valtrex, RxList, https://www.rxlist.com/valtrex-side-effects-drug-center.htm (last visited Aug. 25, 2021).

[10] Methocarbamol is indicated as an adjunct to rest, physical therapy, and other measures for the relief of discomfort associated with acute, painful musculoskeletal conditions. Methocarbamol, RxList, https://www.rxlist.com/consumer_methocarbamol_robaxin/drugs-condition.htm (last visited Aug. 25, 2021).

[11] Effexor (venlafaxine) is used to treat depression, anxiety, panic attacks, and social anxiety disorder (social phobia). Venlafaxine, RxList, https://www.rxlist.com/consumer_venlafaxine_effexor_effexor_xr/drugs-condition.htm (last visited Aug. 25, 2021).

years. See generally Pet. Ex. 8. On October 20, 2015, Dr. Qureshi diagnosed petitioner with post-traumatic stress disorder ("PTSD"). Id. at 6. In April 2016, petitioner reported that he was going through a divorce, had financial stress, and was caring for his two-year-old daughter. Id. at 8.

On August 25, 2017, petitioner underwent a medical examination for a social security disability determination by Dr. Ron Kirkwood. Pet. Ex. 14 at 3. Dr. Kirkwood noted that petitioner continued to have palsy on the left side of his face, and that it affected his eye. Id.

Petitioner presented to Dr. Raghu Athre on April 25, 2018, complaining of tightness in the left side of his face. Pet. Ex. 11 at 1. Dr. Athre documented that petitioner had "complete facial nerve movement on the left side. . . . [Petitioner's] cosmetic outcome after Bell's palsy [was] excellent." Id.

B. Petitioner's Affidavit

Petitioner executed an affidavit on February 28, 2019. In it, petitioner averred that he received the hepatitis B vaccine at issue on Thursday, October 2, 2014. Pet. Ex. 15 at ¶ 1. Afterward, he experienced pain in his left arm where the vaccine was administered. Id. On the evening of October 2, he had "general malaise and soreness." Id. On Friday morning, October 3, 2014, he opened the pharmacy where he worked. Id. at ¶ 2. His arm was sore, but otherwise, he was fine. Id. That afternoon, he began having a headache. Id. His headache continued and became severe, with "sharp piercing pain behind his left ear, and [his] left eye was mildly burning with flowing tears." Id. On Sunday, October 5, 2014, petitioner's pain, eye burning, and tearing continued. Id. at ¶ 3. When he arrived home after work, and looked in the mirror, he saw that his "face was deformed." Id. His left eye did not blink or close, his mouth could not hold water when he tried to brush his teeth, the left side of his face had no feeling, he was unable to chew food, and his mouth was drooping on the left side. Id. Petitioner "thought he was having a stroke," and so he drove himself to an emergency room. Id.

At the emergency room, petitioner was given medication for his severe headache. Pet. Ex. 15 at ¶ 4. The "sharp piercing pain behind [his] left ear continued for 3-4 months" and did not respond to medical treatment and so petitioner had a nerve block. Id. at ¶ 5. Petitioner also had numbness of his "tongue for approximately six months." Id.

As of the date of the affidavit, petitioner continued to "experience tightness and spasms in the left corner of [his] mouth, the left side of his face, and the top of [his] left eye below [the] eyebrow." Pet. Ex. 15 at ¶ 6. Petitioner also has fatigue and spasms of his left eye. Id. He avoids smiling because his smile is not symmetric. Id.

Due to his Bell's palsy, petitioner averred that he "developed chronic anxiety, depressive episodes, nightmares due to panic attacks at night, and chronic insomnia." Pet. Ex. 15 at ¶ 7. He further alleged that he has been "diagnosed with PTSD and chronic insomnia," and that he sees a psychiatrist and takes medication to treat these conditions. Id.

C. Expert Reports

1. Petitioner – Dr. Marcel Kinsbourne

a. Background and Qualifications

Dr. Kinsbourne earned his B.A. from Christ Church at Oxford University. Pet. Ex. 27 at 1. He earned his Bachelor of Medicine and Bachelor of Surgery from Oxford University Medical School. Id. He also earned an M.A. and a Doctor of Medicine from Oxford University. Id. From 1974 to 1980, he was the Senior Staff Physician at the Hospital for Sick Children in Toronto, and also the Director of the Behavioral Neurology Unit at Boston University's Sargent College of Allied Health Professions from 1973 to 1982. Id. at 2. Dr. Kinsbourne also served as the Director of the Behavioral Neurology Department at the Eunice Kennedy Shriver Center from 1980 to 1991. Id. Throughout his career, Dr. Kinsbourne has held teaching positions at various institutions. Id. Dr. Kinsbourne has served and is currently serving on a number of editorial boards, including Archives of Clinical Neuropsychology and Cognitive Neuropsychiatry. Id. at 3. He has authored or co-authored more than 400 publications. Id. at 5-39.

b. Opinion

Dr. Kinsbourne agreed with petitioner's treating physicians that petitioner had Bell's palsy. He explained that Bell's palsy is "either partial or complete isolated ('mononeuritic') paralysis of the seventh facial nerve." Pet. Ex. 16 at 3. The onset is acute, and the paralysis peaks two to three days after onset, and then may gradually decrease, and even completely resolve. Id. Symptoms may also include postauricular pain, as well as changes in sensation of the face and taste perception. Id.

i. Althen Prong One: Medical Theory of Causation

Dr. Kinsbourne proposed an innate immune system theory involving the Toll-like receptor ("TLR") system, resulting in the release of proinflammatory cytokines, to explain how the hepatitis B vaccine can cause Bell's palsy.[12] Pet. Ex. 16 at 5.

The first tenet of petitioner's theory is based on onset as it relates to the immune system. Dr. Kinsbourne opined that the "brief temporal interval between [] vaccination and [] onset of neuropathy" implicates the innate immune system, "which is activated almost immediately after an immune challenge by . . . vaccination." Pet. Ex. 16 at 5. Due to the short onset period, Dr. Kinsbourne opined that the often-cited adaptive immune system theory of molecular mimicry is not applicable here. Id.

The Greco et al. article, referenced by Dr. Kinsbourne, provides an overview of current knowledge about the causes of Bell's palsy. See Pet. Ex. 19. While there are suggested

[12] Dr. Kinsbourne also discussed autoimmune causes of Bell's palsy. However, this Ruling focuses on the theory based on proinflammatory cytokines.

etiologies and mechanisms, the authors emphasized that the cause of the condition is not known. Id. at 3. They opined that viral infection and immune causal mechanisms may be at play.[13] Id. at 3-4.

The second tenet of Dr. Kinsbourne's theory of innate immune system response is that the hepatitis B vaccination "activated the TLRs of the innate immune system, which in turn cause[d] the release of proinflammatory cytokines." Pet. Ex. 16 at 5. Proinflammatory cytokines are accessible to the peripheral nerves (like the facial nerve) because "the blood-nerve-barrier is thinner and more permeable than the blood-brain-barrier." Id. Dr. Kinsbourne stated that the "peripherally produced cytokines caused headache" and demyelination of the seventh cranial nerve. Id.

An article by Zhang and Lu, which discussed the TLR system as it relates to hepatitis B viral infections supports this aspect of Dr. Kinsbourne's proposed theory. Pet. Ex. 35.[14] They explained that TLRs are "a group of highly conserved molecules that play a critical role in the recognition of pathogen-associated molecular patterns (PAMPs) and in the activation of innate immune responses to infectious agents." Id. at 2. TLRs sense pathogen associated molecule patterns and activate antiviral mechanisms, which include "the production of antiviral effectors like interferons [] and proinflammatory cytokines," in an attempt to control the hepatitis B infection.[15] Id. at 1. These proinflammatory cytokines include IL-6, IL-8, and TNF-α. Id. at 2-3.

In addition to being found in patients with hepatitis B viral infections, proinflammatory cytokine levels have been found to be significantly elevated in patients with Bell's palsy. Pet. Ex. 37.[16] In the Yilmaz et al. study, levels of proinflammatory cytokines (IL-6, IL-8, and TNF-α) were significantly higher in patients with Bell's palsy than in controls. Id. at 1. The authors were not able to determine whether the elevated levels were pathogenic or represented a response to the underlying pathology. Id. However, they postulated that proinflammatory cytokines played a role in generating or perpetuating inflammation. Id. at 3. While Yilmaz et al. do not discuss vaccines, they do suggest an inflammatory mechanism. They question, for example,

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[13] The authors explained that while the cause of Bell's palsy is not known, there are two infectious pathogens for which the evidence of causation is "quite sound." Pet. Ex. 19 at 3. "These include *Borrelia burgdorferi* in Lyme disease and [herpes] zoster in Ramsay-Hunt syndrome." Id.

[14] Ejuan Zhang & Mengji Lu, Toll-Like Receptor (TLR)-Mediated Innate Immune Responses in the Control of Hepatitis B Virus (HBV) Infection, 204 Med. Microbiology Immunology 11 (2015).

[15] "Binding of TLR agonist to their receptors initiates the activation of complex networks of intracellular signal transduction pathways to coordinate the inflammatory response." Pet. Ex. 35 at 2.

[16] Mustafa Yilmaz et al., Serum Cytokine Levels in Bell's Palsy, 197 J. Neurological Sci. 69 (2002).

whether an inflammatory mechanism may be caused by the herpes simplex virus ("HSV"). Id. at 1. And significantly, they observed that in Bell's palsy, "there is an inflammatory reaction compressing the facial nerve in the fallopian canal." Id. at 3. The Yilmaz et al. authors further stated that it is "likely that there is demyelination in Bell's palsy."[17] Id. "Since there is demyelination . . . the significantly elevated concentrations of [the cytokine] TNF-α in serum indicate an inflammatory component of the virus-induced demyelination." Id.

The third tenet of petitioner's theory is based on the anatomy of the area through which the facial nerve travels as it innervates the muscles of the face. The relevance of the anatomy is discussed by Jain and Kumar, cited by Dr. Kinsbourne in support of his inflammatory mechanism. See Pet. Ex. 20.[18] The facial nerve travels through the fallopian canal, which provides a bony covering. Id. at 2. While the bony canal protects the nerve, it can also make the nerve "vulnerable to palsy due to entrapment neuropathy." Id. Like Yilmaz et al., Jain and Kumar suggest that the probable mechanism of Bell's palsy is compression of the facial nerve "secondary to any type of inflammatory edema." Id. at 3. "Initially, inflammation causes only a temporary loss of sensory or motor function, but it may result in permanent nerve degeneration due to compression in the fallopian canal." Id.[19]

In addition to citing papers that discuss the TLR system and proinflammatory cytokines as it relates to his proposed theory of inflammation, as well as articles that explain the relevant anatomical considerations, Dr. Kinsbourne also cited papers showing that Bell's palsy has been reported as an adverse reaction following vaccination.

In Zhou et al.,[20] the Centers for Disease Control and Prevention ("CDC") reviewed reports from the Vaccine Adverse Event Reporting System ("VAERS") to evaluate the risk of Bell's palsy following the administration of flu vaccines given by the parenteral route (injection) from 1991 to 2001. Pet. Ex. 44 at 1. They found 197 reports of Bell's palsy. Id. Of these, 145 received a flu vaccine not given in combination with other vaccines, while the balance also received other vaccines. Id. at 3. The authors concluded that the "study provided multiple lines of evidence for a signal that Bell's palsy may be associated with the [flu] vaccine[]." Id. at 4.

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[17] Demyelination is the destruction, removal, or loss of the myelin sheath of a nerve or nerves. Dorland's Illustrated Medical Dictionary 493 (33d ed. 2020).

[18] Shraddha Jain & Sunil Kumar, Bell's Palsy: A Need for Paradigm Shift?, 1 Annals Otology & Neurotology 1 (2018).

[19] Jain and Kumar state, "[a]mong all cranial nerves, [the] facial nerve is the only nerve that travels in a bony canal. Nerve dysfunction may result more easily as the facial nerve swells within the confines of the noncompliant bony facial canal. Endoneural pressure then increases, and neural vasculature is compressed, leading to ischemia . . . and axonal degeneration." Pet. Ex. 20 at 6.

[20] Weigong Zhou et al., A Potential Signal of Bell's Palsy After Parenteral Inactivated Influenza Vaccines: Reports to the Vaccine Adverse Event Reporting System (VAERS)-United States 1991-2001, 13 Pharmacoepidemiological Drug Safety 505 (2004).

Mutsch et al. reported 46 cases of Bell's palsy associated with the intranasal flu vaccine after it was introduced in Switzerland in 2000. Pet. Ex. 21 at 1.[21] The risk of Bell's palsy after intranasal vaccination was 19 times higher than the risk seen in control subjects. Id. at 2. There were also reports of Bell's palsy in those who received the vaccine parenterally (by injection).[22] In conclusion, the authors reported there was "strong evidence that an inactivated intranasal [flu] vaccine caused Bell's palsy," resulting in the Swiss government discontinuing use of the vaccine. Pet. Ex. 16 at 4 (citing Pet. Ex. 21 at 1). Although the authors concluded there was "strong evidence" of vaccine causation with respect to the intranasal flu vaccination, they did not reach any conclusions as to the causal mechanism. Pet. Ex. 21 at 9.

Due to concerns raised by the Zhou et al. and Mutsch et al. studies, a study of the incidence of Bell's palsy following flu parenteral vaccination was undertaken by Stowe et al. in the United Kingdom using the General Practice Research Database for the period of 1992 through 2005. Pet. Ex. 23 at 1.[23] The study did not find evidence of an increased risk, except for an increase on the day of vaccination. Id. The authors stated that the increase was "unlikely to represent a causation association on the grounds of biological plausibility." Id. at 3. They interpreted the increase as an "opportunistic recording of cases at the time of vaccination." Id.

Specific to the hepatitis B vaccine, Dr. Kinsbourne cited an article by Shaw et al., which reported 10 cases of Bell's palsy following hepatitis B vaccination. Pet. Ex. 16 at 4 (citing Pet. Ex. 40 at 1).[24] Shaw et al. reported on neurological adverse events that occurred between 1982 and 1985 related to the "new plasma-derived hepatitis B vaccine." Pet. Ex. 40 at 1. During that time frame, 41 neurologically adverse events were reported, including 10 cases of Bell's palsy. Id. "[N]o conclusive epidemiologic association could be made between any neurologic adverse event and the vaccine." Id.

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[21] Margot Mutsch et al., Use of the Inactivated Intranasal Influenza Vaccine and the Risk of Bell's Palsy in Switzerland, 350 N. Eng. J. Med. 896 (2004).

[22] The authors state that "27 of the 182 patients with Bell's palsy (14.8%) . . . had been immunized with [the] parenteral [flu] vaccine." Pet. Ex. 21 at 6. With regard to this data, the authors stated that "there was essentially no risk of Bell's palsy after receipt of the traditional, parenteral vaccine." Id. These findings were commented on in the Stowe et al. paper as follows: "Although [the Mutsch et al.] study showed no association very few patients had received the parenteral vaccine and the study design had a number of limitations and biases that may have led to missing a true association." Pet. Ex. 23 at 1.

[23] Julia Stowe et al., Bell's Palsy and Parenteral Inactivated Influenza Vaccine, 2 Hum. Vaccines 110 (2006).

[24] Frederic E. Shaw et al., Postmarketing Surveillance for Neurologic Adverse Events Reported After Hepatitis B Vaccination: Experience of the First Three Years, 127 Am. J. Epidemiology 337 (1988).

Dr. Kinsbourne also referenced the hepatitis B vaccine package insert for the vaccine administered to petitioner, ENGERIX-B. See Pet. Ex. 41. Section 6.2, entitled "Postmarketing Experience," stated, "[t]he following adverse reactions have been identified during post-approval use of ENGERIX-B. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to the vaccine." Id. at 8. Following the above statement, under the subsection for nervous system disorders, "Guillain-Barre syndrome and Bell's palsy" are listed as adverse reactions. Id.

Lastly, Dr. Kinsbourne cited a report by Alp et al., describing a case of Bell's palsy following hepatitis B vaccination in a two-year-old child. Pet. Ex. 17 at 1.[25] The child had no upper respiratory tract infection, her MRI of the brain was normal, and testing for viral causes was negative. Id. at 1. No alternative cause was suggested based on the diagnostic workup. Id. "The sole cause suspected was the vaccination against hepatitis B six days before diagnosis of the disease." Id. at 2.

ii. Althen Prong Two: Logical Sequence of Events

It is Dr. Kinsbourne's opinion that petitioner's hepatitis B vaccine caused his Bell's palsy, and that his residual deficits and psychological problems are sequelae of his injury. Pet. Ex. 16 at 6. Dr. Kinsbourne opined that the first manifestation of petitioner's Bell's palsy was the left-sided postauricular headache that he experienced the day after vaccination. Pet. Ex. 16 at 4. The following day, petitioner had "facial muscle weakness." Id. While petitioner's palsy resolved, Dr. Kinsbourne explained that the long-term sequalae included abnormal movements of the left side of his face ("synkinesis") and left eyelid closure with voluntary contraction of the left-sided facial muscles. Id. Synkinesis "is attributed to aberrant reinnervation of the facial muscles during recovery" from Bell's palsy. Id.

Petitioner had a diagnostic workup to determine the cause of his condition, but no other causes were revealed. Pet. Ex. 16 at 1-2. Potential alternative causes such as viral infections (HSV and human herpes virus-6) were not found. Id. There was no evidence of any alternative cause set forth in the medical records. Id. at 6.

Further, Dr. Kinsbourne noted that petitioner's treating neurologist, Dr. Mukardamwala, prescribed prednisone, which suggested that he presumed the cause was immune in nature.[26] Pet. Ex. 28 at 1.

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[25] Handan et al., Bell's Palsy as a Possible Complication of Hepatitis B Vaccination in a Child, 27 J. Health Population & Nutrition 707 (2009).

[26] Dr. Kinsbourne also stated that Dr. Mukardamwala did not prescribe an antiviral agent, which Dr. Kinsbourne indicated to mean that Dr. Mukardamwala did not believe the petitioner's Bell's palsy was caused by a viral infection. Pet. Ex. 28 at 1. However, Dr. Kinsbourne's understanding was erroneous. The medical records show that Dr. Mukardamwala did prescribe Valtrex, an antiviral medication, for seven days, but stopped it after day five due to fatigue. Pet. Ex. 3 at 2-3.

In his affidavit, petitioner described the psychological distress that he has experienced due to his Bell's palsy. See Pet. Ex. 15. Dr. Kinsbourne stated that the medical literature is replete with articles about "the psychological impact of facial palsies." Pet. Ex. 16 at 5. He cited Baugh et al., who noted that "patients with facial paralysis experience psychosocial dysfunction and diminished quality of life as a result of their appearance." Id. at 6 (citing Pet. Ex. 43 at 21).[27] Fu et al. stated that even when the paralysis resolves, "social and psychological problems will remain." Id. (citing Pet. Ex. 18 at 5).[28]

iii. Althen Prong Three: Proximate Temporal Relationship

Dr. Kinsbourne opined that the first indication of petitioner's Bell's palsy was "the left postauricular headache that began one day after the vaccination." Pet. Ex. 16 at 4. Dr. Kinsbourne explained that this type of headache often heralds the onset of the condition, and that it can occur before, during, or after the facial muscles exhibit weakness. Id.

The brief interval between vaccination and onset implicates the innate immune system, which Dr. Kinsbourne asserted is activated "almost immediately after an immune challenge by an infection or vaccination." Pet. Ex. 16 at 5. Dr. Kinsbourne's assertion is supported by an article authored by Talaat et al., which reported rapid responses of cytokines following the inactivated flu vaccination. Resp. Ex. D-2 at 1.[29] Cytokine responses are evident as early as three hours post-vaccination, and peak at 24 hours. Id. While the hepatitis B vaccine was not studied, the data indicated that peripheral cytokines begin to change in the hours immediately following vaccination. Id. Similar findings were reported by Valdez et al. after the pneumococcal polysaccharide vaccine. See Pet. Ex. 30.[30]

2. Petitioner – Dr. Vera S. Byers

a. Background and Qualifications

Dr. Byers works for a consulting company, Immunology Inc. Pet. Ex. 29 at 1. At Immunology Inc. she designs, supervises, and runs epidemiologic studies on populations exposed to carcinogenic environmental chemicals. Id. She is the principal medical witness in

[27] D.F. Baugh et al., Clinical Practice Guideline: Bell's Palsy, 149 Otolaryngology–Head & Neck Surgery S1 (2013).

[28] L. Fu et al., Psychological Distress in People with Disfigurement from Facial Palsy, 25 Eye 1322 (2011).

[29] Kawsar R. Talaat et al., Rapid Changes in Serum Cytokines and Chemokines in Response to Inactivated Influenza Vaccination, 12 Influenza & Other Respiratory Viruses 202 (2018).

[30] Hernan Valdez et al., Levels of Proinflammatory Cytokines in Plasma After Pneumococcal Immunization in Human Immunodeficiency Virus Type 1-Infected Patients, 6 Clinical & Diagnostic Lab'y Immunology 427 (1999).

over 30 cases, involving over 3000 plaintiffs. Pet. Ex. 42 at 1-2. She is board-certified in Internal Medicine and has a Ph.D. in basic immunology awarded in 1969 from the University of California Los Angeles. Pet. Ex. 29 at 1. Dr. Byers received her M.D. from University California San Francisco ("UCSF") followed by a three-year residency in clinical immunology at UCSF. Id. She was an Adjunct Professor of Immunodermatology at UCSF from 1974 to 2008. Id. Dr. Byers has authored or co-authored over 100 journal articles regarding immunology and cancer research. Pet. Ex. 42 at 6-19.

b. Opinion

Dr. Byers agreed with Dr. Kinsbourne that petitioner had an immune-mediated Bell's palsy. Pet. Ex. 29 at 1. She opined that the hepatitis B vaccination that petitioner received was "the cause or a substantial contributor to his Bell's palsy." Id.

Dr. Byers explained that "the understanding of the role of the innate immune system in various infectious diseases is relatively new. [TLRs] are now recognized as the first line of anti-viral immunity." Pet. Ex. 29 at 2. Thus, she, like Dr. Kinsbourne, posited an innate immune system theory involving the TLR system and the production of proinflammatory cytokines.

Citing a paper by Zhang and Lu, Dr. Byers summarized the role of TLR responses to hepatitis B viral infection. Pet. Ex. 29 at 2 (citing Pet. Ex. 35). The authors stated that while the "contribution of innate immune responses to viral control is recognized," it is "not fully understood." Pet. Ex. 35 at 1. In the context of the innate immune response to infections, and specifically infection induced by hepatitis B, Zhang and Lu described how "TLRs initiate intracellular signaling pathways to induce interferons and a cascade of pro-inflammatory cytokines." Pet. Ex. 29 at 2. The authors stated that experimental data indicate that the hepatitis B virus interacts with live cells and "induces the production of IL-6," and within 3 hours proinflammatory cytokines (IL-1, IL-6, IL-8, and TNF-α) are released. Pet. Ex. 35 at 3.

Dr. Byers extended the discussion to show that like the hepatitis viral infection, the recombinant hepatitis B vaccine also evokes cytokine responses. Pet. Ex. 29 at 2. In support of this aspect of her opinion, she cited several studies, including those by Dammermann et al., Campbell, and Chen et al. Collectively, these studies discuss TLRs in different contexts. Dammermann et al. studied the "sensitivity and specificity of a hepatitis cytokine release assay." Pet. Ex. 38 at 1.[31] Campbell discussed clinical testing of surface antigen adjuvant 1018 (a TLR agonist used in a B vaccine HEPLISAV-B). Pet. Ex. 36 at 2.[32] And Chen et al. discussed the genes of TLRs and their "involvement in antigen recognition and immune response activation."

[31] Werner Dammermann et al., CpG Oligonucleotides Increase HBV-Specific Cytokine Responses in Whole Blood and Enhance Cytokine Release Assay Sensitivity, 248 J. Virological Methods 195 (2017).

[32] John D. Campbell, Development of the CpG Adjuvant 1018: A Case Study, in Vaccine Adjuvants: Methods and Protocols, Methods in Molecular Biology 15 (Christopher B. Fox ed., 2017).

Pet. Ex. 31 at 2.[33] Collectively, these articles appear to bolster Dr. Byers's statement that TLRs play a role in the induction of proinflammatory cytokines, in the interplay between the innate and adaptive immune systems, and "influence the efficacy of hepatitis B vaccination." Id.

Like Dr. Kinsbourne, Dr. Byers also cited a study showing that patients with Bell's palsy have elevated proinflammatory cytokines, including IL-6, IL-8, and TNF-α. Pet. Ex. 29 at 2 (citing Pet. Ex. 37). She also cited studies to establish that vaccines cause an increase in these proinflammatory cytokines. Id. Valdez et al., for example, "reported a 2 fold increase in IL-6 after the pneumococcal polysaccharide vaccination." Id. at 1 (citing Pet. Ex. 30 at 1). And Talaat et al. reported an elevation of cytokines within seven hours of administration of the flu vaccination. Id. at 3 (see Resp. Ex. D-2 at 1).

Dr. Byers also cited a case of Bell's palsy after hepatitis B vaccination in a 26-year-old, reported by Paul and Stassen. Pet. Ex. 29 at 2 (citing Pet. Ex. 34).[34] Onset occurred six hours after vaccination. Pet. Ex. 34 at 1. The vaccinee had no signs or symptoms of infection, and no alternative cause was suggested. Id. She received her vaccine in her left deltoid, and she had no local tenderness or infection at the vaccination site. Id. MRI of the brain did not reveal any abnormalities. Id. Paul and Stassen stated that "although the [hepatitis B] vaccine is among the safest of all vaccines, it has been associated with adverse effects." Id. at 2. The authors concluded that the most probable cause of her Bell's palsy was the hepatitis B vaccine. Id. at 3.

3. Respondent – Dr. Subramaniam Sriram

a. Background and Qualifications

Dr. Sriram is board-certified in Internal Medicine and Neurology. Resp. Ex. A at 1. He is Professor of Neurology and Microbiology Immunology and head of the Multiple Sclerosis ("MS") Clinic at Vanderbilt Medical Center, where he takes care of over 1000 patients with MS. Id. He obtained a Bachelor of Medicine and a Bachelor of Surgery from the University of Madras in Madras, India. Resp. Ex. B at 1. He then served as an intern and resident at Wayne State University and completed a residency in neurology at Stanford University, where he also served as chief resident and eventually completed a post-doctoral fellowship in neuroimmunology. Id. Dr. Sriram has published numerous peer-reviewed medical articles regarding demyelinating diseases of the central nervous system. Id. at 9-19.

b. Opinion

[33] Jie Chen et al., Toll-Like Receptors and Cytokines/Cytokine Receptors Polymorphisms Associate with Non-response to Hepatitis B Vaccine, 29 Vaccine 706 (2011).

[34] R. Paul & L.F.A. Stassen, Transient Facial Nerve Paralysis (Bell's Palsy) Following Administration of Hepatitis B Recombinant Vaccine: A Case Report, 216 British Dental J. 69 (2014).

Dr. Sriram agreed with Dr. Kinsbourne and Dr. Byers as to diagnosis. He stated, "[t]here is no question as to the diagnosis of the [petitioner]. He had peripheral cranial nerve VII neuropathy, also known as Bell's palsy." Resp. Ex. A at 3.

i. Althen Prong One: Medical Theory of Causation

While he agreed with petitioner's diagnosis of Bell's palsy, Dr. Sriram disagreed that there is evidence that the hepatitis B vaccine "relates to the development" of the illness. Resp. Ex. A at 4. Specifically, he disagreed with Dr. Kinsbourne's proposed mechanism of innate immune system activation by TLRs. Id. at 5. He opined that there "are no reports that the hepatitis B virus recombinant protein can and/or does act like a [TLR] agonist and does so within 24 hours." Id. Further, he stated that there is "no evidence that cytokines released by [TLR] activation pathway can specifically target the seventh cranial nerve (and avoid all of the nerves) and cause inflammatory demyelination." Id.

Dr. Sriram contended that Dr. Kinsbourne confused "activation of the immune pathway by live and inactivated viruses and that of a cell surface protein belonging to a virus." Resp. Ex. C at 2. He further asserted that there is no "evidence to support the notion that Hepatitis B surface protein activates the TLR pathway" or that "[t]he resultant autoimmune response to hepatitis cell surface protein targets an as yet undefined self-antigen in peripheral cranial [nerve]."[35] Id.

Dr. Sriram contended that "[t]he prevailing opinion is that a direct infection [of the] nerve is [the] most likely cause" of Bell's palsy, although he noted that there is a dispute about whether the illness is caused by a single virus or a number of different viruses. Resp. Ex. A at 4. Some cases are attributed to "ischemic mononeuropathy of other cranial nerves in patients with diabetes." Id. at 3. In most cases of Bell's palsy, Dr. Sriram stated the cause is not known, and thus referred to as idiopathic. Id. In cases where the cause is unknown, Dr. Sriram believed the most likely case is HSV type 1 ("HSV-1"), noting "the current consensus opinion on Bell's palsy is that it is a viral infection of the seventh cranial nerve most likely due to the HSV-1 virus that is reactivated."[36] Id. at 4. "The disease probably reflects virus reactivation from latency in the geniculate ganglia, rather than primary infection." Id.

In reference to the Mutsch et al. article cited by petitioner regarding the incidence of Bell's palsy following the intranasal flu vaccine, Dr. Sriram disagreed that the findings are applicable to vaccines given by injection (parenteral as opposed to nasally). Resp. Ex. C at 1. He further disagreed that findings relative to the flu vaccine provide evidence of causation for the hepatitis B vaccine. Id.

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[35] Dr. Sriram also stated that Dr. Kinsbourne failed to provide evidence that the hepatitis B vaccine (surface protein) "targets [a] . . . self-antigen in peripheral cranial [nerve]." Resp. Ex. C at 2. This comment appears to implicate molecular mimicry, which Dr. Kinsbourne does not believe is applicable in this case due to the short onset. Pet. Ex. 16 at 5.

[36] Dr. Sriram also stated that the "prevailing opinion is that a direct infection" is the cause of Bell's palsy. Resp. Ex. A at 4.

ii. Althen Prong Two: Logical Sequence of Events

Dr. Sriram did not opine as to any alternative causes of petitioner's Bell's palsy. Although he opined that Bell's palsy is thought to be caused by direct infection or reactivation, he did not suggest that petitioner had a primary infection, or that his Bell's palsy was caused by reactivation of a virus. Resp. Ex. C at 2.

iii. Althen Prong Three: Proximate Temporal Relationship

Dr. Sriram agreed with Dr. Kinsbourne that petitioner's symptoms occurred within 24 hours of vaccination. Resp. Ex. A at 3. However, he disagreed that the hepatitis B vaccine can cause inflammatory demyelination of the seventh cranial nerve through the mechanism posited by petitioner's experts within 24 hours. Id. at 5; Resp. Ex. C at 2.

4. Respondent – Dr. Harry W. Schroeder, Jr.

a. Background and Qualifications

Dr. Schroeder is a Professor of Medicine, Microbiology, and Genetics at the School of Medicine at the University of Alabama at Birmingham. Resp. Ex. D at 1. Dr. Schroeder is board-certified in both internal medicine and genetics. Id. He received his bachelor's degree from Texas A&M University, before receiving both his medical degree and Ph.D. from Baylor College of Medicine. Resp. Ex. E at 1. Dr. Schroeder then completed his internship and residency at the University of Kentucky Medical Center. Id. at 2. Since 2001, he has been an editor of the textbook Clinical Immunology: Principles and Practices, which is now in the process of publishing its 6th edition. Resp. Ex. D at 1.

b. Opinion

Consistent with the other experts, Dr. Schroeder agreed with petitioner's diagnosis of Bell's palsy. Resp. Ex. D at 5. He emphasized that Bell's palsy is an idiopathic condition because the cause is not certain. Id. The condition occurs in 15 to 30 per 100,000 persons, and the peak incidence is seen in those ages 15 to 45 years of age. Id. at 6. Dr. Schroeder further explained that the underlying mechanism of the illness remains unknown, but he agreed there may be immune causes. Id.

i. Althen Prong One: Medical Theory of Causation

Unlike Dr. Sriram, Dr. Schroeder agreed with petitioner's experts "that activation of TLR and other components of the innate immune system typically occurs during vaccination." Resp. Ex. D at 9. He also agreed with Dr. Byers' summary of the "role of TLRs in initiating inflammation, evoking cytokine responses, and playing a role in the adjuvant pathways that are activated by the hepatitis vaccine." Id. at 10. Dr. Schroeder noted that instead of invoking a "specific autoimmune reaction due to molecular mimicry, Dr. Byers raises the specter of cytokine activation leading to neurologic damage." Id. at 13.

The causal mechanism proposed by petitioner, is described by Dr. Schroeder as follows:

> Reactogenicity[37] refers to a subset of reactions that occur soon after vaccination, and are a physical manifestation of the inflammatory response to vaccination, which includes cytokine release after activation of [TLR]. As noted by Drs. Kinsbourne and Byers, activation of TLR leads to the synthesis and release of pyrogenic cytokines such as IL-1, IL-6, and TNF-α in the bloodstream, and thus mimics the response to natural infection. Activation of the innate immune system promotes the release of additional inflammatory mediators including chemokines and cytokines, activation of complement, and cellular recruitment. These phenomena are crucial for triggering the adaptive immune system, and can have both local and systemic effects. Local effects include pain, redness[,] and swelling at the site of injection. The mediators and products of inflammation released into the circulation can also cause general systemic side effects such as fever, fatigue, and headache.

Resp. Ex. D at 13.

According to Dr. Schroeder, "the search for a mechanism [for Bell's palsy] has been the subject of research for decades, with the underlying cause still remaining unclear despite several proposed theories." Resp. Ex. D at 6. The proposed theories include, 1) "cell-mediated autoimmune mechanism against myelin basic protein;" 2) "autoimmune demyelinating cranial neuritis . . . (mononeuritis variant of Guillain-Barre Syndrome);" and 3) "autoimmune reaction against peripheral nerve myelin components [are] a result of viral infection or the reactivation of a latent virus." Resp. Ex. D at 6.

He stated that treatment with prednisone is effective, as it may "reduce inflammation and edema, or [] help immunosuppress an autoimmune reaction." Resp. Ex. D at 6.

Dr. Schroeder acknowledged the studies cited by petitioner that reported the incidence of Bell's palsy following flu vaccination (Zhou and Stowe et al.), noting that in Stowe et al., the authors attributed the increased incidence on the day of vaccine administration as an "opportunistic recording of cases." Resp. Ex. D at 7 (citing Pet. Ex. 23 at 1).

Dr. Schroeder also acknowledged the medical literature relevant to the hepatitis B vaccination, cited by Dr. Kinsbourne. Resp. Ex. D at 8. Dr. Schroeder noted that Khamaisi et al. reported that hepatitis B vaccination was associated with Guillain-Barre syndrome ("GBS"). Id.[38] He also cited the case of Bell's palsy following the hepatitis B vaccination reported by Alp et al. Id. (citing Pet. Ex. 17). But he disagreed that the Shaw et al. paper provided any support,

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[37] In referencing the concept of reactogenicity, Dr. Schroeder cited the text by Hervé et al. See Resp. Ex. D at 15 (Caroline Hervé et al., The How's and What's of Vaccine Reactogenicity, 39 NPJ Vaccines 1 (2019)).

[38] Khamaisi et al. was not filed into the record.

and inferred that the incidence of Bell's palsy following vaccination did not exceed the expected baseline numbers. Id. (citing Pet. Ex. 40 at 1).

Dr. Schroeder recognized the fact that the hepatitis B vaccine manufacture's package insert identified an association between the hepatitis B vaccine and Bell's palsy, but he noted that "the basis of this association was not given." Resp. Ex. D at 8.

While Dr. Schroeder agreed with and acknowledged many of Dr. Kinsbourne's statements and opinions, he seemed critical of the fact that Dr. Kinsbourne rejected the adaptive immune system mechanism of molecular mimicry, a mechanism that has been suggested for both GBS and Bell's palsy. Resp. Ex. D at 8. Dr. Schroeder stated, "Dr. Kinsbourne thus demolished the proposed link between vaccine administration and an autoimmune activation of the adaptive immune system as the mechanism underlying the onset of Bell's palsy in the petitioner . . . and then turned to that portion of the immune system that is activated within hours of challenge, the innate immune system." Id. Dr. Schroeder called this a "speculative [] hypothesis," not based on experimental studies or epidemiology. Id.

With regard to the literature cited by Dr. Byers, Dr. Schroeder agreed that the Valdez et al. and Talaat et al. studies reported an increase in proinflammatory cytokines following the administration of the pneumococcal polysaccharide and flu vaccines. Resp. Ex. D at 11-12. However, he noted that neither article referenced the hepatitis B vaccine. Id.

Dr. Schroeder did not consider the findings by Yilmaz et al. to be "conclusive evidence," since they could not distinguish whether the elevated cytokines played a role in the pathogenesis of the disease. Resp. Ex. D at 10. As for the case report by Paul and Strassen, Dr. Schroeder argued that "association does not prove causation." Id. at 11. He concluded his comments about the literature by stating that the epidemiology does not support an association between the hepatitis B vaccine and Bell's palsy, "much less causation." Id. at 12. Generally, Dr. Schroeder opined that the papers cited by Dr. Byers "include[ed] multiple cautionary statements by the authors," and none of them offered support for how "a local inflammatory event" can occur due to a "generalized elevation of cytokines." Id. at 14.

ii. Althen Prong Two: Logical Sequence of Events

According to Dr. Schroeder, after vaccination, petitioner developed "local signs and symptoms of inflammation at the [vaccine] injection site." Resp. Ex. D at 13. Petitioner also had "mild systemic effects including malaise, soreness[,] and mild headache." Id. Dr. Schroeder opined that these symptoms were consistent with "the effect of local activation of the innate immune system . . . includ[ing] activation of [TLR] . . . which can be attributed to the release of cytokines and other mediators." Id. However, Dr. Schroeder contended that petitioner's systemic reaction "resolved within 24 hours of [] vaccination, which is common." Id. He did not believe that any of the symptoms petitioner experienced after that, including the periauricular headache, were vaccine-related. Id. Dr. Schroeder opined that the "activation of the innate system as the cause of this local, unilateral event at a distance from the site of injection is interesting speculation." Id. Dr. Schroeder opined that the "only association between these two

events [vaccination and Bell's palsy] appears to be a temporal coincidence and thus most likely due to chance alone." Id. at 15.

Dr. Schroeder did not opine as to any alternative causes of petitioner's Bell's palsy. He stated that "the lack of an alternative causation in [petitioner's] case could be considered to be 'par for the course,' i.e., another reflection of the fact that at present we do not know with certainty what the pathogenetic cause of Bell's palsy might be and thus we placed it in the idiopathic (i.e., we don't know) category." Resp. Ex. D at 10.

iii. Althen Prong Three: Proximate Temporal Relationship

Dr. Schroeder agreed with Dr. Kinsbourne that petitioner's symptoms occurred within 24 hours of vaccination. Resp. Ex. D at 10. Likewise, Dr. Schroeder agreed that there was a temporal association between petitioner's vaccination and his Bell's palsy. Id. However, he did not believe there was any evidence that the hepatitis B vaccine can cause inflammatory demyelination of the seventh cranial nerve through the mechanism posited by petitioner's experts within 24 hours. Id. at 14. He asserted that activation of the TLR system triggers "activation of the adaptive immune system involving cell mediated immunity (T cells) and humoral immunity (B cells and their antibody products) . . . which is attributed to molecular mimicry and takes days, not hours, to develop." Id. at 9. Thus, Dr. Schroeder concluded the timeframe of onset here is too short. Id. at 14. He attributed the temporal association between vaccination and onset of petitioner's Bell's palsy to "chance alone." Id. at 15.

VI. DISCUSSION

A. Standards for Adjudication – Causation

The Vaccine Act was established to compensate vaccine-related injuries and deaths. § 10(a). "Congress designed the Vaccine Program to supplement the state law civil tort system as a simple, fair and expeditious means for compensating vaccine-related injured persons. The Program was established to award 'vaccine-injured persons quickly, easily, and with certainty and generosity.'" Rooks v. Sec'y of Health & Hum. Servs., 35 Fed. Cl. 1, 7 (1996) (quoting H.R. Rep. No. 908 at 3, reprinted in 1986 U.S.C.C.A.N. at 6287, 6344).

Petitioner's burden of proof is by a preponderance of the evidence. § 13(a)(1). The preponderance standard requires a petitioner to demonstrate that it is more likely than not that the vaccine at issue caused the injury. Moberly v. Sec'y of Health & Hum. Servs., 592 F.3d 1315, 1322 n.2 (Fed. Cir. 2010). Proof of medical certainty is not required. Bunting v. Sec'y of Health & Hum. Servs., 931 F.2d 867, 873 (Fed. Cir. 1991). The petitioner need not make a specific type of evidentiary showing, i.e., "epidemiologic studies, rechallenge, the presence of pathological markers or genetic predisposition, or general acceptance in the scientific or medical communities to establish a logical sequence of cause and effect." Capizzano v. Sec'y of Health & Hum. Servs., 440 F.3d 1317, 1325 (Fed. Cir. 2006). Instead, petitioner may satisfy his burden by presenting circumstantial evidence and reliable medical opinions. Id. at 1325-26.

In particular, petitioner must prove that the vaccine was "not only [the] but-for cause of the injury but also a substantial factor in bringing about the injury." Moberly, 592 F.3d at 1321 (quoting Shyface v. Sec'y of Health & Hum. Servs., 165 F.3d 1344, 1352-53 (Fed. Cir. 1999)); see also Pafford v. Sec'y of Health & Hum. Servs., 451 F.3d 1352, 1355 (Fed. Cir. 2006). The received vaccine, however, need not be the predominant cause of the injury. Shyface, 165 F.3d at 1351. A petitioner who satisfies this burden is entitled to compensation unless respondent can prove, by a preponderance of the evidence, that the vaccinee's injury is "due to factors unrelated to the administration of the vaccine." § 13(a)(1)(B).

To receive compensation through the Program, petitioner must prove either (1) that he suffered a "Table Injury"—i.e., an injury listed on the Vaccine Injury Table—corresponding to a vaccine that he received, or (2) that he suffered an injury that was actually caused by a vaccination. See §§ 13(a)(1)(A), 11(c)(1); Capizzano, 440 F.3d at 1319-20. Because petitioner's claim is not a Table claim, he must prove his claim by showing that his injury was caused-in-fact by the vaccination in question. § 11(c)(1)(C)(ii). To do so, petitioner must establish, by preponderant evidence: "(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.

The causation theory must relate to the injury alleged. The petitioner must provide a sound and reliable medical or scientific explanation that pertains specifically to this case, although the explanation need only be "legally probable, not medically or scientifically certain." Knudsen v. Sec'y of Health & Hum. Servs., 35 F.3d 543, 548-49 (Fed. Cir. 1994). Petitioner cannot establish entitlement to compensation based solely on his assertions; rather, a vaccine claim must be supported either by medical records or by the opinion of a medical doctor. § 13(a)(1). In determining whether petitioner is entitled to compensation, the special master shall consider all material in the record, including "any . . . conclusion, [or] medical judgment . . . which is contained in the record regarding . . . causation." § 13(b)(1)(A). The undersigned must weigh the submitted evidence and the testimony of the parties' proffered experts and rule in petitioner's favor when the evidence weighs in his favor. See Moberly, 592 F.3d at 1325-26 ("Finders of fact are entitled—indeed, expected—to make determinations as to the reliability of the evidence presented to them and, if appropriate, as to the credibility of the persons presenting that evidence."); Althen, 418 F.3d at 1280 (noting that "close calls" are resolved in petitioner's favor).

B. Causation Analysis

1. Althen Prong One: Medical Theory of Causation

Under Althen Prong One, petitioner must set forth a medical theory explaining how the received vaccine could have caused the sustained injury. Andreu v. Sec'y of Health & Hum. Servs., 569 F.3d 1367, 1375 (Fed. Cir. 2009); Pafford, 451 F.3d at 1355-56. Petitioner's theory of causation need not be medically or scientifically certain, but it must be informed by a "sound and reliable" medical or scientific explanation. Boatmon v. Sec'y of Health & Hum. Servs., 941 F.3d 1351, 1359 (Fed. Cir. 2019); see also Knudsen, 35 F.3d at 548; Veryzer v. Sec'y of Health

& Hum. Servs., 98 Fed. Cl. 214, 223 (2011) (noting that special masters are bound by both § 13(b)(1) and Vaccine Rule 8(b)(1) to consider only evidence that is both "relevant" and "reliable"). If petitioner relies upon a medical opinion to support his theory, the basis for the opinion and the reliability of that basis must be considered in the determination of how much weight to afford the offered opinion. See Broekelschen v. Sec'y of Health & Hum. Servs., 618 F.3d 1339, 1347 (Fed. Cir. 2010) ("The special master's decision often times is based on the credibility of the experts and the relative persuasiveness of their competing theories."); Perreira v. Sec'y of Health & Hum. Servs., 33 F.3d 1375, 1377 n.6 (Fed. Cir. 1994) (stating that an "expert opinion is no better than the soundness of the reasons supporting it" (citing Fehrs v. United States, 620 F.2d 255, 265 (Ct. Cl. 1980))).

The undersigned finds that the petitioner has set forth a sound and reliable medical theory to explain how the hepatitis B vaccine can cause Bell's palsy. This finding is based on the following reasons.

First, that the innate immune system's TLR system plays a role the release of proinflammatory cytokines after vaccination is well-described in the medical literature and acknowledged by petitioner's experts and respondent's expert, Dr. Schroeder. Zhang and Lu discuss the TLR system in the context of hepatitis B viral infections. TLRs sense pathogen-associated molecule patterns and activate antiviral mechanisms which include proinflammatory cytokines. Dr. Schroeder describes the process whereby TLRs release proinflammatory cytokines following vaccination, and describes the process as one that "mimics the response to natural infection." Resp. Ex. D at 13. Thus, the causal theory appears to be well-accepted as an explanation for how the innate immune system responds to viral infections.

Second, studies published by Yilmaz et al. and Talaat et al. show that proinflammatory cytokine levels are elevated in patients who have Bell's palsy. While the authors did not reach any conclusions as to whether the elevated cytokines constitute evidence of pathogenesis, Yilmaz et al. did suggest that an inflammatory demyelinating mechanism may be the cause of Bell's palsy in the context of viral infections.

Third, the relevant anatomy and the vulnerability of the facial nerve as it passes through the bony fallopian canal has been implicated as playing a causal role in the medical literature. Yilmaz et al. observed that Bell's palsy involves "an inflammatory reaction compressing the facial nerve in the fallopian canal." Pet. Ex. 37 at 3. Jain and Kumar suggest that the probable mechanism is compression of the facial nerve "secondary to any type of inflammatory edema." Pet. Ex. 20 at 3. They state that "inflammation . . . may result in permanent nerve degeneration due to compression in the fallopian canal." Id.

Petitioner's causal theory combines a sound and reliable mechanism of inflammatory demyelination (like that which may occur with infection) with the known anatomical vulnerability of the facial nerve to inflammation in the fallopian canal. Further evidence in support of this theory is provided by histological evidence of inflammation found in the facial nerve of patients with Bell's palsy. Thus, the basic underpinnings of the causal theory are all well-supported by existing knowledge of immunology, anatomy, and histology.

Moreover, Bell's palsy has been identified as a potential adverse reaction to the hepatitis B vaccine by the vaccine manufacturer and there are supportive case reports.

The lack of supportive epidemiological evidence is not dispositive. It is difficult to use epidemiology to determine whether a vaccine is implicated in causation. Moreover, "[r]equiring epidemiologic studies . . . or general acceptance in the scientific or medical communities . . . impermissibly raises a claimant's burden under the Vaccine Act and hinders the system created by Congress, in which close calls regarding causation are resolved in favor of injured claimants." Andreu, 569 F.3d at 1378 (quoting Capizzano, 440 F.3d at 132-26); see also Althen, 418 F.3d at 1280 (noting that "close calls" are resolved in petitioner's favor).

For these reasons, the undersigned finds that petitioner has provided preponderant evidence of a sound and reliable causal theory, satisfying Althen Prong One.

2. Althen Prong Two: Logical Sequence of Cause and Effect

Under Althen Prong Two, petitioner must prove by a preponderance of the evidence that there is a "logical sequence of cause and effect showing that the vaccination was the reason for the injury." Capizzano, 440 F.3d at 1324 (quoting Althen, 418 F.3d at 1278). "Petitioner must show that the vaccine was the 'but for' cause of the harm . . . or in other words, that the vaccine was the 'reason for the injury.'" Pafford, 451 F.3d at 1356 (internal citations omitted).

In evaluating whether this prong is satisfied, the opinions and views of the vaccinee's treating physicians are entitled to some weight. Andreu, 569 F.3d at 1367; Capizzano, 440 F.3d at 1326 ("[M]edical records and medical opinion testimony are favored in vaccine cases, as treating physicians are likely to be in the best position to determine whether a 'logical sequence of cause and effect show[s] that the vaccination was the reason for the injury.'" (quoting Althen, 418 F.3d at 1280)). Medical records are generally viewed as trustworthy evidence, since they are created contemporaneously with the treatment of the vaccinee. Cucuras, 993 F.2d at 1528. The petitioner need not make a specific type of evidentiary showing, i.e., "epidemiologic studies, rechallenge, the presence of pathological markers or genetic predisposition, 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, petitioner may satisfy his burden by presenting circumstantial evidence and reliable medical opinions. Id. at 1325-26.

In regard to Althen Prong Two, the undersigned finds petitioner provided preponderant evidence of a logical sequence of cause and effect showing that his vaccination was the cause of his Bell's palsy. Although his treating physicians did not provide any opinions that support or negate a finding that petitioner's vaccine was causal, his medical records show that his clinical course is consistent with the proposed causal mechanism.

After vaccination, petitioner developed local signs and symptoms of inflammation at the site of his vaccination. Petitioner had malaise, arm soreness, and mild headache. Dr. Schroeder opined that these symptoms were consistent with "the effect of local activation of the innate immune system . . . includ[ing] activation of [TLRs] . . . which can be attributed to the release of cytokines and other mediators." Resp. Ex. D at 13. Petitioner then had the onset of his Bell's

palsy, the left-sided postauricular headache the day after vaccination. The following day, petitioner had "facial muscle weakness." Id. These symptoms are consistent with the injury to the facial nerve secondary to inflammatory demyelination due to compression in the fallopian canal.

Lastly, there is no evidence of any alternative cause for petitioner's illness. Petitioner did not have a urinary tract infection, upper respiratory tract infection, herpetic or zoster infection or evidence of reactivation, or evidence of any other cause. Respondent's experts do not identify any other cause for petitioner's Bell's palsy.

Thus, the undersigned finds that petitioner provided preponderant evidence of a logical sequence of cause and effect, satisfying Althen Prong Two.

3. Althen Prong Three: Proximate Temporal Relationship

Althen Prong Three requires petitioner to establish a "proximate temporal relationship" between the vaccination and the injury alleged. Althen, 418 F.3d at 1281. That term has been equated to mean a "medically acceptable temporal relationship." Id. The petitioner must offer "preponderant proof that the onset of symptoms occurred within a timeframe which, given the medical understanding of the disease's etiology, it is medically acceptable to infer causation-in-fact." de Bazan v. Sec'y of Health & Hum. Servs., 539 F.3d 1347, 1352 (Fed. Cir. 2008). The explanation for what is a medically acceptable time frame must also coincide with the theory of how the relevant vaccine can cause the injury alleged (under Althen Prong One). Id.; Koehn v. Sec'y of Health & Hum. Servs., 773 F.3d 1239, 1243 (Fed. Cir. 2014); Shapiro v. Sec'y of Health & Hum. Servs., 101 Fed. Cl. 532, 542 (2011), recons. den'd after remand, 105 Fed. Cl. 353 (2012), aff'd mem., 503 F. App'x 952 (Fed. Cir. 2013).

The hepatitis B vaccination was administered to petitioner on October 2, 2014. The experts agree that petitioner's severe postauricular pain which began on Friday afternoon, October 3, 2014, heralded the onset of petitioner's Bell's palsy. Petitioner's experts agree that the innate immune system is activated almost immediately following vaccination. Both Dr. Kinsbourne and Dr. Byers cited medical literature to support their assertions that cytokine responses begin as early as three to seven hours after vaccination and peak at 24 hours. This timeframe is appropriate given the petitioner's causal theory of inflammation leading to injury of the facial nerve. Therefore, petitioner has provided preponderant evidence satisfying Althen Prong Three.

VII. CONCLUSION

Based on the record as a whole, the undersigned finds there is preponderant evidence to satisfy all three Althen prongs and to establish petitioner's vaccination caused his Bell's palsy. Thus, the undersigned finds petitioner has established by preponderant evidence that he is entitled to compensation. A separate damages order will issue.

IT IS SO ORDERED.

s/Nora Beth Dorsey
Nora Beth Dorsey
Special Master