In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

No. 07-173V
Filed: May 11, 2011

GEORGE A. DAILY,	)	
	)	
Petitioner,	)	FOR PUBLICATION
	)	
v.	)	Entitlement; cause-in-fact;
	)	Guillain-Barré Syndrome; GBS;
SECRETARY OF	)	Chronic Inflammatory
HEALTH AND HUMAN SERVICES,	)	Demyelinating Polyneuropathy;
	)	CIDP
Respondent.	)	
	)	

David L. Terzian, Rawls & McNelis P.C., Richmond, VA, 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 George Daily filed a petition under the National Childhood Vaccine Injury Act ("Vaccine Act" or "Act"), alleging he suffered a neurological injury that was caused in fact by a trivalent influenza vaccination he received on November 28, 2000.[2] On December 11, 2000, Petitioner began to experience neurological symptoms that were initially diagnosed as Guillain-

[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.

Barré Syndrome (GBS).[3] After several relapses and years of partially effective or ineffective treatment, his diagnosis was changed from GBS to Chronic Inflammatory Demyelinating Polyneuropathy (CIDP).[4] Petitioner contends that this condition was triggered by his flu vaccination, which caused an autoimmune reaction by way of a biological process identified as molecular mimicry.[5]

Petitioner's case depends on extrapolation by his medical experts concerning biological processes that are not well understood. Under the Vaccine Act, this type of evidence is permitted as long as it is plausible and based on reliable science.

Respondent counters Petitioner's allegations with expert testimony that no epidemiological studies or animal models have demonstrated the validity of the causation theories presented. While Respondent is correct, the standards she relies upon are those of the laboratorian, not the Vaccine Program. I conclude that the testimony presented by Petitioner's experts is based in part on reliable science and in part on reliable inferences from that science. Considered from this vantage, Petitioner has presented a winning case, although it is unproven scientifically.

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[3] GBS is a group of disorders that cause peripheral polyneuropathy (destruction of nerve cells outside of the central nervous system). Allan H. Ropper & Martin A. Samuels, Adams and Victor's Principles of Neurology 1261-62 (9th ed. 2009). The main form of GBS is Acute Inflammatory Demyelinating Polyneuropathy (AIDP) (attacks the protective cells that surround motor nerves), and the terms AIDP and GBS sometimes are used synonymously. Id. at 1261-64; see Respt's Ex. B at 1. Another form of GBS is Acute Motor Axonal Neuropathy (AMAN) (attacks the motor nerves). Ropper & Samuels, supra, at 1261-64; see also Hugh J. Willison, Gangliosides as Targets for Autoimmune Injury to the Nervous System, J. Neurochemistry, 2007;103 (Suppl. 1);143-49 (Petr's Ex. 41). AIDP is characterized by a symmetrical weakness that usually begins in the lower extremities and progresses into the trunk and upper limbs. Ropper & Samuels, supra, at 1263. Tingling in the fingers and toes is the earliest symptom. Id. "A mild respiratory or gastrointestinal infection or immunization precedes the neuropathic symptoms by 1 to 3 weeks in approximately 60[%] of cases." Id. at 1261.

[4] CIDP and GBS are two forms of polyneuropathy, and they share many of the same symptoms. Ropper & Samuels, supra, at 1292. CIDP is similar to GBS in a variety of ways, but differs in its "modes of evolution, responses to treatment, and prognosis." Ropper & Samuels, supra, at 1292. In addition, "[a]n antecedent infection is usually not identified in patients with CIDP as it is in GBS." Id. at 1292. In a small proportion of patients, CIDP first emerges as GBS, and then becomes relapsing or simply worsens progressively. Id. at 1292; see Respt's Ex. B at 3.

[5] When the immune system responds to an infectious organism, it often identifies the organism by certain features on the cell wall of the organism. As posited by scientists, "molecular mimicry" occurs when the identifying feature on an infectious organism is also found on the cell wall of certain cells. K. A. Sheikh et al., Molecular Mimicry in Guillain-Barré Syndrome, Ann NY Acad Sciences 845:307-21, at 308, 1998 (Petr's Ex. 27). The result is that the body attacks its own cells. Id.; see also Petr's Ex. 24 at 2.

II. FACTUAL AND PROCEDURAL BACKGROUND

A. Procedural History

This was originally Special Master Abell's case. He conducted a hearing on May 29, 2009. The case was assigned to me on December 7, 2010. On February 9, 2011, I convened a status conference where counsel for both parties expressed their desire for the Court to reach a decision based on the existing record, without an additional hearing. See Order, Feb. 9, 2011. Subsequently, the parties filed a Joint Motion for a Ruling on the Record.

In the Motion, the parties agreed "there is no dispute concerning the material facts of the case, which are contained in the medical records filed with the petition." Am. Jt. Mot. for Ruling on Record, at 1 (Mar. 22, 2011). The parties also agreed that while "the reliability and persuasiveness of the respective medical experts' opinions are disputed," resolution of the dispute does not require "the special master to have observed the demeanor of the expert witness while testifying." Id. at 1-2. Accordingly, the parties jointly moved for a decision "based upon the existing record as a whole, including, but not limited to, all motions, pleadings, and exhibits filed with the court; the transcript of testimony of the experts at the hearing held on May 29, 2009, in Washington, D.C., before Special Master Richard B. Abell; and the post-hearing submissions filed by the parties following the aforesaid Hearing." Id. at 1.

B. Pertinent Facts

1. Petitioner's Case

Petitioner alleged that he suffered GBS as a result of receiving the flu vaccine, and that this injury evolved into CIDP. Although he was initially diagnosed with GBS, following several relapses and ineffective treatment, Petitioner was diagnosed with CIDP. Petitioner maintained that his injury resulted from his reaction to the flu vaccine, based on the testimony of his experts.

a. Dr. Reed Perron

Dr. Reed Perron is a neurologist in private practice and Petitioner's treating physician. Tr. at 13. In his expert report, Dr. Perron stated that Petitioner initially was diagnosed with GBS but that, as Petitioner's symptoms persisted despite treatment, Dr. Perron "began to suspect that he might be in the early stages of CIDP." Petr's Ex. 24 at 2. Dr. Perron noted that early in the course of the two diseases it may be difficult to distinguish between them. Id. Accordingly, he felt it was acceptable to use the experience with flu vaccine and GBS as a model for Petitioner's injury, notwithstanding that, in Dr. Perron's view, Petitioner actually suffered from CIDP, not GBS. Tr. at 23, 26-27; see Petr's Ex. 32 at 2.

Dr. Perron opined that the causal connection between Petitioner's flu vaccination and his condition was based on molecular mimicry. Petr's Ex. 24 at 2. Under that theory, Dr. Perron explained in his report, the body mistakes an antigen in the vaccine for "a similar protein structure" in the vaccinee's own nervous system. Id. When that happens, the body's immune mechanism, primed by the vaccination, attacks the self-protein, resulting in neurologic damage. Id.

In support of his opinion, Dr. Perron referred to experience with the swine flu vaccination program in the mid-1970s, noting that the "period of risk" following vaccination with swine flu vaccine "was concentrated primarily within the five week period after vaccination." Id. at 3. He cited a "proximate temporal relationship" of about two weeks between Petitioner's symptoms and his vaccination, which was consistent with the swine flu vaccine/GBS experience. Id.

At hearing, Dr. Perron conceded that he was not a specialist in neuromuscular diseases. Tr. at 25. He stated that, in addition to the temporal relationship between vaccination and the onset of Petitioner's injury, his opinion was based on the "close relationship" between GBS and CIDP. Tr. at 26. He testified that the two disorders are so closely related that generally they are considered to be "different forms of the same disease." Id. Accordingly, Dr. Perron based his causation opinion in Petitioner's case on medical literature linking vaccination and GBS. Id. In addition, Dr. Perron relied on a case report in which an 84-year-old woman developed symptoms of CIDP 21 days after receiving the flu vaccine. Tr. at 36-37; see Praful Kelfar, Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) with Rapid Progression after Influenza Vaccination: a Report of Three Cases, J. Clinical Neuromuscular Disease Vol. 8(1), 20-25 (Sept. 2006) (Petr's Ex. 34). He conceded that his opinion as to causation was based on temporal association in combination with the absence of any other identifiable cause. Tr. at 31-32 ("So by exclusion, I felt it reasonable to attribute it to the flu shot").

b. Dr. Ahmet Höke

Dr. Ahmet Höke, an Associate Professor of Neurology and Neuroscience and Director of the Neuromuscular Division of the Department of Neurology at Johns Hopkins Hospital, specializes in peripheral neuropathy and demyelinating disorders such as GBS and CIDP. See Petr's Ex. 36 (Dr. Höke's report); Tr. at 39-40. He opined that Petitioner, at the outset of his illness, had GBS. Petr's Ex. 36 at 1; Tr. at 44-45. He explained, however, that "clinically it can be very difficult to really differentiate between the case of a GBS that recurred and then developed into a chronic form which we would then call CIDP." Petr's Ex. 36 at 2; Tr. at 48. "[W]e're dealing with a spectrum of a same illness, pathogenic mechanisms are probably similar." Tr. at 48. Both are autoimmune disorders, and they "respond to the similar type of treatments, including IVIG and plasma exchange, so it's really semantics that differentiate between these two diseases." Petr's Ex. 36 at 2; Tr. at 48. In his testimony, Dr. Höke explained that in the vast majority of cases "CIDP doesn't start as GBS . . . . It just starts slowly." Tr. at 50. He further testified that a small percentage of patients "really ha[ve] an overlapped syndrome that is very difficult to differentiate between the two conditions." Id.

According to Dr. Höke, the mechanism of molecular mimicry has been identified in the disorder of AIDP. Tr. at 50.[6] A large body of literature links gangliosides and antibodies against certain gangliosides as causal agents of GBS. Id.[7] It is unknown, however, whether the same type of gangliosides are associated with CIDP. Id.

As to vaccines, he conceded that no experimental proof has shown that vaccination can induce GBS or CIDP, but he opined that the association was strong enough that causation is likely. Tr. at 55-56. In support of his opinion, Dr. Höke relied on a study of patients with GBS or CIDP who suffered a recurrence of their disorders following flu vaccination. Id. at 56-57; see J.M. Brostoff et al., Post-Influenza Vaccine Chronic Inflammatory Demyelinating Polyneuropathy, Age and Ageing 2008;37; 229-30 (Petr's Ex. 39); J. Pritchard et al., Risk of Relapse of Gullain-Barré or Chronic Inflammatory Demyelinating Polyradiculoneuropathy Following Immunisation, J. Neurol. Neurosurg. Psychiatry 2002; 73; 348-49 (Petr's Ex. 40). Dr. Höke characterized the results of the study as indicative of a type of "challenge" that "puts a stronger relationship between the vaccine and the plausible relationship or induction of the immune attack." Tr. at 58. Dr. Höke testified that GBS patients, as with other neurological disorders, can present with a "wide spectrum of presentations." Tr. at 64-65. Although the majority of GBS patients has a monophasic illness, a "very small percentage of patients will go on to develop CIDP," as occurred in Petitioner's case. Tr. at 65.[8]

On cross-examination, Dr. Höke conceded that the "inciting trigger" for autoimmune diseases is "not always clear-cut." Tr. at 74. He distinguished between monophasic disorders like GBS and "more of a classical remitting and relapsing type of a disease" like MS, which may be characterized as "multiple monophasic illnesses." Tr. at 77. He conceded that wild influenza virus does not target the nervous system. Tr. at 88. He cited studies showing "that there is still a persistently high risk of GBS after flu vaccination; not as high as after the swine flu [shot]," and conceded that despite case reports, no epidemiological studies have shown an increase in CIDP following flu vaccination." Tr. at 91-92. Petitioner's illness was an unusual presentation: "classical GBS" at the start that later "evolved" into CIDP." Tr. at 84. Dr. Höke would not have asserted a similar causal connection between "classic CIDP" and flu vaccination. Tr. at 104.

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[6] As discussed above, AIDP is a form of GBS, and the two terms often are used synonymously. See Respt's Ex. B at 1.

[7] Gangliosides are a class of chemicals (a type of lipid) that often appear on cell-surface membranes. Nobuhiro Yuki, Ganglioside Mimicry and Peripheral Nerve Disease, Muscle & Nerve, June 2007, 691-711, at 693 (Petr's Ex. 42).

[8] Monophasic means occurring in only one phase or variation (Diphasic would be in two stages or phases). Dorland's Illustrated Medical Dictionary (31st ed. 2007) at 530, 1197.

2. Respondent's Case: Dr. Subramaniam Sriram

Dr. Sriram is Professor of Neurology and Microbiology Immunology and head of the Multiple Sclerosis Clinic at Vanderbilt Medical Center. He has particular expertise in demyelinating disorders of the central nervous system. Tr. at 111; see Respt's Ex. B at 1. Dr. Sriram challenged the link between GBS and CIDP, stating "CIDP and GBS are two different diseases even though they share similarities in pathology and in electrodiagnostic studies." Respt's Ex. B at 1-2. He cited certain clinical differences in patients suffering from the disorders and asserted that "there is insufficient evidence to suggest that CIDP represents a chronic variant of AIDP." Id. at 3-4; see Tr. at 126-28. In his view, it would be necessary to demonstrate "a common underpinning of the pathobiology between the two disease states" before concluding that CIDP was a chronic form of GBS. Respt's Ex. B at 4. "Since there is very little evidence that AIDP and CIDP share any commonality in the reactivity to self antigens responsible for the autoimmune process, it is therefore premature to conclude that they represent two ends of a spectrum of a common disease." Id.

As a result, Dr. Sriram disputed the applicability of information concerning a possible link between GBS and flu vaccination to the context of CIDP. Id. at 1. He asserted that there are "no infectious etiologies or vaccinations that are linked to the development of CIDP." Id.

In a supplemental report, Dr. Sriram took issue more specifically with the opinion submitted by Dr. Höke. He asserted that the autoantigens associated with GBS have been identified in only about 10 percent of patients; "in the rest of the patients with AIDP the autoantigen is not known." Respt's Ex. E at 2. He also stated that GBS "is in fact not a single disease entity." Id. He noted certain clinical and experimental results that call into question whether GBS is "necessarily" an autoimmune disorder. Id. Dr. Sriram asserted that evidence for an antecedent infection in CIDP is "extremely weak," between 10-15 percent, "which is not different from that seen in a general population." Id. "Most important," Dr. Sriram stated, "surveys done after swine flu vaccination . . . have failed to identify a single case of CIDP after influenza vaccination." Id.

Dr. Sriram asserted that, to make an association between vaccine and disease there must be "clinical observation that is then supported by larger studies." Id. Such associations "do not rest on a theoretical possibility. . . ." Id.

Dr. Sriram testified that Petitioner suffered acute onset CIDP. Tr. at 141. He explained that he was not excluding the possibility that molecular mimicry causes CIDP, but he characterized that possibility as "pure speculation," and noted that "people have looked" for evidence to support the hypothesis and not found it. Tr. at 126, 161-64. More than "just a hypothesis" is needed to prove vaccine causation, Dr. Sriram stated, "[w]e need some more tangible evidence." Tr. at 168.

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 Health & Human Servs., 617 F.3d 1328, 1338 (Fed. Cir. 2010); Shyface v. Sec'y of Health & Human Servs., 165 F.3d 1344, 1352 (Fed. Cir. 1999).[9] 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 Health & Human Servs., 592 F.3d 1315, 1322 (Fed. Cir. 2010) (quoting Knudsen v. Sec'y of Health & Human Servs., 35 F.3d 543, 548-49 (Fed. Cir. 1994)); see also Grant v. Sec'y 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.

Petitioner's burden is to 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. 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. Id. If Petitioner fails to establish a prima facie case of causation, however, the burden does not shift. Doe 11 v. Sec'y 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)).

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 ("'[a]n expert opinion is no better than the soundness of the reasons supporting it'") (citing and quoting Perreira v. Sec'y of Health & Human Servs., 33 F.3d 543, 548 (Fed. Cir.1994)).

[9] Petitioner has not alleged a "Table" injury. Petr's Post-Hr'g Br. at 1; see 42 C.F.R. § 100.3.

Assessing the reliability of an expert opinion in Vaccine Act cases can be challenging, because often there is little supporting evidence. See Althen, 418 F.3d at 1280 (noting that the "field [is] bereft of complete and direct proof of how vaccines affect the human body"). Consequently, most expert opinions extrapolate from existing data and knowledge. The weight to be given to an expert's opinion is based in part on the size of the gap between the science and the opinion proffered. Cedillo, 617 F.3d at 1339 (quoting Joiner, 522 U.S. at 146). Evidence should be viewed under the preponderance standard as it is understood in civil courts and "not 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).

B. Analysis

1. Althen Prong 1

Under Althen prong 1, a petitioner must set forth a biologically plausible theory explaining how the vaccine could cause the injury complained of. This requirement has been interpreted as "can the vaccine(s) at issue cause the type of injury alleged?" Pafford v. Sec'y of Dep't of Health & Human Servs., 451 F.3d 1352, 1355-56 (Fed. Cir. 2006). Although the theory of causation need not be corroborated by medical literature or epidemiological evidence, the theory must be sound, reliable, and reputable -- in other words, the theory need not be scientifically certain, but it must have a scientific basis. See id. at 1379-80.

Dr. Höke and Dr. Perron adopted the theory of molecular mimicry to explain Petitioner's vaccine reaction. To support the theory, Petitioner submitted articles demonstrating that molecular mimicry explains some forms of GBS that are triggered by bacterial infection. See, e.g., Petr's Ex. 27; Petr's Ex. 41. No articles were submitted that scientifically confirmed the process of molecular mimicry in any cases of CIDP.

Dr. Höke and Respondent's expert, Dr. Sriram, disagreed about the diagnosis of Petitioner's disorder, while Dr. Perron, the treating physician, agreed with Dr. Sriram that Petitioner had CIDP from the start, not GBS. The experts also disagreed about underlying issues, such as whether GBS and CIDP are similar conditions on a spectrum or represent different disease states. On the evidence of record, it appears that, at present, medical science cannot resolve these questions with any degree of assurance. They are matters concerning which reasonable medical minds may legitimately differ.

Dr. Sriram makes a strong argument that Dr. Höke's theory is merely speculative and not supported by epidemiological evidence or animal models. From the scientific perspective, he is correct. The law, however, requires much less to establish a possible 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. Höke's opinion to see whether it is plausible and reliable, knowing that it does not prove causation under rigorous scientific standards. See Hocraffer v. Sec'y of Dep't of Health & Human Servs., 63 Fed. Cl. 765, 779 (2005).[10]

Dr. Höke is an expert in the area of peripheral neuropathy and demyelinating disorders; he is well qualified to opine in this case. His testimony is based on extensive medical knowledge as well as treatment, at an outstanding medical institution, of patients with GBS and other neuromuscular disorders. See Tr. at 40. He believes that GBS and CIDP are similar conditions and that, if vaccination can cause GBS, it can cause some cases of CIDP. There is scant evidence in the medical literature confirming his theory.

Petitioner's Exhibit 34 presents three case reports of CIDP following flu vaccination. Kelkar, supra Petr's Ex. 34. The article described three patients who "developed CIDP with rapid onset in close proximity to influenza vaccination followed by relapsing or chronic course." Id. The article recognized that the relationship between CIDP and vaccination is less clear than with GBS. Id. The authors suggested that vaccination may trigger CIDP in patients who have a "rapid onset in close proximity to influenza vaccination." Id.

Petitioner's Exhibit 39 is a report in a peer-reviewed journal presenting a case of CIDP occurring after flu vaccination in a 74-year-old man with no previous neurological history. Brostoff et al., supra Petr's Ex. 39. This article not only reports the case of CIDP but notes "the relatively rapid onset of symptoms compared with the latent period of approximately 2 weeks between vaccination and onset of [GBS] (which shares a similar aetiopathogenesis) in affected individuals." Id. at 229. The authors indicate a link between the disease process that results in GBS and the process that leads to CIDP.

Petitioner's Exhibit 40 reported a survey of patients with GBS and CIDP. Following flu vaccination, two out of 46 CIDP patients experienced relapsing or recurring symptoms. Tr. at 57-58; Pritchard et al., supra Petr's Ex. 40, at 348. In Dr. Höke's view, "this type of challenge. . . puts a stronger relationship between the vaccine and the plausible relationship or induction of the immune attack." Tr. at 58. The cited article itself, however, notes the "difficulties" in drawing conclusions from this type of study, and that "the true risks of relapse following immunizations after GBS or in CIDP

[10] Dr. Sriram noted that researchers have tried without success to identify an autoimmune etiology for CIDP. See Tr. at 164. Indeed, a link between molecular mimicry and most forms of GBS has yet to be discovered. See Tr. at 153-56; see Petr's Ex. 42 at 707. Nevertheless, a possible link between GBS and vaccination has been recognized for some time. See Lawrence B. Schonberger et al., Guillain-Barré Syndrome Following Vaccination in the National Influenza Immunization Program, United States, 1976-1977, Am. J. Epidemiology Vol. 110:105-23, 1979 (Petr's Ex. 29).

may be less than those discovered in this audit." Pritchard et al., supra Petr's Ex. 40, at 349.

Petitioner's Exhibits 41 and 42 describe how molecular mimicry explains the biological mechanism of certain sub-types of GBS, which are known to be triggered by bacterial infection. The limitations of these articles reduce their ability to demonstrate a similar mechanism in a case of CIDP of unknown etiology, and these were pointed out effectively by Respondent's expert, Dr. Sriram. See Tr. 161-65.[11]

Petitioner's Exhibit 42 is instructive in another way, however, in that it highlights the differences between causation as it is understood in the scientific community and the legal criteria applicable to proving causation under the Vaccine Act. The article lists "four criteria" that "must be satisfied to conclude that a disease is triggered by molecular mimicry:"

> – establishment of an epidemiological association between the infectious agent and the immune-mediated disease;
>
> – identification of T cells or antibodies directed against the patient's target antigens;
>
> -- identification of microbial mimics of the target antigen;
>
> – reproduction of the disease in an animal model.

Yuki, supra Petr's Ex. 42, at 691-92.[12]

Immediately apparent upon review of these scientific standards of proof is that Petitioner's presentation does not begin to satisfy them. Under pertinent law, however, the scientific shortcomings of Petitioner's case -- lack of scientific literature or confirmatory studies -- do not preclude a finding of causation-in-fact. See Cedillo, 617 F.3d at 1339 (noting a petitioner's injury is not required to be recognized by the medical community or in the literature). The pertinent standards are not those of the 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.

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[11] Even the authorities cited by Petitioner affirm that medical experts generally agree that vaccine injuries are extremely rare. See, e.g., Brostoff et al., supra, Petr's Ex. 39 ("Rarely, individual patients may develop certain restricted patterns of autoimmune neurological damage . . . The risk factors for such reactions remain unknown, and for the overwhelming majority of patients viral vaccines carry no risk of systemic autoimmune disease. . . .").

[12] As expounded by Dr. Sriram on behalf of Respondent, the requirements are similarly stringent: "You would want at least two areas to be fulfilled in some way or the other. One is to have an animal model of the disease . . . the other . . . to have some data set that tells you that the immune system is directed against peripheral nerve tissue in some way or form." Tr. at 128.

On its face, Dr. Höke's theory is plausible. The premises of Dr. Höke's theory are: 1) flu vaccination can cause GBS in rare instances, 2) molecular mimicry can cause GBS in at least some cases, and 3) there is a biological basis (though this is contested) to assume some similarity between GBS and CIDP. From these premises, Dr. Höke concludes that vaccination could cause CIDP by a process of molecular mimicry. This theory makes sense. It is based on science and reliable inferences therefrom. Absent persuasive refutation from Respondent, I accept the theory in satisfaction of Althen prong 1.

When I turn to Dr. Sriram's testimony, I do not find that he challenges the plausibility of Dr. Höke's theory. Instead, he points out that the theory is unproven.[13] So far as I can tell from the record, Dr. Sriram is correct. Since he has not negated the plausibility of Dr. Höke's theory, however, Petitioner has carried the burden under Althen prong 1. 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).

2. Althen Prongs 2 and 3

Dr. Höke testified that Petitioner initially developed GBS from his flu vaccination, which later evolved into CIDP. See Tr. 58, 83-84, 104. Dr. Perron testified that Petitioner's disorder initially was misdiagnosed as GBS, but was in fact CIDP. Tr. 16, 23. Dr. Perron testified, "it's often very difficult to distinguish one disease from the other early on." Id. at 23. Some of the ambiguity, however, may be semantic or due to nomenclature. Tr. at 48. When a patient has a "monophasic course that responds to treatment, to me it is GBS by definition. Whether you [instead] call it acute onset CIDP . . . [is] splitting hairs there in terms of nomenclature." Tr. at 98. Dr. Höke's testimony concerning GBS is key, because Dr. Höke admitted that if Petitioner suffered a "classic" case of CIDP without the acute onset, he would not have opined that the flu vaccine caused the condition. Tr. at 104.[14]

As Dr. Höke explained it, Petitioner "at the beginning" had GBS "by definition." Tr. at 44. This was based on Petitioner's clinical presentation. Tr. at 45. Some GBS

[13] For example, Dr. Sriram questions the link between GBS and CIDP, stating, "[a]lthough AIDP and CIDP share many electrophysiological features pertaining to loss of nerve function, there is insufficient evidence to suggest that CIDP represents a chronic variant of AIDP." Respt's Ex. B at 3. Dr. Sriram is not necessarily saying that Petitioner's experts are wrong, rather that there is insufficient evidence to determine that they are right. In an area bereft of scientific knowledge, this often will be the case.

[14] Dr. Höke's opinion to the same effect in a similar case was deemed sufficient, in the absence of a rebutting submission from Respondent, to award compensation. See Goza v. Sec'y of Dep't of Health & Human Servs., No. 07-290V, 2008 WL 6082761, *4 (Aug. 1, 2008) ("Ms. Goza had developed an atypical onset GBS that turned into a CIDP within weeks of vaccination with the influenza vaccine").

cases "later on act like CIDP," in that "some of those patients go on to have recurrences that are partially responsive to treatment . . . and . . . in this case. . . he responded later on to the treatment that we normally use for CIDP." Tr. at 44-45. Essentially, the damage to the peripheral nerves from GBS sometimes is "so severe that the axons start to degenerate [resulting in CIDP]." Tr. at 47. Dr. Höke based this opinion on his general understanding of the relevant medical literature, as well as discussions with his colleagues, observing that "clinically it can be very difficult to really differentiate between the case of a GBS that recurred and then developed into a chronic form which we would then call CIDP, or perhaps a more acute form of a CIDP that would start -- that looks like GBS but in reality is a type of CIDP." Tr. at 47-48.

If Dr. Höke is correct and a vaccination could cause an autoimmune response resulting in a GBS-type syndrome that later evolved into CIDP, the course of Petitioner's illness would comport with the theory. The onset of Petitioner's neurological symptoms followed his vaccination by about two weeks, an appropriate time frame in which an autoimmune response could occur. Tr. at 58, 68 ("within weeks").[15]

Dr. Sriram disputed the idea that CIDP represents a "chronic variant" of GBS. Tr. at 125-26. He cited specific studies, which were admitted into evidence. See Tr. at 126-38. He pointed out that, in one study, no instances of AIDP evolved into CIDP. Tr. at 126; see Allan Ropper et al., Limited Relapse in Guillain-Barré Syndrome After Plasma Exchange, Arch. Neurology 1988;45(3); 314-15 (Respt's Ex. D-10) (of 94 patients with GBS, none developed CIDP). What actually occurs, Dr. Sriram explained, is that patients with CIDP are initially misdiagnosed as having AIDP, but AIDP does not evolve into CIDP. Tr. at 127. That comports with Dr. Perron's (treating physician) testimony concerning what happened in this case.

Dr. Sriram also contested the sufficiency of the evidence to support a cause-and-effect relationship between vaccination and Petitioner's CIDP. He testified, "I'd like to have something -- some evidence in his blood, a serum or something like that showing antibodies to . . . myelin antigens, something of that order to make it likely that this was vaccine related." Tr. at 137. Again, Dr. Sriram's opinion sets the bar too high. In this context, the question is whether the relationship between vaccine and injury is logical. It does not appear to me that Dr. Sriram's testimony or the medical literature submitted by Respondent challenges the logic of the asserted causal relationship in Petitioner's case.

That studies have failed to uncover more instances of the phenomenon Dr. Höke described does not invalidate his opinion. If the phenomenon is as rare as even Dr. Höke believes it to be, it is quite likely that studies of a few hundred individuals would

[15] I do note that on cross-examination Dr. Höke conceded that in one of the case reports of an individual who developed CIDP following flu vaccination, the time between vaccination and onset was only two days. Tr. at 96. Dr. Höke explained that, although in that case it would appear that the onset was too soon to be related to the flu vaccination, in CIDP cases it's very difficult to determine the exact onset of symptoms. Id. This explanation is only faintly persuasive.

not necessarily detect it. Further, as noted above, clinical confirmation of cause and effect is not required. Andreu, 569 F.3d at 1378.

This record reveals a vigorous dispute among highly-qualified professionals regarding questions that have yet to be determined one way or the other by medical science. I find confirmation of this conclusion even in the medical literature submitted by Respondent, which discusses the many similarities between GBS and CIDP and the difficulties of diagnosis. See, e.g., F. Grand'Maison et al., Recurrent Guillain-Barré Syndrome: Clinical and Laboratory Features, Brain (1992), 115, 1093-1106, at 1094 (Respt's Ex. D-2) ("Differentiation of the two disorders relies on arbitrary clinical criteria: the time to reach maximum disability . . . . The difficulty of classifying inflammatory polyneuropathies is illustrated by the occasional patient with attacks of both acute and more chronic onset." (emphasis added)). In these circumstances, it is appropriate to defer to Petitioner's experts, recognizing that the Vaccine Act allows for a finding of causation in field bereft of direct proof, and the applicable case law instructs a special master to err if necessary on the side of petitioners.

IV. CONCLUSION

Petitioner has satisfied the legal requirements for proving that his November 28, 2000, trivalent influenza vaccination was a legal cause of his GBS and CIDP. 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