In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS
No. 16-1548V
Filed: October 18, 2022
PUBLISHED

KEVIN KELLY,

Petitioner,

v.

SECRETARY OF HEALTH AND HUMAN SERVICES,

Respondent.

Special Master Horner

Myasthenia Gravis; Diplopia; Ptosis; Influenza (flu) Vaccine; Ruling on the Written Record

Ronald Craig Homer, Conway, Homer, P.C., Boston, MA, for petitioner.
Lauren Kells, U.S. Department of Justice, Washington, DC, for respondent.

DECISION ON ENTITLEMENT[1]

On November 18, 2016, petitioner, Kevin Kelly, filed a petition under the National Childhood Vaccine Injury Act, 42 U.S.C. § 300aa-10-34 (2012),[2] alleging that he suffers diplopia, ptosis, and myasthenia gravis caused-in-fact by his December 17, 2013 influenza ("flu") vaccination. (ECF No. 1.) For the reasons set forth below, I conclude that petitioner is not entitled to compensation.

I. Applicable Statutory Scheme

Under the National Vaccine Injury Compensation Program, compensation awards are made to individuals who have suffered injuries after receiving vaccines. In general, to gain an award, a petitioner must make a number of factual demonstrations, including showing that an individual received a vaccination covered by the statute;

[1] Because this decision contains a reasoned explanation for the special master's action in this case, it will be posted on the United States Court of Federal Claims' website in accordance with the E-Government Act of 2002. *See* 44 U.S.C. § 3501 note (2012) (Federal Management and Promotion of Electronic Government Services). **This means the decision will be available to anyone with access to the Internet.** In accordance with Vaccine Rule 18(b), 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 the special master, upon review, agrees that the identified material fits within this definition, it will be redacted from public access.

[2] Within this decision, all citations to § 300aa will be the relevant sections of the Vaccine Act at 42 U.S.C. § 300aa-10-34.

received it in the United States; suffered a serious, long-standing injury; and has received no previous award or settlement on account of the injury. Finally – and the key question in most cases under the Program – the petitioner must also establish a *causal link* between the vaccination and the injury. In some cases, the petitioner may simply demonstrate the occurrence of what has been called a "Table Injury." That is, it may be shown that the vaccine recipient suffered an injury of the type enumerated in the "Vaccine Injury Table," corresponding to the vaccination in question, within an applicable time period following the vaccination also specified in the Table. If so, the Table Injury is presumed to have been caused by the vaccination, and the petitioner is automatically entitled to compensation, unless it is affirmatively shown that the injury was caused by some factor other than the vaccination. § 300aa-13(a)(1)(A); § 300 aa-11(c)(1)(C)(i); § 300aa-14(a); § 300aa-13(a)(1)(B).

In many cases, however, the vaccine recipient may have suffered an injury *not* of the type covered in the Vaccine Injury Table. In such instances, an alternative means exists to demonstrate entitlement to a Program award. That is, the petitioner may gain an award by showing that the recipient's injury was "caused-in-fact" by the vaccination in question. § 300aa-13(a)(1)(B); § 300aa-11(c)(1)(C)(ii). In such a situation the presumptions available under the Vaccine Injury Table are inoperative. The burden is on the petitioner to introduce evidence demonstrating that the vaccination actually caused the injury in question. *Althen v. Sec'y of Health & Human Servs.*, 418 F.3d 1274, 1278 (Fed. Cir. 2005); *Hines v. Sec'y of Health & Human Servs.*, 940 F.2d 1518, 1525 (Fed. Cir. 1991). Here, the conditions alleged by petitioner – diplopia, ptosis, and myasthenia gravis – are not listed on the Vaccine Injury Table. Accordingly, petitioner must satisfy the burden of proof for an injury alleged to have been caused-in-fact by his flu vaccine.

The showing of "causation-in-fact" must satisfy the "preponderance of the evidence" standard, the same standard ordinarily used in tort litigation. § 300aa-13(a)(1)(A); *see also Althen*, 418 F.3d at 1279; *Hines*, 940 F.2d at 1525. Under that standard, the petitioner must show that it is "more probable than not" that the vaccination was the cause of the injury. *Althen*, 418 F.3d at 1279. The petitioner need not show that the vaccination was the sole cause but must demonstrate that the vaccination was at least a "substantial factor" in causing the condition, and was a "but for" cause. *Shyface v. Sec'y of Health & Human Servs.*, 165 F.3d 1344, 1352 (Fed. Cir. 1999). Thus, the petitioner must supply "proof of a logical sequence of cause and effect showing that the vaccination was the reason for the injury[,]" with the logical sequence being supported by "reputable medical or scientific explanation, *i.e.*, evidence in the form of scientific studies or expert medical testimony." *Althen*, 418 F.3d at 1278; *Grant v. Sec'y of Health & Human Servs.*, 956 F.2d 1144, 1148 (Fed. Cir. 1992). A petitioner may not receive a Vaccine Program award based solely on his or her assertions; rather, the petition must be supported by either medical records or by the opinion of a competent physician. § 300aa-13(a)(1).

In what has become the predominant framing of this burden of proof, the *Althen* court described the "causation-in-fact" standard, as follows:

> Concisely stated, Althen's burden is to show by preponderant evidence that the vaccination brought about her injury by providing: (1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of proximate temporal relationship between vaccination and injury. If Althen satisfies this burden, she is "entitled to recover unless the [government] shows, also by a preponderance of the evidence, that the injury was in fact caused by factors unrelated to the vaccine."

Althen, 418 F.3d at 1278 (citations omitted). The *Althen* court noted that a petitioner need not necessarily supply evidence from medical literature supporting petitioner's causation contention, so long as the petitioner supplies the medical opinion of an expert. *Id*. at 1279-80. The court also indicated that, in finding causation, a Program fact-finder may rely upon "circumstantial evidence," which the court found to be consistent with the "system created by Congress, in which close calls regarding causation are resolved in favor of injured claimants." *Id*. at 1280.

II. Procedural History

This case was initially assigned to Special Master Millman. (ECF No. 4.) Petitioner filed his medical records between November of 2016 and March of 2017. (ECF Nos. 6-7, 12; Exs. 1-15.) Thereafter, respondent confirmed his intention to defend the case and petitioner was ordered to file an expert report. (ECF Nos. 14, 15.)

Petitioner filed additional medical records in July of 2017 (ECF No. 19; Exs. 16-17) and an expert report by neurologist Thomas Morgan, M.D., in September of 2017 (ECF No. 20; Exs. 18-19). In November of 2017, respondent filed his Rule 4 Report and a responsive expert report by immunologist Neil Romberg, M.D. (ECF Nos. 23-25; Ex. A (inc. Tabs 1-12).) Petitioner then filed a supplemental expert report in April of 2018. (ECF No. 28; Ex. 20 (inc. Tabs A-C).)

Thereafter, a follow up status conference was held. (ECF No. 30.) During the status conference, respondent announced his intention of filing a motion for summary judgment in lieu of filing a further expert report. (*Id.*) That motion was filed on June 8, 2018. (ECF No. 31.) In the course of briefing, respondent filed two additional medical articles marked as Exhibits B and C. (ECF No. 34.) On July 9, 2018, Special Master Millman denied respondent's motion for summary judgment, concluding that the experts had raised issues that would likely be "fleshed out at trial" and that Vaccine Rule 3(d) therefore counseled in favor of allowing petitioner further opportunity to develop the record. (ECF No. 36.) The special master urged the parties to explore settlement; however, no further action was taken in the case until it was reassigned to the undersigned in June of 2019. (ECF Nos. 37-40.)

After the case was reassigned, an entitlement hearing was set for October of 2021. (ECF No. 47.) However, during a status conference held July 8, 2021, petitioner advised that Dr. Morgan is no longer available to participate in the case. (ECF No. 48.) The petitioner was given the option of either filing a report from a different expert and rescheduling the hearing or proceeding to a ruling on the written record. (*Id*.) Petitioner was ordered to confer with respondent and file a follow up status report on behalf of both parties indicating how they proposed to proceed. (*Id*.) Petitioner advised that the parties wished to proceed to a ruling on the written record. (ECF No. 49.)

Petitioner filed his motion for a ruling on the written record on August 30, 2021, along with an additional piece of medical literature marked as Exhibit 21. (ECF Nos. 50, 52.) Respondent filed a response on October 15, 2021. (ECF No. 53.) Petitioner filed a reply on November 12, 2021. (ECF No. 57.) However, petitioner also filed updated medical records at that time. (ECF No. 55; Ex. 22.) The parties therefore agreed that respondent should have an opportunity for sur-reply, which was filed on January 13, 2022. (ECF No. 58.)

I have determined that the parties have had a full and fair opportunity to present their cases and that it is appropriate to resolve this issue without a hearing. *See* Vaccine Rule 8(d); Vaccine Rule 3(b)(2); *Kreizenbeck v. Sec'y of Health & Human Servs*., 945 F.3d 1362, 1366 (Fed. Cir. 2020) (noting that "special masters must determine that the record is comprehensive and fully developed before ruling on the record."). Accordingly, this matter is now ripe for resolution.

III. Factual History

Petitioner received the flu vaccination at issue in this case on December 17, 2013. (Ex. 1, pp. 1-2.) About two weeks later, on December 31, 2013, petitioner presented to an ophthalmologist (Dr. Sharp) with a history of one and a half weeks of diplopia[3] and three days of headache. (Ex. 7, p. 8.) He reported no recent trauma. (*Id*.) He returned on January 3, 2018, with a further complaint of two to three days of foreign body sensation under his right upper eyelid. (*Id*. at 7.) He was diagnosed with persistent diplopia and nonspecific conjunctivitis. (*Id*.)

On January 24, 2014, petitioner followed up with his primary care physician (Dr. Tribuzio) during a routine wellness exam. (Ex. 4, p. 23.) Petitioner had complaints of fatigue, lower back pain, and hyperopia[4] for which he was seeing Dr. Sharp. Petitioner

[3] "The perception of two images of a single object; called also *ambiopia, double vision,* and *binocular polyopia." Diplopia,* DORLAND'S MEDICAL DICTIONARY ONLINE, https://www.dorlandsonline.com/dorland/definition?id=14354&searchterm=diplopia (last accessed Oct. 14, 2022).

[4] "An error of refraction in which rays of light entering the eye parallel to the optic axis are brought to a focus behind the retina, as a result of the eyeball being too short from front to back. [] Called also *farsightedness*[.]" *Hyperopia,* DORLAND'S MEDICAL DICTIONARY ONLINE, https://www.dorlandsonline.com/dorland/definition?id=23917&searchterm=hyperopia (last accessed Oct. 14, 2022).

also had high cholesterol and ALT. (*Id.*) He returned to Dr. Sharp on January 28, 2014. (Ex. 7, p. 6.) The diplopia and foreign body sensation persisted. (*Id*.)

On March 24, 2014, petitioner sought a second opinion from another ophthalmologist (Dr. Myers). (Ex. 11, pp. 1-3.) Dr. Myers recorded a history of intermittent diplopia since the prior November and a three-month history of foreign body sensation in the right eye. (*Id*. at 1.) Dr. Myers diagnosed blepharitis with mild allergic conjunctivitis and diplopia, which he questioned as being related to a mild decompensating phoria.[5] (*Id*. at 3.)

On April 7, 2014, petitioner consulted a neuro-ophthalmologist (Dr. Sergott). (Ex. 8, pp. 9-18; Ex. 7, pp. 33-36.) Petitioner reported intermittent diplopia since December that returned in early April as well as ptosis of the left eye beginning April 5th. (Ex. 8, p. 9.) Dr. Sergott's assessment was ptosis of the left eye with motility deficits in both eyes, which he felt was consistent with ocular myasthenia.[6] He prescribed Mestinon[7] and recommended anti-acetylcholine receptor antibody and thyroid testing. (*Id*. at 11.) Petitioner followed up with Dr. Sergott on April 17, 2014, and again on May 2, 2014. (*Id*. at 5-8.) Petitioner had only an "incomplete" response to Mestinon and his blood studies were normal. (*Id.* at 5.) Dr. Sergott therefore recommended imaging as well as an increased dose of Mestinon. (*Id*.) However, an MRI of petitioner's orbits dated May 2, 2014, showed no abnormalities. (Ex. 10, p. 30; Ex. 9, p. 3.)

Petitioner was seen for a neurology consultation (Dr. Bird) on May 8, 2014. (Ex. 9, pp. 2-4.) Petitioner provided a history consistent with the above and reported that the Mestinon was partly helping with his ptosis but not his diplopia. (*Id*. at 2.) Based on

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[5] "Failure of the visual axes to remain parallel after the visual fusional stimuli have been eliminated." *Heterophoria,* DORLAND'S MEDICAL DICTIONARY ONLINE, https://www.dorlandsonline.com/dorland/definition?id=22486 (last accessed Oct. 14, 2022). Heterophoria is usually asymptomatic. *Heterophoria,* WIKIPEDIA, https://en.wikipedia.org/wiki/Heterophoria (last accessed Oct. 14, 2022). This is when it is said to be "compensated". *Id.* When fusional reserve is used to compensate for heterophoria, it is known as compensating vergence. *Id.* In severe cases, when the heterophoria is not overcome by fusional vergence, sign and symptoms appear. *Id.* This is called "decompensated" heterophoria. *Id.*

[6] "Ocular myasthenia gravis is a form of myasthenia gravis (MG) in which the muscles that move the eyes and control the eyelids are easily fatigued and weakened." *Ocular MG,* Myasthenia.org, https://myasthenia.org/MG-Education/Learn-More-About-MG-Treatments/MG-Brochures/ocular-mg (last access Oct. 14, 2022). "Muscular weakness; any constitutional anomaly of muscle." *Myasthenia,* DORLAND'S MEDICAL DICTIONARY ONLINE, https://www.dorlandsonline.com/dorland/definition?id=32596&searchterm=myasthenia (last accessed Oct. 14, 2022).

[7] Mestinon is the trademark for preparations of pyridostigmine bromide. *Mestinon,* DORLAND'S MEDICAL DICTIONARY ONLINE, https://www.dorlandsonline.com/dorland/definition?id=30704&searchterm=Mestinon (last accessed Oct. 14, 2022). Pyridostigmine bromide is a cholinesterase inhibitor, "which acts by inhibiting destruction of acetylcholine and so facilitating transmission of impulses across the neuromuscular junction." *Pyridostigmaine bromide,* DORLAND'S MEDICAL DICTIONARY ONLINE, https://www.dorlandsonline.com/dorland/definition?id=42398 (last accessed Oct. 14, 2022). It's used as a "cholinergic in the symptomatic treatment of myasthenia gravis and for reversal of the effects of nondepolarizing neuromuscular blocking agents such as tubocurarine after surgery." *Id.*

history and exam, Dr. Bird concluded "He certainly has a history and examination typical of ocular myasthenia gravis. Given his symptoms and their fluctuation, I am not certain that this could be anything else other than ocular myasthenia gravis." (*Id*. at 3.) Given that his antibody results were negative, Dr. Bird recommended a single fiber EMG to try to confirm the diagnosis. He also suggested a chest MRI and to check MuSK antibodies. (*Id*.) A subsequent chest MRI on May 12, 2014, was unrevealing of any cause for petitioner's symptoms. (Ex. 10, p. 29.) Dr. Bird indicated that about half of patients with ocular myasthenia gravis develop generalized disease, typically within two to three years. (Ex. 9, p. 3.) Dr. Bird added prednisone to petitioner's treatment. (*Id*. at 4.)

On June 2, 2014, petitioner sought a second neurology opinion (Dr. Rakocevic). (Ex. 10, pp. 6-10.) Petitioner reported a history of diplopia beginning eight days post-vaccination and occurring off and on for about three weeks, followed by a more acute recurrence in late March of 2014 with left eyelid ptosis occurring about one week later. (*Id*. at 6.) He reported that the prednisone prescribed by Dr. Bird was helping his symptoms "significantly" and he felt he was nearly back to baseline. (*Id*. at 7.) MuSK antibodies were noted to be negative. (*Id*. at 8.) Dr. Rakocevic's impression was seronegative myasthenia gravis with ocular myasthenic syndrome. (*Id*.) Dr. Rakocevic recommended continuing the current treatment plan but tapering prednisone in the near future. He recommended further bloodwork to check for conditions, such as Lyme disease, that may mimic myasthenia gravis. (*Id*.) Petitioner returned to Dr. Sergott on June 6, 2014. (Ex. 8, p. 1; Ex. 7, p. 29.) Dr. Sergott indicated petitioner was "absolutely asymptomatic." (Ex. 1, p. 1.) He confirmed much of petitioner's workup had been unrevealing and indicated that he would "step into the background" and have petitioner continue with Dr. Rakocevic for ongoing management unless any specific neuro-ophthalmology issues arise. (*Id*.)

On October 6, 2014, petitioner's neurologist (Dr. Rakocevic) recorded that petitioner had successfully tapered off prednisone with no relapse having occurred during the past two months without the medication. (Ex. 10, pp. 1-2.) He recommended continuing on Mestinon. However, on the same date, petitioner's ophthalmologist (Dr. Myers) recorded that petitioner had been experiencing foreign body sensation in his right eye for the past six months. (Ex. 11, pp. 4-6.) He confirmed the myasthenia gravis had improved with prednisone and again diagnosed blepharitis and mild allergic conjunctivitis. (*Id*. at 6.)

On December 18, 2014, petitioner returned to Dr. Myers indicating that his myasthenia gravis symptoms had returned. (Ex. 7, p. 15; Ex. 11, p. 10.) He did not report diplopia but indicated that he was slow to focus each eye. (*Id*.) Petitioner returned to Dr. Myers on January 29, 2015. (Ex. 11, p. 15.) At that time Dr. Myers noted that petitioner was continuing to taper his prednisone, currently on 10mg and planning to reduce to 5mg. (*Id*.) Given that Dr. Rakocevic's prior record of October 6, 2014 indicated petitioner was off prednisone, it is not clear when he resumed. (*Compare* Ex. 11, p. 15, *and* Ex. 10, pp. 1-2.) Dr. Myers reported as of April 28, 2015,

that during that month petitioner had increased from 10 mg of prednisone to 30 mg. (Ex. 7, p. 5.)

Dr. Tribuzio later noted during petitioner's July 14, 2015, annual exam that he was concerned petitioner was "on and off prednisone" and recommended considering IVIG and a bone density test. (Ex. 4, pp. 18-22.) It is noted that petitioner would be asking neurology about vaccines, with Dr. Tribuzio noting that "I suspect he is no longer going to receive his flu vaccine with concern[] that this started afterwards." (*Id*. at 18.) In March of 2016, petitioner returned to his primary care physician complaining of insomnia he felt was related to his use of prednisone. (*Id*. at 7-9.) He noted that he had started a higher dose does to a recent flare of his myasthenia gravis. (*Id*. at 8.) However, on March 29, 2016, his myasthenia gravis was noted to be stable. (Ex. 7, p. 4.) As of June 2016, petitioner was again tapering his prednisone with concerns that it was causing anxiety. (Ex. 4, pp. 1-3, 4-6; Ex. 11, pp. 16-20.)

On October 24, 2016, petitioner reported that his diplopia had been worse over the past month and that he planned to seek a second opinion at Johns Hopkins. (Ex. 14, pp. 1-3.) Since tapering his prednisone during the summer of 2016, petitioner was experiencing new weakness in his arms and legs as well as fatigue and difficulty swallowing. (*Id.* at 1.) He was also noticing tremors in his thumb and toes. (*Id*. at 2.) Increasing prednisone again was not helping. (*Id*.)

On November 30, 2016, petitioner had a neurology consultation with Dr. Corse at Johns Hopkins. (Ex. 15, pp. 21-24.) Dr. Corse felt petitioner had a history suggestive of seronegative autoimmune generalized myasthenia gravis, which she intended to confirm. (*Id.* at 23.) Dr. Corse ordered repeat bloodwork and a single fiber EMG, though she was concerned petitioner mild symptomatology and rigorous prednisone treatment would reduce the sensitivity of the test. (*Id*.) Dr. Corse was concerned petitioner's prednisone dose was too high to be safe for long term management and felt he would be a good candidate for an immunosuppressive treatment to spare steroids. (*Id*.) Both the bloodwork and EMG were normal, but Dr. Corse still felt seronegative autoimmune myasthenia gravis was the correct diagnosis and started petitioner on mycophenolate (an immunosuppressive). (*Id.*)

Petitioner saw a new ophthalmologist (Dr. Silbert) on April 14, 2017, complaining of tearing, worse in the right eye, since December. (Ex. 16, p. 10.) On examination, petitioner had nasolacrimal obstruction in both eyes, near complete in the left eye and partial in the right. Surgery was recommended. (*Id*.) Petitioner had eye surgery on May 12, 2017. (*Id.* at 18.)

In his motion for a ruling on the record, petitioner asserts that he has continued to experienced symptoms of his myasthenia gravis, including diplopia, ptosis, limb fatigue and difficulties with speech, chewing, and swallowing. (ECF No. 52, p. 16.) The updated medical records subsequently filed by petitioner confirm as of February 25, 2019, that petitioner remained symptomatic, most notably with worsening diplopia, but at least as of that most recent evaluation, without significant limb weakness or difficulty

speaking, swallowing, chewing. (Ex. 22, p. 24.) However, these updated records confirm that as of December 2018 he tested positive for AChR antibodies, making his myasthenia gravis seropositive. (*Id*. at 28.)

IV. Expert Opinions

Petitioner relies on an expert opinion by neurologist Thomas F. Morgan, M.D., to support his claim.[8] (Exs. 18, 20.) Dr. Morgan agrees with petitioner's clinical diagnosis of generalized and ocular myasthenia gravis, which was still seronegative at the time he created his report. (Ex. 18, p. 5.) He explains that, in addition to genetic susceptibility, myasthenia gravis is explained by an autoimmune mechanism involving the formation of antibodies to acetylcholine receptors at the neuromuscular junction. (*Id.*) He asserts that it can be caused by antibodies formed either post-viral infection or post immunization. (*Id.* (citing IOM (Institute of Medicine), *Adverse Effects of Vaccines: Evidence and Causality,* National Academies Press: Washington, DC (2011), pp. 51-52, 61-63 (Ex. 18, Tab D)).)[9] Dr. Morgan opines that onset of petitioner's myasthenia gravis symptoms, occurring three days post flu vaccination, is consistent with an autoimmune mechanism. (*Id*. at 6.)

Dr. Morgan cites literature referencing post-hepatitis B vaccine myasthenia gravis. (Meng-Ying Hsieh et al., *Combined Guillain-Barre syndrome and myasthenia gravis,* 35 BRAIN & DEV. 865 (2013) (Ex. 18, Tab G, Table 1, Ref 14); Joerg-Patrick Stubgen, *Neuromuscular disorders associated with Hepatitis B vaccination;* 202 J. NEUROLOGICAL SCI. 1 (2010) (Ex. 18, Tab H)).) Additionally, small studies have experimentally shown cross reaction between herpes simplex and other microbial peptides and human sera; however, these studies were deemed too small to determine the significance of the cross reaction. (Anne Eroclini & Stephen Miller, *Role of immunologic cross-reactivity in neurological diseases,* 27(7) NEUROLOGICAL RES. 726, 730 (2005) (Ex. 18, Tab F).) He states that "[a]lthough there are no specific case reports of flu vaccine causally related to myasthenia gravis, a characterized autoimmune mechanism of molecular mimicry with antibodies to vaccinations and

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[8] Dr. Morgan received his medical degree from Meharry Medical College in 1970. (Ex. 19, p. 1.) He is board certified by the American Board of Independent Medical Examiners, the American Board of Psychiatry and Neurology, and the Rhode Island Board of Medical Licensure and Discipline. (*Id*. at 3.) As of the date of his curriculum vitae, Dr. Morgan is an assistant clinical professor at Brown University where he also serves on the university healthcare team and as a neurology consultant. (*Id*. at 4.) Dr. Morgan has authored numerous publications relating to neurology and neuropathology and has conducted a variety of neurological studies. (*Id*. at 4-5.)

[9] The 2012 IOM publication cited by Dr. Morgan is over 800 pages and assesses epidemiologic and mechanistic evidence bearing on proposed relationships between a number of specific vaccines and specific disorders. However, the specific pages excerpted by Dr. Morgan include a general discussion of immune mechanisms that do not specifically address the causes of myasthenia gravis. (IOM Report, *supra,* at Ex. 18, Tab D.) Included in the excerpted pages is a discussion of molecular mimicry and the fact that cross reaction can occur following antigen exposure from natural infection, vaccine, or drug exposure. (*Id.* at 61-62.) However, although that section includes some specific examples, neither AChR antibodies nor myasthenia gravis are discussed. (*Id*.) In fact, upon my own review of the complete publication, the IOM did not address myasthenia gravis at all.

viruses makes the flu vaccine more probable than not the cause of [petitioner's] seronegative myasthenia gravis." (Ex. 18, p. 5.) In support of this proposition, Dr. Morgan cites a case report of a 17-year-old who experienced both GBS and myasthenia gravis, though there was no suggestion of vaccine causation either in that case or in a discussion of eleven prior cases discussed as part of a literature review. (Hsieh et al., *supra,* at Ex. 18, Tab G.) Although the authors noted that GBS and myasthenia gravis have some similarities, they stressed that the conditions involved different autoantibodies against different tissues (peripheral nerves and neuro-muscular junctions respectively). (*Id*. at 868-69.)

In response to Dr. Morgan's first report, respondent filed a report by immunologist Neil Romberg, M.D.[10] (Ex. A.) Dr. Romberg does not disagree with the general proposition that myasthenia gravis represents an autoimmune condition involving autoantibodies against neuromuscular junctions. (*Id*. at 2.) However, he does disagree that there is evidence to implicate the flu vaccine as a cause of myasthenia gravis via a theory of molecular mimicry involving cross-reaction between vaccine antigen and neuromuscular junction proteins. (*Id*.) Dr. Romberg confirms Dr. Morgan's acknowledgement that no case reports of post-flu vaccine myasthenia gravis exist. He further notes that a study of 3,667 hospitalizations among 513 myasthenia gravis patients in Canada showed that administration of the flu vaccine did not lead to an increased risk of disease flare within the weeks after vaccination. (*Id*. at 3 (citing Lorne Zinman et al., *Safety of Influenza vaccination in patients with myasthenia gravis: a population-based study,* 40 MUSCLE & NERVE 947 (2009) (Ex. A, Tab 6).) According to Dr. Romberg, the type of epidemiologic association lacking here, is one of the lines of evidence that can support a theory of molecular mimicry. (*Id*. at 4.)

Dr. Romberg also agrees that AChR autoantibodies are the primary driver of myasthenia gravis. (Ex. A, p. 4.) However, he explains two studies that suggest molecular mimicry is not involved. First, researchers studying B cells from the thymuses of myasthenia gravis patients found their immunoglobulin genes to be highly mutated. (*Id.* (citing Gary Sims et al., *Somatic hypermutation and selection of B cells in thymic germinal centers responding to acetylcholine receptor in myasthenia gravis,* 167 J. IMMUNOL. 1935 (2001) (Ex. A, Tab 14)).) According to the authors, the study provides "direct evidence that ectopic [germinal centers] are responsible for maintaining an autoimmune response through selection of specific self-reactive B cells." (Sims et al., *supra,* at Ex. A, Tab 14, p. 1943.) Second, a separate study indicates that autoantibodies from myasthenia gravis patients bind with high affinity to the same AChR

[10] Dr. Romberg received his medical degree from Pennsylvania State College of Medicine in 2004. (Ex. D, p. 1.) He is board certified by the American Board of Pediatrics and the American Board of Allergy and Immunology, and he holds a Pennsylvania State Medical License. (*Id*. at 2.) Dr. Romberg is an assistant professor of pediatrics at the Children's Hospital of Philadelphia for the University of Pennsylvania School of Medicine. (*Id*. at 1.) He also serves as an attending physician (immunology) at Children's Hospital of Philadelphia. (*Id.*) Dr. Romberg is a founding member of the Dysregulated Immunity Program at Children's Hospital of Philadelphia. (*Id.*) His career has focused on caring for patients with inherited immunological disorders and investigating the molecular mechanism that underlie their diseases. (Ex. A, p. 1.)

sites as those from AChR sensitized mice. (Ex. A, p. 4 (citing Socrates Tzartos et al., *Specificities of antibodies to acetylcholine receptors in sera from myasthenia gravis patients measured by monoclonal antibodies,* 79 PROC. NATL. ACAD. SCI. USA 188 (1982) (Ex. A, Tab 15)).) According to Dr. Romberg these studies together suggest that it is unlikely molecular mimicry is a meaningful contributor to the immunopathology of myasthenia gravis. (Ex. A, pp. 4-5.) Specifically, Dr. Romberg explains that "the antigen driving [myasthenia gravis] autoantibody production in humans is highly likely to be AChR, the same antigen driving autoantibody production and not cross-reacting viral or vaccine containing antigen." (*Id*. at 4.) Dr. Romberg further notes that the published literature includes no animal model in which influenza vaccine antigen has been shown to cause features of myasthenia gravis. (*Id*. at 4.) Moreover, he notes that myasthenia gravis patients benefit from the flu vaccine given that they are a population at high risk of influenza-related complications. (*Id*. at 3.)

Finally, Dr. Romberg opines that the onset of petitioner's own myasthenia gravis, occurring only three to four days post-vaccination, is too early to have been the result of a primary humoral immune response. (Ex. A, p. 5.) Specifically, he indicates that the lag phase between a primary antigen exposure and develop of an antibody response is at least seven to ten days. (*Id*. (citing IOM Report, *supra,* at Ex. 18, Tab D).)

In response to Dr. Romberg's opinion, Dr. Morgan filed a supplemental report. (Ex. 20.) Dr. Morgan agrees there is no epidemiology to support this theory. (*Id*. at 2.) He also agrees that myasthenia gravis patients should, in general, be vaccinated for influenza. (*Id*.) Nonetheless, he opines that there can be cross-reaction to peptides within the flu vaccine in some patients having underlying predisposition. (*Id*.) He maintains that molecular mimicry is an important hypothesis in this context and suggests that there is recent data to suggest cross reactivity between several microbial antigens and acetylcholine receptor subunits. (*Id*. (citing S. Lee & M. C. Levin, *Molecular mimicry in neurological disease: what is the evidence?* 65 CELL. MOL. LIFE SCI. 1161 (2008) (Ex. 20, Tab A)).) Citing the Institute of Medicine, Dr. Morgan identifies the following as "essential" to concluding molecular mimicry explains a given condition: (1) a susceptible host allowing for emergence of self-reactive immunity, (2) exposure to an exogenous agent with antigens immunologically similar to self-antigens, and (3) an immune response to that exogenous agent that cross reacts with biologically relevant tissue structures leading to clinical disease. (*Id*.)

V. Additional Medical Literature

In this case, both parties filed additional medical literature that was not directly addressed by the experts. First, when respondent filed his motion for summary judgment, he also filed two articles marked as Exhibits B and C. (Michael Nicolle, *Myasthenia gravis and Lamber-Eaton myasthenic syndrome,* 22(6) CONTINUUM 1978 (2005) (Ex. B); Perry B. Shieh, *Congenital Myasthenic Syndromes,* 36 NEUROL. CLIN. 367 (2018) (Ex. C).) According to respondent, these papers reflect the distinction between myasthenia gravis and myasthenic syndrome, a distinction relevant to a dispute between the parties regarding searches of the Vaccine Adverse Events

Reporting System ("VAERS") that I do not find it necessary to address. (ECF No. 33, p. 5.) Later, when petitioner filed his motion for a ruling on the record, he filed an article marked as Exhibit 21. (Hung Youl Seok et al., *The impacts of influenza infection and vaccination on exacerbation of myasthenia gravis,* 13(4) J. CLIN. NEUROL. 325 (2017) (Ex. 21).) Petitioner cited this study for the proposition that the fact that the flu vaccination has a protective effect for myasthenia gravis patients is not evidence that the vaccine is entirely risk free. (ECF No. 52, p. 29 (citing Seok et al., *supra,* at Ex. 21).)

VI. Discussion

a. *Althen* prong one

Under *Althen* prong one, a petitioner must provide a "reputable medical theory," demonstrating that the vaccine received can cause the type of injury alleged. *Pafford v. Sec'y of Health & Human Servs.*, 451 F.3d 1352, 1355–56 (Fed. Cir. 2006) (citations omitted). To satisfy this prong, petitioner's theory must be based on a "sound and reliable medical or scientific explanation." *Knudsen v. Sec'y of Health & Human Servs.*, 35 F.3d 543, 548 (Fed. Cir. 1994). Such a theory must only be "legally probable, not medically or scientifically certain." *Id.* at 549. Generally, however, petitioners may satisfy the first *Althen* prong without resort to medical literature, epidemiological studies, demonstration of a specific mechanism, or a generally accepted medical theory. *Andreu v. Sec'y of Health & Human Servs.,* 569 F.3d 1367, 1378-79 (Fed. Cir. 2009) (citing *Capizzano v. Sec'y of Health & Human Servs.*, 440 F.3d 1317, 1325-26 (Fed. Cir. 2006)).

Here, Dr. Morgan successfully establishes two broad predicates for his theory of causation. There is little debate that myasthenia gravis is an autoimmune neuromuscular disorder and there is little debate that molecular mimicry is, in general, a viable theory of autoimmunity that can in at least some contexts implicate vaccination. Importantly, however, these predicates are not enough to meet petitioner's burden of proof. *W.C. v. Sec'y of Health & Human Servs.,* 704 F.3d 1352, 1360-61 (Fed. Cir 2013); *Tullio v. Sec'y of Health & Human Servs.,* 149 Fed.Cl. 448, 468 (2020); *Deshler v. Sec'y of Health & Human Servs*., No. 16-1070V, 2020 WL 4593162, at *20 (Fed. Cl. Spec. Mstr. July 1, 2020); *McKown v. Sec'y of Health & Human Servs.,* No. 15-1451V, 2019 WL 4072113, at *50 (Fed. Cl. Spec. Mstr. July 15, 2019). Dr. Morgan fails to link the influenza vaccine to myasthenia gravis in any meaningful way.

As a threshold matter, Dr. Romberg suggests that there is literature available (citing Sims and Tzartos respectively) that undermines the notion of molecular mimicry contributing to myasthenia gravis specifically. In response, Dr. Morgan cites to literature that suspects that some antigens, most notably herpes simplex virus and hepatitis B vaccine, might cross react with neuromuscular junction proteins. (Stubgen, *supra,* at Ex. 18, Tab H; Lee & Levin, *supra,* at Ex. 20, Tab A.) This is enough to show that Dr. Romberg's reliance on the Sims and Tzartos studies does not definitively *disprove* that molecular mimicry is a relevant concept for myasthenia gravis. (Ex. A, pp. 4 (citing

Sims et al., *supra,* at Ex. A, Tab 14; Tzartos et al., *supra,* at Ex. A, Tab 15).) (Nor does Dr. Romberg push his assertion that far.) However, the record as a whole suggests that the question of whether molecular mimicry plays a role in causing myasthenia gravis is best characterized as unsettled.

In any event, even assuming molecular mimicry is an established contributor to myasthenia gravis, Dr. Morgan identifies evidence of cross-reaction between the exogenous agent at issue and a relevant host tissue as "essential" to concluding that molecular mimicry is at work.[11] (Ex. 20, p. 2.) This further requires that the exogenous agent have some immunologic similarity to a self-antigen, in this case AChR. (*Id*.) But evidence favoring either of these points is lacking in this case vis-à-vis the flu vaccine.

Dr. Morgan agrees that no epidemiology is available to support the theory. (Ex. 20, p. 2.) Dr. Romberg, in contrast, cites the Zinman study as some evidence tending to suggest the flu vaccine is safe for myasthenia gravis patients.[12] (Zinman et al., *supra,* at Ex. A, Tab 6.) Dr. Morgan also acknowledges that there are no published case reports to support the theory. (Ex. 18, p. 5.) Further to this, Dr. Romberg asserts that there is no relevant animal model demonstrating the cross-reaction experimentally, a point that Dr. Morgan did not counter. (Ex. A, p. 4.) Petitioner has filed a study that shows "influenza infection constitutes a specific and important risk factor for [myasthenia gravis] symptom exacerbation," however, the same study confirmed that the same risk is not present following influenza vaccination. (Seok et al., *supra,* at Ex. 21, p. 5.) Petitioner points out that two patients out of 133 experienced an aggravation post-vaccination and argues that "that the wild virus itself is a more significant risk compared to vaccination does not mitigate all risk." (ECF No. 52, p. 30.) This is true as far as it goes, but relative risk is not the issue given that the study result was not considered significant compared to unvaccinated controls. In fact, the authors noted their results to be consistent with two prior studies that found no increased risk of exacerbation following influenza vaccination. (Seok et al., *supra,* at Ex. 21, p. 4.) Otherwise, as noted above, the record of this case suggests that it is other antigens, such as Hepatis B or herpes simplex, that may be suspected of being capable of the relevant cross-reaction.

Petitioner stresses that he is not obligated to come forward with medical literature or other documentation objectively confirming his expert's theory or establishing general acceptance. (ECF No. 52, pp. 27-28 (citing *Andreu*, 569 F.3d at 1378).) However, it is

[11] In his motion for a ruling on the written record, petitioner argues that Dr. Romberg applies too-elevated a standard for assessing molecular mimicry. (ECF No. 52, pp. 26-27.) Importantly, however, I am applying Dr. Morgan's assessment of what is necessary to invoke molecular mimicry.

[12] Although petitioner is not obligated to come forward with epidemiologic proof, special masters do weigh the epidemiology that is filed. *D'Tiole v. Sec'y of Health & Human Servs.*, 726 F. App'x 809, 811 (Fed. Cir. 2018) (citing *Andreu*, 569 F.3d at 1379 ("Although *Althen* and *Capizzano* make clear that a claimant need not produce medical literature or epidemiological evidence to establish causation under the Vaccine Act, *where such evidence is submitted*, the Special Master can consider it in reaching an informed judgment as to whether a particular vaccination likely caused a particular injury." (emphasis added)); *Grant*, 956 F.2d at 1148-49 (considering negative epidemiological studies).

necessary that petitioner come forward with expert opinion that is sound and reliable. *Boatmon v. Sec'y of Health & Human Servs.*, 941 F.3d 1351, 1359-60 (Fed. Cir. 2019). Special masters are not required to accept an expert's *ipse dixit*. *Snyder v. Sec'y of Health & Human Servs.,* 88 Fed. Cl. 706, 743 (2009). Here, Dr. Morgan opines in favor of vaccine causation despite clearly failing to support the three-part test he himself set forth for establishing the relevance of molecular mimicry. (Ex. 20, p. 2.)

In light of the above, petitioner has not met his preponderant burden of proof with respect to *Althen* prong one.

b. *Althen* prong two

The second *Althen* prong requires proof of a logical sequence of cause and effect, usually supported by facts derived from a petitioner's medical records. *Althen*, 418 F.3d at 1278; *Andreu*, 569 F.3d at 1375-77; *Capizzano*, 440 F.3d at 1326; *Grant*, 956 F.2d at 1148. In establishing that a vaccine "did cause" injury, the opinions and views of the injured party's treating physicians are entitled to some weight. *Andreu*, 569 F.3d at 1367; *Capizzano*, 440 F.3d at 1326 (quoting *Althen*, 418 F.3d at 1280) (stating that "medical 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'"). However, medical records and/or statements of a treating physician's views do not *per se* bind the special master to adopt the conclusions of such an individual, even if they must be considered and carefully evaluated. *See* Section 13(b)(1) (providing that "[a]ny such diagnosis, conclusion, judgment, test result, report, or summary shall not be binding on the special master or court"); *Snyder*, 88 Fed. Cl. at 746 n.67 (stating that "there is nothing . . . that mandates that the testimony of a treating physician is sacrosanct—that it must be accepted in its entirety and cannot be rebutted").

In this case, petitioner identifies the following factors as bearing on vaccine causation: petitioner was healthy prior to vaccination; his symptoms of myasthenia gravis arose in a medically acceptable timeframe post-vaccination; three of his physicians recorded that there was a temporal association to the vaccination[13]; and no other cause for petitioner's condition (such as thymoma, paraneoplastic syndrome, Lyme disease, or thyroid disease) was discovered after extensive evaluation. (ECF No. 52, p. 31-32; ECF No. 57, p. 5.) Petitioner stresses that "medical records and medical opinion can satisfy *Althen* prong two, and [. . .] evidence used to satisfy one of the *Althen* prongs can overlap to satisfy another prong." (ECF No. 52, p. 31 (quoting *Lozano v. Sec'y of Health & Human Servs.*, 958 F.3d 1363 (Fed. Cir. 2020).) Thus, petitioner asserts that, because he has demonstrated a reliable medical theory and a

[13] Specifically, petitioner cites Dr. Rakocevic as noting that "[h]e had a flu shot and about eight days later he had the onset of double vision." (Ex. 10, p. 6.) Petitioner also cites Dr. Corse as noting "[h]e dates the onset of his symptoms to 3 days after a flu shot in December 2013, 3 years ago." (Ex. 15, p. 21.) And petitioner cites Dr. Goyal as observing symptoms began after petitioner's December 2013 flu vaccine. (Ex. 22, pp. 12, 15.) I also note that Dr. Tribuzio recorded that "I suspect he is no longer going to receive his flu vaccine with concern[] that this started afterwards." (Ex. 4, p. 18.) However, my interpretation of this medical record is that Dr. Tribuzio is referring to petitioner's own subjective concern.

temporal relationship, the above-discussed factors are sufficient to substantiate that his vaccine was a substantial contributing factor in the development of his condition as required by *Althen* prong two. (*Id*. at 32.)

Here, petitioner's argument is unavailing given that he did not, in fact, present a reliable medical theory for all the reasons discussed above. Dr. Morgan's causal opinion therefore does not meet petitioner's burden with respect to either *Althen* prong one or *Althen* prong two. Additionally, none of petitioner's treating physicians otherwise actually opined that petitioner's condition was vaccine-caused. While treating physician records are given significant weight, "[a] treating physician's recognition of a temporal relationship does not advance the analysis of causation." *Isaac v. Sec'y of Health & Human Servs*., No. 08-601V, 2012 WL 3609993, at *26 (Fed. Cl. Spec. Mstr. July 30, 2012); *see also Devonshire v. Sec'y of Health & Human Servs.*, No. 99-031V, 2006 WL 2970418, at *19 (Fed. Cl. Spec. Mstr. Sept. 28, 2006) (medical expert's "*post hoc ergo prompter hoc* reasoning . . . has been consistently rejected by the Court and is 'regarded as neither good logic nor good law'") (quoting *Fricano v. U.S.*, 22 Cl. Ct. 796, 800 (1991) (emphasis in original)). Nor is a temporal relationship standing alone sufficient to meet *Althen* prong two. *See*, *e.g.*, *Veryzer v. Sec'y of Health & Human Servs.*, 100 Fed. Cl. 344, 356 (2011) (explaining that "a temporal relationship alone will not demonstrate the requisite causal link and that petitioner must posit a medical theory causally connecting the vaccine and injury"). In his reply, petitioner stresses that treating physicians may rely on a close temporal proximity to inform their causal opinion. (ECF No. 57, p. 6, n. 12 (citing *Andreu*, 569, 569 F.3d at 1376).) Here, however, the physician statements are better characterized as merely noting the temporality as history rather than agreeing that it is causally relevant.

An additional point warrants mention. Subsequent to the filing of the expert reports in this case, petitioner tested positive for AChR antibodies in December of 2018. (Ex. 22, p. 28.) Thus, petitioner is seropositive for the antibodies that both experts agree are likely relevant to the etiopathogenesis of myasthenia gravis. (Ex. A, p. 4; Ex. 18, p. 5.) Importantly, however, these autoantibodies are expected regardless of what, if anything, triggered the disorder. For example, Dr. Romberg explains that these autoantibodies are present in 90% of cases. (Ex. A, p. 4.) Thus, while the presence of these autoantibodies is helpful in tending to clinically confirm that the relevant autoimmune process is occurring, it is not dispositive with respect to vaccine-causation.[14]

In light of the above, petitioner has not met his preponderant burden of proof with respect to *Althen* prong two.

[14] For this reason it is not necessary to resolve the significance of the fact that the antibodies were first detected five years after vaccination. Respondent appears to suggest that the causal significance of the result should be viewed with suspicion given that it is remote to vaccination and there were intervening negative results. (ECF No. 58, p. 2.) Petitioner suggests, however, that it is simply the case that the later test was more sensitive than the prior tests, implying the prior tests may have been inadequate. (ECF No. 57, p. 5.)

c. *Althen* prong three

The third *Althen* prong requires establishing a "proximate temporal relationship" between the vaccination and the injury alleged. *Althen*, 418 F.3d at 1281. That term has been equated to the phrase "medically-acceptable temporal relationship." *Id.* A petitioner must offer "preponderant proof that the onset of symptoms occurred within a timeframe which, given the medical understanding of the disorder's etiology, it is medically acceptable to infer causation." *de Bazan v. Sec'y of Health & Human Servs.*, 539 F.3d 1347, 1352 (Fed. Cir. 2008). The explanation for what is a medically acceptable timeframe must coincide with the theory of how the relevant vaccine can cause an injury (*Althen* prong one's requirement). *Id.* at 1352; *Shapiro v. Sec'y of Health & Human Servs.*, 101 Fed. Cl. 532, 542 (2011), *recons. den'd after remand*, 105 Fed. Cl. 353 (2012), *aff'd mem.*, 503 Fed. Appx. 952 (Fed. Cir. 2013); *Koehn v. Sec'y of Health & Human Servs.*, No. 11-355V, 2013 WL 3214877 (Fed. Cl. Spec. Mstr. May 30, 2013), *mot. for review den'd,* (Fed. Cl. Dec. 3, 2013), *aff'd*, 773 F.3d 1239 (Fed. Cir. 2014).

As discussed in more detail within the factual summary, petitioner first presented with a complaint of diplopia two weeks post-vaccination and at that time indicated it had been present for about a week and a half. (Ex. 7, p. 8.) This places onset about three to four days post-vaccination. Although there are some inconsistencies in the later reports, both experts discuss latency on the assumption that onset occurred three to four days post-vaccination, differing only on whether this is medically reasonable in light of Dr. Morgan's theory. (Ex. 18, p. 6; Ex. A, p. 5.) Citing to the IOM excerpt originally included with Dr. Morgan's report, Dr. Romberg asserts that it takes at least seven to ten days of lag phase to develop the type of antibody response implicated in Dr. Morgan's theory. (Ex. A, p. 5 (citing IOM Report, *supra,* at Ex. 18, Tab D).) Importantly, however, Dr. Romberg cites the primary response time discussed by the IOM while also stressing that petitioner had also been vaccinated with the prior year's flu vaccine that contained "nearly identical strains" as the vaccine at issue in this case. (*Id*.) In the context of a second exposure, the IOM suggests a shorter latency, with a lag phase of one to three days. (IOM Report, *supra,* at Ex. 18, Tab D, p. 52.)

Thus, petitioner has preponderantly established that onset of petitioner's myasthenia gravis occurred within a timeframe consistent with molecular mimicry. Accordingly, assuming arguendo petitioner had met his burden of proof under *Althen* prong one and successfully showed molecular mimicry to be relevant to the cause(s) of myasthenia gravis, then he also would have satisfied *Althen* prong three.

VII. Conclusion

Petitioner has my sympathy for what he has endured. However, for all the reasons discussed above, he has not preponderantly established that his diplopia, ptosis, and myasthenia gravis were caused-in-fact by his December 17, 2013 flu

vaccination. Accordingly, petitioner is not entitled to compensation. Therefore, this case is dismissed.[15]

IT IS SO ORDERED.

s/Daniel T. Horner
Daniel T. Horner
Special Master

[15] In the absence of a timely-filed motion for review of this Decision, the Clerk of the Court shall enter judgment accordingly.