In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

No. 17-722V

(To be published)

L.C., parent of K.N., a minor, Petitioner, v. SECRETARY OF HEALTH AND HUMAN SERVICES, Respondent.	Chief Special Master Corcoran Dated: July 2, 2021

Ronald Craig Homer, Conway, Homer, P.C., Boston, MA, for Petitioner.

Mollie Gorney, U.S. Department of Justice, Washington, DC, for Respondent.

ENTITLEMENT RULING[1]

On May 31, 2017, L.C. filed a claim filed on behalf of her minor daughter, K.N., for compensation pursuant to the National Vaccine Injury Compensation Program (the "Vaccine Program").[2] The Petition alleged that K.N. suffered from a neurological demyelinating disorder as a result of her receipt of a Tetanus-diphtheria-acellular pertussis ("Tdap") vaccine on June 7, 2014. Petition (ECF No.1) at 1. An entitlement hearing in the matter was held on March 16, 2021.

Having reviewed the materials filed in this case and considered the parties' arguments, I hereby find that Petitioner has met her burden of proof, and is therefore entitled to damages. As discussed in greater detail below, the experts on both sides agreed that K.N. likely suffered from

[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, upon review, I agree that the identified material fits within this definition, it will be redacted from public access.

[2] The Vaccine Program comprises Part 2 of the National Childhood Vaccine Injury Act of 1986, Pub. L. No. 99-660, 100 Stat. 3755 (codified as amended at 42 U.S.C. §§ 300aa-10–34 (2012)) (hereinafter "Vaccine Act" or "the Act"). All subsequent references to sections of the Vaccine Act shall be to the pertinent subparagraph of 42 U.S.C. § 300aa.

Myelin Oligodendrocyte Glycoprotein ("MOG") Antibody Disease ("MOGAD"), a neuroinflammatory condition and recently-coined diagnostic concept. Although not much is yet known about MOGAD's pathogenesis, I find sufficient preponderant evidence was offered in this case to support Petitioner's contention that the Tdap vaccine could cause MOGAD, and did so here.

I. Medical History

K.N. was born in 2004. Ex. 1 at 1. Prior to vaccination, she was a healthy ten year-old girl. *See generally* Ex. 2. On June 7, 2014, K.N. received the Tdap vaccine. Ex. 1 at 2; Ex. 2 at 9. Afterwards, K.N. traveled to France for a family vacation, during which time her mother reported she experienced no medical issues. Ex. 3 at 24-26. Within a couple of weeks of receiving the vaccine, however, Petitioner asserts that K.N. started complaining of headaches, and then at the beginning of July began having problems with her vision. Ex. 10 at 2. On July 4, 2014, K.N. woke up crying, telling her mother that she could not see anything. *Id.* L.C. therefore rushed K.N. to the emergency room at the California Pacific Medical Center in San Francisco, California. *Id.*

Emergency care treaters recorded K.N. as experiencing bilateral vision loss which had started approximately two to three days earlier. Ex. 3 at 4, 24, 175. It was also noted that K.N. had a "recent sick contact" with her cousin, who had a fever, but K.N. had not felt ill herself. *Id.* at 24. The results of a brain MRI showed "[s]uspected bilateral optic neuritis." *Id.* at 168. She received treatment with high-dose steroids, and on July 5, 2014, was transferred out of the intensive care unit. *Id.* at 175. Her pediatric neurologist proposed K.N. had acute disseminated encephalomyelitis ("ADEM"). *Id.* at 146.

K.N. remained hospitalized until July 7, 2014, and during that time her vision improved following treatment with steroids. Ex. 3 at 5. Upon discharge, K.N.'s diagnosis was parainfectious optic neuritis ("ON"), and her prognosis was deemed excellent. *Id.* On July 8, 2014, K.N. underwent a neuro-ophthalmology evaluation with Richard Imes, M.D. Ex. 2 at 50. Petitioner reported that K.N. "may have [had] a mild fever with a headache a couple of weeks prior to losing [her] vision." *Id.* K.N.'s optic disc swelling had improved, and Dr. Imes recommended tapering her steroid treatment over the next ten days. *Id.* He concluded that K.N. most likely had experienced ON "despite the vague history of an antecedent viral illness… Post-immunization bilateral optic neuritis is well reported but not after DTaP vaccine." *Id.*

On July 23, 2014, K.N. had a follow-up appointment for her ON. Ex. 4 at 1083. Her vision was 20/150 in her right eye and 20/200 in her left eye. *Id.* at 1084. The impression was that K.N. had isolated papillitis bilaterally, and her treater noted it was "[v]ery unlikely to be [multiple sclerosis] or other systemic pathology and ot [sic] related to recent vaccination as no other cortical

leukoencephalopathy [was] seen. This condition is thought to be post-viral." *Id.* at 1086. On July 29, 2014, K.N. visited ophthalmology for another follow-up and the record noted that the "[p]atient feels like visual acuity improved…Medications: stopped steroids 2 days ago… Assessment/plan: optic neuritis: Improving, now feels like visual acuity almost back to baseline." Ex. 8 at 1.

On August 26, 2014, K.N.'s pediatrician examined her for a recent headache with a fever (which improved with ibuprofen) and vomiting. Ex. 2 at 8. K.N. also reported decreased energy, but she denied eye pain or blurriness. *Id.* Two days later, on August 28, 2014, K.N. presented to the emergency room at the University of California – San Francisco due to acute onset left-sided "body shaking, numbness, and weakness." Ex. 4 at 56. By this time, K.N.'s ON had "nearly completely resolved." *Id.* at 56-57. She was admitted to the pediatric intensive care unit and underwent a lumbar puncture; the results were "concerning for infection [versus] inflammatory process." *Id.* at 57. An MRI angiography did not show signs of a stroke, mass, or a demyelinating process, but revealed an "abnormal vascular flow in [the right] hemisphere including the occipital lobe possibly concerning for a vasculitis." *Id.* The attending neurologist added:

> Acute onset weakness in tri-phasic illness with multiple lesions not severe appearing in MRI. This is mostly consistent with an auto-immune reaction… She had NMO [neuromyelitis optica] negative titers, but will need to follow up on this, as this seems most likely. She is of Japanese descent, which also increases the risk for NMO. For follow up and prognostic purposes, would also consider [lumbar puncture] to get repeat titers and to get spinal MRI. Treat with pulse steroids with taper. If she does not respond to this, would consider IVIg or PLEX.

Id. at 299.

K.N. thereafter had an infectious disease consultation on August 29, 2014 with Dr. Nicole Learned, who noted that lab findings were not consistent with any particular infectious etiology, and that instead a vasculitic or immune-modulated process was the more likely causal. Ex. 4 at 297. After improvement with steroid treatment, K.N. was discharged on September 5, 2014. *Id.* at 67. The discharge summary stated that a "very broad laboratory work-up has returned all negative data," and K.N.'s neurological function had improved such that she was "nearly back to baseline." Ex. 2 at 120; Ex. 4 at 67. Her diagnosis was left-sided weakness, and she remained on many medications, including prednisone. Ex. 2 at 61, 77. K.N. also developed a urinary tract infection, and antibiotics were prescribed. *Id.* at 77-78.

On September 11, 2014, K.N. saw Dr. Creig Hoyt, a neuro-ophthalmologist, who noted that her "optic neuritis with edema of optic disc" had "completely resolved." Ex. 4 at 1089. Approximately one month later, on October 9, 2014, K.N. began outpatient physical therapy for muscle weakness secondary to encephalitis. Ex. 3 at 213. The notes state that "[diagnosis] still

under investigation but MD suspects viral infection, possibly from Tdap vaccine." *Id.* at 222. Fatigue and mild gait deviation were also observed. *Id.* at 215; *see also Id.* at 242-43, 258-59, 274-75 (documenting additional sessions).

On October 13, 2014, K.N. was assessed at the University of California – San Francisco pediatric multiple sclerosis ("MS") clinic by Dr. Jennifer Graves. Ex. 2 at 176-92. Following a thorough examination, K.N.'s treating physician concluded that her symptoms and response to steroids in July 2014 were consistent with acute demyelinating ON. *Id.* at 191. The "second clinical event occurred in the setting of 5-7 days of fever and has some features consistent and others less consistent with a prolonged (20 [minute]) seizure and sequelae… She may have had an infectious related encephalopathy." *Id.* K.N. was instructed to complete the steroid taper and to follow-up with the clinic; the recommendations also state to "[a]void live vaccines if possible, but vaccines in the setting of prior optic neuritis can be evaluated with a risk benefit approach." *Id.* at 192. The record from this assessment also contains the first reference to K.M. testing positive for MOG antibodies, although Dr. Graves only deemed their presence of "possible interest." *Id.* at 191.

From October 29-31, 2014, K.N. was hospitalized at the University of California – San Francisco following an episode of pain with eye movement and blurred vision. Ex. 2 at 203. K.N.'s treating neurologist and rheumatologist concurred that her MRI imaging was "most consistent with [a] vasculitic process, not MS." *Id.* at 205. Upon discharge, K.N.'s working diagnosis was "autoimmune [central nervous system] vasculitis." *Id.*; Ex. 4 at 943.

K.N. continued to follow-up with numerous doctors, and on November 21, 2014, she was evaluated by her rheumatologist for her "steroid-dependent [central nervous system] inflammatory condition associated with abnormal MRI findings." Ex. 2 at 228. Her vision had returned to normal, but she still reported left-sided weakness with physical activity; she was participating in physical therapy. *Id.* K.N. was tolerating her medications, and continued monitoring was recommended. *Id.* at 228, 232.

Throughout 2015, K.N. had multiple appointments with various treating physicians. *E.g.*, Ex. 4 at 1134-96, 1213, 1442. As of June 11, 2015, possible diagnoses included central nervous system ("CNS") vasculitis, MS with MOG antibodies of unclear significance, or NMO, although the latter was deemed unlikely. *Id.* at 1183. K.N. continued to follow-up with neurology, ophthalmology, gastroenterology, and rheumatology throughout 2016, 2017, and 2018. *See, e.g.*, Ex. 34 at 244. She stopped taking immunosuppressant medication in January 2018, and in August 2018 was noted to be in remission, with migraine headaches and fatigue as remaining issues. Ex. 34 at 247, 269. In February 2019, the headaches that she was having were considered to be unrelated to her "recurrent ON." Ex. 35 at 31.

On February 18, 2020, K.N. had a follow-up pediatric neurology visit. Ex. 36 at 5-13. The record noted that K.N. had remained MOG antibody-positive 1/100 over the past two years, and lab worked revealed that testing confirmed she remained positive that day as well. *Id.* at 5-13, 18.

II. Expert Testimony

A. *Petitioner's Expert – Dr. Robert Thompson Stone, M.D.*

Dr. Stone, a pediatric neurologist, was Petitioner's sole expert, and he both testified at hearing and offered two written expert reports. Tr. at 4-54; Report, dated March 16, 2018, filed as Ex. 11 (ECF No. 28-1) ("Stone Rep."); Report, October 10, 2018, filed as Ex. 32 (ECF No. 35-1) ("Stone Supp. Rep."). Dr. Stone contended that it was more likely than not that the Tdap vaccination K.N. received on June 7, 2014, caused the onset of MOGAD—manifesting as two episodes of ON and one episode of ADEM-like illness. Stone Rep. at 10.

Dr. Stone obtained his medical degree from New York University School of Medicine, and his residency training in Adult and Child Neurology at the University of Rochester School of Medicine and Dentistry. Curriculum Vitae, filed as Ex. 11 on March 16, 2018 (ECF No. 28-1) ("Stone CV") at 2. He is licensed to practice medicine in the state of New York and board certified in neurology with special qualifications in child neurology. Stone CV at 4. Dr. Stone was appointed in 2011 to a faculty position as Assistant Professor in the Department of Neurology and Pediatrics where he still currently serves. *Id.* at 2. He is also Director of the Rochester Pediatric Multiple Sclerosis and Neuroimmunology Program. *Id.* Dr. Stone has authored numerous articles and publications on various topics within the field of neurology and has received several grants for neurological research. *Id.* at 4-5.

Dr. Stone began with an overview of MOGAD. As he explained, MOGAD is a CNS inflammatory disorder that in recent years has been more fully described to be a distinct entity from neuromyelitis optica ("NMO"), multiple sclerosis, and other acute demyelinating conditions like ON or transverse myelitis ("TM"). Tr. at 16; First Stone Rep. at 7; E. Hennes et al., *Prognostic Relevance of MOG Antibodies in Children with an Acquired Demyelinating Syndrome*, 89 Neurology 900-908 (2017), filed as Ex. 13 on Feb. 16, 2021 (ECF No. 74-1) ("Hennes"); Y. Hacohen et al., *Diagnostic Algorithm for Relapsing Acquired Demyelinating Syndromes in Children*, 89 Neurology 269-278 (2017), filed as Ex. 14 on Feb. 16, 2021 (ECF No. 74-2) ("Hacohen"); Tr. at 13. MOGAD is associated with the presence of the anti-MOG antibodies. Stone Rep. at 7. Those antibodies are thought to cause an attack on the MOG, or myelin oligodendrocyte glycoprotein, a minor myelin protein expressed on the surface of the myelin sheaths that wrap around the nerve cells. Tr. at 26.

MOGAD manifests symptomatically as ADEM, ON,[3] and/or TM, any of which could constitute a singular and distinct disorder. Tr. at 41. Since MOGAD's classification, however, paitents presenting with ON and/or ADEM-like symptoms will now be tested for anti-MOG antibodies. *Id.* Approximately sixty percent of children with MOGAD experience a monophasic course, with the remainder suffering some symptoms relapse. *Id.* at 13-14. The risk of relapse is higher in children who have not been immunosuppressed after the initial episode for at least three months, with relapses occurring after immunosuppression (usually via corticosteroids) is ceased. *Id*. at 14. Dr. Stone's review of relevant literature revealed that it is common in patients with MOGAD (even those whose course is self-limiting) to persistently test positive for the antibody—with seventy percent of patients having persistent antibodies (although typically low titer) after the condition goes into remission. *Id*. at 15.[4]

The cause of MOGAD is still currently unknown. It is understood that the target of the autoimmune attack that results in the myelin destruction manifesting in CNS clinical symptoms are the oligodendrocytes on the myelin surface, and that factors making MOGAD more likely include gender and a genetic susceptibility. Tr. at 68-69. But much of what is known about comparable acute/monophasic demyelinating conditions, like ADEM, could also be applicable. *Id.* at 42. Indeed, Dr. Stone felt it likely that medical science had (before MOGAD was better understood) likely misconstrued many cases of MOGAD as instead ADEM, which in the past was not diagnosed with serologic tests. *Id.* at 66-67. But ADEM could have different causes and pathologic paths—from a prior infection to the first manifestation of neuromyelitis optica spectrum disorder ("NMOSD"), which is well understood to be propelled by a different autoantibody—despite a common phenotype. *Id.* at 67-68.

Research has revealed that MOGAD has been around for quite some time, although it was only recently proposed as a disease/condition entity. Tr. at 49. As a result, at the time of K.N.'s inflammatory episodes (2014), her medical team unsurprisingly did not discern the diagnostic importance of the positive MOG antibody finding that testing had revealed. Stone Rep. at 6; Ex. 2 at 191 ("[s]he has positive anti-MOG antibodies, and while these are of possible interest, a clear syndrome involving these antibodies or treatment for such a syndrome have not been clearly

[3] Dr. Stone described ON as inflammation of the optic nerve which can have a variety of causes (including idiopathic, post-infectious, or post-vaccination), and can be a single event or the precursor/presenting symptom of a larger and more chronic demyelinating disease, like multiple sclerosis or NMO Tr. at 16. ON leads to acute or subacute pain with eye movement, vision loss, color desaturation, and decreased visual acuity on exam. *Id.*

[4] At hearing, Dr. Stone also discussed how the difference in pathology between NMO spectrum disorder, a longer-term and chronic condition, and the more acute/monophasic MOGAD is mirrored by the differences in treatment. Tr. at 62. If NMO spectrum disorder is left untreated, many patients die within ten years or are left blind. *Id.* Modern medicine has discovered the most effective treatment for NMO spectrum disorder is a medication called Rituximab. *Id.* Patients treated with Rituximab, which depletes antibodies, see a far lower relapse risk. *Id.* In contrast, Rituximab does not seem to be a particularly good treatment for MOG antibody disease. *Id.* at 63.

defined in the literature). However, by the latter half of 2017, knowledge of MOGAD was increasing, and commercial testing for the antibody became more widely available. *Id*.; Tr. at 13.

Dr. Stone reviewed a number of items of literature shedding light on the nature of MOGAD. Stone Rep. at 6. Hacohen, for example, evaluated a cohort of 26 children who tested positive for the anti-MOG antibody. Hacohen at 269. These children had initially presented with what had appeared to be either an NMO spectrum disorder, multiphasic ADEM, or relapsing ON—with 43.2% of these children presenting initially with ON (like K.N.). Hacohen at 273. 46.2% of children with MRI abnormalities had "predominantly confluent, hazy/poor marginated lesions involving both gray and white matter." *Id,* at 274. Thus, MOGAD likely has some kind of impact on the CNS (and the brain particularly) that has something to do with its varied presentation.

Another published report detailed the clinical presentation in MOGAD based on 252 patients found positive for the antibody. Stone Rep. at 7; M. Jurynczyk et al., *Clinical Presentation and Prognosis in MOG-Antibody Disease: a UK Study*, 140 Brain 3128-3138 (2017), filed as Ex. 15 on Feb. 16, 2021 (ECF No. 74-3) ("Jurynczyk"). Jurynczyk observed that 55% of the studied subjects presented with unilateral or bilateral ON, and 18% with ADEM or an "ADEM-like" illness. Jurynczyk at 3128. In addition, 44% were relapsing, and 78% of patients had full or good recovery in patients with ADEM-like or ON presentations. *Id.*

Review of K.N.'s medical history from July to October-November 2014 persuaded Dr. Stone that she likely suffered from MOGAD. Stone Rep. at 2-6; Tr. at 15. Her first and third inflammatory events (in July[5] and October 2014, respectively) were consistent with ON, based on her clinical findings, neuroimaging, and her treating physician's impressions. Stone Rep. at 6. By August, she began also to experience different recurring neurologic symptoms, plus fever and fatigue, and cerebrospinal fluid ("CSF") testing and MRIs both revealed the presence of inflammation. Tr. at 18-19.

Dr. Stone acknowledged that this intervening set of symptoms proved to be a more challenging assessment for her treating physicians, but it was nevertheless consistent with an ADEM-like inflammatory event that in turn could constitute part of a MOGAD presentation. Stone Rep. at 6. This was because the nature of these ADEM-like symptoms were not particularly consistent with a monophasic case of classic ADEM, which would not typically follow ON, as occurred in K.N.'s case. Tr. at 20. Its specific features herein, moreover—*focal* neurologic deficits, including left hemiparesis, left facial weakness, and left visual field abnormality—were not

[5] Dr. Stone commented on the July 29th record (Ex. 4 at 1086) in which a treater suggests that K.N.'s ON might not be vaccine-related, testifying that he did not give great weight to the suggestion that the absence of cortical leukoencephalopathy evidence made other etiologies, like a viral infection, more likely. TR 97-99. Ultimately, this record comment is too vague and off-hand to give it significant evidentiary value—especially since a more holistic and contextual consideration of the record (through at least October/November 2014) reveals that the true nature of K.N.'s condition was not fully grasped at the time she received treatment for her initial ON symptoms.

particularly consistent with classic ADEM.[6] Stone Rep. at 7. K.N.'s MRI scan was also considered atypical for ADEM, since it included gray matter lesions. MOGAD disease, by contrast, can produce lesions involving both the gray *and* white matter. *Id.* at 7; Ex. 4 at 57.

Even before the second ON occurrence (and third event in total), K.N.'s disease progression continued, in Dr. Stone's reading, to reflect something other than ON. A follow-up MRI in September 2014 revealed "cellular swelling injury," plus changes in cerebral blood flow, all of which looked somewhat like a noninfectious inflammatory disease. Tr. at 19. K.N. also began to display oligoclonal bands in CSF testing, an indicator of CNS inflammation. *Id.* At this point, Dr. Stone deemed K.N.'s diagnosis to be "a bit elusive," although the record pointed to "a single process that was most likely consistent with an inflammatory or immune etiology." *Id.* at 20.

Then, in October 2014, K.N. was seen by a pediatric neurologist, and at that time her positive anti-MOG results were observed, along with new MRI scans showing resolution of signal abnormalities (which Dr. Stone deemed "typical for ADEM"), plus decreased thickness of retinal neurofiber, likely a function of her prior ON. Tr. at 22. Now (and in particular after her second occurrence of ON), K.N. began to receive the kind of immunosuppressive treatment that in Dr. Stone's understanding would be appropriate in addressing injury attributable to the anti-MOG antibody. *Id.* at 23. Indeed, Dr. Stone felt K.N. likely would have experienced *more* attacks after October but for these treatments. *Id.* at 64-65. And in fact, her disease course was far less acute thereafter (although Dr. Stone opined that the correct and effective treatment intervention made it difficult to assess what would otherwise have befallen K.N. in the absence of treatment). *Id.* at 92.

Dr. Stone went on to discuss what is known about MOGAD's potential association with vaccination. Stone Rep. at 7. MOGAD is part of the spectrum of autoimmune, inflammatory CNS demyelinating disorders, which also includes MS, TM, ON, ADEM, and NMO. *Id.* It is known by medical science that both genetic and environmental factors contribute to developing such conditions. *Id.* And recent infection or vaccinations (which mimic infectious processes) have been clearly shown to trigger the onset of some of these disorders. *Id.*; *see also* E. Applebaum et al., *Neurological Complications Following Antirabies Vaccination*, 151(3) JAMA 188-191 (1953), filed as Ex. 18 on Feb. 16, 2021 (ECF No. 74-6) ("Applebaum"); W. Huynh et al., *Post-Vaccination Encephalomyelitis: Literature Review and Illustrative Case*, 15 J. Clinical Neuroscience 1315-1322 (2008), filed as Ex. 20 on Feb. 16, 2021 (ECF No. 74-8) ("Huynh").

For example, it was initially shown in 1953 that the Semple rabies vaccine had a strong association with the development of ADEM. Stone Rep. at 7; Applebaum at 188. Since then, ADEM has been found to be associated with multiple vaccines, including smallpox, MMR,

[6] ADEM or ADEM-like inflammatory events typically feature initial non-specific symptoms like fever, headache, or fatigue. Tr. at 20-22. Patients may also have polyfocal neurologic deficits, and an MRI scan usually shows bilateral multifocal lesions. *Id.* at 22.

Japanese B encephalitis, pertussis, influenza, and hepatitis B. Stone Rep. at 7; Huynh; D. Karussis et al., *The Spectrum of Post-Vaccination Inflammatory CNS Demyelinating Syndromes*, 13 Autoimmunity Rev. 215-224 (2014), filed as Ex. 24 on Feb. 16, 2021 (ECF No. 75-2) ("Karussis"); R. Baxter et al., *Acute Demyelinating Events Following Vaccines: A Case-Centered Analysis*, 63(11) Clinical Infectious Diseases 1456-62 (2016), filed as Ex. 21 on Feb. 16, 2021 (ECF No. 74-9) ("Baxter"). Baxter was particularly relevant, observing a statistically significant risk for developing ADEM after the Tdap vaccine (based on >9 million subjects), with an odds ratio of 15.8. Baxter at 1456. While Dr. Stone acknowledged that Baxter's findings were based on a small sample, and that the frequency of vaccine-driven ADEM would have to be very uncommon, his experience as a child neurologist and neuroimmunologist treating and managing children with extremely rare diseases suggested to him that its findings still carried weight. Tr. at 70-72; Stone Supp. Rep. at 2. ON is also commonly associated with vaccinations in the literature. Stone Rep. at 8; C. Ray et al., *Bilateral Optic Neuropathy Associated with Influenza Vaccination*, 16 J. Neuroophthalmology, 182-184 (1996), filed as Ex. 25 on Feb. 16, 2021 (ECF No. 75-3).

Dr. Stone could not identify literature specifically associating MOGAD with vaccination. At best, he referenced a single case report involving a boy who developed multi-phasic ADEM ("MDEM") associated with MOG antibodies after vaccination in the setting of a subclinical infection. Stone Rep. at 8; K. Azumagawa et al., *Post-Vaccination MDEM Associated with MOG Antibody in a Subclinical Chlamydia Infected Boy*, 38 Brain and Development 690-693 (2016), filed as Ex. 28 on Feb. 16, 2021 (ECF No. 75-6) ("Azumagawa"); *see also* N. Kumar et al., *Case Report: Postvaccination Anti-Myelin Oligodendrocyte Glycoprotein Neuromyelitis Optica Spectrum Disorder: A Case Report and Literature Review of Postvaccination Demyelination*, 22(2) Int. J. MS Care 85-90, filed as Ex. 37 on Feb. 16, 2020 (ECF No. 72-1) ("Kumar") (37-year-old woman presented with viral prodromal symptoms three weeks after receiving the tetanus vaccine and two weeks after receiving the measles, mumps, and rubella and the varicella vaccines).

But Dr. Stone stressed that MOGAD's novelty as a diagnostic category explained the dearth of relevant literature studying it. Tr. at 34; Stone Rep. at 8. And he did not deem it unreasonable to consider what was already known about comparable acute/monophasic demyelinating conditions and their vaccine associations. It is well known that CNS demyelinating diseases share certain characteristics with regard to their risk factors, pathophysiology, and treatment strategies. Stone Supp. Rep. at 1. Thus, while neuroinflammatory autoimmune diseases are not "interchangeable," it is fair to make associations between conditions with similar mechanisms. *Id.* This is especially the case given that such diseases are generally treated in a common manner (i.e., with immunosuppression and/or steroids). *Id.* In addition, research has revealed that forty to fifty percent of children previously diagnosed with ADEM actually likely had MOGAD. Thus, reliance on literature regarding vaccine association with ADEM and ON is fair, given the pathologic and symptomatic overlap for these related diseases. Tr. at 32.

In addition, Dr. Stone maintained that some MOGAD-specific articles suggested a possible vaccine association. S. Jarius et al., *MOB-IgG in NMO and Related Disorders: A Multicenter Study of 50 Patients*, 13(280) J. Neuroinflamm. (2016) 1-45, filed as Ex. 32 Tab C on Feb. 16, 2021 (ECF No. 76-2) ("Jarius"). In Jarius, one out of fifty patients had disease onset of recurrent myelitis and ON two weeks after receipt of a polyvalent vaccine against tetanus, diphtheria, and pertussis. Tr. at 43; Jarius at 41. Although Jarius's authors accepted that a causal link between the two events could not be conclusively proven on this basis, "the close temporal association is highly suggestive of vaccine-medicated immune activation." Jarius at 41; Stone Supp. Rep. at 2. Moreover, symptoms started within two weeks after a polyvalent vaccination against tetanus, diphtheria, and pertussis (as well as polio and influenza virus) in a second MOG-IgG positive patient in this cohort. *Id.*

Dr. Stone also attempted to distinguish certain items of literature that Respondent's expert offered to rebut a MOGAD-vaccine association. One, a large-scale French study, looked at the clinical and radiologic features of MOGAD in nearly 200 adults. A. Cobo-Calvo et al., *Clinical Spectrum and Prognostic Value of CNS MOG Autoimmunity in Adults*, 90 Neurology 1858-1869 (2018), filed as Ex. 32 Tab A on Feb. 16, 2021 (ECF No. 76-1) ("Cobo-Calvo"). Dr. Stone, however, noted that Cobo-Calvo did not involve children, and otherwise said nothing about vaccine causality, as this was not the study's intent. Stone Supp. Rep. at 1.

Dr. Stone further underscored the significance of patient age as a factor in associating vaccination with MOGAD. Stone Rep. at 8. One recent study suggested that vaccination of any type received by individuals younger than 50 years old was statistically associated with an increased risk of CNS acute demyelinating syndromes. *Id.*; Tr. at 30; A. Langer-Gould et al., *Vaccines and the Risk of Multiple Sclerosis and Other Central Nervous System Demyelinating Disorders*, 71(12) JAMA Neurology 1506-1513 (2014), filed as Ex. 27 on Feb. 16, 2021 (ECF No. 75-5), refiled as Ex. 32 Tab E on Oct. 10, 2018 (ECF No. 35-6) ("Langer-Gould"). Langer-Gould specifically observed a two-fold increase in the first 30 days after vaccination—roughly the same timeframe at issue for K.N. Stone Supp. Rep. at 2; Langer-Gould at 1506. MOGAD's similarity to other autoimmune CNS demyelinating conditions meant the same could be true here, in Dr. Stone's view, even though Langer-Gould could be read to apply only to demyelination associated with more classically-monophasic conditions. Tr. at 81.

Besides a possible general association between MOGAD and vaccination, Dr. Stone proposed two potential mechanisms to explain how K.N.'s vaccination could have initiated an autoimmune inflammatory process. Stone Rep. at 8. First, he opined that molecular mimicry could explain K.N.'s autoimmune inflammatory reaction. *Id.* He described molecular mimicry as occurring where antigenic epitopes (i.e., pieces of a molecule in a vaccine or wild virus that can induce an immune response) are similar or identical to a relevant CNS protein (here, MOG). *Id.* Autoreactive immune cells induced by vaccine response could develop that can enter the CNS

during routine immune surveillance and cause inflammation by reacting against homologous self-targets. *Id.* at 8-9. The inflammatory response then leads to demyelination, and the clinical symptoms of ADEM and ON. *Id.*; Tr. at 28; Huynh; R. Fujinami et al., *Molecular Mimicry, Bystander Activation, or Viral Persistence: Infections and Autoimmune Disease*, 19(1) Clinical Microbiology Reviews 80-94 (2006), filed as Ex. 29 on Feb. 16, 2021 (ECF No. 75-7) ("Fujinami").[7] Alternatively, stimulation of preexisting anti-myelin-specific "bystander" T cells already present in the body, but quiescent due to suppression by regulatory immune cells in an effort to maintain tolerance to self, could be stimulated by the immune response elicited by vaccination, which would then engage in an autoimmune reaction. Stone Rep. at 9; Tr. at 28; Fujinami (modeling the experimental autoimmune encephalomyelitis model of MS).

Finally, Dr. Stone opined that the timing of K.N.'s MOGAD onset post-vaccination was medically acceptable. Her first ON episode occurred approximately three weeks post-vaccination, which he deemed typical for a vaccine-caused autoimmune CNS injury. Stone Rep. at 9; Tr. at 30; A. Rowhani-Rahbar et al., *Biologically Plausible and Evidence-Based Risk Intervals in Immunization Safety Research*, 31(1) Vaccine 271-277 (2012), filed as Ex. 31 on Feb. 16, 2021 (ECF No. 75-9) (neurological symptoms presenting in patients between six days and six weeks). And he saw no other preceding incident to explain K.N.'s symptoms. Stone Rep. at 9; Tr. at 31. K.N. had experienced no clear prior infection, for example, and the angiitis considered as diagnostic for her second demyelinating episode could be ruled out, given that her recovery was rapid with corticosteroids alone and there was significant resolution of the lesions on repeated MRI imaging. Stone Rep. at 9.

B. *Respondent's Expert – Marc Albert Bouffard, M.D.*

Dr. Bouffard, a neurologist with a specialty in neuro-ophthalmology, provided two written reports and testified at hearing on behalf of Respondent. Tr. at 55-106; Report, dated July 12, 2018, filed as Ex. A (ECF No. 33-1) ("Bouffard Rep."); Report, March 5, 2019, filed as Ex. C (ECF No. 42-1) ("Bouffard Supp. Rep."). Dr. Bouffard opined that it is more likely than not that the Tdap vaccine did not cause K.N.'s MOGAD-related symptoms.

[7] To support this argument, Dr. Stone cited literature involving T-cell mediated MS (*see* Stone Rep. at 8 n.18)—despite the fact, as Respondent's expert noted, that MOGAD is understood to be *B cell* mediated (since it is the anti-MOG antibodies that drive the pathologic cross-reaction). Stone Supp. Rep. at 2. In response, Dr. Stone maintained that denoting an autoimmune process as driven solely by B cells or T cells is overly simplistic, since (a) both interact in an autoimmune process, and (b) literature suggests that molecular mimicry can arguably stimulate production of either kind of immune cell. *Id.*; L. Albert, *Molecular Mimicry and Autoimmunity*, 34(27) New England J. of Med. 2068-2074, filed as Ex. 32 Tab F on Feb. 16, 2021 (ECF No. 76-3).

Respondent's criticism of this component of Dr. Stone's opinion is apt. This is amplified by the fact that Dr. Stone lacks expertise in immunology (although that limitation in expert credentials is shared by Respondent's expert). However, and as discussed below, proof of mechanism is not required in vaccine cases generally, and I still find preponderant evidence supports Petitioner's "can cause" showing—even if mechanism *itself* was not well supported.

Dr. Bouffard obtained his medical degree from Tufts University School of Medicine in Boston, Massachusetts. Curriculum Vitae, filed as Ex. B on July 12, 2018 (ECF No. 33-14) ("Bouffard CV") at 1. He completed a neurology residency at Beth Israel Deaconess Medical Center, a neuro-ophthalmology fellowship at the Massachusetts Eye and Ear Infirmary, and a fellowship in Advanced General and Autoimmune Neurology at the Massachusetts General Hospital. Bouffard CV at 1. Dr. Bouffard is licensed to practice medicine in the Commonwealth of Massachusetts and is currently employed by the Harvard Faculty of Medical Physicians and sees patients at the Beth Israel Deaconess Medical Center. *Id.* He routinely evaluates patients with a variety of autoimmune disorders and currently treats a dozen patients with MOG antibody associated disorders. Tr. at 57; Bouffard Rep. at 1. Dr. Bouffard has also published several articles and book chapters in the field of neurology. Bouffard CV at 1-2.

Dr. Bouffard began with a review of MOGAD, which largely paralleled Dr. Stone's testimony. *See generally* Tr. at 59-61. He did not dispute the legitimacy of MOGAD diagnostically, and accepted the likelihood that K.N. had experienced it. Bouffard Rep. at 4; Tr. at 64. He emphasized that MOGAD is understood to involve specific antibodies, and thus B cells are of primary importance in its pathogenesis. Bouffard Rep. at 5; Tr. at 53; L. Chen et al., *Different Features Between Pediatric-Onset and Adult-Onset Patients Who are Seropositive For MOG-IGG: A Multicenter Study in Southern China*, 321 J. Neuroimmunol. 83-91 (2018), filed as Ex. A Tab 7 on July 12, 2018 (ECF No. 33-8) ("Chen"), at 89. But it remains unclear if the anti-MOG antibodies are truly pathologic themselves. Tr. at 61; Karussis. At most, he speculated that the anti-MOG antibody might influence the structural integrity of the target antigen, the oligodendrocyte, which provides the fatty insulation around nerve axons that permits them to conduct electrical signals from one place to another. Tr. at 61-62. Dr. Bouffard admitted, however, that recent research about antibody-mediated diseases reveals they also involve abnormal function of "cell-mediated" immunity, or T cells, in stimulating an inflammatory response. *Id.* at 53.

Dr. Bouffard noted some distinctions in MOGAD depending upon the age of the patient. The constituent parts of the CNS impacted by MOGAD are similar for children and adults: the optic nerve, the spinal cord, and/or brain. Tr. at 63. However, less than ten percent of adult cases entail primarily an ADEM-like inflammation of the brain, while for children approximately fifty percent do. *Id.*[8] Otherwise the differences in adults and children with MOGAD were subtle (and studies like Hacohen had relevance to pediatric cases). Bouffard Rep. at 4; Chen at 83.

[8] Dr. Bouffard also testified that ADEM overall is more commonly monophasic when experienced by children, although many children may subsequently experience chronic relapse or characteristic clusters of attacks when treatments are suspended or limited. Tr. at 64.

There is, however, in Dr. Bouffard's view limited to no reliable evidence associating vaccination and MOGAD's initiation. Bouffard Rep. at 4.[9] He noted, for example, a lack of published epidemiologic data linking vaccines to MOGAD, adding that Dr. Stone seemed to accept this absence of evidence as well. *Id.* at 4-5. Further, he rejected the notion that what was known about other comparable neuroinflammatory conditions and illnesses could be applied herein, arguing that such other diseases were not interchangeable with MOGAD. Thus, while it is believed at the present that the anti-MOG antibodies central to MOGAD are likely pathogenic (as opposed to the unexplained byproduct of the disease), the pathogenesis of comparable CNS demyelinating conditions, such as ADEM, is far less understood, with no similar causative antibody having been identified. *Id.*[10] Indeed, Dr. Bouffard maintained that drawing a link between MOGAD and ADEM was "particularly fraught," noting that pediatric MOGAD cases who experience an ADEM-like phenotype usually retain a progressive, relapsing course, whereas classic ADEM tends to be monophasic, suggesting a fundamentally different mechanism by which both initiate and are propagated. Bouffard Supp. Rep. at 2, 3.

Dr. Bouffard further opined that the scientific evidence connecting comparable autoimmune neuroinflammatory diseases to vaccines was itself not especially robust, criticizing some of the ADEM-oriented literature Dr. Stone offered. Bouffard Rep. at 5. Baxter, for example, may have observed an increased incidence of post-Tdap ADEM, but this conclusion was based only on the experience of *two* patients in total. Bouffard Rep. at 5; Baxter at 1456.[11] Baxter's authors in fact disclaimed that their findings proved a causal link. Tr. at 70. And (since ADEM is not per se interchangeable with MOGAD) Baxter's findings were even less probative. *Id.* at 70-72, 96. Langer-Gould's observation of an increased risk of CNS demyelinating disease in the first 30 days following vaccination diminished in the subsequent timeframe, suggesting an absence of long-term risk of disease—which in turn indicated to Dr. Bouffard that vaccination at best could cause symptoms flare but not the underlying disease itself. Bouffard Rep. at 5; Langer-Gould at 1506.

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[9] Dr. Bouffard's reports also both included lengthy sections where he addressed the "Hill criteria" for evaluating scientific causation as a general matter. *E.g.*, Bouffard Rep. at 6-7. Although interesting, this aspect of Dr. Bouffard's report revealed more about how he personally evaluated the persuasiveness of arguments regarding causation in this case than their *actual* persuasiveness as a legal matter—a determination that I must make based on principles applicable in Vaccine Program cases that are independent of the logical structures a given expert relies upon to decide if the evidence for a causation is persuasive. I will therefore disregard these components of his opinion.

[10] Dr. Bouffard also highlighted differences between NMO and MS to demonstrate the invalidity of applying conclusions drawn from one disease to another. Bouffard Rep. at 5. NMO is understood to be mediated by the aquaporin-4 antibody, whereas no pathologic antibody has ever been identified for MS. *Id.* In addition, the disease processes for these two conditions vary for different populations, present differently, and require distinct treating strategies. *Id.*; M. Jurynczyk et al., *Overlapping CNS Inflammatory Disease: Differentiating Features of NMO and MS*, 86 J. Neurol. Neurosurg. Psychiatry 20-25 (2015), filed as Ex. A Tab 8 on July 12, 2018 (ECF No. 33-9).

[11] On cross-examination, however, Dr. Bouffard admitted that Baxter's findings regarding ADEM were statistically significant. Tr. at 87.

Other items of literature, Dr. Bouffard proposed, were no more supportive of Petitioner's theory. He acknowledged that studies like Cobo-Calvo or Hacohen did not seek to examine a putative link between vaccination and MOGAD, but pointed out each included thorough chart reviews of medical events antecedent to diagnosis—neither of which mentioned vaccines as a likely cause. Bouffard Supp. Rep. at 1; Cobo-Calvo at 1862; Hacohen at 482. Jarius only observed temporal vaccine associations to MOGAD, in circumstances with confounding facts such as concurrent diseases. Jarius at 15, 26, 41, 42. Thus, Dr. Bouffard denied that "two cases of a temporal association between rarely correlated events" was a sufficient basis for causation. Bouffard Supp. Rep. at 2.

Dr. Bouffard also attempted to distinguished case reports cited by Dr. Stone. For example, the Huynh case report involved ON after receipt of a flu vaccine—not Tdap—and discussed only associations between ADEM and the flu vaccine. Huynh at 1315; Tr. at 35-36. The Cheong case report also involved the flu vaccine and ADEM, and featured a patient with an identified infection—a much more common trigger than vaccination. Tr. at 36-37. The Azumagawa case report involved ADEM after a measles, mumps, and rubella ("MMR") vaccination plus a Japanese encephalopathy vaccine—again distinguishable from K.N.'s case. Azumagawa at 690; Tr. at 38. And Kumar involved anti-MOG demyelination two and three weeks after MMR and tetanus vaccination, respectively. Kumar at 85-86. Other case reports, like Applebaum, involve the rabies vaccine, which contained brain tissue (an ingredient not included in Tdap), and hence "the incidence of post-vaccination CNS demyelination was a lot higher" for reasons having to do with the specific vaccine's composition. Tr. at 25.

More specifically, Dr. Bouffard questioned the persuasiveness of Petitioner's proposed causation mechanism. In so doing, he reiterated his prior arguments about the problem of relying on what is known about facially-comparable autoimmune CNS demyelinating diseases, observing that because so little is known about most demyelinating conditions understood to involve autoantibodies (whether NMO or MOGAD), it is difficult to delineate a coherent mechanism by which the Tdap vaccine could specifically cause the production of the antibodies. Tr. at 61. Dr. Bouffard also acknowledged the scientific legitimacy of molecular mimicry, but noted that the fact that the anti-MOG antibodies might not drive the disease process diminished the utility of the theory—especially since cross-reactivity featuring antibodies attacking homologous structures would be the product of a B cell process. *Id.*; Tr. at 61.

Dr. Bouffard also considered K.N.'s actual medical history, but he did not seem to identify much about it that suggested Dr. Stone's causation theory was wrong. Bouffard Rep. at 1-3. He deemed K.N.'s course to be "fairly typical for anti-MOG antibody mediated neuroinflammation." *Id.* at 4. Dr. Bouffard compared K.N.'s case to those described in Jarius, noting that clinically-apparent attacks in these patients affected the optic nerve at some point for the majority of patients,

consistent with what K.N. experienced. Jarius at 5. The response to steroids was also often marked, as was K.N.'s case. *Id.*; Bouffard Rep. at 4. In addition, MRI brain abnormalities were common and affected both the white matter and meninges, as seen in K.N. Jarius at 8; Bouffard Rep. at 4. And he agreed that K.N.'s positive anti-MOG testing results would not have been understood in 2014 to have the same significance as today. Bouffard Rep. at 3.

Dr. Bouffard did, however, suggest that K.N.'s course—which featured three intervening events separated by a few weeks—was not wholly consistent with the contention that the Tdap vaccine caused upregulation of the anti-MOG antibodies. Even if vaccination could cause an initial increase in antibodies, titer levels would likely drop once the effect of the vaccine's initial immune stimulation wore off, diminishing the likelihood of further attacks—as the record revealed occurred here. Tr. at 75-76.

The timing of K.N.'s disease onset was not medically acceptable in Dr. Bouffard's estimation. Although he admitted that Langer-Gould observed a higher odds ratio for demyelinating injuries in 30 days after vaccination, he disputed whether the finding had statistical significance, adding that because half of its of subjects had MS, with only one ADEM occurrence, "it doesn't translate to our patient's disease" in this case. Tr. at 74.

Dr. Bouffard also proposed that there could be alternative explanations for K.N.'s MOGAD—which, if potentially vaccine-caused, could be attributable as well to other "pathogenic exposures." Tr. at 78. He highlighted the fact that some of the case reports filed in this matter often showed preexisting infection as confounding factor in development of a CNS autoimmune inflammatory illness. *Id.* at 78-79. And he stressed that the record revealed K.N. had traveled abroad prior to her vaccination, raising the possibility that K.N.'s travel could have constituted sufficient antigenic stimulation to reduce the likelihood the vaccine was the instigating factor. Bouffard Rep. at 6. She also had been exposed to family member with a reported upper respiratory infection. TR at 79, 93-94. But Dr. Bouffard ultimately admitted that these alternatives were speculative in nature, and could not be corroborated by record proof (for example, a test result establishing the existence of a viral infection). *Id.* at 78, 93.

III. Procedural History

This matter commenced with the filing of the Petition on May 31, 2017 and was originally assigned to Special Master Sanders. Over the following months, Petitioner filed medical records in support of her claim. Respondent thereafter filed a Rule 4(c) Report on November 6, 2017 asserting that compensation was not appropriate in this case. Respondent's Report, filed Nov. 6, 2017 (ECF No. 22). After the scheduling and canceling of a Rule 5 conference, Petitioner was ordered to submit an expert report in support of her claim no later than February 14, 2018. *See*

Docket Entry, dated Nov. 16, 2017. Following an extension, Petitioner subsequently filed expert reports from Dr. Stone and accompanying medical literature on March 16, 2018.

Respondent filed a responsive report by Dr. Bouffard on July 12, 2018 along with literature in opposition to Petitioner's position. Petitioner filed an amended Petition on October 10, 2018. After an interim fees motion, this matter was transferred to Special Master Danial Horner on August 28, 2019. Both parties then filed supplemental expert reports. An Interim Fees Decision was issued on September 9, 2019. The matter was reassigned to me on July 29, 2020, after which I set it down for a hearing. A one-day entitlement hearing took place on March 16, 2021. The parties elected to file post-hearing briefs, doing so on May 28, 2021. Petitioner's Brief (ECF No. 86) ("Petitioner's Post-Hearing Br."); Respondent's Brief (ECF No. 87). The matter is now fully ripe for resolution.

IV. Applicable Law

A. *Petitioner's Overall Burden in Vaccine Program Cases*

To receive compensation in the Vaccine Program, a petitioner must prove either: (1) that he suffered a "Table Injury"—i.e., an injury falling within the Vaccine Injury Table—corresponding to one of the vaccinations in question within a statutorily prescribed period of time or, in the alternative, (2) that his illnesses were actually caused by a vaccine (a "Non-Table Injury"). *See* Sections 13(a)(1)(A), 11(c)(1), and 14(a), as amended by 42 C.F.R. § 100.3; § 11(c)(1)(C)(ii)(I); *see also Moberly v. Sec'y of Health & Hum. Servs.*, 592 F.3d 1315, 1321 (Fed. Cir. 2010); *Capizzano v. Sec'y of Health & Hum. Servs.*, 440 F.3d 1317, 1320 (Fed. Cir. 2006). In this case, Petitioner does not assert a Table claim.

For both Table and Non-Table claims, Vaccine Program petitioners bear a "preponderance of the evidence" burden of proof. Section 13(1)(a). That is, a petitioner must offer evidence that leads the "trier of fact to believe that the existence of a fact is more probable than its nonexistence before [he] may find in favor of the party who has the burden to persuade the judge of the fact's existence." *Moberly*, 592 F.3d at 1322 n.2; *see also Snowbank Enter. v. United States*, 6 Cl. Ct. 476, 486 (1984) (mere conjecture or speculation is insufficient under a preponderance standard). Proof of medical certainty is not required. *Bunting v. Sec'y of Health & Hum. Servs.*, 931 F.2d 867, 873 (Fed. Cir. 1991). In particular, a petitioner must demonstrate 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)); *Pafford v. Sec'y of Health & Hum. Servs*., 451 F.3d 1352, 1355 (Fed. Cir. 2006). A petitioner may not receive a Vaccine Program award based solely on his assertions; rather, the petition must be supported by either medical records or by the opinion of a competent physician. Section 13(a)(1).

In attempting to establish entitlement to a Vaccine Program award of compensation for a Non-Table claim, a petitioner must satisfy all three of the elements established by the Federal Circuit in *Althen v. Secretary of Health and Hum. Servs.*, 418 F.3d 1274, 1278 (2005): "(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."

Each of the *Althen* prongs requires a different showing. Under *Althen* prong one, petitioners must provide a "reputable medical theory," demonstrating that the vaccine received *can cause* the type of injury alleged. *Pafford*, 451 F.3d at 1355–56 (citations omitted). To satisfy this prong, a petitioner's theory must be based on a "sound and reliable medical or scientific explanation." *Knudsen v. Sec'y of Health & Hum. 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.

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 & Hum. Servs.*, 569 F.3d 1367, 1378–79 (Fed. Cir. 2009) (citing *Capizzano*, 440 F.3d at 1325–26). Special masters, despite their expertise, are not empowered by statute to conclusively resolve what are essentially thorny scientific and medical questions, and thus scientific evidence offered to establish *Althen* prong one is viewed "not through the lens of the laboratorian, but instead from the vantage point of the Vaccine Act's preponderant evidence standard." *Andreu*, 569 F.3d 1367, 1380. Accordingly, special masters must take care not to increase the burden placed on petitioners in offering a scientific theory linking vaccine to injury.

The Federal Circuit has consistently rejected the contention that the first *Althen* prong can be satisfied merely by establishing a proposed causal theory's scientific or medical *plausibility*. *See Boatmon v. Sec'y of Health & Hum. Servs.*, 941 F.3d 1351, 1359 (Fed. Cir. 2019); *see also LaLonde v. Sec'y of Health & Hum. Servs.*, 746 F.3d 1334, 1339 (Fed. Cir. 2014) ("[h]owever, in the past we have made clear that simply identifying a 'plausible' theory of causation is insufficient for a petitioner to meet her burden of proof." (citing *Moberly*, 592 F.3d at 1322)). Rather, this prong (like the other two) requires a preponderant showing. This naturally flows from the overarching fact that Program petitioners *always* have the ultimate burden of establishing their claim with preponderant evidence. *W.C. v. Sec'y of Health & Hum. Servs.*, 704 F.3d 1352, 1356 (Fed. Cir. 2013) (citations omitted); *Tarsell v. United States*, 133 Fed. Cl. 782, 793 (2017) (noting that *Moberly* "addresses the petitioner's overall burden of proving causation-in-fact under the Vaccine Act" by a preponderance standard).

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 v. Sec'y of Health & Hum. Servs.*, 956 F.2d 1144, 1148 (Fed. Cir. 1992). 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 ("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'") (quoting *Althen*, 418 F.3d at 1280). Medical records are generally viewed as particularly trustworthy evidence, since they are created contemporaneously with the treatment of the patient. *Cucuras v. Sec'y of Health & Hum. Servs.*, 993 F.2d 1525, 1528 (Fed. Cir. 1993).

Medical records and statements of a treating physician, however, 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. 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 v. Sec'y of Health & Hum. Servs.*, 88 Fed. Cl. 706, 746 n.67 (2009) ("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"). As with expert testimony offered to establish a theory of causation, the opinions or diagnoses of treating physicians are only as trustworthy as the reasonableness of their suppositions or bases. The views of treating physicians should be weighed against other, contrary evidence also present in the record—including conflicting opinions among such individuals. *Hibbard v. Sec'y of Health & Hum. Servs.*, 100 Fed. Cl. 742, 749 (2011) (not arbitrary or capricious for special master to weigh competing treating physicians' conclusions against each other), *aff'd*, 698 F.3d 1355 (Fed. Cir. 2012); *Veryzer v. Sec'y of Dept. of Health & Hum. Servs.*, No. 06-522V, 2011 WL 1935813, at *17 (Fed. Cl. Spec. Mstr. Apr. 29, 2011), *mot. for review denied*, 100 Fed. Cl. 344, 356 (2011), *aff'd without opinion*, 475 F. Appx. 765 (Fed. Cir. 2012).

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 & Hum. Servs.*, 539 F.3d 1347, 1352 (Fed. Cir. 2008). The explanation for what is a medically acceptable timeframe must align 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 & Hum. Servs.*, 101 Fed. Cl. 532, 542 (2011), *recons. denied after remand*, 105 Fed. Cl. 353 (2012), *aff'd mem.*, 503 F. Appx. 952 (Fed. Cir. 2013); *Koehn v. Sec'y of Health & Hum. Servs.*, No. 11-355V, 2013 WL 3214877 (Fed. Cl. Spec. Mstr. May 30, 2013), *mot. for rev. denied* (Fed. Cl. Dec. 3, 2013), *aff'd*, 773 F.3d 1239 (Fed. Cir. 2014).

B. *Legal Standards Governing Factual Determinations*

The process for making determinations in Vaccine Program cases regarding factual issues begins with consideration of the medical records. Section 11(c)(2). The special master is required to consider "all [] relevant medical and scientific evidence contained in the record," including "any diagnosis, conclusion, medical judgment, or autopsy or coroner's report which is contained in the record regarding the nature, causation, and aggravation of the petitioner's illness, disability, injury, condition, or death," as well as the "results of any diagnostic or evaluative test which are contained in the record and the summaries and conclusions." Section 13(b)(1)(A). The special master is then required to weigh the evidence presented, including contemporaneous medical records and testimony. *See Burns v. Sec'y of Health & Hum. Servs.*, 3 F.3d 415, 417 (Fed. Cir. 1993) (it is within the special master's discretion to determine whether to afford greater weight to contemporaneous medical records than to other evidence, such as oral testimony surrounding the events in question that was given at a later date, provided that such determination is evidenced by a rational determination).

Medical records that are created contemporaneously with the events they describe are presumed to be accurate and "complete" (i.e., presenting all relevant information on a patient's health problems). *Cucuras*, 993 F.2d at 1528; *Doe/70 v. Sec'y of Health & Hum. Servs.*, 95 Fed. Cl. 598, 608 (2010) ("[g]iven the inconsistencies between petitioner's testimony and his contemporaneous medical records, the special master's decision to rely on petitioner's medical records was rational and consistent with applicable law"), *aff'd sub nom. Rickett v. Sec'y of Health & Hum. Servs.*, 468 F. Appx. 952 (Fed. Cir. 2011) (non-precedential opinion). This presumption is based on the linked propositions that (i) sick people visit medical professionals; (ii) sick people honestly report their health problems to those professionals; and (iii) medical professionals record what they are told or observe when examining their patients in as accurate a manner as possible, so that they are aware of enough relevant facts to make appropriate treatment decisions. *Sanchez v. Sec'y of Health & Hum. Servs.*, No. 11-685V, 2013 WL 1880825, at *2 (Fed. Cl. Spec. Mstr. Apr. 10, 2013); *Cucuras v. Sec'y of Health & Hum. Servs.*, 26 Cl. Ct. 537, 543 (1992), *aff'd*, 993 F.2d at 1525 (Fed. Cir. 1993) ("[i]t strains reason to conclude that petitioners would fail to accurately report the onset of their daughter's symptoms").

Accordingly, if the medical records are clear, consistent, and complete, then they should be afforded substantial weight. *Lowrie v. Sec'y of Health & Hum. Servs.*, No. 03-1585V, 2005 WL 6117475, at *20 (Fed. Cl. Spec. Mstr. Dec. 12, 2005). Indeed, contemporaneous medical records are generally found to be deserving of greater evidentiary weight than oral testimony—especially where such testimony conflicts with the record evidence. *Cucuras*, 993 F.2d at 1528; *see also Murphy v. Sec'y of Dep't of Health & Hum. Servs.*, 23 Cl. Ct. 726, 733 (1991) (citing *United States v. United States Gypsum Co.*, 333 U.S. 364, 396 (1947) ("[i]t has generally been held that oral

testimony which is in conflict with contemporaneous documents is entitled to little evidentiary weight.")).

There are, however, situations in which compelling testimony may be more persuasive than written records, such as where records are deemed to be incomplete or inaccurate. *Campbell v. Sec'y of Health & Hum. Servs*., 69 Fed. Cl. 775, 779 (2006) ("like any norm based upon common sense and experience, this rule should not be treated as an absolute and must yield where the factual predicates for its application are weak or lacking"); *Lowrie*, 2005 WL 6117475, at *19 ("'[w]ritten records which are, themselves, inconsistent, should be accorded less deference than those which are internally consistent'") (quoting *Murphy*, 23 Cl. Ct. at 733)). Ultimately, a determination regarding a witness's credibility is needed when determining the weight that such testimony should be afforded. *Andreu*, 569 F.3d at 1379; *Bradley v. Sec'y of Health & Hum. Servs*., 991 F.2d 1570, 1575 (Fed. Cir. 1993).

When witness testimony is offered to overcome the presumption of accuracy afforded to contemporaneous medical records, such testimony must be "consistent, clear, cogent, and compelling." *Sanchez*, 2013 WL 1880825, at *3 (citing *Blutstein v. Sec'y of Health & Hum. Servs*., No. 90-2808V, 1998 WL 408611, at *5 (Fed. Cl. Spec. Mstr. June 30, 1998)). In determining the accuracy and completeness of medical records, the Court of Federal Claims has listed four possible explanations for inconsistencies between contemporaneously created medical records and later testimony: (1) a person's failure to recount to the medical professional everything that happened during the relevant time period; (2) the medical professional's failure to document everything reported to her or him; (3) a person's faulty recollection of the events when presenting testimony; or (4) a person's purposeful recounting of symptoms that did not exist. *Lalonde v. Sec'y of Health & Hum. Servs*., 110 Fed. Cl. 184, 203–04 (2013), *aff'd*, 746 F.3d 1334 (Fed. Cir. 2014). In making a determination regarding whether to afford greater weight to contemporaneous medical records or other evidence, there must be evidence that this decision was the result of a rational determination. *Burns*, 3 F.3d at 417.

C. *Analysis of Expert Testimony*

Establishing a sound and reliable medical theory often requires a petitioner to present expert testimony in support of his claim. *Lampe v. Sec'y of Health & Hum. Servs.*, 219 F.3d 1357, 1361 (Fed. Cir. 2000). Vaccine Program expert testimony is usually evaluated according to the factors for analyzing scientific reliability set forth in *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 509 U.S. 579, 594–96 (1993). *See Cedillo v. Sec'y of Health & Hum. Servs*., 617 F.3d 1328, 1339 (Fed. Cir. 2010) (citing *Terran v. Sec'y of Health & Hum. Servs.*, 195 F.3d 1302, 1316 (Fed. Cir. 1999)). "The *Daubert* factors for analyzing the reliability of testimony are: (1) whether a theory or technique can be (and has been) tested; (2) whether the theory or technique has been subjected to peer review and publication; (3) whether there is a known or potential rate of error

and whether there are standards for controlling the error; and (4) whether the theory or technique enjoys general acceptance within a relevant scientific community." *Terran*, 195 F.3d at 1316 n.2 (citing *Daubert*, 509 U.S. at 592–95).

The *Daubert* factors play a slightly different role in Vaccine Program cases than they do when applied in other federal judicial fora (such as the district courts). *Daubert* factors are usually employed by judges (in the performance of their evidentiary gatekeeper roles) to exclude evidence that is unreliable and/or could confuse a jury. In Vaccine Program cases, by contrast, these factors are used in the *weighing* of the reliability of scientific evidence proffered. *Davis v. Sec'y of Health & Hum. Servs.*, 94 Fed. Cl. 53, 66–67 (2010) ("uniquely in this Circuit, the *Daubert* factors have been employed also as an acceptable evidentiary-gauging tool with respect to persuasiveness of expert testimony already admitted"). The flexible use of the *Daubert* factors to evaluate the persuasiveness and reliability of expert testimony has routinely been upheld. *See, e.g.*, *Snyder*, 88 Fed. Cl. at 742–45. In this matter (as in numerous other Vaccine Program cases), *Daubert* has not been employed at the threshold, to determine what evidence should be admitted, but instead to determine whether expert testimony offered is reliable and/or persuasive.

A special master's decision may be "based on the credibility of the experts and the relative persuasiveness of their competing theories." *Broekelschen v. Sec'y of Health & Hum. Servs.*, 618 F.3d 1339, 1347 (Fed. Cir. 2010) (citing *Lampe*, 219 F.3d at 1362). However, nothing requires the acceptance of an expert's conclusion "connected to existing data only by the *ipse dixit* of the expert," especially if "there is simply too great an analytical gap between the data and the opinion proffered." *Snyder*, 88 Fed. Cl. at 743 (quoting *Gen. Elec. Co. v. Joiner*, 522 U.S. 136, 146 (1997)); *see also Isaac v. Sec'y of Health & Hum. Servs.*, No. 08-601V, 2012 WL 3609993, at *17 (Fed. Cl. Spec. Mstr. July 30, 2012), *mot. for rev. denied*, 108 Fed. Cl. 743 (2013), *aff'd*, 540 F. Appx. 999 (Fed. Cir. 2013) (citing *Cedillo*, 617 F.3d at 1339). Weighing the relative persuasiveness of expert testimony, based on a particular expert's credibility, is part of the overall reliability analysis to which special masters must subject expert testimony in Vaccine Program cases. *Moberly*, 592 F.3d at 1325–26 ("[a]ssessments as to the reliability of expert testimony often turn on credibility determinations"); *see also Porter v. Sec'y of Health & Hum. Servs.*, 663 F.3d 1242, 1250 (Fed. Cir. 2011) ("this court has unambiguously explained that special masters are expected to consider the credibility of expert witnesses in evaluating petitions for compensation under the Vaccine Act").

Expert opinions based on unsupported facts may be given relatively little weight. *See Dobrydnev v. Sec'y of Health & Hum. Servs.*, 556 F. Appx. 976, 992–93 (Fed. Cir. 2014) ("[a] doctor's conclusion is only as good as the facts upon which it is based") (citing *Brooke Group Ltd. v. Brown & Williamson Tobacco Corp.*, 509 U.S. 209, 242 (1993) ("[w]hen an expert assumes facts that are not supported by a preponderance of the evidence, a finder of fact may properly reject the expert's opinion")). Expert opinions that fail to address or are at odds with contemporaneous

medical records may therefore be less persuasive than those which correspond to such records. *See Gerami v. Sec'y of Health & Hum. Servs.*, No. 12-442V, 2013 WL 5998109, at *4 (Fed. Cl. Spec. Mstr. Oct. 11, 2013), *aff'd*, 127 Fed. Cl. 299 (2014).

D. *Consideration of Medical Literature*

Petitioner has filed medical and scientific literature in this case, but not every filed item factors into the outcome of this decision. While I have reviewed all the medical literature submitted in this case, I discuss only those articles that are most relevant to my determination and/or are central to Petitioner's case—just as I have not exhaustively discussed every individual medical record filed. *Moriarty v. Sec'y of Health & Hum. Servs.*, 844 F.3d 1322, 1328 (Fed. Cir. 2016) ("[w]e generally presume that a special master considered the relevant record evidence even though he does not explicitly reference such evidence in his decision") (citation omitted); *see also Paterek v. Sec'y of Health & Hum. Servs.,* 527 F. Appx. 875, 884 (Fed. Cir. 2013) ("[f]inding certain information not relevant does not lead to—and likely undermines—the conclusion that it was not considered").

E. *Evaluation of Expert Credentials and Professional Competence*

It is common in Program cases for special masters to evaluate competing expert opinions when deciding non-Table claims—and that process can be very difficult when the experts are equally well-credentialed and qualified to provide the opinion offered. Under such circumstances, resolution of a claimant's success in establishing causation turns on the comparative reliability of the scientific/medical contentions each side makes, rather than a measure of each particular expert's baseline qualifications against the other. *See, e.g., D'Tiole v. Sec'y of Health & Hum. Servs.*, No. 15-085V, 2016 WL 7664475, at *20 (Fed. Cl. Nov. 28, 2016) (determination that causation theory was unreliable did not arise from adequacy of Petitioner's expert, who was expressly deemed well-qualified to provide the opinion given), *mot. for review den'd,* 132 Fed. Cl. 421 (2017), *aff'd*, 726 F. App'x 809 (Fed. Cir. 2018).

In other circumstances, however, weighing the probative value of an expert's opinion fairly takes into account that same expert's qualifications or professional experience. This is most obviously necessary when an expert offers an opinion that plainly exceeds his training or individual competence. *Domeny v. Sec'y of Health & Hum. Servs.,* No. 94-1086V, 1999 WL 199059, at * 15 (Fed. Cl. Spec. Mstr. Mar. 15, 1999) (dentist not qualified to offer diagnostic opinion on whether petitioner had experienced a neuropathy), *mot. for review den'd,* slip op., May 25, 1999 (Fed. Cl.), *aff'd*, 232 F.3d 912 (Fed. Cir. 2000). But it can even be an issue with experts who possess immense and impressive credentials, and who in prior cases may have offered reliable opinions. *See, e.g.*, *Rolshoven v. Sec'y of Health & Hum. Servs.,* No. 14-439V, 2018 WL 1124737, at *21 (Fed. Cl. Spec. Mstr. Jan. 11, 2018) (otherwise-competent expert with significant Vaccine

Program experience undermined his credibility in part with constant commentary about relevant legal standards to be applied in case).

ANALYSIS

Petitioner Has Established Each of the Althen Prongs

A. Prong One

As described in detail above, a Program petitioner must show that the vaccine at issue "can cause" the alleged injury, by proposing a scientifically and medically reliable causation theory. Here, Dr. Stone offered his opinion as to causation, bulwarked with literature suggesting that individuals at risk for developing MOGAD could have their disease process triggered or accelerated by receiving a vaccination, and emphasized that comparable diseases in scope and nature had been vaccine-associated. He also presented two possible mechanisms—molecular mimicry and bystander activation—by which the Tdap vaccine could precipitate an autoimmune response. Although Petitioner's showing was far from robust, it was sufficiently preponderant to carry her *Althen* prong one burden.

I begin with some discussion of other relevant decisions for guidance.[12] I have not identified cases in which a petitioner successfully demonstrated a vaccine triggered or caused MOGAD—but this is probably attributable to the newness of the diagnostic classification, and accompanying lack of literature/research on the topic—as both experts acknowledged to be the case. Bouffard Rep. at 4; Stone Rep. at 7. Other petitioners have, however, successfully demonstrated that the anti-MOG antibody was vaccine-induced, causing an individual to experience a CNS demyelinating injury. *See, e.g.*, *White v. Sec'y of Health & Hum. Servs.,* No. 15-1521V, 2019 WL 7563239 (Fed. Cl. Spec. Mstr. Dec. 19, 2019) (HPV vaccine caused anti-MOG antibody-mediated TM). There is thus *some* recognition in the Program that vaccination could play a role in the propagation of these antibodies, even if the greater disease itself has not previously been evaluated in a reasoned decision.

[12] It is certainly correct that prior decisions from different cases do not *control* my decision in this case. Only Federal Circuit rulings concerning legal issues are generally binding on special masters in all cases. *Guillory v. Sec'y of Health & Hum. Servs*., 59 Fed. Cl. 121, 124 (2003), *aff'd* 104 F. Appx. 712 (Fed. Cir. 2004). But it is reasonable, and in fact prudent, when deciding a Vaccine Act case to consider and be guided by other relevant reasoned decisions involving the same theory, injury, and/or vaccine. This flows from the fact that special masters reasonably draw upon their experience in resolving Vaccine Act claims. *Doe v. Sec'y of Health & Hum. Servs.,* 76 Fed. Cl. 328, 338–39 (2007) ("[o]ne reason that proceedings are more expeditious in the hands of special masters is that the special masters have the *expertise and experience to know the type of information that is most probative of a claim*") (emphasis added). They would therefore be remiss in ignoring prior cases presenting similar theories or factual circumstances, along with the reasoning employed in reaching such decisions.

There are, however, numerous reasoned decisions in which special masters determined that a petitioner had successfully established that an acute and monophasic CNS demyelinating injury was vaccine-caused—including due to the Tdap vaccine. *See generally*, *Kennedy v. Sec'y of Health & Hum. Servs.,* No. 09–474V, 2012 WL 1929801 (Fed. Cl. Spec. Mstr. May 8, 2012) (petitioner who received the meningococcal and Tdap vaccines and then developed ADEM was entitled to compensation based on the theory of molecular mimicry); *Lerwick v. Sec'y of Health & Hum. Servs.,* No. 06–847V, 2011 WL 4537874 (Fed. Cl. Spec. Mstr. Sept. 8, 2011) (ADEM and DTaP/Hep B vaccines); *Kuperus v. Sec'y of Health & Hum. Servs.,* No. 01–0060V, 2003 WL 22912885 (Fed. Cl. Spec. Mstr. Oct. 23, 2003) (awarding compensation in a DTaP/ADEM case based on the theory of immune-mediated attack); *Johnson v. Sec'y of Health & Hum. Servs.,* No. 99–0219V, 2000 WL 1141582 (Fed. Cl. Spec. Mstr. July 27, 2000) (ADEM and Tdap vaccine).[13]

I acknowledge Dr. Bouffard's point that separate categories of CNS-demyelinating injuries are not interchangeable—and that distinctions between them, particularly with respect to pathology, often matter when evaluating causation.[14] I nevertheless deem these prior determinations helpful to the decision I must reach in this action. Dr. Stone persuasively established that even if MOGAD featured more than one demyelinating incident (here, two flares of ON with ADEM-like symptoms in the middle), it is likely (especially when experienced by children) to feature a cluster of related demyelinating events, with greater relapse only likely if prompt treatment does not arrest the overall disease process. Thus, although MOGAD may be driven by a specific antibody distinct from whatever underlies the pathogenesis of a single occurrence of TM or ON, Dr. Stone persuasively established that it is sufficiently akin to the CNS demyelinating injuries that are more acute in nature to rely somewhat on what is known about them for comparative purposes. Stone Rep. at 8; Tr. at 23-32. Indeed, certain instances of ADEM diagnosed in the past may actually have constituted MOGAD. Tr. at 32.

[13] By contrast, I have denied compensation in some recent cases alleging comparable acute demyelinating injuries after the Tdap vaccine. *See, e.g.*, *I.J. v. Sec'y of Health & Hum. Servs*., No. 16-864V, 2021 WL 1232733 (Fed. Cl. Spec. Mstr. Jan. 4, 2021) (TM not caused by Tdap vaccine). However, *I.J.* is facially distinguishable. There, the petitioner's expert relied on Baxter, the same study cited herein—but *despite* the fact that Baxter expressly did not find a statistically significant relationship between TM and the Tdap vaccine. Baxter is far *more* supportive of this claim, since it did find an association between ADEM and Tdap (and ADEM is more comparable to some of K.N.'s symptoms than TM).

[14] I would particularly distinguish cases involving acute and monophasic CNS demyelinating diseases from those where a *chronic* demyelinating injury, like MS, is experienced. I have generally not found that the latter are likely vaccine-caused, since it cannot usually be reliably established that a vaccine would (alone or predominantly) set into motion a chronic/relapsing disease process, with no predictable course or treatment that could stop it thereafter. *See Morgan v. Sec'y of Health & Hum. Servs.*, 148 Fed. Cl. 454, 466-67 (Fed. Cl. 2020) (citing *Morgan v. Sec'y of Health & Hum. Servs.* No. 15-1137V, 2019 WL 7498665 at 16 (Fed. Cl. Spec. Mstr. Dec. 4, 2019)), *aff'd,* No. 2020-2107, 2021 WL 1115436 (Fed. Cir. Mar. 24, 2021). Self-limiting acute disease processes, by contrast, more credibly could be attributed to a single vaccination event, which itself is self-limiting.

With the foregoing as backdrop, Dr. Stone presented a persuasive theory that the Tdap vaccine could cause MOGAD, by stimulating production of the anti-MOG antibodies. Tr. at 25, 46-47. These antibodies, in turn, cause CNS demyelination, which can present as ON or ADEM-like episodes. *Id.* at 25-26, 47. Dr. Stone also proposed reliable mechanisms that could explain MOGAD's pathogenesis. Molecular mimicry and bystander activation have been accepted in other Program cases as scientifically-accepted mechanistic explanations for the progression of comparable autoimmune-mediated demyelinating illnesses. *Raymo v. Sec'y of Health & Hum. Servs.,* No. 11–0654V, 2014 WL 1092274 (Fed. Cl. Spec. Mstr. Feb. 24, 2014), *rev. den'd, aff'd* 129 Fed.Cl. 691 (Fed. Cl. 2016).

Admittedly, Petitioner's evidence regarding mechanism constituted a weak link in her causation theory. Dr. Stone's reliance on evidence relating to T cell-driven autoimmune processes was inconsistent with the fact that MOGAD, as an antibody-oriented disease, would be B cell-driven. Yet both experts in this case agreed that the relevant cross-reactive process herein is "more complicated than simple amino acid sequence homology." Tr. at 28-29, 77; Langer-Gould at 1511-12 ("[v]accines could theoretically increase the risk of CNS ADS [acquired central nervous system demyelinating syndromes] through mechanisms similar to those induced by infection. Infections are known to cause or enhance autoimmunity through expansion of autoreactive T-cell clones by molecular mimicry, later stimulation of autoreactive T-cell clones, or enhancement of antigen presentation by bystander activation, epitope spreading, adjuvant effect, and enhanced antigen presentation"). Dr. Stone in fact opined that MOGAD "isn't purely a B-cell driven disease, but there's also abnormal function of cell-mediated immunity or T cells" (Tr. at 53), and that the pathogenic nature of the anti-MOG autoantibody might only be exhibited in the presence of a T cell-mediated inflammatory response. Tr. at 53-54 (citing Azumagawa at 690). This (plus the fact that mechanism need not even be proved in a Vaccine Act case) leads me to find that the evidence offered on potential MOGAD mechanisms stimulated by vaccination was adequately substantiated (although barely so).

Respondent also raised valid arguments about the absence of more direct evidence establishing that the Tdap vaccine could stimulate production of the MOGAD-related autoantibodies. Tr. at 76-77. But I return to the fact that somewhat comparable acute demyelinating CNS illnesses, like ON or ADEM, have been linked to the same vaccine—and, as Dr. Stone noted, it is likely that up to forty or fifty percent of patients so previously diagnosed actually had MOGAD. Tr. at 32. Since "the purpose of the Vaccine Act's preponderance standard is to allow the finding of causation in a field bereft of complete and direct proof [as to] how vaccines affect the human body" (*Althen* at 1280), and given MOGAD's diagnostic novelty, I do not find Respondent's objections in this case to causation merit the same weight they might receive in a case involving a more-studied illness, or where more substantial rebutting evidence was offered.

In sum, the evidence supporting Petitioner's contention that the Tdap vaccine could be causal of MOGAD is far from overwhelming. Certainly the limited science studying what is a fairly recent diagnostic classification provides some explanation for this paucity—although I must be careful in accepting such excuses, since *all* vaccine cases involve matters not fully understood by medicine or science. Petitioners are still required to meet the preponderant burden of proof, which is recognized to be substantial. *Hodges v. Secretary of Health & Hum. Servs*., 9 F.3d 958, 961 (Fed.Cir.1993) (while "the [Vaccine Act] does the heavy lifting" when a claimant seeks to establish a Table injury, in the causation-in-fact context "the heavy lifting must be done by the petitioner, and it is heavy indeed"). Nevertheless, Petitioner did persuasively establish through Dr. Stone's credible testimony that it may be scientifically correct to think of MOGAD as a refinement and expansion on what was previously understood about related acute/monophasic illnesses like TM or ADEM—injuries that are frequently compensated in the Program, via reasoned decisions.

I thus find that this is no worse than a "close" case—and such circumstances counsel for a determination in the Petitioner's favor on this prong of the *Althen* test. *Andreu*, 569 F.3d at 1378. Of course, my determination leaves ample room for doubt—as indeed, *any* determination that a claimant has carried his preponderant burden on the "can cause" prong is not akin to a finding that a vaccine is medically certain to cause injury. As scientific understanding of MOGAD, and the role that anti-MOG antibodies play in its pathogenesis, expands and develops, evidence far more convincing than offered in this matter may come into existence suggesting that the Tdap vaccine does *not* likely cause MOGAD. If such evidence is offered in a future case, it could well result in a denial of entitlement. But Respondent did not so establish *here*, and/or rebut Petitioner's otherwise barely-preponderant showing herein.

B. Prong Two

The record in this case is generally consistent with the conclusion that the Tdap vaccine likely caused K.N.'s MOGAD. Both experts agreed she had MOGAD. Stone Rep. at 6; Bouffard Rep. at 4. K.N.'s course began with the onset of severe neurological symptoms approximately three weeks after receipt of the Tdap vaccine. Tr. at 31. K.N. suffered from "frontal headaches" approximately one week following vaccination, and then experienced an episode of optic neuritis approximately three weeks post-vaccination, in July 2014. *Id.* at 16. MRI imaging showed abnormal optic nerve enhancement plus swelling/edema which confirmed the existence of bilateral optic neuritis. *Id.* at 17. There was no evidence of prior infection or illness to explain a possible pathology, and testing was negative for antibodies associated with other CNS demyelinating diseases. *Id.* at 16, 17, 19-20. Thus, these initial symptoms, leading up to what looked (at first) like ON alone, are consistent with the conclusion that K.N. had begun experiencing an autoimmune inflammatory process characteristic of MOGAD, even if she had not yet been tested for anti-MOG antibodies (which as of 2014 were not understood to be as significant as they are today).

K.N. was prescribed steroids and then prednisone which resulted in a good recovery of vision and a subsequent steroidal taper by her treaters in August 2014. Tr. at 18. However, shortly after the steroid taper, K.N. experienced recurrent neurological symptoms presenting as ADEM-like inflammatory event and an episode of left optic neuritis. Although the second event proved to be more of a diagnostic dilemma for her medical treaters, in retrospect was most likely an "ADEM-like" event consistent with MOGAD. Stone Rep. at 7. Between the second and third event, testing revealed K.N. was positive for MOG antibodies (although their significance was less understood in 2014 than today). Tr. at 24-25. She later had a second bout with ON, and then steroid treatments proved effective in arresting her disease course. Although K.N.'s overall course was not classically monophasic (in that it featured a cluster of three related events within five months, rather than a single event), Dr. Stone persuasively established that MOGAD's kind of course often presents in this way.

Petitioner's medical treaters also documented the development of symptoms in the context of vaccination on several occasions. For example, in a July 17, 2014 letter, Dr. Imes, a neuro-ophthalmologist, wrote that K.N. "had a DTAP immunization a month earlier and an insect bite the same day she told her parents she was having difficulty seeing." Ex. 8 at 2. The next month, on August 29, 2014, Dr. Von Scheven, a rheumatologist, wrote, "[i]mmunizations up to date; in fact she received Tdap on 6/7 which was about a week before her symptoms of headache first began." Ex. 4 at 262. And on October 13, 2014, K.N.'s treating pediatric neurologist, Dr. Graves, wrote:

> Her first visual or neurological symptom[] was in July 2014…Before this episode, June 7th she had a TDAP vaccine, she had frontal headaches around June 17th while[e] on trip to France but no clear vision symptoms…Avoid live vaccines if possible, but vaccines in the setting of prior optic neuritis can be evaluated with a risk benefit approach.

Ex. 4 at 1090-1105. Such treater evidence also supports the conclusion that K.N.'s receipt of the Tdap vaccine likely played a role in her subsequent symptoms.

C. Prong Three

The third *Althen* prong also finds support in the record, and the evidence of the timing for symptoms onset is consistent with Petitioner's causation theory. As Petitioner and her expert established, an acceptable range of onset for immune-mediated CNS demyelinating reactions triggered by vaccination is within thirty days/three to four weeks following vaccination. Tr. at 30; Langer-Gould; Karussis. Here, Petitioner's onset fell squarely within that range, since she experienced her symptoms within one to three weeks after receiving the Tdap vaccine. Respondent for his part did not establish that this timing was not medically acceptable or unreliable—in fact,

Respondent's expert agreed at hearing that a three-to-four week onset was an appropriate timeframe for an immune-mediated reaction. Tr. at 94. I therefore find that Petitioner has offered preponderant evidence in support of the conclusion that the timeframe for post-vaccination onset of K.N.'s symptoms was medically acceptable.

CONCLUSION

Not nearly enough is currently known about MOGAD to say more definitively that it likely can be, or cannot be, caused by vaccination. In a case with more evidence directly involving MOGAD, I might well have determined that the causal association had not been demonstrated. But a combination of Petitioner's persuasive expert, apt analogies to recognized Program injuries, and the general novelty of MOGAD from a diagnostic standpoint, all lead me to conclude that the preponderant "line" was crossed herein—and thus that damages for K.N.'s vaccine-caused injury are warranted.

In order to guide the parties through the damages phase of the action, a separate damages order will issue.

IT IS SO ORDERED.

s/Brian H. Corcoran
Brian H. Corcoran
Chief Special Master