In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS
No. 18-757V
Filed: May 28, 2024

DEREK GRACE,

Petitioner,

v.

SECRETARY OF HEALTH AND HUMAN SERVICES,

Respondent.

Diana Lynn Stadelnikas, Magio Christopher & Toale, PA, Sarasota, FL, for petitioner
Voris Edward Johnson, U.S. Department of Justice, Washington, DC, for respondent

Decision[1]

On May 29, 2018, petitioner, Derek Grace, filed a petition under the National Childhood Vaccine Injury Act, 42 U.S.C. § 300aa-10-34 (2012)[2], alleging that an influenza ("flu") vaccination he received on November 9, 2016, caused him to develop IgA vasculitis or Henoch-Schonlein purpura ("HSP"). (ECF No. 1, pp. 1-2; ECF No. 9, pp. 1-2.) For the reasons set forth below, I conclude that petitioner is *not* entitled to an award of 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 document contains a reasoned explanation for the action taken in this case, it must be made publicly accessible and will be posted on the United States Court of Federal Claims' website, and/or at https://www.govinfo.gov/app/collection/uscourts/national/cofc, in accordance with the E-Government Act of 2002. 44 U.S.C. § 3501 note (2018) (Federal Management and Promotion of Electronic Government Services). **This means the document 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, I will redact such material from public access.

[2] Within this decision, all citation 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)-(B); § 300aa-11(c)(1)(C)(i); § 300aa-14(a).

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)(A); § 300aa-11(c)(1)(C)(ii). In such a situation, of course, 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). In this case, petitioner's alleged injury is not listed on the Vaccine Injury Table relative to the flu vaccine. Petitioner must therefore meet the burden of proof for establishing causation-in-fact.

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 another special master. (ECF No. 4.) It was reassigned to the undersigned on August 27, 2019. (ECF Nos. 36-37.)

Petitioner filed medical records and a Statement of Completion in June of 2018. (ECF Nos. 10-12; Exs. 1-12.) In February of 2019, respondent filed a Rule 4 Report recommending against compensation. (ECF No. 21.) In addition to contending petitioner had not met his burden of proof under any of the *Althen* prongs, respondent also asserted that his treatment with Humira may have caused his condition. (*Id*. at 7.) Respondent also filed three medical articles to support this proposition. (ECF No. 22; Exs. A-C.)

Thereafter, petitioner filed additional medical records (Ex. 13), photographs of his rash (Ex. 14), and an affidavit regarding his alleged damages (Ex. 15). (ECF Nos. 23, 29-30.) On December 16, 2019, petitioner filed an expert report by rheumatologist Lindsay Lally, M.D., with supporting materials. (ECF Nos. 40-41; Exs. 16-27.) Respondent filed a responsive report by Mehrdad Matloubian, M.D., Ph.D., on June 3, 2020. (ECF No. 45; Exs. D-P.) Petitioner then filed additional medical records (Ex. 28) and a supplemental expert report and further supporting materials (Exs. 29-31). (ECF Nos. 49, 51.) Respondent filed a responsive supplemental expert report. (ECF No. 53; Ex. Q.) Petitioner filed still further medical records (Exs. 32-41) and a second supplemental report by Dr. Lally (Exs. 42-48). (ECF Nos. 54-55, 60.)

On November 22, 2021, I held a Rule 5 conference. (ECF No. 62.) I noted that Dr. Matloubian's opinion as stated to that point was inadequate to support respondent's contention that Humira was a likely cause of petitioner's condition. (*Id*. at 1-2.) Instead, I advised that my preliminary view was that the case would turn on *Althen* prongs one

and three, which I felt were interrelated. (*Id*. at 1.) Petitioner requested an opportunity to file a further supplemental report, and I instructed the parties identify dates on which to schedule an entitlement hearing. (*Id*. at 3.)

In June of 2022, petitioner filed a fourth report by Dr. Lally (Exs. 49-52) and additional medical records (Ex. 53). (ECF Nos. 67-68.) Respondent filed a final report by Dr. Matloubian in August of 2022. (ECF No. 70; Ex. R.) An entitlement hearing was set, but then cancelled after the parties jointly requested that the case be decided on the written record. (ECF Nos. 72-73; Order (Non-PDF), 2/16/2023.) Petitioner explained on behalf of the parties that "[u]pon review of the evidentiary record, in preparation for the entitlement proceedings and after discussion with Respondent's counsel, the parties believe the issues at question to be clear and evidentiary record to be complete in terms of resolving the issues." (ECF No. 73, p. 1.)

Petitioner filed his motion for a ruling on the written record on June 2, 2023. (ECF No. 75.) Respondent filed a response on July 6, 2023, and petitioner filed his reply on August 18, 2023. (ECF Nos. 76, 78.) Accompanying his reply, petitioner filed updated medical records and a declaration. (ECF No. 79; Exs. 54-59.)

This matter is now ripe for resolution. I have concluded that the parties have had a full and fair opportunity to develop the record and that it is appropriate to resolve this case without an entitlement hearing. *See Kreizenbeck ex rel. C.J.K. v. Sec'y of Health & Human Servs*., 945 F.3d 1362, 1366 (Fed. Cir. 2020) (citing *Simanski v. Sec'y of Health & Human Servs*., 671 F.3d 1368, 1385 (Fed. Cir. 2012)); *see also* Vaccine Rule 8(d); Vaccine Rule 3(b)(2).

III. Factual History

a. Medical Records

Although I have reviewed the complete medical records filed in this case, it is not necessary to discuss the records in detail because the operative facts are undisputed. Petitioner received a flu vaccine on November 9, 2016, at age 48. (Ex. 1, p. 5.) He had a longstanding prior history of psoriasis and psoriatic arthritis for which he initially treated with methotrexate but later switched to adalimumab, which was more effective. (*See* Ex. 10, p. 281.) At the time of vaccination, petitioner was taking adalimumab once monthly. (*Id.* at 245.) Typically, however, it is administered once every two weeks. (Ex. D, p. 2.)

Following the vaccination, petitioner presented to an urgent care clinic on November 14, 2016, with a complaint of "rash since 11/9/16." (Ex. 2, p. 3.) Petitioner explained that after he was administered his vaccination, he "noticed a rash later that night." (*Id*.) He subsequently developed diarrhea as well as joint, muscle and abdominal pain, though he had no fever or chills. (*Id.*; Ex. 5, p. 3.) At urgent care, it was initially felt that petitioner's rash was "probably an immune response to vaccination." (Ex. 5, p. 4.) He was subsequently seen at the emergency department

and then evaluated by a dermatologist and was ultimately diagnosed with IgA vasculitis/Henoch Schonlein Purpura following a skin biopsy. (Ex. 10, p. 81.) As discussed below, both parties' experts accept this diagnosis. (*See* Ex. 16, p. 2; Ex. D, p. 2.) Petitioner was started on prednisone. (Ex. 10, p. 251.)

As of a follow up on November 18, 2016, petitioner's skin lesions had improved significantly, but he had severe abdominal pain and a CT scan suggested intestinal inflammation. (Ex. 10, pp. 241, 136-37.) He was hospitalized from November 18, 2016 until November 22, 2016. (*Id.* at 556.) Petitioner reported to his rheumatologist that his condition arose following vaccination, but the rheumatologist was more concerned that the vasculitis could have been caused by his Humira treatment. (*Id.* at 565-66 (discussing case reports regarding adalimumab induced IgA vasculitis).)

By November 30, 2016, petitioner was noted to be "essentially symptom free" after steroid treatment. (Ex. 10, p. 217.) However, he did later have some recurrent skin lesions after tapering from his prednisone. (*Id.* at 196, 173.) Petitioner was later seen at the Cleveland Clinic, where rheumatology felt petitioner's vasculitis was either idiopathic or secondary to his Humira treatment. (Ex. 7, p. 4.) One of the Cleveland Clinic rheumatologists, Dr. Villa-Forte, ultimately noted the vasculitis "might still have been caused by [H]umira – we can't prove one way or another." (*Id.* at 19.)

I have not located any instance within the medical records where any of petitioner's treating physicians ever attributed his condition to his flu vaccination subsequent to his IgA vasculitis diagnosis. Nor has petitioner identified any such notation. (ECF No. 75, pp. 3-6, 43-45; ECF No. 78, pp. 6-7.)

b. Declaration

Petitioner explains that prior to his vaccination he had an active lifestyle and a good quality of life. (Ex. 59, p. 1.) He explains that he began noticing spots on his arms during the evening following his vaccination. (*Id.*) Within a week, the spots became painful and had spread, most severely on his legs. (*Id.*) Initially he went to urgent care, but they were confused by his presentation and recommended he go to the emergency department, which he did immediately. (*Id*.) Petitioner indicates he was in a constant state of worry during his hospitalization and that "[t]hese were difficult times." (*Id*. at 2.) Even after his hospitalization he remained worried about the long-term effects of taking large doses of steroids. (*Id*.) He describes recurrences of his condition as "unpredictable and devastating" and a source of newfound worry. (*Id.*) He considers himself "forever changed" and indicates he will never feel mentally and physically safe again. (*Id.* at 5.)

IV. Expert Opinions and Qualifications

a. Petitioner's expert, Lindsay Lally, M.D.[3]

Dr. Lally explains that IgA vasculitis, also known as Henoch-Schonlein Purpura, is a form of systemic vasculitis more often seen in children than adults. (Ex. 16, p. 3.) It has a presumed infectious trigger, which is consistent with observed increased incidences occurring in fall and winter months. (*Id.*) Classic findings of the condition include nonthrombocytopenic purpura,[4] arthritis, abdominal pain, and proteinuria[5] or hematuria.[6] (*Id*.) Skin involvement is generally most prominent on the lower extremities. (*Id.*) Skin biopsy will show evidence of leukocytoclastic vasculitis with IgA deposits in the vasculature observable on immunofluorescence. (*Id*.)

In petitioner's case, he presented with a rash consistent with IgA vasculitis as well as abdominal symptoms supportive of IgA affecting his gastrointestinal tract. He also had findings of proteinuria and intermittent hematuria consistent with IgA vasculitis renal involvement. (Ex. 16, p. 3.) Onset of his cutaneous lesions occurred within 24

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[3] Dr. Lally is a board certified rheumatologist, specializing in systemic vasculitis. (Ex. 16, p. 1; Ex. 17, p. 3.) She received her undergraduate degree from Princeton University and her medical degree from Weill Cornell Medical College. (Ex. 17, p. 2.) She completed an internship and residency at New York Presbyterian Hospital Weill Cornell Medical Center and a rheumatology fellowship at New York Presbyterian Hospital and Hospital for Special Surgery. (*Id.*) She currently works as an Assistant Professor of Medicine at both Weill Cornell Medical College and Hospital for Special Surgery. (*Id.* at 5.) At the time her CV was filed in this case, she had written six peer-reviewed articles, six reviews, and three chapters. (*Id.* at 11-12.) Dr. Lally has seen over "100 patients with various forms of small vessel vasculitis." (Ex. 16, p. 1.) Petitioner argues that I should place more weight on Dr. Lally's opinion because of her specific specialization in vasculitis. (ECF No. 75-1, pp. 8-10.) I have considered this point, but do not find that this factor overcomes the shortcomings of petitioner's showing under *Althen* as discussed in the analysis below. Additionally, while Dr. Lally has greater specialization in vasculitis, Dr. Matloubian is likewise a rheumatologist with the requisite clinical experience to offer his own competing medical opinion and it must be further noted that Dr. Matloubian has added qualifications in immunology that are particularly germane to several of his criticisms of Dr. Lally's opinion as it pertains to *Althen* prongs one and three.

[4] "Purpura" refers to a group of conditions characterized by small hemorrhages in the skin or other membrane surfaces, which may be due to blood disorders, vascular abnormalities, or trauma. *Purpura*, DORLAND'S MEDICAL DICTIONARY ONLINE, HTTPS://WWW.DORLANDSONLINE.COM/DORLAND/DEFINITION?ID=42170, (last visited May, 24, 2024). "Nonthrombocytopenic purpura" is "purpura without any decrease in platelet count of the blood." *Nonthrombocytopenic purpura,* DORLAND'S MEDICAL DICTIONARY ONLINE, https://www.dorlandsonline.com/dorland/definition?id=101157&searchterm=nonthrombocytopenic+purpua (last visited May, 24, 2024).

[5] "Proteinuria" refers to "excessive serum proteins in urine, such as in renal disease, after strenuous exercise, and with dehydration." *Proteinuria,* DORLAND'S MEDICAL DICTIONARY ONLINE, https://www.dorlandsonline.com/dorland/definition?id=41409&searchterm=proteinuria (last visited May 24, 2024).

[6] "Hematuria" refers to "blood (erythrocytes) in the urine." *Hematuria,* DORLAND'S MEDICAL DICTIONARY ONLINE, https://www.dorlandsonline.com/dorland/definition?id=21814&searchterm=hematuria (last visited May 24, 2024).

hours of his vaccination. (*Id.* at 2; Ex. 29, p. 2.) IgA vasculitis can have a relapsing course, which petitioner did. (Ex. 29, p. 1.) Prior to onset of his IgA vasculitis, petitioner had a history of psoriasis, which placed him at increased risk of IgA vasculitis. (Ex. 16, p. 5.) Petitioner treated his psoriasis with adalimumab (brand name Humira), which is a type of biologic treatment known as a "TNF inhibitor or "TNFi" because it blocks a particular inflammatory cytokine known Tumor Necrosing Factor alpha. (Ex. 16, pp. 3-4.) Dr. Lally observes that IgA vasculitis has rarely been reported following this type of treatment. (*Id*. at 3.) However, these reports generally show that the vasculitis is self-limited and resolves when the treatment is discounted. (*Id*. at 3-4; Ex. 29, pp. 1-2.) Because petitioner continued to have a relapsing course of IgA vasculitis after discontinuance of adalimumab, and because he had been treating with adalimumab for a decade prior to onset of his IgA vasculitis, it is unlikely his condition was related to that treatment. (Ex. 16, pp. 3-4; Ex. 44, p. 2.)

Dr. Lally acknowledges that the casual mechanism of IgA vasculitis is unknown but proposes that, as an autoimmune condition, the pathogenesis involves genetic and environmental factors interacting to lead to IgA complex formation and deposition that then leads to recruitment of pro-inflammatory neutrophils and results in tissue destruction. (Ex. 16, p. 4 (citing Marieke H. Heineke et al., *New Insights in the Pathogenesis of Immunoglobulin A Vasculitis (Henoch-Schonlein Purpura,* 16 AUTOIMMUNITY REVS. 1246 (2017) (Ex. 21)).) Citing a case series of 13 reported cases of IgA vasculitis following vaccination (including four cases following the flu vaccine), Dr. Lally asserts that vaccination can be implicated as among the environmental factors leading to IgA vasculitis, along with infections and drugs. (*Id*. (citing Andreas Woerner et al., *IgA Vasculitis (Henoch-Schonlein): Case Definition and Guidelines for Data Collection, Analysis, and Presentation of Immunisation Safety Data,* 35 VACCINE 1559 (2017) (Ex. 27)); *see also* Rachael Kantor et al., *Henoch-Schonlein Purpura Post-Vaccination in a Pediatric Patient: A Rare but Possible Adverse Reaction to Vaccine,* 22 ISR. MED. ASS'N J. 654 (2020) (Ex. 45).) Although she agrees the available evidence supporting this link is "limited," she suggests that research has been hampered by underreporting of the condition and the lack of a uniform disease definition. (Ex. 16, p. 4; Ex. 29, p. 1.) She notes that other forms of vasculitis have also been reported as adverse events following vaccination. (Ex. 16, p. 4-5 (citing Caterina Bonetto et al., *Vasculitis as an Adverse Event Following Immunization – Systematic Literature Review,* 34 VACCINE 6641 (2016) (Ex. 18)).) Dr. Lally agrees that immunizations are not a "major" etiologic factor for IgA vasculitis but contends that they may be a trigger in "select cases." (Ex. 29, p. 1.)

Dr. Lally suggests that, because pre-existing psoriasis is an autoimmune condition involving T cell dysregulation and autoreactive T cells, petitioner was more susceptible to other autoimmune conditions. (Ex. 29, p. 2 (citing Yihua Cai et al., *New Insights of T Cells in the Pathogenesis of Psoriasis,* 9 CELLULAR & MOLECULAR IMMUNOLOGY 302 (2012) (Ex. 30)).) She proposes that petitioner's vaccination upregulated his immune response and led to an "exuberant host response." (*Id.*) This response resulted in bystander activation whereby activated antigen presenting cells in turn activated pre-primed autoreactive T cells that initiated the autoimmune disease,

ultimately leading to the inappropriate IgA production and immune complex formation seen in IgA vasculitis. (*Id.*) Dr. Lally acknowledges that IgA response following influenza vaccination is "poorly understood," but cites a study that she indicates shows successive exposures to influenza infection and vaccination does increase IgA response to vaccination. (Ex. 44, pp. 2-3 (citing Rodrigo B. Abreu et al., *IgA Responses Following Recurrent Influenza Virus Vaccination,* 11 FRONTIERS IMMUNOLOGY 1 (2020) (Ex. 48)).)

Dr. Lally acknowledges that the immune process she describes typically peaks around 7 days after an exposure. (Ex. 49, p. 1.) However, she does not agree that this implies a brisker response is not possible. (*Id.*) She cites a case series of 19 IgA vasculitis cases following Covid-19 vaccination, where the mean onset was 4 days, but the most frequent interval was 1-2 days. (*Id*. (citing Hideo Hashizume et al., *Immunoglobulin A Vasculitis Post-Severe Acute Respiratory Syndrome Coronavirus 2 Vaccination and Review of Reported Cases,* 49 J. DERMATOLOGY 560 (2022) (Ex. 50)).) She opines that, especially considering petitioner's underlying psoriatic condition, the proposed mechanism could unfold within 24 hours. (Ex. 29, p. 2.) She notes that it is possible (but unknown) that petitioner may already have had elevated circulating IgA at the time of his vaccination due to his psoriasis. (Ex. 49, p. 1 (citing E. Maverakis et al., *The Psoriasis Glycome: Differential Expression of Cholesterol Particle Glycans and IgA Glycans Linked to Disease Severity,* J. INVESTIGATIVE DERMATOLOGY 1 (2022) (Ex. 51); A. Damasiewicz-Bodzek & T. Wielkoszynski, *Advanced Protein Glycation in Psoriasis,* 26 J. EUR. ACAD. DERMATOLOGY 172 (2012) (Ex. 52)).)

b. Respondent's expert, Mehrdad Matloubian, M.D., Ph.D.[7]

Dr. Matloubian agrees that petitioner suffered IgA vasculitis that was heralded by onset of a rash occurring the day of his vaccination. (Ex. D, pp. 5, 14.) Specifically, Dr. Matloubian places onset between 12-16 hours post-vaccination. (*Id.* at 9.) Treatment with azathioprine resolved his major symptoms, but he then continued to have occasional mild flares. (*Id*. at 5.) As Dr. Lally did, Dr. Matloubian discussed literature that suggests there could be a causal relationship between TNFi treatment and vasculitis. (*Id*. at 12-13.) He disagrees that petitioner's later flares are a reason for either favoring vaccine-causation or eliminating adalimumab as a causal factor (Ex. D, p. 14; Ex. R, p. 2), but ultimately opined that "I do not know what causes petitioner's IgA/HSP and agree with Dr. Villa-Forte's statement on 4/23/2017 that his vasculitis

[7] Dr. Matloubian is a board certified rheumatologist. (Ex. E, p. 2.) He received an undergraduate degree, medical degree, and Ph.D. in virology/immunology from the University of California, Los Angeles. (*Id.* at 1.) He also completed an internship, residency, fellowship in rheumatology, and a post-doctoral fellowship at the University of California, San Francisco. (*Id.*) He is currently an associate adjunct professor at the University of California, San Francisco. (*Id.* at 2.) His "areas of expertise include T and B cell responses, especially to viruses as well as factors that regulate lymphocyte circulation and trafficking." (Ex. D, p. 1.) his research focuses on "innate and adaptive immune responses, including those of T and B cells, to acute and chronic viral infections." (*Id.*) Dr. Matloubian has published 36 peer reviewed articles, and two review articles. (Ex. E, pp. 10-13.) Additionally, he "actively evaluates and treats patients with complex autoimmune diseases at a tertiary referral center." (Ex. D, p. 1.)

'might still have been caused by [H]umira – we can't prove one way or another.'" (Ex. D, p. 12 (quoting Ex. 7, p. 19).)

Like Dr. Lally, Dr. Matloubian explains that IgA vasculitis involves immune complex formation and deposition in tissue and, while the cause of IgA vasculitis is not known, as an autoimmune condition genetic and environmental factors are thought to be implicated. (Ex. D, p. 5) In particular, infection is thought to play a role. (*Id*.) However, half or more of IgA cases do not have any identified environmental factor. (*Id*.) Dr. Matloubian cites a literature review that observed that a majority of studies have failed to show a causal association between vaccination and vasculitides, including IgA vasculitis. (*Id*. (citing Fatma Dedeoglu & Susan Kim, *IgA Vasculitis (Henoch-Schonlein Purpura): Clinical Manifestations and Diagnosis,* UPTODATE (last updated Nov. 1, 2019) (Ex. I)).) Dr. Matloubian suggests that Dr. Lally's theory of causation is essentially based on temporality alone, given that she has not cited any literature to support her specific invocation of bystander activation. (*Id*. at 6.) Further, he asserts that Dr. Lally's single supporting citation – Bonetto, et al. – does not actually provide meaningful support for her opinion. (*Id*. at 6-7 (discussing Bonetto et al., *supra,* at Ex. 18).) Although the Bonetto authors noted case reports purporting to link vasculitis to vaccination, they present reasons for questioning the significance of those case reports and ultimately concluded based on their further literature review that the existing literature does not support the causative link. (*Id*. at 7 (discussing Bonetto et al., *supra,* at Ex. 18, pp. 8-9).) Dr. Matloubian cites two small studies that he indicates show patients with psoriatic arthritis treating with TNFi do not have increased risk of adverse events after flu vaccination. (*Id*. at 8 (citing A. Polachek et al., *Immunogenicity and Safety of Vaccination Against Seasonal 2012 Influenza Virus Among Patients with Psoriatic Arthritis and Psoriasis,* 33 CLINICAL & EXPERIMENTAL RHEUMATOLOGY 181 (2015) (Ex. L); Odile Launay et al., *Immunogenicity and Safety of Influenza Vaccine in Inflammatory Bowel Disease Patients Treated or Not with Immunomodulators and/or Biologics: A Two-Year Prospective Study,* 2015 J. CROHN'S & COLITIS 1096 (2015) (Ex. M)).)

Further, Dr. Matloubian observes that IgA is typically produced by mucosal infections (or intranasal live vaccines) whereas the flu vaccine generally results in IgG antibodies. (Ex. D, p, 9 (citing CLAIRE-ANNE SIEGRIST, *General Aspects of Vaccination, in* VACCINE IMMUNOLOGY (Ex. O)).) In any event, Dr. Matloubian suggests that the Lee study he cites shows that the flu vaccine results in activation of influenza specific antibody secreting cells, but not those that make antibodies to other antigens, suggesting bystander activation, as invoked by Dr. Lally, is unlikely to result from a flu vaccination. (*Id.* at 10-11 (discussing F. Eun-Hyung Lee et al., *Circulating Human Antibody-Secreting Cells During Vaccinations and Respiratory Viral Infections are Characterized by High Specificity and Lack of Bystander Effect,* 186 J. IMMUNOLOGY 5514 (2011) (Ex. N)).) Even following the stronger immune response experienced during infection, onset of IgA vasculitis usually occurs after one to two weeks. (*Id*. at 11 (citing Woerner et al., *supra,* at Ex. 27, p. 2).) Dr. Matloubian acknowledges that the Abrue, et al., study cited by Dr. Lally did measure serum IgA post flu vaccination; however, he stresses that these measurements were taken 21-28 days post-vaccination

and the increase was only "minor," being less than 2-fold. (Ex. R, p. 1 (discussing Abreu et al., *supra,* at Ex. 48, p. 2).) Thus, he opines that these findings are not supportive of an exaggerated IgA response to vaccination. (*Id*.) To the extent Dr. Lally cites petitioner's preexisting psoriasis as a source of T cell dysfunction, Dr. Matloubian indicates that such abnormalities are not unique to psoriasis and that vaccines are recommended as safe for people with various autoimmune diseases, including psoriasis. (Ex. Q, pp. 2-3 (citing Christien Rondaan et al., *Efficacy, Immunogenicity and Safety of Vaccination in Adult Patients with Autoimmune Inflammatory Rheumatic Diseases: A Systematic Literature Review for the 2019 Update of EULAR Recommendations,* 5 RHEUMATIC & MUSCULOSKELETAL DISEASES OPEN 1 (2019) (Ex. J); Johanna Westra et al., *Vaccination of Patients with Autoimmune Inflammatory Rheumatic Diseases,* 11 NATURE REV. IMMUNOLOGY 135 (2015) (Ex. K); Polachek et al., *supra,* at Ex. L; Launay et al., *supra,* at Ex. M).) Dr. Matloubian stresses that there is no evidence within petitioner's own clinical history that he experienced the "exuberant" immune response to vaccination that Dr. Lally proposes. (Ex. R, p. 1.)

Dr. Matloubian also opines that it is "extremely unlikely" that the immune process that Dr. Lally theorizes could occur within 12-16 hours. (Ex. D, p. 9.) Dr. Matloubian explains that circulating antibodies, including IgA, are produced by plasma cells which, in turn, are produced by either naïve or memory B cells. (*Id*.) It generally takes at least four days for plasma cells to appear in circulation after vaccination. (*Id*. (citing Lee et al., *supra,* at Ex. N).) Even accounting for Dr. Lally's invocation of a recall response, this still would take 2-3 days. (Ex. Q, p. 2 (citing Ex. D, p. 10 (fig.).) It then typically takes several more days for secreted antibody cells to accumulate. (Ex. D, p. 9.) By invoking bystander activation, Dr. Lally's theory seeks an alternative to this process whereby IgA secreting plasma cells are directly stimulated to produce more IgA. (*Id*. at 9-10.) However, Dr. Matloubian raises several issues with this alternative. First, unlike B cells, plasma cells do not respond strongly to stimulation by their specific antigen. (*Id*. at 9.) Thus, Dr. Matloubian suggests he is not aware of any cytokine or immunologic agent that could do this. (*Id*. at 10.) Second, if this were possible, it would still involve a multi-step process whereby antigen presenting cells migrate to the lymph nodes to produce more circulating cytokines to activate more IgA secreting plasma cells that in turn have to accumulate to a sufficient degree to deposit in tissue and recruit neutrophils. (*Id*.) Dr. Matloubian opines that it is also difficult to see how this alternative process could unfold in 12-16 hours. (*Id*.) Dr. Lally's reliance on pre-primed autoreactive T cells does not overcome the timing issue, because T cells would still need to activate IgA producing B cells, which would in turn need to differentiate into plasma cells. (Ex. Q, p. 2.)

V. Analysis

As discussed above, petitioner's burden of proof in a cause-in-fact claim is to meet the three-part *Althen* test, which includes (1) a general theory of causation implicating the vaccine as a cause of the alleged condition, (2) a logical sequence of cause and effect implicating the vaccination as a cause of petitioner's own condition,

and (3) appropriate timing of onset based on the theory of causation. 418 F.3d at 1278. In this case, the parties present issues with respect to all three *Althen* prongs.

a. *Althen* prong one

Under *Althen* prong one, petitioner must provide a "reputable medical theory," demonstrating that the vaccine received can cause the type of injury alleged. *Pafford ex rel. Pafford v. Sec'y of Health & Human Servs.,* 451 F.3d 1352, 1355-56 (Fed. Cir. 2006) (quoting *Pafford ex rel. Pafford v. Sec'y of Health & Human Servs.*, No. 01-0165V, 2004 WL 1717359, at *4 (Fed. Cl. Spec. Mstr. July 16, 2004)). Such a theory must only be "legally probable, not medically or scientifically certain." *Knudsen ex rel. Knudsen v. Sec'y of Health & Human Servs.,* 35 F.3d 543, 548-49 (Fed. Cir. 1994). Petitioner may satisfy the first *Althen* prong without resort to medical literature, epidemiological studies, demonstration of a specific mechanism, or a generally accepted medical theory. *See Andreu ex rel. 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)). However, "[a] petitioner must provide a 'reputable medical or scientific explanation' for [her] theory. While it does not require medical or scientific certainty, it must still be 'sound and reliable.'" *Boatmon v. Sec'y of Health & Human Servs.,* 941 F.3d 1351, 1359 (quoting *Knudsen*, 35 F.3d at 548-49).

Dr. Lally opines that bystander activation can explain how the flu vaccine can results in an exuberant immune response that in turn triggers an overproduction of IgA leading to IgA vasculitis. (*See* Ex. 29, p. 2.) It must be stressed, however, that Dr. Lally acknowledges that the evidence supporting any link between the flu vaccine and IgA vasculitis is "limited" and that IgA response to the flu vaccination is "poorly understood." (*Id.* at 1; Ex. 44, p. 1.) Although there is no dispute that bystander activation is a valid concept, Dr. Matloubian is persuasive in observing that Dr. Lally has provided no support for her assertion that bystander activation can be invoked in this context. Moreover, he has cited a study that shows that the flu vaccine results in activation of influenza specific antibody secreting cells, but not those that make antibodies to other antigens, suggesting bystander activation, as invoked by Dr. Lally, is unlikely to result from a flu vaccination. (Ex. D, pp. 10-11 (discussing Lee et al., *supra,* at Ex. N).) Dr. Lally did not rebut this point. Further, Dr. Matloubian explains that IgA is usually produced by mucosal infection and the flu vaccine, by contrast, has been shown to produce primarily IgG. (*Id*. at 9 (citing Siegrist, *supra,* at Ex. O, p. 3 (Table 2-2)).) Dr. Lally cited Abrue, et al, for the proposition that the flu vaccine can produce IgA. (Ex. 44, pp. 2-3 (citing Abrue et al., *supra,* at Ex. 48).) However, Dr. Matloubian is persuasive in opining that the minor IgA findings observed in Abrue et al. are not consistent with the type of exuberant immune response that Dr. Lally proposes would lead to an overproduction of IgA. (Ex. R, p. 1.)

This leaves the case reports cited by Dr. Lally as the only remaining support for her theory of causation. Dr. Matloubian has suggested reason to doubt the particular case reports at issue, stressing that the Bonetto authors themselves did not believe a

causal link was established despite having raised the case reports as some evidence. (Ex. D, pp. 6-7 (citing Bonetto et al., *supra,* at Ex. 18, p. 3).) But in any event, though they are some evidence, case reports are a particularly weak form of evidence. *E.g. Crutchfield v. Sec'y of Health & Human Servs.*, No. 09-39V, 2014 WL 1665227, at *19 (Fed. Cl. Spec. Mstr. Apr. 7, 2014) ("single case reports of Disease X occurring after Factor Y . . . do not offer strong evidence that the *temporal* relationship is a *causal* one—the temporal relationship could be pure random chance"), ***aff'd***, 125 Fed. Cl. 251 (2014); *see also Paluck v. Sec'y of Health & Human Servs.*, 104 Fed. Cl. 457, 475 (2012) (indicating that case reports "'do not purport to establish causation definitively, and this deficiency does indeed reduce their evidentiary value'. . . [but] 'the fact that case reports can by their nature only present indicia of causation does not deprive them of all evidentiary weight."), ***aff'd***, 786 F.3d 1373 (Fed. Cir. 2015)). Especially given the significant shortcomings in Dr. Lally's reliance on bystander activation, the case reports in evidence are inadequate to support Dr. Lally's proposed theory.

For all these reasons, petitioner has not met his preponderant burden of proof with respect to *Althen* prong one.

b. *Althen* prong three

The third *Althen* prong requires establishing a "proximate temporal relationship" between the vaccination and the injury alleged. 418 F.3d at 1278. A petitioner must offer "preponderant proof that the onset of symptoms occurred within a timeframe for which, given the medical understanding of the disorder's etiology, it is medically acceptable to infer causation-in-fact." *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), ***mot. for recons. den'd after remand***, 105 Fed. Cl. 353 (2012), ***aff'd***, 503 Fed. Appx. 952 (Fed. Cir. 2013); *Koehn ex rel. Koehn v. Sec'y of Health & Human Servs.*, No. 11-355V, 2013 WL 3214877, at *26 (Fed. Cl. Spec. Mstr. May 30, 2013), ***aff'd***, 773 F.3d 1239 (Fed. Cir. 2014).

Dr. Lally has not provided any support for her assertion that bystander activation leading to IgA vasculitis can occur in less than a single day. Instead, she has acknowledged that the immune process underlying her opinion typically peaks after 7 days. (Ex. 49, p. 1.) She contends that this "does not imply that a brisker onset of IgA vasculitis is not possible." (*Id*.) However, Dr. Matloubian's opinion is not based merely on the "peak" of the immune response. He has explained in detail why the mechanisms involved make it "extremely unlikely" that the process could result in disease within the timeframe at issue in this case. (Ex. D, p. 9.) Dr. Lally has not rebutted Dr. Matloubian's detailed explanation of the multi-step immune process *at all*. To the extent Dr. Lally referenced memory recall response and/or pre-existing autoimmunity as reasons for suspecting a brisker onset, Dr. Matloubian addressed why neither concept fundamentally changes the timing with respect to the overall multi-step immune process at issue. (Ex. Q, p. 2 (citing Ex. D, p. 10 (fig.).)

Even following infection, Dr. Matloubian suggests that onset of IgA vasculitis usually occurs at least a week later. (Ex. D, p. 11 (citing Woerner et al., *supra,* at Ex. 27, p. 2).) Dr. Lally cited a case series of 19 cases of IgA vasculitis occurring after Covid-19 vaccination. (Hashizume et al., *supra,* at Ex. 50, p. 1.) She stresses that the series showed that onset most often occurred 1-2 days post-vaccination. (Ex. 49, p. 1.) Critically, however, even if this series was sufficient to show that onset can occur more quickly than Dr. Matloubian would accept,[8] none of the reported cases had onset occurring less than a day post-vaccination as seen in this particular case. (Hashizume et al., *supra,* at Ex. 50, p. 3 (Table 1).)

For all these reasons, petitioner has not met his preponderant burden of proof with respect to *Althen* prong three.

c. *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 1326-27; *Grant*, 956 F.2d at 1147-48. Medical records are generally viewed as particularly trustworthy evidence. *Cucuras ex rel. Cucuras v. Sec'y of Health & Human Servs.*, 993 F.2d 1525, 1528 (Fed. Cir. 1993). However, medical records and/or statements of a treating physician's views do not *per se* bind the special master. *See* § 300aa-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 ex rel. Snyder v. Sec'y of Health & Human Servs.,* 88 Fed. Cl. 706, 745 n. 67 ("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.") A petitioner may support a cause-in-fact claim through either medical records or expert medical opinion. § 300aa-13(a). The special master is required to consider all the relevant evidence of record, draw plausible inferences, and articulate a rational basis for the decision. *Winkler v. Sec'y of Health & Human Servs.,* 88 F.4th 958, 963 (Fed. Cir. 2023) (citing *Hines,* 940 F.2d at 1528).

For the reasons discussed above, petitioner has not preponderantly established that the flu vaccine can cause IgA vasculitis. Nor, even assuming *arguendo* that it could, has he preponderantly established that the onset of his own condition arose within a timeframe from which vaccine causation could be inferred based on Dr. Lally's theory. Accordingly, he is not in a position to prevail under *Althen* prong two. It is also worth noting that none of petitioner's treating physicians opined that his IgA vasculitis was vaccine caused and, moreover, as Dr. Matloubian observes, Dr. Lally has cited no

[8] It should be noted that this case series involved a different vaccine. Some of the disagreement between the experts as discussed under *Althen* prong one involves specific evidence regarding bystander activation and IgA response specific to the flu vaccine. Accordingly, while I do not entirely discount this case series, it cannot necessarily be assumed that what is true of the immune response to the Covid-19 vaccine would also be true of the flu vaccine given the experts' differences under *Althen* prong one.

aspect of petitioner's own clinical history that would support the assertion that he experienced a particular "exuberant" immune response. (Ex. R, p. 1.) Dr. Lally speculates that petitioner's pre-existing psoriasis may have resulted in already circulating IgA at the time of vaccination, but acknowledges that this remains unknown. (Ex. 29, p. 2.) She asserts that his psoriasis left him susceptible to additional autoimmunity, but as explained in her first report, petitioner's history of psoriasis *alone* left him at a five-times greater risk of developing additional immune-mediated disease. (Ex. 16, p. 5 (citing Yuki M.F. Andersen et al., *Chronologic Order of Appearance of Immune-Mediated Inflammatory Diseases Relative to Diagnosis of Psoriasis,* 81 J. AM. ACAD. DERMATOLOGY 1283 (2019) (Ex. 20)).) In that regard, Dr. Matloubian has stresses that vaccination is considered safe and is recommended for patients with autoimmune conditions. (Ex. Q, pp. 2-3.)

Further to this, respondent continues to highlight the possibility that petitioner's treatment with adalimumab may be a more likely explanation for his condition. (ECF No. 76, p. 16.) Because petitioner cannot prevail in any event, it is not necessary to resolve this question. However, I note in the interest of completeness that, regardless of how well a causal relationship is supported by literature, Dr. Matloubian's opinion does not ultimately support adalimumab as a cause of petitioner's own condition. Dr. Matloubian indicated that "I do not know what caused petitioner's IgA/HSP and agree with Dr. Villa-Forte's statement on 4/23/2017 that his vasculitis 'might still have been caused by [H]umira – we can't prove one way or another.'" (Ex. D, p. 12 (quoting Ex. 7, p. 19).) Accordingly, the outcome of this case does not turn on whether there is any casual relationship between petitioner's adalimumab treatment and his IgA vasculitis.

For all the reasons discussed above, petitioner has not met his preponderant burden of proof with respect to *Althen* prong two.

VI. Conclusion

Petitioner has suffered and for that he has my sympathy. However, for all the reasons discussed above, petitioner has not demonstrated by preponderant evidence that his condition was caused by his vaccination. Accordingly, this case is dismissed.[9]

IT IS SO ORDERED.

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

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