In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

LAURIE BISHARA,	*	
	*	No. 19-115V
Petitioner,	*	Special Master Christian J. Moran
	*	
v.	*	Filed: January 27, 2023
	*	
SECRETARY OF HEALTH AND HUMAN SERVICES,	*	Entitlement, scleroderma, tetanus, diphtheria, acellular pertussis (Tdap), molecular mimicry, case reports
	*	
Respondent.	*	

Edward Kraus, Kraus Law Group, LLC, Chicago, IL, for petitioner;
Voris Edward Johnson, United States Dep't of Justice, Washington, D.C., for respondent.

PUBLISHED DECISION DENYING COMPENSATION[1]

Ms. Laurie Bishara alleges that the tetanus-diphtheria-acellular-pertussis (Tdap) vaccine that she received at her annual physical appointment caused her to suffer scleroderma. The Secretary disputed this allegation, contending that Ms. Bishara failed to prove that there is a causal link between her Tdap vaccination and her scleroderma. The parties developed their positions by retaining experts who wrote reports, arguing through legal memoranda, and presenting testimony.

The evidence, viewed in its entirety, does not preponderate in favor of finding that the Tdap vaccine caused Ms. Bishara's scleroderma. The evidence is not persuasive to demonstrate that molecular mimicry is a reliable basis for causally connecting the Tdap vaccine to scleroderma. Accordingly, Ms. Bishara is not entitled to compensation.

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[1] The E-Government Act, 44 U.S.C. § 3501 note (2012) (Federal Management and Promotion of Electronic Government Services), requires that the Court post this decision on its website. This posting will make the decision available to anyone with the internet. Pursuant to Vaccine Rule 18(b), the parties have 14 days to file a motion proposing redaction of medical information or other information described in 42 U.S.C. § 300aa-12(d)(4). Any redactions ordered by the special master will appear in the document posted on the website.

I. Facts

Ms. Bishara was born in 1972. She could not produce medical records created in the three years before the allegedly causal vaccination.[2]

According to two medical histories obtained after the vaccination, Ms. Bishara experienced some symptoms, which could be associated with scleroderma, in 2015. See exhibit 5 at 78-84; Exhibit 4 at 24. However, Ms. Bishara contested the accuracy of those histories and the inference that she was suffering from scleroderma before the vaccination. See exhibit 16 (affidavit, signed May 22, 2020).

Ms. Bishara saw her primary care physician, Sharon Morris, M.D. on February 8, 2016 for an annual physical. Exhibit 4 at 1-4. Ms. Bishara did not report any problems with her skin at this appointment. She received the Tdap vaccination during this appointment.

Ms. Bishara averred that within two days of the vaccination, she felt exhausted and achy. Exhibit 16 at 2. She returned to the office of her primary care physician and saw Kamaljit Kaur, M.D. on February 23, 2016. Exhibit 4 at 17. Ms. Bishara complained that her fingertips were swollen and changing colors from white to blue. Id. Dr. Kaur diagnosed her with Raynaud's phenomenon and ordered a lab test for antinuclear antibodies ("ANA"). Id. at 19. Dr. Kaur also referred Ms. Bishara to a rheumatologist. Id.

Ms. Bishara's blood was drawn for the ANA test on February 24, 2016, and the results, which became available two days later, revealed that Ms. Bishara had an elevated antibody level. Id. at 22.

Ms. Bishara consulted the rheumatologist to whom she had been referred, Hossam Elzawawy, M.D. on March 14, 2016. Id. at 24-30. Dr. Elzawawy was aware of Ms. Bishara's positive ANA results and history of Raynaud's phenomenon. Dr. Elzawawy ordered additional lab tests to rule out scleroderma and other autoimmune diseases. Id. at 30.

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[2] According to Ms. Bishara's attorney, when Ms. Bishara's primary care physician died, her medical records were not transferred to another doctor because she did not transfer her care. See Pet'r's Mot. for Extension of Time, filed Apr. 24, 2019. To ameliorate the lack of medical records, Ms. Bishara submitted information from her medical insurance companies. These lists of claims did not suggest that she was having significant health problems before the vaccination. See Exhibits 14&15. In the January 31, 2020 status conference, the Secretary accepted the completeness of the records.

In April 2016, swelling in Ms. Bishara's fingers prompted her to resize her rings. Exhibit 50 at 1. Around this time, she began an anti-inflammatory diet to try to minimize swelling. Exhibit 16 at 2.

Ms. Bishara consulted a second rheumatologist, Eric Greidinger, M.D. who was affiliated with the University of Miami Hospital and Clinics., reporting "feeling generally well until receiving a vaccination booster approximately six months ago, with subsequent onset of fatigue and cold-induced color changes in her fingers, [primarily] with blue attacks with tingling." Exhibit 3 at 1 (July 7, 2016). Dr. Greidinger assessed her as having "diffuse cutaneous scleroderma with Scl-70 positivity." Id. at 2. He discussed treatment options for her and planned a return visit in three months. Id.

Ms. Bishara periodically returned for appointments with Dr. Greidinger over the next one and a half years. See exhibit 3, passim. Reports from these visits show the ups and downs of Ms. Bishara's scleroderma, but do not provide any meaningful information about the cause of the scleroderma.

On December 19, 2017, Ms. Bishara consulted her third rheumatologist, Ami Shah, M.D., who is affiliated with Johns Hopkins Medicine, for an initial evaluation of "diffuse cutaneous systemic sclerosis." Exhibit 5 at 78-86. Dr. Shah obtained medical history from Ms. Bishara in which Ms. Bishara recounted, among other points, that she was having difficulty removing her rings in March 2015." Id. at 78. Dr. Shah diagnosed Ms. Bishara as suffering from systemic sclerosis and formulated a care plan for Ms. Bishara. Id. at 85-86.

After the December 19, 2017 appointment with Dr. Shah, Ms. Bishara continued to seek treatment from her doctors for her scleroderma. However, the parties and the experts whom they retained, agreed that the more recent medical records do not contribute to determining whether the Tdap vaccination caused Ms. Bishara's scleroderma. Thus, these records are not summarized here.

Ms. Bishara testified how the scleroderma was affecting her. Tr. 9-63.

II. Procedural History

Ms. Bishara alleged that the Tdap vaccination caused her to suffer scleroderma. Pet., filed Jan. 22, 2019. She filed medical records and then assessed the record as complete on July 17, 2019.

The Secretary expressed an interest in defending the case. Resp't's Status Rep., filed Jan. 21, 2020. Thus, to advance the case, Ms. Bishara intended to obtain a report from an expert. To assist in the process of presenting reports from experts, a set of instructions were proposed and then made final. Orders, issued February 7, 2020 and February 26, 2020.

Ms. Bishara filed a report from a rheumatologist whom she had retained, Samar Gupta, M.D. on June 5, 2020. Exhibit 17. Dr. Gupta asserted that before the vaccination, Ms. Bishara "was in excellent health with no acute conditions." Id. at 2. In Dr. Gupta's view, after the vaccination, Ms. Bishara developed scleroderma, which is a rare condition. Id. at 4, 8. Dr. Gupta generally opined that the Tdap vaccination caused Ms. Bishara's scleroderma. He maintained that molecular mimicry "may serve to explain potential development of autoimmune phenomena post vaccination." Id. at 7. Dr. Gupta acknowledged "a paucity in literature of vaccine induced Scleroderma cases due to its rare nature." Id. at 8. However, Dr. Gupta analogized scleroderma to another condition, morphea. Id.

Dr. Gupta's opinion regarding when Ms. Bishara began to manifest symptoms of scleroderma was conclusory. See Exhibit 17 at 9. Therefore, Ms. Bishara was directed to obtain a more detailed opinion. Order, issued June 24, 2020. Ms. Bishara did so. In Dr. Gupta's supplemental report, he stated that the positive ANA test from February 23, 2016 was the first diagnostic feature of scleroderma and Ms. Bishara "displayed the full spectrum of Scleroderma disease" by March 14, 2016. Exhibit 35 at 1-2.

The Secretary responded by submitting a report from a rheumatologist whom he had retained, Chester Oddis, M.D. and a report from an immunologist whom he had retained, You-Wen He, M.D., Ph.D. Exhibit A&B. Dr. Oddis began his summary of medical events by noting that Dr. Shah had recorded that Ms. Bishara developed swollen fingers in March 2015. Exhibit A at 2; see also id. at 6-7 (acknowledging a discrepancy in the evidence that Dr. Oddis cannot resolve). On the other hand, when Dr. Oddis presented his opinion regarding the onset of Ms. Bishara's scleroderma, he does not refer to this history. Instead, Dr. Oddis maintains that the positive ANA, which was detected two weeks after vaccination, could not have been produced in response to vaccination because the body takes more than two weeks to produce antibodies. Id. at 7-8, 10.

Apart from the question of onset, Dr. Oddis agreed that Ms. Bishara suffers from scleroderma. Exhibit A at 6. Dr. Oddis did not address the theory of molecular mimicry. See Id. at 8-9. But, Dr. Oddis challenges Dr. Gupta's opinion that an antibody can be developed and detected two weeks after vaccination. Dr.

Oddis also indicated that morphea is not analogous to scleroderma. Id. at 8-9. He stated the "etiology of scleroderma . . . is unknown." Id. at 11.

The Secretary's second expert, Dr. He, also opined that the "etiology of Scleroderma is currently unknown" and the "pathogenesis of Scleroderma is very complex." Exhibit B at 3. Like Dr. Oddis, Dr. He recognized that the history from Dr. Shah raised a question as to whether Ms. Bishara "had some levels of autoimmune disease prior to her Tdap vaccination." Id. at 3, 8.

Dr. He challenged the theory of molecular mimicry. He stated that recent scientific evidence shows that "viral and human proteomes have massive peptide sharing." Exhibit B at 4, citing three articles.[3] Dr. He maintained that Dr. Gupta had not demonstrated that molecular mimicry could explain how vaccines can cause an autoimmune disease. Further, Dr. He also asserted that the "fact that not a single published report described Tdap vaccine and Scleroderma indicates that Tdap vaccine is highly unlikely to cause Scleroderma." Id. at 7.

The Secretary incorporated the assessments of Dr. Oddis and Dr. He in recommending against compensation. Resp't's Rep., filed Jan. 21, 2021. The Secretary maintained that despite Dr. Gupta's reports, Ms. Bishara had failed to present a persuasive medical theory to explain how the Tdap vaccine can cause scleroderma. Id. at 7-10. With respect to the onset of Ms. Bishara's scleroderma, the Secretary did not directly address that issue. Id. at 12.

After reviewing the reports from Dr. Oddis and Dr. He, Dr. Gupta authored another report. Exhibit 40. Dr. Gupta defended his opinion that Ms. Bishara's scleroderma started after the vaccination and explained why he did not accept the history Dr. Shah created. Id. at 1. Dr. Gupta also defended the reliability of molecular mimicry as a theory, noting molecular mimicry was suggested as a way that the Covid virus could cause damage to the nervous system. Id. at 1.[4] Dr. Gupta explained why antibodies could develop within two weeks of the vaccination. Id. at 2.

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[3] Dr. He cited D. Kanduc et al., "Massive peptide sharing between viral and human proteomes," 29(10) Peptides 1755 (2008), filed as Exhibit B.4; Trost et al., "Bacterial peptides are intensively present throughout the human proteome," 1(1) Self Nonself 71 (2010), filed as Exhibit B.5; and A. Kusalik, et al., "Widespread and ample peptide overlapping between HCV and Homo sapiens proteomes," 28(6) Peptides 1260 (2007), filed as Exhibit B.6.

[4] Dr. Gupta cited A. Gammazza et al., "Molecular mimicry in the post-COVID 19 signs and symptoms of neurovegetative disorders," 2(3) The Lancet Microbe Correspondence E94 (2021), filed as Exhibit 43.

Dr. Gupta's report appeared to complete the disclosure of expert opinions. The parties were, accordingly, directed to advocate for their positions in written submissions. Order, issued April 19, 2021.

Ms. Bishara submitted her materials, including a brief, on June 25, 2021. About three months later, the Secretary submitted his materials, which also included a brief. Ms. Bishara replied on October 25, 2021.

It appeared that the parties disagreed about the significance of the history that Dr. Shah recorded on December 19, 2017. The Secretary expressed an interest in calling Dr. Shah as a witness, either during a hearing or at a remote video deposition. Resp't's Status Rep., filed Jan. 14, 2022. To clarify Ms. Bishara's health before vaccination, the parties were directed to attempt to obtain additional evidence. Ms. Bishara described her activities around the time of the February 2016 Tdap vaccination. Exhibit 56 (affidavit, filed Mar. 11, 2022). The parties also informally sought more information from Dr. Shah through a letter but did not receive any response from her. Pet'r's Status Rep., filed June 27, 2022. In a July 18, 2022 status conference, the Secretary was offered an opportunity to compel the testimony of Dr. Shah because the Secretary was relying upon a history that she obtained and to which Ms. Bishara contested. The Secretary declined this opportunity. Order, issued July 19, 2022.

A hearing was held on November 17-18, 2022. Ms. Bishara testified. Dr. Gupta, Dr. Oddis, and Dr. He testified in accord with their reports. With the submission of this testimony, the case is ready for adjudication.

III. Standards for Adjudication

A petitioner is required to establish her case by a preponderance of the evidence. 42 U.S.C. § 300aa-13(1)(a). The preponderance of the evidence standard requires a "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 v. Sec'y of Health & Hum. Servs., 592 F.3d 1315, 1322 n.2 (Fed. Cir. 2010) (citations omitted). Proof of medical certainty is not required. Bunting v. Sec'y of Health & Hum. Servs., 931 F.2d 867, 873 (Fed. Cir. 1991).

Distinguishing between "preponderant evidence" and "medical certainty" is important because a special master should not impose an evidentiary burden that is too high. Andreu v. Sec'y of Health & Hum. Servs., 569 F.3d 1367, 1379-80 (Fed.

Cir. 2009) (reversing a special master's decision that petitioners were not entitled to compensation); see also Lampe v. Sec'y of Health & Hum. Servs., 219 F.3d 1357 (Fed. Cir. 2000); Hodges v. Sec'y of Health & Hum. Servs., 9 F.3d 958, 961 (Fed. Cir. 1993) (disagreeing with the dissenting judge's contention that the special master confused preponderance of the evidence with medical certainty).

When pursuing an off-Table injury, a petitioner bears a burden "to show by preponderant evidence that the vaccination brought about [the vaccinee's] injury by providing: (1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of a proximate temporal relationship between vaccination and injury." Althen v. Sec'y of Health & Hum. Servs., 418 F.3d 1274, 1278 (Fed. Cir. 2005).

IV. Analysis

Ms. Bishara and her expert, Dr. Gupta, advance the theory of molecular mimicry to explain how a Tdap vaccination could cause scleroderma. Thus, appellate cases regarding molecular mimicry are reviewed in section A. Section B contains an assessment of the evidence that Ms. Bishara put forward in an effort to demonstrate the persuasiveness of molecular mimicry as a theory in this context.

A. Appellate Guidance regarding Molecular Mimicry

Because special masters are often called upon to evaluate the persuasiveness of the theory of molecular mimicry, the Court of Federal Claims and the Court of Appeals for the Federal Circuit have considered molecular mimicry in their appellate role opinions from special masters. In December 2019, the undersigned identified the leading precedents as W.C. v. Sec'y of Health & Hum. Servs., 704 F.3d 1352 (Fed. Cir. 2013), and Caves v. Sec'y of Dep't. of Health & Hum. Servs., 100 Fed. Cl. 119 (2011), aff'd sub nom., 463 F. App'x 932 (Fed. Cir. 2012). Tullio v. Sec'y of Health & Hum. Servs., No. 15-51V, 2019 WL 7580149, at *12-14 (Fed. Cl. Spec. Mstr. Dec. 19, 2019), mot. for rev. denied, 149 Fed. Cl. 448 (2020). While Tullio describes those cases in more detail, their essence appears to be that although molecular mimicry is accepted in some contexts, special masters may properly require some empirical evidence to show that a particular vaccine can cause a particular disease.

In the next approximately three years, appellate authorities reviewing decisions involving molecular mimicry have generally endorsed the approach of looking for some evidence that persuasively shows that a portion of a vaccine resembles a portion of human tissue, which contributes to causing the disease, and

that the immune system will respond to the relevant amino acid sequence.[5] Chronologically, the list of more recent appellate cases begins with the opinion in Tullio, which denied the motion for review. 149 Fed. Cl. 448, 467-68 (2020).

Another example in which the Court of Federal Claims held that the special master did not elevate the petitioner's burden of proof in the context of evaluating the theory of molecular mimicry is Morgan v. Sec'y of Health & Hum. Servs., 148 Fed. Cl. 454, 476-77 (2020), aff'd in non-precedential opinion, 850 F. App'x 775 (Fed. Cir. 2021). In Morgan, the Chief Special Master found that petitioner had not presented persuasive evidence about a relevant antibody. Id. at 477. The Chief Special Master also noted that the articles about the relevant disease do not list the wild flu virus as potentially causing the disease. Id. When examining this analysis, the Court of Federal Claims concluded: "the Chief Special Master did not raise the burden of causation in this case; petitioner simply failed to meet it." Id.

The Federal Circuit also evaluated the Chief Special Master's approach in Morgan. The Federal Circuit concluded: "We discern no error in the special master's causation analysis." 850 F. App'x 775, 784 (Fed. Cir. 2021).

Most other recent appellate cases follow this path. See, e.g., Duncan v. Sec'y of Health & Hum. Servs., 153 Fed. Cl. 642, 661 (2021) (finding the special master did not err in rejecting a bare assertion of molecular mimicry); Caredio v. Sec'y of Health & Hum. Servs., No. 17-79V, 2021 WL 6058835, at *11 (Fed. Cl. Dec. 3, 2021) (indicating that a special master did not err in requiring more than homology and citing Tullio); Yalacki v. Sec'y of Health & Hum. Servs., 146 Fed. Cl. 80, 91-92 (2019) (ruling that special master did not err in looking for reliable evidence to support molecular mimicry as a theory); but see Patton v. Sec'y of Health & Hum. Servs., 157 Fed. Cl. 159, 169 (2021) (finding that a special master erred in requiring petitioner submit a study to establish medical theory causally connecting flu vaccine to brachial neuritis).

Based upon this guidance, a relevant question is whether Ms. Bishara has presented any evidence that makes the theory of molecular mimicry a reliable theory in the context of a Tdap vaccine causing scleroderma. The evidence is taken up in the following section.

[5] The term "homology" is used when discussing molecular mimicry. "Homology" is defined as "the quality of being homologous; the morphological identity of corresponding parts; structural similarity due to descent from a common form." *Dorland's* at 868.

B. Evidence regarding Tdap Vaccine and Scleroderma

Ms. Bishara's evidence with respect to the first Althen prong can be placed into two categories. First, Dr. Gupta asserts an unidentified homology between the Tdap vaccine and tissues affected in scleroderma supports a causal connection. Second, Dr. Gupta relies upon case reports.

1. Homology

The primary sources of support for Ms. Bishara's proposal of molecular mimicry are Dr. Gupta's May 31, 2020 report and his March 15, 2021 report. Exhibits 17&40. In his earlier report, Dr. Gupta asserts that a person with genetic susceptibility could develop an autoimmune disease when the person is exposed to foreign peptides homologous to human peptides. Exhibit 17 at 7; see also Tr. 160. He further asserts that scleroderma resembles morphea and case reports have associated the receipt of Tdap vaccine as occurring before instances of morphea. Id. at 8; Tr. 102-05.[6]

In response to Dr. Gupta's May 31, 2020 report, the Secretary presented a contrary opinion from Dr. He. Dr. He questioned the value of the molecular mimicry theory because, according to Dr. He, recent scientific studies on viral and human proteomes have shown "massive peptide sharing." Exhibit B at 4. To support his opinion regarding the significant degree of overlap, Dr. He cited three articles: Kanduc, Trost, and Kusalik. With regard to the case reports, Dr. He emphasized that he could not locate any case reports about Tdap vaccine and either scleroderma or systemic sclerosis. Dr. He stated: "Tens of millions of Tdap vaccine doses have been administered to the general population worldwide. The fact that not a single published report described Tdap vaccine and Scleroderma indicates that Tdap vaccine is highly unlikely to cause Scleroderma." Id. at 7; accord Tr. 274-75. The Secretary's challenge to the usefulness of the case reports was reinforced by Dr. Oddis, who opined that morphea is not comparable to scleroderma. Exhibit A at 9; Tr. 187-88.

In Dr. Gupta's final report, he defends the value of molecular mimicry as a theory. He asserts: "To date, molecular mimicry is the most widely accepted theory for autoimmune disease development." Exhibit 40 at 1. For this

[6] Dr. Gupta also discusses adjuvants and cites some articles discussing autoimmune syndrome induced by adjuvants ("ASIA"). Exhibit 17 at 7-8. However, Ms. Bishara did not advance a theory based upon adjuvants. See Pet'r's Br. at 7-13. In any event, special masters have consistently rejected a theory based upon ASIA.

proposition, Dr. Gupta cites one article about how inflammatory bowel disease might cause arthritis and one article about how the Covid virus might cause neurovegetative disorders. Dr. Gupta also contends that morphea and scleroderma "share[] the same histopathology." Id. at 2.

Here, Ms. Bishara has presented little, if any, persuasive evidence to demonstrate that molecular mimicry is a reliable basis for causally connecting the Tdap vaccine to scleroderma. At a fundamental level, Dr. Gupta did not identify any homology between any component of the Tdap vaccine and any tissue that has been linked to scleroderma. Tr. 126. Without this basic step, Ms. Bishara's case is on par with Caves and Duncan in which appellate judges ruled that the special master did not err in declining to credit molecular mimicry. In Caves, "[w]hile the special master acknowledged that [] [petitioner's] submitted articles supported the general theory of molecular mimicry . . . he [] held that the articles do not provide any support for the more specific theory that the influenza vaccine can serve as the antigenic trigger that sets that autoimmune process into motion." 100 Fed. Cl. at 129. Furthermore, in Duncan, while "[t]he Special Master acknowledged that medical literature submitted by [petitioner] indicated that strep infections can lead to PANDAS through the process of molecular mimicry, [] [petitioner]'s experts did not identify any link between the molecular structures of strep bacteria and the HPV vaccine." 153 Fed. Cl. at 653.

Moreover, a showing of homology alone does not meaningfully advance a petitioner's support for molecular mimicry as the Kanduc, Trost, and Kusalik articles demonstrate. Special masters have, on occasion, discussed these Kanduc and Trost articles and found that they show homology is common. See, e.g., Nifakos v. Sec'y of Health & Hum. Servs., No. 14-236V, 2021 WL 1345218, at *12, *20-21 (Fed. Cl. Spec. Mstr. Mar. 4, 2021); McKown v. Sec'y of Health & Hum. Servs., No. 15-1451V, 2019 WL 4072113, at *36, *50 (Fed. Cl. Spec. Mstr. July 15, 2019); Tarsell v. Sec'y of Health & Hum. Servs., No. 10-251V, 2016 WL 880223, at *10-12 (Fed. Cl. Spec. Mstr. Feb. 16, 2016), mot. for rev. granted after an intervening remand, 133 Fed. Cl. 782 (2017). Ms. Bishara submitted an article expressing the idea: "the presence of cellular mimicry does not guarantee the clinical manifestations of autoimmune conditions." Exhibit 65 (Daniil Hammoudi et al., "Induction of Autoimmune Diseases Following Vaccinations: A Review," 1(3) SM Vaccine Vaccin. 1011 (2015)) at 2. It bears repeating that the discussion of homology and cellular mimicry is merely academic because Ms. Bishara has not actually presented any evidence showing that a portion of the Tdap vaccine is homologous with tissue involved in the pathogenesis of scleroderma. In other words, Ms. Bishara presented an abstract theory but failed to present evidence on how this theory applied to her in the instant case.

Shortly before the hearing, Ms. Bishara submitted an article to offer some support for the opinion that vaccines can cause scleroderma.[7] Three researchers discussed environmental factors that could trigger systemic sclerosis. Exhibit 64 (Hana Alahmari, "Environmental Risks for Systemic Sclerosis," 48 Rheum Dis Clin N Am 845 (2022)). They focused on occupational exposures, such as epoxy resin, asbestos, and heavy metals. But, they also considered the possibility that infectious agents, such as herpes viruses, parvovirus B19, retrovirus, and *Helicobacter pylori* could lead to systemic sclerosis. In doing so, the authors listed more than 75 articles about systemic sclerosis.

Alahmari has limited, if any, relevance in determining whether the Tdap vaccination can cause scleroderma. First, the article does not discuss vaccines or immunizations at all. Tr. 133. Second, to the extent that the article's list of infectious agents might be extended to a vaccine against those infectious agents, the article does not discuss tetanus, diphtheria, or pertussis. Tr. 135.

2. Reliance on Case Reports

Without any evidence that directly connects the Tdap vaccine with scleroderma, Ms. Bishara relies upon case reports about a tetanus vaccine preceding the onset of morphea to support the claim that a Tdap vaccine can cause scleroderma. See Pet'r's Br. at 11-12; Pet'r's Reply at 4-5; Tr. 168-70. This position is flawed because case reports provide little, if any, meaningful information about causation. At best, they show temporal data but not necessarily that a Tdap vaccine can cause scleroderma.

Various authorities have commented on the value of case reports. To start, the Federal Judicial Center has published a series of guides designed "to assist judges . . . in reaching an informed and reasoned assessment concerning the basis of expert evidence." Jerome P. Kassirer and Gladys Kessler, Reference Manual on Scientific Evidence, Preface (3d ed. 2011) ("Reference Manual"). The guidance from the Federal Judicial Center translates to the Vaccine Program because causation for off-Table injuries in the Vaccine Program is the same as traditional causation. See Moberly, 592 F.3d at 1322-23; Shyface v. Sec'y of Health & Human Servs., 165 F.3d 1344, 1351 (Fed. Cir. 1999) ("The absence of elaboration of the law of causation in the legislative history leads us to conclude that the Vaccine Act's requirement of causation in non-Table cases was not viewed as distinct from causation in the tort law."). For examples in which appellate

[7] The Secretary did not oppose the submission of this article shortly before the hearing.

authorities within the Vaccine Program have cited the Reference Manual, see Germaine v. Sec'y of Health & Hum. Servs., 155 Fed. Cl. 226, 228-29 (2021), and Hart v. Sec'y of Health & Hum. Servs., 60 Fed. Cl. 598, 607 n.20 (2004).

A pertinent guide in the Reference Manual states "[a]necdotal evidence usually amounts to reports that events of one kind are followed by events of another kind. Typically, the reports are not even sufficient to show association, because there is no comparison group." David H. Kaye and David A. Freedman, Reference Manual on Scientific Evidence, Reference Guide on Statistics, at 218. These authors also state "some courts have suggested that attempts to infer causation from anecdotal reports are inadmissible as unsound methodology under Daubert." Id. at 217 n. 14 (citing cases)."

Within the Vaccine Program, the Federal Circuit has endorsed, albeit indirectly, a view that case reports merit little weight. In a series of five cases involving auto-immune hepatitis, the (undersigned) special master rejected case reports as evidence of causation. Porter v. Sec'y of Health & Hum. Servs., No. 99–639V, 2008 WL 4483740, at *13 (Fed. Cl. Spec. Mstr. Oct. 2, 2008). Under the caption of a different case, a judge at the Court of Federal Claims disagreed with this weighing of evidence. Rotoli v. Sec'y of Health & Hum. Servs., 89 Fed. Cl. 71, 86–87 (2009). When the Federal Circuit reviewed the special master's decision, the Federal Circuit stated that "[t]he special master found that the remaining two articles, both describing single case studies, did not contain any meaningful analysis about causation." Porter v. Sec'y of Health & Human Servs., 663 F.3d 1242, 1253 (Fed. Cir. 2012). The Federal Circuit also stated that the "decision reveals a thorough and careful evaluation of all the evidence including . . . medical literature." Id. at 1254.

Similar indirect support from the Federal Circuit is found in W.C. W.C. v. Sec'y of Health & Hum. Servs., No. 07-456V, 2011 WL 4537877, at *13 (Fed. Cl. Spec. Mstr. Feb. 22, 2011), mot. for rev. denied on this point, 100 Fed. Cl. 440, 456 (2011), aff'd, 704 F.3d 1352 (Fed. Cir. 2013). At the trial level, the (undersigned) special master declined to rely upon case reports because, among other reasons, "case reports cannot distinguish a temporal association from a causal relationship." Id. at *13. At the Federal Circuit, the appellate court focused primarily upon epidemiologic studies, which undermined the claim that the vaccine significantly aggravated the petitioner's illness. W.C. v. Sec'y of Health & Hum. Servs., 704 F.3d 1352, 1360-61 (Fed. Cir. 2013). However, at the end of its opinion, the Federal Circuit stated that it "cannot say that the special master's . . . weighing of the scientific evidence was arbitrary or capricious." Id. at 1361.

Without citing either Federal Circuit case (Porter or W.C.), Ms. Bishara asserts that "case reports are an important contribution to supporting the understanding of the pathogenesis of autoimmune disease." Pet'r's Br. at 10. For this proposition, Ms. Bishara cites Paluck v. Sec'y of Health & Hum. Servs., 104 Fed. Cl. 457, 475 (2012).

Paluck generally supports Ms. Bishara's assertion as Paluck states "case reports 'do not purport to establish causation definitively, and this deficiency does indeed reduce their evidentiary value. Nonetheless, the fact that case reports can by their nature only present indicia of causation does not deprive them of all evidentiary weight.'" Paluck, 104 Fed. Cl. at 475, quoting Campbell v. Sec'y of Health & Hum. Servs., 97 Fed. Cl. 650, 668 (2011). The case Paluck quotes, Campbell, cites to Rotoli v. Sec'y of Health & Hum. Servs., 89 Fed. Cl. 71, 86-87 (2009). However, the value of the opinion by the Court of Federal Claims seems questionable as the Federal Circuit, as noted above, reversed the outcome in Rotoli, and reinstated the special master's decision, which gave little weight to the case reports. Porter, 663 F.3d at 1253.[8]

Much of the foregoing analysis regarding case reports was set forth in K.O. v. Sec'y of Health & Human Servs., No. 13-472V, 2016 WL 7634491, at *11-12 (Fed. Cl. Spec. Mstr. July 7, 2016). After K.O., the Federal Circuit has not discussed case reports in a precedential opinion, leaving Porter and W.C. as the leading, although muted, words on the subject. Consequently, judges from the Court of Federal Claims have tended to defer to the special master's assessment of case reports. See, e.g., Kelly v. Sec'y of Health & Hum. Servs., 160 Fed. Cl. 316, 319 (2022) (indicating that the special master was not arbitrary in finding that case reports have limited or nonexistent value); Rus v. Sec'y of Health & Hum. Servs., 129 Fed. Cl. 672, 682 (2016) (noting the special master could reasonably afford little weight to the medical literature, including case reports). An exception to this trend is Patton v. Sec'y of Health & Hum. Servs., 157 Fed. Cl. 159 (2021). In Patton, the Court ruled that the special master "erred in his prong one analysis by discounting the evidentiary value of the case reports [petitioner's expert] submitted." Id. at 168. But, Patton does not discuss Porter or W.C. Instead, Patton relies upon Paluck, which has a questionable value as discussed above.

Outside of the Vaccine Program, district courts have examined the value of case reports in the context of claims that drugs or a medical device harmed a person. Recent examples include: In re: Abilify (Aripriprazole) Products Liability Litigation, 299 F.Supp.3d 1291, 1309 (N.D. Fla. 2018) ("The difficulty with case

[8] Paluck, which cited Rotoli, was issued before the Federal Circuit reversed Rotoli.

reports is distinguishing between association and causation"); In re Tylenol (Acetaminophen) Marketing, Sales Practice, and Products Liability Litigation, 198 F.Supp.3d 446, 461 (E.D. Pa. 2016) ("It is true that case reports and anecdotal evidence alone may not be sufficient support for a causation opinion. . . . However, case reports considered in conjunction with other evidence may be an appropriate basis for an expert's causation opinion."); In re Mirena IUD Products Liability Litigation, 169 F.Supp.3d 396, 451 (S.D.N.Y. 2016) ("Case reports are generally disfavored by courts as evidence of causation because they merely describe 'reported phenomena without comparison to the rate at which the phenomena occur in the general population or in a defined control group; [they] do not isolate and exclude potentially alternative causes; and [they] do not investigate or explain the mechanism of causation.'") (citation omitted).

Through Dr. Gupta, Ms. Bishara has presented case reports. See Tr. 102-05. As these case reports are part of the record, the undersigned must consider them and has considered them. See 42 U.S.C. § 300aa–13(a)(1) (requiring a special master to evaluate the "record as a whole"). As Dr. Gupta testified, "a lot of case reports don't add up to making a well designed data." Tr. 114. Thus, the evidentiary value of case reports is negligible, at best. See Whitecotton v. Sec'y of Health & Human Servs., 81 F.3d 1099, 1104 (Fed. Cir. 1996) (indicating that special masters have discretion in how they weigh evidence).

Moreover, the case reports submitted here are further removed because the subjects of the case reports did not develop the same condition, scleroderma, as Ms. Bishara did. Tr. 131, 170. Dr. Oddis testified that morphea is different from scleroderma. Tr. 187-88. When case reports do not match the alleged vaccine-injury combination, special masters may further discount the value of the case reports. Temes v. Sec'y of Health & Hum. Servs., 151 Fed. Cl. 448, 462-63 (2020). Thus, resolving the controversy as the degree to which scleroderma does (or does not) resemble morphea is not needed.

In sum, Dr. Gupta essentially proposes molecular mimicry with little, if any, persuasive evidence to make that theory reliable in the context of Tdap vaccine as potentially causing scleroderma. Dr. Gupta has not identified any homology. Medical articles have not listed tetanus, diphtheria, and/or pertussis as infections often preceding the onset of scleroderma. Case reports, strictly speaking, do not link Tdap vaccine to scleroderma. Under these circumstances, Ms. Bishara has failed to meet her burden regarding Althen prong one. As such, the other Althen prongs do not need to be addressed.

V. Conclusion

For the foregoing reasons, Ms. Bishara has not presented sufficient evidence to show that the Tdap vaccine caused her to develop systemic scleroderma. Accordingly, her claim for compensation is DENIED.

The Clerk's Office is instructed to enter judgment in accord with this decision unless a motion for review is filed. Information about filing a motion for review, including the deadline, can be found in the Vaccine Rules, which are available on the website for the Court of Federal Claims.

IT IS SO ORDERED.

s/Christian J. Moran
Christian J. Moran
Special Master