In the United States Court of Federal Claims

No. 11-693V
(Filed: January 23, 2019)[1]

OLIVIA BENDER, **Petitioner,** **v.** **SECRETARY OF HEALTH AND HUMAN SERVICES,** **Respondent.**	**National Childhood Injury Vaccination Act, 42 U.S.C. §§ 300aa-1 et seq.; Causation in Fact; Hepatitis A Vaccine; Meningococcal Vaccine; Menactra; Transverse Myelitis; Expert Testimony; Molecular Mimicry; Remand.**

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OPINION AND ORDER

WILLIAMS, Senior Judge.

This Vaccine Act case comes before the Court following a remand. In the underlying action before the Special Master, Petitioner claimed that she developed transverse myelitis ("TM") as a result of receiving the meningococcal and Hepatitis A vaccines and sought compensation under the National Vaccine Injury Compensation Program. The Special Master denied compensation, finding that Petitioner failed to prove that her vaccinations caused her TM, and Petitioner filed a Motion for Review. This Court granted Petitioner's motion, finding that the Special Master misconstrued Petitioner's expert's testimony and remanded the matter directing the Special Master to reevaluate the expert's opinion considering the entirety of her testimony and the

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[1] Pursuant to Vaccine Rule 18 of the Rules of the United States Court of Federal Claims, the Court issued its Opinion under seal to provide the parties an opportunity to submit redactions. The parties did not propose any redactions. Accordingly, the Court publishes this Opinion.

medical evidence. In his decision on remand, the Special Master again denied compensation, which prompted this second Motion for Review.

Petitioner claims that the Special Master again erred in basing his causation analysis on the misconstruction and mischaracterization of the testimony of Petitioner's expert immunologist, Dr. Vera Byers, and that he impermissibly raised Petitioner's burden of proof by requiring specific medical literature to establish causation. For the reasons stated below, the Court denies Petitioner's Motion for Review and sustains the Special Master's decision on remand.

Background[2]

On May 29, 2009, Petitioner—a then 14-year old with no prior health problems—received her first meningococcal vaccine (marketed as "Menactra") and her second Hepatitis A vaccine (having suffered no adverse reactions to her first Hepatitis A vaccine eight years earlier). On July 10, 2009, while traveling through Arizona by bus with other teenagers, Petitioner suffered a sudden loss of sensation in her legs that caused her to collapse as she walked off the bus. Petitioner was immediately brought to the nearest hospital where several tests were performed, including CT scans of her spine, a urinalysis, and a complete blood count. Upon examination, Petitioner had no sensation below her umbilicus and no reflexes in her lower extremities.

That same day, Petitioner was transferred to a second hospital in Nevada for further testing. Two MRIs of Petitioner's spine indicated acute transverse myelitis. See Pet'r's Ex. 15, at 146-53. A mycoplasma IgM serology, which would have indicated a prior infection, came back negative, but the treating physicians mistakenly listed positive results. Petitioner's doctors initially relied upon the false IgM reading, diagnosing her with TM secondary to a mycoplasma infection and treating her in accordance with that incorrect diagnosis.

On July 21, 2009, Petitioner was transferred to Blythedale Children's Hospital in Valhalla, New York for inpatient rehabilitation and was discharged in September after months of physical and occupational therapy. Petitioner then consulted two specialists in an effort to identify her TM's etiology. First she saw a pediatric hematologist, Dr. Oya Tugal, who performed additional MRIs and concluded that the prior TM diagnosis was correct, but did not opine on the cause of Petitioner's TM. In December 2009, Petitioner saw Dr. Douglas Kerr, a neurologist with recognized expertise in TM and a co-author of one of the supporting medical papers submitted by Petitioner. Dr. Kerr avoided the diagnostic error made by initial providers concerning the false indicator of a prior mycoplasma infection and concluded that the medical evidence suggested an "unknown etiology." Dr. Kerr's records do not mention the vaccines received prior to onset. Pet'r's Ex. 13, at 1-3. Despite continuing rigorous rehabilitative therapies, Petitioner has not regained motor or sensory functions in her lower extremities.

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[2] A fuller statement of facts is set forth in the Special Master's Decision on Remand and the Court's first opinion. See Bender v. Sec'y of Health & Human Servs., No. 11-693V, 2018 WL 3679637, at *1-4 (Fed. Cl. Spec. Mstr. Jul. 2, 2018) ("SM Dec."); Bender v. Sec'y of Health & Human Servs., 138 Fed. Cl. 197, 198-99 (2018) ("Dec.").

In her original Motion for Review, Petitioner argued that, in analyzing Althen prong one,[3] the Special Master erroneously determined that Dr. Byers had excluded molecular mimicry as a plausible mechanism that could have caused Petitioner's TM. This Court determined that, while Dr. Byers' testimony was not a model of clarity and while she did reject "widespread" molecular mimicry as a causal mechanism, she nevertheless embraced individualized molecular mimicry as a causal mechanism. The Court found that the Special Master's misconstruction of Dr. Byers' testimony may have impacted his legal analysis and issued the following remand order:

> 1. On remand, the Special Master shall reevaluate the opinion of Dr. Byers, considering the entirety of her testimony and her distinction between widespread and individualized molecular mimicry.
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> 2. Because the Special Master's interpretation of Dr. Byers' testimony affected his entire causation analysis, the Special Master shall reevaluate the evidence—including the medical literature and records, such as test results—based upon his reconsideration of Dr. Byers' testimony.

Dec. 206.

Discussion

Legal Standard

In Vaccine Act cases, the Court of Federal Claims reviews findings of fact under the "arbitrary and capricious" standard, legal questions under the "not in accordance with law" standard, and discretionary rulings under the "abuse of discretion" standard. Althen v. Secretary of Health & Human Services, 418 F.3d 1274, 1277-78 (Fed. Cir. 2005); Saunders v. Sec'y of Health & Human Servs., 25 F.3d 1031, 1033 (Fed. Cir. 1994). In reviewing a Special Master's factual findings and legal conclusions, the court's role is not to "reweigh the factual evidence," "assess whether the Special Master correctly evaluated the evidence," or "examine the probative value of the evidence or the credibility of the witnesses." Lampe v. Sec'y of Health & Human Servs., 219 F.3d 1357, 1360 (Fed. Cir. 2000) (internal citation and quotation marks omitted). The court should "not . . . second guess the Special Master[']s fact intensive conclusions," particularly when "the medical evidence of causation is in dispute." Cedillo v. Sec'y of Health & Human Servs., 617 F.3d 1328, 1338 (Fed. Cir. 2010) (quoting Hodges v. Sec'y of Health & Human Servs., 9 F.3d 958, 961 (Fed. Cir. 1993)). Reversible error is "extremely difficult to demonstrate" if the Special Master has "considered the relevant evidence of record, drawn plausible inferences and articulated a rational basis for the decision . . . ." Hines ex rel. Sevier v. Sec'y of Dep't of Health & Human Servs., 940 F.2d 1518, 1528 (Fed. Cir. 1991).

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[3] In Althen v. Secretary of Health & Human Services, the Federal Circuit set forth a three-pronged test for proving causation in vaccine cases: "(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." 418 F.3d 1274, 1278 (Fed. Cir. 2005).

The Special Master Reasonably Evaluated the Expert Testimony and Medical Evidence on Remand

In a 50-page decision on remand, the Special Master denied entitlement, finding that Petitioner had failed to meet her burden on all three Althen prongs. The Special Master cited logical and evidentiary gaps in Petitioner's overall causation theory and found Petitioner's experts "significantly less persuasive" than Respondent's experts. SM Dec. *31. On remand the Special Master followed this Court's directive and explained his evaluation of the opinions of both Dr. Byers and Respondent's expert, Dr. Thomas Forsthuber, and his basis for finding Dr. Forsthuber's opinions more reliable than those of Dr. Byers. In general, the Special Master determined that Dr. Byers:

> conveyed her opinions in a haphazard, facially-contradictory manner . . . . She appeared unprepared to testify at many points. She also relied heavily on general propositions about cytokines or mechanistic theories that were at best loosely connected to the record evidence.

Id. The Special Master found that Dr. Byers relied "simply on the absence of other contrary causation evidence" as proof that certain components of her medical theory, such as her theory of cytokine upregulation and her proposed mechanism of bystander activation, were plausible. SM Dec. *8, 10 (citing Tr. at 46, 138, 373). Contrary to his findings on Dr. Byers' reliability, the Special Master found Dr. Forsthuber, Respondent's expert in immunology, highly persuasive:

> [Dr. Forsthuber] explained complex immunologic and scientific issues in a cogent and logical manner. He also has direct, demonstrated understanding of one of Petitioner's chosen mechanisms, epitope spreading, having written on the subject in an article cited by Petitioner . . . . [He and Dr. Lotze] provided more scientifically reliable, logical opinions that were better supported by the record and the literature they offered, and their expertise was well-matched to the questions upon which they were asked to opine.

Id. at *32 (internal citation omitted).

There is no basis for this Court to disturb the Special Master's determinations on the competing experts' opinions. Where, as in this case, both sides offer expert testimony, the Special Master may base his decision on "the credibility of the experts and the relative persuasiveness of their competing theories." Broekelschen v. Sec'y of Health & Human Servs., 618 F.3d 1339, 1347 (Fed. Cir. 2010) (citing Lampe, 219 F.3d at 1362); see Porter v. Sec'y of Health & Human Servs., 663 F.3d 1242, 1250 (Fed. Cir. 2011) ("[T]his 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."); Moberly ex rel. Moberly v. Sec'y of Health & Human Servs., 592 F.3d 1315, 1325-26 (Fed. Cir. 2010) ("Assessments as to the reliability of expert testimony often turn on credibility determinations, particularly in cases such as this one where there is little supporting evidence for the expert's opinion."). Such credibility determinations are "virtually unreviewable" on appeal. Lampe, 219 F.3d at 1362. Furthermore, 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 v. Sec'y of Health & Human Servs., 88 Fed. Cl. 706, 743 (2009) (internal citation and quotation marks omitted).

The Special Master concluded that Dr. Byers' overarching theory—that the vaccines promoted pro-inflammatory cytokines that in turn promoted "an inflammatory, demyelinating process leading to TM"—was scientifically unreliable and implausible. SM Dec. *27. He found that Dr. Byers' testimony was too generalized and lacked "reliable support linking cytokine production in the periphery to CNS demyelinating conditions like TM." Id.

The Special Master found that Dr. Byers cited no evidence to explain how the mere presence of cytokines could instigate an autoimmune process that results in a demyelinating condition in the central nervous system ("CNS"), particularly when the vaccines were injected in the periphery. See id. at *33 (finding that Dr. Byers did not establish that "any vaccine could instigate the chronic production of cytokines for a long enough period of time, sufficient in severity and degree, to cause an acutely-presenting autoimmune condition like TM via the proposed mechanisms"). In contrast, the Special Master found that Dr. Forsthuber had reliably established that there was no evidence of any such "initiatory" mechanism here. SM Dec. *28.

In rejecting Dr. Byers' theories, the Special Master neither required conclusive proof of a biological mechanism nor cloaked "the application of an erroneous legal standard in the guise of a credibility determination, and thereby shield it from appellate review." Andreu v. Sec'y of Health & Human Servs., 569 F.3d 1367, 1378 (Fed. Cir. 2009). The Special Master considered the Agmon-Levin case studies and VAERS reports that Dr. Byers offered as direct evidence of her theory, but nevertheless agreed with Dr. Forsthuber's opinion that this evidence was unreliable. SM Dec. *39 (finding the case studies inapposite because they did not involve the vaccines at issue); *40 (finding the VAERS reports unreliable in general because "special masters do not typically afford great weight to VAERS data in determining causation – and their evaluation of the deficiencies of such evidence has been affirmed"); N. Agmon-Levin, et al., Transverse Myelitis and Vaccines: A Multi-Analysis, 18 Lupus 1198-1204 (2009), filed as Ex. 30, Tab 1 (ECF No. 104-1). The Special Master accorded weight to the Baxter study proffered by Respondent that suggested "there is no statistically significant association between Menactra and/or Hep A and TM." SM Dec. *40; see R. Baxter, et al., Acute Demyelinating Events Following Vaccines: A Case-Centered Analysis, 63 Clinical Infectious Diseases 1456-61 (2016), filed as Ex. C, Tab 4 (ECF No. 114-5)("Baxter").

In addressing this Court's directive that he reexamine Dr. Byers' opinion on molecular mimicry, the Special Master acknowledged that, although Dr. Byers rejected widespread molecular mimicry as a plausible biological mechanism, she in fact embraced individualized molecular mimicry as a potential cause of Petitioner's TM, equating it with epitope spreading. SM Dec. *7 & n.22. The Special Master reasonably rejected epitope spreading as a plausible causal factor for Petitioner's TM based on his assessment of the reliability of the competing experts. Noting that in Dr. Byers' view, epitope spreading "causes T cells highly reactive to other self structures to initiate an autoimmune reaction, in a molecular mimicry-like attack," the Special Master reasonably credited Dr. Forsthuber's opinion that epitope spreading is more properly

viewed as a mechanism for the "continuation" of an already-underway autoimmune process - - not its initiation. Id. at *8, 16-17, 28.

The Special Master also reasonably rejected Dr. Byers' other proposed mechanism, bystander activation, which occurs when cytokines are "released by either an infection or a vaccination which not only activates [the] antigen-specific immune system, but also activates other reactive cells as well, so they . . . can go after their true target, which is actually autologous self-antigens." Tr. 53. The Special Master concluded that Dr. Byers did not offer any theoretical evidence explaining how the specific vaccines at issue could "cause the kind of cytokine-driven, non-antigen-specific inflammatory response that she was proposing could become pathogenic via this mechanism." SM Dec. *8.

The Special Master reasonably credited Dr. Forsthuber's opinion that Dr. Byers' bystander activation theory lacked "some initial pathogenic T cell response in the CNS," an opinion supported by recent studies including the Murali-Krishna study cited favorably by Dr. Byers. Id. at *16; see K. Murali-Krishna, et al., Counting Antigen-Specific CD8 T Cells: A Reevaluation of Bystander Activation During Viral Infection, Immunity, 177–87 (1998), filed as Exhibit 30, Tab 18 (ECF No. 104-1)("Murali-Krishna").

In sum, the record supports the Special Master's reliance on Dr. Forsthuber's opinion that neither epitope spreading nor bystander activation "was supported by sufficient medical or scientific evidence to constitute reliable explanations for how TM could occur in connection with the relevant vaccinations." SM Dec. *15.

Absent a showing that the Special Master's causation analysis on remand was tainted by any misconstruction of Dr. Byers' testimony, Petitioner's remaining challenges fail, as Petitioner provided no other persuasive evidence—in the form of medical records, testimony of treating physicians or otherwise—that supported the proposition that the subject vaccines did cause her TM.

Although Petitioner submits that the onset of TM in this case, having occurred within 42 days, was an appropriate interval, the Special Master reasonably found that a 42-day onset "has been deemed acceptable with respect to other vaccines and different autoimmune diseases. But most cases involving claims of vaccine-induced TM (in keeping with its acute nature) resulting in a successful entitlement decision involve a far shorter timeframe." SM Dec. *32 (emphasis in original) (internal citations omitted).

Finally, Petitioner contends that the Special Master impermissibly raised Petitioner's burden of proof by requiring specific medical literature supporting a causal connection between the vaccinations and TM. Pet'r's Mot. 18. However, the Special Master's decision reflects that he did not elevate Petitioner's burden of proof or err in his consideration of medical literature. See, e.g., SM Dec. *14, 30. Rather, the Special Master acknowledged that some literature Petitioner had submitted supported parts of her argument, such as on components of the theory of cytokine upregulation. See e.g., id. at *27, 35. He also found, however, that Petitioner failed to cite any medical literature to support the other components of her theory or to rebut Dr. Forsthuber's opinions. Id. at *27, 35. The Special Master noted Dr. Forsthuber knew of no reliable medical

literature causally linking TM to the vaccines and referenced a recent epidemiologic, case-centered study that found "[n]o statistically significant heightened risk of TM" in either the 5-28 days, or 2-42 days, following the two vaccinations Petitioner received. SM Dec. *14 (citing Tr. 310, Forsthuber Rep. 17); see R. Baxter, et al., Acute Demyelinating Events Following Vaccines: A Case-Centered Analysis, 63 Clinical Infectious Diseases 1456-61 (2016), filed as Ex. C, Tab 4 (ECF No. 114-5)("Baxter"). The Special Master noted that the Agmon-Levin study, cited by Petitioner, did not involve the vaccines at issue. SM Dec. *9 (citing Tr. 74, 76, 83, 132-33, 137-38); N. Agmon-Levin, et al., Transverse Myelitis and Vaccines: A Multi-Analysis, 18 Lupus 1198-1204 (2009), filed as Ex. 30, Tab 1 (ECF No. 104-1).

Conclusion

The Court denies Petitioner's second Motion for Review and sustains the decision of the Special Master.

s/Mary Ellen Coster Williams
MARY ELLEN COSTER WILLIAMS
Senior Judge