In the United States Court of Federal Claims

No 12-631V
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GRZEGORZ RUS and AGNIESZKA RUS, as Parents and Natural Guardians of A.R., a minor, Petitioners, v. SECRETARY OF HEALTH AND HUMAN SERVICES, Respondent.	)	National Childhood Vaccine Injury Act ("Vaccine Act"), 42 U.S.C. § 300aa–1 to –34 (2012).

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MEMORANDUM OPINION AND ORDER

GRIGGSBY, Judge

I. INTRODUCTION

Petitioners, Grzegorz and Agnieszka Rus, parents of A.R., a minor child, seek review of the June 23, 2016, decision of the special master denying their claim for compensation under the National Childhood Vaccine Injury Act ("Vaccine Act"), 42 U.S.C. § 300aa–1 to –34 (2012).

* This Memorandum Opinion and Order was originally filed under seal on December 8, 2016 (docket entry no. 90). The parties were given an opportunity to advise the Court of their views with respect to what information, if any, should be redacted. The parties filed a joint status report on December 30, 2016, notifying the Court that they do not believe any information should be redacted (docket entry no. 92). And so, the Court is reissuing its Memorandum Opinion and Order dated December 8, 2016 without redactions.

Petitioners allege that their minor child suffers from nephrotic syndrome, resulting from a hepatitis A vaccination that she received on October 30, 2009. For the reasons set forth below, the Court **DENIES** petitioners' motion for review and **SUSTAINS** the decision of the special master.

II. FACTUAL AND PROCEDURAL BACKGROUND[1]

A. Factual Background

1. A.R.'s Medical History

The medical history of petitioners' daughter, A.R., is discussed in detail in the special master's June 23, 2016, decision ("Special Master's Decision") and can be briefly summarized here. *Rus v. Sec'y of Health & Human Servs*., No. 12-631V, 2016 WL 4013709 (Fed. Cl. Spec. Mstr. June 23, 2016). A.R. was born on August 31, 2006. Dec. at *2; Pet. Ex. 1 at 1. A.R. has no family history of kidney or renal disease, or nephrotic syndrome. Dec. at *1; TR at 12. Today, A.R. has nephrotic syndrome, defined by symptoms such as protein in the urine, low blood protein levels, edema (swelling) and high cholesterol. TR at 46; Resp. Brief at n.2.

On October 30, 2009, A.R. visited her pediatrician for her 3-year well-child visit, where she was noted to be a healthy child that was developing normally. Dec. at *1; TR at 30-32. During this visit, A.R. received her first hepatitis A vaccination. Dec. at *1; TR at 32; Pet. Ex. 2 at 1.

On October 31, 2009, A.R. was taken to the hospital due to fever and a febrile seizure. Dec. at *2; TR at 33-34, 40; Pet. Ex. 3 at 46. A.R.'s hospital records show that A.R. had a body temperature of 104.1 F at the time, and that A.R. did not present with edema. Pet. Ex. 3 at 46; TR at 39. The attending physician's notes in A.R.'s hospital record for this visit state that "I

[1] The facts recounted in this Memorandum Opinion and Order are taken from the special master's April 25, 2016, decision in *Rus v. Sec'y of Health & Human Servs*., No. 12-631V, 2016 WL 4013709 (Fed. Cl. Spec. Mstr. June 23, 2016) ("Dec."); the transcript of the entitlement hearing before the special master held on September 17, 2015 ("Tr."); petitioners' exhibits filed before the Office of Special Master ("Pet. Ex."); petitioners' motion for review ("Pet. Mot."); and respondent's response to petitioners' motion for review ("Resp. Brief"). Except where otherwise noted, the facts recited herein are undisputed.

suspect that the child had a febrile seizure tonight, which was brought on by the fever, which is likely secondary to her being vaccinated 2 days ago." Pet. Ex. 3 at 46; *see also* Dec. at *2.

Laboratory results from tests done on November 1, 2009, show that A.R.'s albumin–a blood protein that when low, indicates malnutrition, liver problems, or that the patient is spilling protein into the urine–was normal. Dec. at *2; TR at 37-38; Pet. Ex. 12 at 3. In addition, these tests show that A.R.'s total blood protein was slightly decreased, and her urine protein was elevated. Dec. at *2; TR at 36; Pet. Ex. 12 at 3.

After being discharged from the hospital, A.R. visited her pediatrician on November 1, 2009. Dec. at *2. During this visit, A.R.'s pediatrician noted that A.R. had a wet cough and an upper respiratory infection. *Id*. On November 4, 2009, A.R. visited her pediatrician again. *Id*.; TR at 42. During this subsequent visit, A.R.'s pediatrician observed that A.R. had facial swelling. Dec. at *2. During this visit, A.R.'s pediatrician performed laboratory tests which showed decreased albumin, decreased total blood protein, marked proteinuria[2], high triglycerides and high cholesterol. *Id*.; Pet. Ex. 3 at 79. It is undisputed in this matter that A.R. suffered from diagnosable nephrotic syndrome at the time of her November 4, 2009, visit to the pediatrician. Dec. at *8; Pet. Mot. at 10-11; TR at 47-50.

A.R. subsequently visited her pediatrician on November 5, 2009, and November 9, 2009. Dec. at *2. During these visits, the pediatrician observed that A.R.'s facial swelling had decreased and that she seemed to be recovering. *Id*. On November 11, 2009, A.R. visited a nephrologist, Dr. Jeff Stein. TR at 171.

In January 2010, A.R.'s nephrotic syndrome went into remission. Pet. Ex. 4 at 8. However, A.R. has experienced at least two relapses of these symptoms since that time. Dec. at *2.

[2] Proteinuria is the "[p]resence of urinary protein in amounts exceeding 0.3 g in a 24-hour urine collection or in concentrations more than 1 g per liter in a random urine collection on two or more occasions at least 6 hours apart." Stedman's Medical Dictionary 730680 (updated Nov. 2014).

2. Nephrotic Syndrome

Nephrotic syndrome is a kidney disorder that causes, among other things, the body to excrete too much protein into the urine. TR at 46. Nephrotic syndrome commonly involves symptoms such as protein in the urine, low blood protein levels, edema and high cholesterol. TR at 46; Resp. Ex. A at 2, 6.

When a person suffers from nephrotic syndrome, a breakdown in the kidney's ability to keep proteins in the blood and out of the urine occurs. TR at 76-78. In this regard, the glomerular basement membrane ("GBM") in the kidneys is responsible for keeping blood out of the urine. *Id.* at 72, 76. The GBM is comprised of several different types of cells, including podocytes and foot processes. *Id*. at 76–77.

3. The Entitlement Hearing

On September 25, 2012, petitioners filed a petition for vaccine compensation on behalf of A.R. under the Vaccine Act. Dec. at *1; *see generally* Pet. Petition. The special master convened an entitlement hearing on petitioners' claim for compensation under the Vaccine Act on September 17, 2015. Dec. at *1; *see generally* TR.

During the entitlement hearing, Agnieszka Rus and petitioners' medical expert, Dr. Jan T. Kielstein, testified on behalf of the petitioners. S*ee generally* TR. The government's medical expert, Dr. Bernard S. Kaplan, testified on behalf of the respondent. *Id*.

Ms. Rus testified that A.R. was a healthy, lively child prior to October 30, 2009. *Id*. at 9. Ms. Rus further testified that A.R. did not have a family history of nephrotic syndrome. *Id*. at 12.

Dr. Kielstein is currently an Associate Professor of Medicine at the Department of Internal Medicine in the Division of Nephrology and Hypertension at the Medical School in Hannover, Germany. Pet. Ex. 13 at 1. During the entitlement hearing, Dr. Kielstein opined that the hepatitis A vaccination caused A.R.'s nephrotic syndrome. TR at 86-87. Dr. Kielstein also put forward two medical theories to support this opinion: (1) a specific T-cell response (the "T-cell medical theory") and (2) an inflammatory cykotine response to the vaccination that alters a unspecific pathway involving angiopoietin-like 4 ("ANGPTL4 medical theory"). *Id*. at 72-86.

With respect to the T-cell medical theory, Dr. Kielstein testified that all vaccinations are intended to cause an adaptive immune response, and this response occurs primarily in the T-cells in the case of the hepatitis A vaccine. TR at 115; Dec. at *10. And so, he theorized that nephrotic syndrome could be caused by a T-cell response to the vaccination, whereby T-cell dysfunction results in the production of a circulating glomerular permeability factor. Pet. Ex. 12 at 5. Dr. Kielstein also theorized that the circulating glomerular permeability factor could "directly induce[ ] foot process fusion resulting in severe alteration of the glomerular filter system and resulting in marked proteinuria." *Id*.; *see also* TR at 86.

With respect to the timing associated with the T-cell medical theory, Dr. Kielstein also testified that "we need more than a day or two for a T-cell response, and so the lowest time span we are talking about here is about four days." TR at 75. He acknowledged, however, that A.R.'s nephrotic syndrome symptoms began 36-40 hours after vaccine. *Id*. at 49, 73-75, 107, 116.

With respect to the ANGPTL4 medical theory, Dr. Kielstein testified that ANGPTL4 is analogous to barbed wire that covers a fence–in this case, the GBM–to help keep proteins out of the urine. *Id*. at 77. Dr. Kielstein theorized that any vaccination could cause an inflammatory response in the body that alters the production of ANGPTL4. *Id*. at 80-84. Specifically, Dr. Kielstein testified that such inflammatory response may cause overproduction of a form of ANGPTL4 lacking sialic acid residues would cause binding of ANGPTL4 to the glomerular basement membrane, thereby inducing the development of nephrotic-range proteinuria. TR at 81-92; *see also* Dec. at *9; Pet. Mot. at 13-14.

In addition, to support his theory that vaccinations set off an inflammatory response that may cause nephrotic syndrome, Dr. Kielstein offered anecdotal case reports and medical studies finding that the meningococcal and hepatitis B vaccinations may cause relapses in cases of established nephrotic syndrome. Pet. Ex. 15, 25. He also put forward case reports showing that certain vaccinations, other than the hepatitis A vaccine, may cause other diseases or syndromes, one case report demonstrating that nephrotic syndrome occurred after a hepatitis B vaccination, a case report demonstrating that the hepatitis A vaccine allegedly caused autoimmune hepatitis and A.R.'s medical history from October 30, 2009, onward. Pet. Ex. 12, 16-20, 22-24, 26-27. Dr. Kielstein acknowledged, however, that he was not aware of any cases demonstrating that the hepatitis A vaccination caused nephrotic syndrome. TR at 118.

Dr. Kielstein also relied upon two 2014 medical studies−Lionel C. Clement *et al*., *Circulating Angiopoietin–Like 4 Links Proteinuria With Hypertriglyceridemia in Nephrotic Syndrome*, 20 Nature Medicine 37 (2014) and Sumant S. Chugh, *et al*., *Angiopoietin–Like 4 Based Therapeutics for Proteinuria and Kidney Disease*, 5 Frontiers in Pharmacology 23/1 (2014)−to support the ANGPTL4 medical theory. Dec. at *10; Pet. Ex. 34, 35. The Clement study demonstrates that the manipulation of a certain type of ANGPTL4 is an important mediator of nephrotic syndrome and a critical link between proteinuria and hypertriglyceridemia. Pet. Ex. 34. The Chugh study demonstrates that the manipulation of a certain type of ANGPTL4 may improve proteinuria. Pet. Ex. 35.

The government's medical expert, Dr. Bernard Kaplan, testified that he did not find any evidence in the record that the hepatitis A vaccination that A.R. received on October 30, 2009, contributed to her nephrotic syndrome.[4] TR at 131. In this regard, Dr. Kaplan testified that there is no medical literature showing that the hepatitis A vaccine precipitates nephrotic syndrome. *Id*. at 132. He also offered an opinion about the medical literature relied upon by the petitioners to support their T-Cell and ANGPTL4 medical theories. Dr. Kaplan also testified that there is no medical literature showing that vaccines affect ANGPTL4 production. *Id*. at 143-44. Dr. Kaplan further testified that there are "gaping holes" in the T-cell medical theory. *Id*. at 146-47; Resp. Ex. C at 2.

Dr. Kaplan also opined that, if nephrotic syndrome was caused by an inflammatory response to any vaccination as the petitioners suggests, diagnoses of nephrotic syndrome should have risen over the past 50 years, as vaccinations have increased during this time period. TR at 149-50. He noted, however, that diagnoses of nephrotic syndrome have remained "absolutely constant." *Id*. at 132. And so, Dr. Kaplan concluded that the case reports and medical literature cited by Dr. Kielstein do not demonstrate that the hepatitis A vaccination is linked to the new-onset nephrotic syndrome. *Id*. at 160-61.

[3] Dr. Kaplan is a pediatric nephrologist in the Division of Nephrology in the Children's Hospital of Philadelphia. Resp. Ex. B at 2.

4. The Special Master's Decision

On June 23, 2016, the special master issued a decision denying petitioners' claim for compensation under the Vaccine Act. *See generally* Dec. In the decision, the special master determined that petitioners had failed to prove by preponderant evidence that the hepatitis A vaccination caused A.R.'s nephrotic syndrome under *Althen* Prong I. *Id*. at *1; *see Althen v. Sec'y of Health & Human Servs*., 418 F.3d 1274, 1278 (Fed. Cir. 2005).

As an initial matter, the special master addressed the legal standard petitioners are required to meet to receive compensation under the Vaccine Program. Dec. at *3. Specifically relevant here, the special master determined that petitioners were required to prove each *Althen* prong by preponderant evidence, including *Althen* Prong I which requires petitioners to provide "a medical theory causally connecting the vaccination and the injury." *Id*. (citing *Althen*, 418 F.3d at 1278). The special master also determined that, in presenting a theory causally connecting the vaccination and the injury, "a claimant need not produce medical literature or epidemiological evidence to establish causation under the Vaccine Act. . . ." *Id*. at *4. But, the special master determined that petitioners' causation theory must be supported by a "'sound and reliable' medical or scientific explanation." *Id*. at *7 (quoting *Knudsen ex rel. Knudsen v. Sec'y of Health & Human Servs.*, 35 F.3d 543, 548 (Fed. Cir. 1994)).

Applying the aforementioned standard, the special master determined that the petitioners had met their burden of proof with respect to *Althen* Prongs II and III, but that the petitioners failed to meet their burden with respect to *Althen* Prong I. *Id*. at *9, 12. In reaching this conclusion, the special master found that:

> In determining whether petitioner is entitled to compensation, a special master must consider the entire record and is not bound by any particular piece of evidence. § 13(b)(1) (stating a special master is not bound by any "diagnosis, conclusion, judgment, test result, report, or summary" contained in the record). Thus a special master must weigh and evaluate opposing expert opinions, medical and scientific evidence, and the evidentiary record in deciding whether petitioners have met their burden of proof.

Id. at *4.

To determine whether petitioners had met their burden with respect to *Althen* Prong I, the special master reviewed petitioners' two medical causation theories, the T-cell medical theory

and the ANGPTL4 medical theory. The special master characterized petitioners' T-cell medical theory as proposing that nephrotic syndrome:

> [C]ould be caused by a "specific" T-cell response to vaccination where systemic T-cell dysfunction results in the production of a circulating glomerular permeability factor, which directly induces podocyte foot process fusion. . . . The foot process fusion would severely alter the glomerular filter system, resulting in proteinuria.

Id. at *5. To that end, the special master also found that the timing of the T-cell medical theory put forward by Dr. Kielstein did not comport with the progression of A.R.'s symptoms. *Id*. at *8.

In this regard, the special master noted that Dr. Kielstein testified that a T-cell response to a vaccination would take about four days. *Id*. (citing TR at 75). But, the special master also noted that Dr. Kielstein testified that the likely onset of A.R.'s nephrotic syndrome occurred within 36 to 40 hours of the vaccination. *Id*. at *12 (citing TR at 73-75).

The special master also considered the petitioners' ANGPTL4 medical theory, and he noted that Dr. Kielstein offered anecdotal case reports, medical studies finding that the meningococcal and hepatitis B vaccinations may cause relapses in cases of established nephrotic syndrome, case reports showing that certain vaccinations other than hepatitis A may cause other diseases or syndromes, one case report demonstrating that the hepatitis A vaccine allegedly caused autoimmune hepatitis, and A.R.'s own medical progression from October 30, 2009 onward, to support this theory. Dec. at *6, 11. The special master also noted that, during the entitlement hearing, Dr. Kielstein admitted he was not aware of any cases demonstrating that the hepatitis A vaccination caused nephrotic syndrome. *Id*. at *6; TR at 118.

With respect to the Clement medical study that the petitioners put forward to support their ANGPTL4 medical theory, the special master determined that "the Clement study appeared to demonstrate that enhancement of ANGPTL4 reduced existing proteinuria, but did not address how the ANGPTL4 may have been altered in the podocytes in the first place, leading to the onset of the disease." Dec. at *12 (citing Pet. Ex. 34).

The special master also determined that "[w]hile innate or inflammatory disruption of the angiopoietin-like 4 pathway may, at some point, prove to be a viable theory, at the present time it appears to be a bridge too far, too vague and too uncertain in terms of the triggering mechanism

and sequence of the events in this case." *Id*. And so, the special master concluded that Dr. Kielstein:

> [A]cknowledged that there remains great mystery in the understanding of the causation of this disease. Without an understanding of the causation of the disease, it is not possible to come to a conclusion about vaccine causation or causation by a specific vaccine such as a hepatitis A.

Id.

And so, on June 23, 2016, the special master issued a decision denying petitioners' request for compensation. *See generally* Dec. Petitioners, alleging error, seek review of the Special Master's Decision.

B. Procedural Background

On June 22, 2016, petitioners filed a motion for review of the Special Master's Decision. *See generally* Pet. Mot. The government filed a response to petitioners' motion for review on August 22, 2016. *See generally* Resp. Brief. Petitioners' motion for review having been fully briefed, the Court resolves the pending motion.

III. STANDARDS FOR DECISION

A. Standard Of Review

The United States Court of Federal Claims has jurisdiction to review the record of the proceedings before a special master and, upon such review, may:

> (A) uphold the findings of fact and conclusions of law of the special master and sustain the special master's decision,
>
> (B) set aside any findings of fact or conclusions of law of the special master found to be arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law and issue its own findings of fact and conclusions of law, or
>
> (C) remand the petition to the special master for further action in accordance with the court's direction.

42 U.S.C. § 300aa–12(e)(2).

The special master's determinations of law are reviewed *de novo*. *Andreu ex rel. Andreu v. Sec'y of Health & Human Servs.*, 569 F.3d 1367, 1373 (Fed. Cir. 2009). The special master's findings of fact are reviewed for clear error. *Id.*; *see also Broekelschen v. Sec'y of Health &*

Human Servs., 618 F.3d 1339, 1345 (Fed. Cir. 2010) ("We uphold the special master's findings of fact unless they are arbitrary or capricious.") (citation omitted). In addition, a special master's findings regarding the probative value of the evidence and the credibility of witnesses will not be disturbed so long as they are "supported by substantial evidence." *Doe v. Sec'y of Health & Human Servs*., 601 F.3d 1349, 1355 (Fed. Cir. 2010) (citation omitted); *see also Burns v. Sec'y of Health & Human Servs.*, 3 F.3d 415, 417 (Fed. Cir. 1993) (holding that the decision of whether to accord greater weight to contemporaneous medical records or later given testimony is "uniquely within the purview of the special master"). This "level of deference is especially apt in a case in which the medical evidence of causation is in dispute." *Hodges v. Sec'y of Health & Human Servs.*, 9 F.3d 958, 961 (Fed. Cir. 1993). And so, the Court will "not substitute its own judgment for that of the special master if the special master has considered all relevant factors, and has made no clear error of judgment." *Lonergan v. Sec'y of Health & Human Servs.*, 27 Fed. Cl. 579, 580 (1993).

B. Vaccine Injury Claims

Pursuant to the Vaccine Act, the Court shall award compensation if a petitioner proves, by a preponderance of the evidence, all of the elements set forth in 42 U.S.C. § 300aa–11(c)(1), unless there is a preponderance of evidence that the illness is due to factors unrelated to the administration of the vaccine. 42 U.S.C. § 300aa–13(a)(1). A petitioner can recover either by proving an injury listed on the Vaccine Injury Table ("Table"), or by proving causation-in-fact. *See* 42 U.S.C. §§ 300aa–11(c)(1)(C); *Althen,* 418 F.3d at 1278. And so, to receive compensation under the National Vaccine Injury Compensation Program, a petitioner must prove either that: (1) the petitioner suffered a "Table Injury" that corresponds to one of the vaccinations in question within a statutorily prescribed period of time or, in the alternative, (2) the petitioner's illnesses were actually caused by a vaccine. *See* 42 U.S.C. §§ 300aa–13(a)(1)(A), 300aa–11(c)(1)(C)(i-ii), 300aa–14(a); *see also Moberly v. Sec'y of Health & Human Servs*., 592 F.3d 1315, 1321 (Fed. Cir. 2010); *Capizzano v. Sec'y of Health & Human Servs.,* 440 F.3d 1317, 1320 (Fed. Cir. 2006).

In addition, in Table and non-Table cases, a petitioner bears a "preponderance of the evidence" burden of proof. 42 U.S.C. §§ 300aa–13(a)(1)(A); *Althen*, 418 F.3d at 1278 (citing *Shyface v. Sec'y of Health & Human Servs*., 165 F.3d 1344, 1352-53 (Fed. Cir. 1999)). And so,

a petitioner must offer evidence that leads the "trier of fact to believe that the existence of a fact is more probable than its nonexistence before [he] may find in favor of the party who has the burden to persuade the [judge] of the fact's existence." *Moberly*, 592 F.3d at 1322 n.2 (brackets existing) (internal quotation omitted); *see also Snowbank Enter. v. United States*, 6 Cl. Ct. 476, 486 (1984) (holding that mere conjecture or speculation is insufficient under a preponderance standard).

To establish a *prima facie* case when proceeding on a causation-in-fact theory, as petitioners seek to do in this matter, a petitioner must "prove, by a preponderance of the evidence, that the vaccine was not only a but-for cause of the injury but also a substantial factor in bringing about the injury." *Shyface*, 165 F.3d at 1352. "[T]o show that the vaccine was a substantial factor in bringing about the injury, the petitioner must show 'a medical theory causally connecting the vaccination and the injury.'" *Id.* at 1352-53 (quoting *Grant v. Sec'y of Health & Human Servs.*, 956 F.2d 1144, 1148 (Fed. Cir. 1992) (*per curiam*)). In other words, "[t]here must be a 'logical sequence of cause and effect showing that the vaccination was the reason for the injury,'" *id.* at 1353 (quoting *Grant*, 956 F.2d at 1148), and "[t]his 'logical sequence of cause and effect' must be supported by a sound and reliable medical or scientific explanation." *Knudsen*, 35 F.3d at 548 (quoting *Jay v. Sec'y of Health & Human Servs.*, 998 F.2d 979, 984 (Fed. Cir. 1993)); *see also* 42 U.S.C. § 300aa–13(a)(1) ("The special master or court may not make such a finding based on the claims of a petitioner alone, unsubstantiated by medical records or by medical opinion."). However, medical or scientific certainty is not required. *Knudsen*, 35 F.3d at 548-49.

In *Althen*, the Federal Circuit addressed the three elements that a petitioner must provide to prove causation-in-fact:

> (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, 418 F.3d at 1278. All three prongs "must cumulatively show that the vaccination was a 'but-for' cause of the harm, rather than just an insubstantial contributor in, or one among several possible causes of, the harm." *Pafford v. Sec'y of Health & Human Servs.*, 451 F.3d 1352, 1355 (Fed. Cir. 2006). In addition, if a petitioner establishes a *prima facie* case, the burden shifts to

the respondent to show, by a preponderance of the evidence, that the injury was caused by a factor unrelated to the vaccine. *See* 42 U.S.C. § 300aa–13(a)(1)(B); *Shalala*, 514 U.S. at 270-71. But, regardless of whether the burden of proof ever shifts to the respondent, the special master may consider the evidence presented by the respondent in determining whether the petitioner has established a *prima facie* case. *See Stone v. Sec'y of Health & Human Servs.*, 676 F.3d 1373, 1379 (Fed. Cir. 2012) ("[E]vidence of other possible sources of injury can be relevant not only to the 'factors unrelated' defense, but also to whether a prima facie showing has been made that the vaccine was a substantial factor in causing the injury in question."); *de Bazan v. Sec'y of Health & Human Servs.*, 539 F.3d 1347, 1353 (Fed. Cir. 2008) ("The government, like any defendant, is permitted to offer evidence to demonstrate the inadequacy of the petitioner's evidence on a requisite element of the petitioner's case[-]in-chief.").

IV. LEGAL ANALYSIS

Petitioners enumerate three objections to the special master's decision. *See generally* Pet. Mot. First, petitioners argue that the special master erred as a matter of law by holding petitioners to a higher burden of proof than required under the Vaccine Act to prove the causal relationship between the vaccination and the injury under *Althen* Prong I. Pet. Mot. at 2, 17. Second, petitioners argue that the special master "failed to consider the medical and scientific evidence contained in the record as a whole" in evaluating their claim under the first prong of *Althen*. *Id*. at 2. Finally, petitioners also argue that the special master erred in finding that petitioners' expert, Dr. Kielstein, testified that there was "great mystery in the understanding of the causation of" nephrotic syndrome. *Id*. at 3 (quoting Dec. at *12).

The government counters that the special master's decision to deny compensation in this case is reasonable, in accordance with law and supported by the record evidence. *See generally* Resp. Brief. For the reasons discussed below, the Court agrees. And so, the Court **SUSTAINS** the decision of the special master.

A. The Special Master Applied The Correct Burden Of Proof

As an initial matter, the record demonstrates that the special master correctly applied the law in determining the burden of proof that petitioners must meet to satisfy the medical theory prong of *Althen*. In their motion for review, petitioners argue that the special master imposed too high of a burden of proof on petitioners to prove "a medical theory causally connecting the

vaccination and the injury." Pet. Mot. at 2; 15 (citing *Althen*, 418 F.3d at 1278). The Court reviews the special master's determination of law *de novo*. *Andreu*, 569 F.3d at 1373.

The record evidence shows that the special master correctly applied the burden of proof for petitioners' vaccine injury claim. In his decision, the special master determined that petitioners were required to prove each prong under the Federal Circuit's decision in *Althen v. Secretary of Health and Human Services* by a preponderance of the evidence. Dec. at *7 (citing *Althen*, 418 F.3d at 1278). The special master also determined that, in putting forth their theory causally connecting the vaccination and the injury the petitioners "need not produce medical literature or epidemiological evidence to establish causation under the Vaccine Act." *Id*. at *4. In addition, the special master concluded that petitioners' medical theories in this case must be supported by a "'sound and reliable' medical or scientific explanation" under *Althen* Prong I. *Id*. at *7 (quoting *Knudsen*, 35 F.3d at 548).

The special master's decision correctly states the legal standard under the Federal Circuit's decision in *Althen*. *Althen*, 418 F.3d at 1278. And so, the special master did not err as a matter of law in determining the burden of proof for the petitioners' claim in this action.

The record evidence also shows that the special master correctly applied this burden of proof to the medical theories put forward by the petitioners to support their vaccine injury claim. In this regard, the special master determined that petitioners' T-cell medical theory−that nephrotic syndrome could be caused by a T-cell response to the vaccination−did not fit within the timeline that the petitioners' medical expert identified for the onset of A.R.'s symptoms. Dec. at *12. Specifically, Dr. Kielstein testified during the entitlement hearing that it would take approximately four days for a T-cell reaction to occur after a vaccination. *Id*. (citing TR at 73-75). But, as the special master noted in his decision, Dr. Kielstein acknowledged in his testimony that A.R.'s nephrotic syndrome symptoms first occurred just 36-40 hours after A.R. received the hepatitis A vaccination. *Id*.

Given this, the special master appropriately determined that petitioners had not shown, by a preponderance of the evidence, that their T-cell medical theory could causally connect the hepatitis A vaccination that A.R. received on October 30, 2009 to the onset of A.R.'s nephrotic syndrome. *Id*. at *8, 12. And so, the special master did not err as a matter of law in reaching this conclusion.

The special master also properly applied the legal standard under *Althen* in considering the petitioners' ANGPTL4 medical theory. In this regard, the record evidence shows that the special master determined that the medical literature upon which the petitioners relied to support this medical theory did not link any vaccines to dysfunction in the ANGPTL4. *Id*. at *11. The special master also noted that the government's expert, Dr. Kaplan, testified that "in spite of "hundreds of millions of vaccines" administered worldwide over the last 50 years," the prevalence of nephrotic syndrome has remained "absolutely constant." Dec. at *11 (quoting TR at 132). And so, the special master concluded that the absence of a correlation between the increase in the number of vaccinations and the prevalence of nephrotic syndrome cast doubt upon the petitioners' ANGPTL4 medical theory. Dec. at *11.

Given the lack of evidence to support either of petitioners' medical theories, the special master found that "[t]he bigger problem is that there seems to be a genuine lack of understanding about the cause of this disease entity among nephrologists even though nephrotic syndrome has been studied for many years." *Id*. And so, the special master reasonably concluded there was insufficient evidence for the petitioners to meet their burden of proof under *Althen* Prong I. *Id*. at *12.

B. The Special Master Appropriately Considered The Medical And Scientific Evidence In The Record

Petitioners' argument that the special master erred by failing to consider the medical and scientific evidence contained in the record is similarly unsupported by the evidence. Pet. Mot. at 2. As discussed above, the special master's findings of fact are reviewed for clear error. *Andreu*, 569 F.3d at 1373; *see also Broekelschen*, 618 F.3d at 1345. In addition, the special master's findings regarding the probative value of the evidence and the credibility of witnesses will not be disturbed so long as they are "supported by substantial evidence." *Doe*, 601 F.3d at 1355 (citations omitted); *see also Burns*, 3 F.3d at 417.

The record evidence shows that special master properly considered the medical literature relied upon by the petitioners in reaching his decision. Dec. at *11. In particular, the special master specifically considered the Chugh medical study put forward by the petitioners, and the special master noted in his decision that, "Chugh reported that "the central role played by [angiopoietin-like 4] in nephrotic syndrome . . . suggests that manipulating [angiopoietin-like 4]

related pathways in the context of therapeutics has a high chance of success." *Id*. at *10 (citing Pet. Ex. 35).

The special master also considered the Clement medical study, which the petitioners also advanced to support their claim. In this regard, the special master acknowledged that the Clement medical study "demonstrated that angiopoietin-like 4 is an important biological mediator of nephrotic syndrome and is a critical link between proteinuria and hypertriglyceridemia." *Id*. at *10 (citing Pet. Ex. 34). The special master ultimately determined, however, that neither the Clement nor the Chugh medical study linked the hepatitis A vaccination−or any vaccine−to dysfunction in the ANGPTL4. Dec. at *11-12. And so, the special master reasonably concluded that the medical literature relied upon by the petitioners did not support their ANGPTL4 medical theory.

The record evidence also shows that the special master appropriately considered Dr. Kielstein's expert reports and testimony in support of the petitioners' claim. *See generally* Dec.; Pet. Mot. at 7-8; TR at 24-118; Pet. Ex. 14-20, 22-27, 32-35. For example, the special master notes in his decision that Dr. Kielstein attempted to relate the medical theories discussed in the Chugh and Clements medical studies to A.R.'s case in his testimony. Dec. at *11 (citing TR at 83).

With respect to the ANGPTL4 medical theory, the special master also notes in his decision that Dr. Kielstein testified that the high fever that A.R. experienced during her October 31, 2009, visit to the emergency room suggested a cytokine response that could have been secondary to the hepatitis A vaccine. Dec. at *11. The special master further notes, however, that Dr. Kielstein testified that he did not know whether a cytokine response could have caused A.R.'s symptoms, "because we are making the data, looking at that, and this is a very fascinating field." *Id*.; TR at 84. And so, the evidentiary record shows that the special master reasonably concluded that Dr. Kielstein was unable to link the hepatitis A vaccination to A.R.'s nephrotic syndrome. Dec. at *11.

In addition, the record evidence demonstrates that the special master considered the case reports that the petitioners put forward to support their medical theories. Specifically, the special master noted in his decision that Dr. Kielstein provided case reports demonstrating that vaccines other than the hepatitis A vaccine may cause nephrotic syndrome. Dec. at *6; *see also* Pet. Ex.

15-20, 22. The special master also noted in his decision that two of the case reports provided by petitioners show that diseases other than nephrotic syndrome have occurred following vaccinations other than the hepatitis A vaccination. Dec. at *6; *see* Pet. Ex. 23-24. But, as the special master correctly concluded in his decision, none of these case reports show that the hepatitis A vaccination causes nephrotic syndrome. Dec. at *6, 11; *see also* Pet. Ex. 15-20, 22-24, 27.

Lastly, the record before the Court makes clear that the special master afforded appropriate weight to all of the evidence discussed above. The special master notes in his decision that Dr. Kielstein testified that "he was not aware of any case reports showing the development of nephrotic syndrome following a Hep A vaccine, and he was not aware of any medical literature where the authors assert a causal connection between Hep A and nephrotic syndrome." *Id*. at *6 (citing TR at 118). In addition, the special master noted that Dr. Kielstein also testified that "the existing literature was a 'low-quality database,' as the studies are not 'prospective, randomized studies.'" *Id*. (quoting TR at 65). Given Dr. Kielstein's testimony, it was certainly reasonable for the special master to afford limited weight to the medical literature and case studies advanced by the petitioners. And so, the Court will not disturb the special master's findings regarding the probative value of this evidence. *Doe*, 601 F.3d at 1355.

In sum, given the evidence in the record, it is not surprising that the petitioners do not point to any specific medical or scientific evidence that the special master failed to consider in deciding their vaccine injury claim. *See generally* Pet. Mot. Nor do petitioners demonstrate that the special master failed to properly weigh this evidence in reaching his decision on that claim. And so, the evidentiary record here demonstrates that the special master did not err in considering the medical and scientific evidence to support petitioners' claim.

C. The Special Master Correctly Characterized Dr. Kielstein's Testimony As Conveying That The Cause Of Nephrotic Syndrome Remains Unknown

Lastly, petitioners' final challenge–that the special master erred in characterizing Dr. Kielstein's testimony as conveying that there was "great mystery in the understanding of the causation of [nephrotic syndrome]"–is equally without evidentiary support. Dec. at *12; Pet. Mot. at 12-13.

In this regard, the record evidence shows that Dr. Kielstein made several statements in his expert reports and during his expert testimony that support the special master's factual finding that there is uncertainty about the causes of nephrotic syndrome. *See* TR; Pet. Ex. 12, 30, 31. Specifically, the record before the Court shows that Dr. Kielstein states in his expert report dated August 15, 2014, that "the exact underlying cause of [nephrotic syndrome] is not fully understood." Pet. Ex. 12. In his supplemental expert report, dated March 6, 2014, Dr. Kielstein also states that "[u]nraveling the pathophysiology of minimal change nephritic [sic] syndrome is an ongoing endeavor." Pet. Ex. 30.

Dr. Kielstein expressed a similar view during the entitlement hearing. For example, the following exchange occurred during Dr. Kielstein's testimony about the petitioners' ANGPTL4 medical theory:

> THE COURT: And are you suggesting that the injury [the inflammatory response to the vaccination] causes some loss of the angiopoietin-like 4?" . . .
>
> DR. KIELSTEIN: "The question is can we, from the data we have, identify the single mechanism that is – that is inducing that [the nephrotic syndrome]? I'm not able to do that. What I am doing is to offer possible explanations. . . ."

TR at 80-81.

Dr. Kielstein's own testimony and expert reports make clear that Dr. Kielstein represented to the Court that the cause of nephrotic syndrome remains undetermined. Given this, the special master did not err in characterizing Dr. Kielstein's testimony as conveying that there remains "great mystery in the understanding of the causation of this disease." Dec. at *12. And so, the Court will not set aside the findings of the special master.

V. CONCLUSION

In sum, the record evidence in this case demonstrates that petitioners have not demonstrated that the special master erred in considering their vaccine injury claim. To the contrary, the record evidence in this matter demonstrates that the special master's decision was reasonable, supported by the evidence and in accordance with law.

And so, for the foregoing reasons, the Court **DENIES** petitioners' motion for review and **SUSTAINS** the decision of the special master.

The Clerk is directed to enter judgment accordingly.

Each party to bear their own costs.

Some of the information contained in this Memorandum Opinion and Order may be considered privileged, confidential, or sensitive personally-identifiable information that should be protected from disclosure. Accordingly, this Memorandum Opinion and Order shall be **FILED UNDER SEAL**. The parties shall review the Memorandum Opinion and Order to determine whether, in their view, any information should be redacted prior to publication. The parties shall also **FILE**, by **December 30, 2016**, a joint status report identifying the information, if any, that they contend should be redacted, together with an explanation of the basis for each proposed redaction.

IT IS SO ORDERED.

s/ Lydia Kay Griggsby
LYDIA KAY GRIGGSBY
Judge