United States Court of Appeals for the Federal Circuit

JENNIFER STONE AND GARY STONE, PARENTS AND NEXT FRIENDS OF AMELIA STONE, A MINOR,
Petitioners-Appellants,

v.

SECRETARY OF HEALTH AND HUMAN SERVICES,
Respondent-Appellee.

2011-5109

Appeal from the United States Court of Federal Claims in Case No. 04-VV-1041, Senior Judge Lawrence S. Margolis.

SCOTT R. HAMMITT, AS THE LEGAL REPRESENTATIVE OF HIS MINOR DAUGHTER, RACHEL HAMMITT,
Petitioner-Appellant,

v.

SECRETARY OF HEALTH AND HUMAN SERVICES,

Respondent-Appellee.

2011-5117

Appeal from the United States Court of Federal Claims in Case No. 07-VV-170, Judge Thomas C. Wheeler.

Decided: April 26, 2012

RICHARD GAGE, Richard Gage, P.C., of Cheyenne, Wyoming, argued for petitioners-appellants in appeal no. 2011-5109.

CURTIS R. WEBB, of Twin Falls, Idaho, argued for petitioner-appellant in appeal no. 2011-5117.

ALEXIS B. BABCOCK, Trial Attorney, Torts Branch, Civil Division, United States Department of Justice, of Washington, DC, argued for respondent-appellee in appeal no. 2011-5109. With her on the brief were TONY WEST, Assistant Attorney General, MARK W. ROGERS, Acting Director, VINCENT J. MATANOSKI, Acting Deputy Director, and CATHARINE E. REEVES, Assistant Director.

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Acting Director, VINCENT J. MATANOSKI, Acting Deputy Director, and GABRIELLE M. FIELDING, Assistant Director.

Before RADER, *Chief Judge*, SCHALL and BRYSON, *Circuit Judges*.

BRYSON, *Circuit Judge*.

In separate proceedings, petitioners Jennifer and Gary Stone and petitioner Scott Hammitt sought compensation under the National Vaccine Injury Compensation Program for injuries to their children allegedly caused by the Diptheria-Tetanus-acellular Pertussis ("DTaP") vaccine. The Stones alleged that the administration of the DTaP vaccine to their daughter Amelia was a substantial cause of a seizure disorder from which she suffers, known as Severe Myoclonic Epilepsy of Infancy ("SMEI").[1] Mr. Hammitt made the same allegation with respect to his daughter Rachel, who also suffers from SMEI. The same special master presided over both cases and determined that the petitioners failed to show entitlement to compensation because in both cases the evidence showed that a gene mutation present in both children was the sole cause of their injuries. The Court of Federal Claims affirmed both decisions.

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[1] SMEI is also known as Dravet Syndrome. As the special master explained, it is an epilepsy syndrome that "begins in the first year of life in previously healthy children. Hemiclonic seizures, which may be long lasting, are characteristic and can be associated with fever. Myoclonic, absence, tonic-clonic, and partial seizures also occur. The epilepsy is refractory and developmental regression ensues." *Stone v. Sec'y of Health & Human Servs.*, No. 04-1041V, at 1 n.2 (Fed. Cl. Spec. Mstr. Apr. 15, 2010).

I

A

Amelia Stone was born on April 17, 2001, and received a DTaP vaccination on August 27, 2001. The day after her DTaP vaccination, Amelia experienced a febrile seizure. She was treated at a hospital and released several days later. The special master and the trial court found that Amelia suffered no brain damage as a result of the seizure. On September 26, 2001, Amelia experienced a second febrile seizure. She was again treated at the hospital, and no evidence of brain damage was discovered.

Amelia continued to experience seizures, both febrile and afebrile. At a check-up on December 19, 2001, her doctor noted that "[i]t appears now that [Amelia] has a primary seizure disorder," but that her "neurologic development has been appropriate." In October 2003, Amelia's seizure disorder was diagnosed as SMEI. In January 2005, genetic testing revealed that Amelia has a de novo mutation in her SCN1A gene. The records accompanying the results noted that "[t]his finding is most consistent with this DNA variant being associated with a severe phenotype (SMEI or SMEB) rather than a mild or normal phenotype."

B

Rachel Hammitt was born on November 9, 2003. She received her second DTaP, IPV, Hepatitis B, Hib, and Pneumococcal Conjugate vaccinations on March 15, 2004. That evening, Rachel experienced a febrile seizure. She was treated at a hospital and released several days later. The special master and the trial court found that Rachel suffered no brain damage as a result of that seizure. On

April 22, 2004, Rachel experienced a second seizure. She was again treated at the hospital and released several days later.

Thereafter, Rachel continued to experience intermittent seizures. Records from her 12-month check-up on November 12, 2004, showed a diagnosis of epilepsy but reported normal growth and development. However, at her 14-month checkup, Rachel's pediatrician recorded delayed verbal and gross motor development and recommended that she be evaluated for global developmental delays. Genetic testing ordered on May 3, 2005, revealed that Rachel has a mutation in her SCN1A gene. The records accompanying the results stated that the mutation is "associated with a severe phenotype (SMEI or SMEB) rather than a mild or normal phenotype." At a follow-up appointment, a physician noted that Rachel's "clinical course, EEG, and SCN1A test . . . are suggestive of [SMEI]."

C

The petitioners in both cases sought compensation under the National Childhood Vaccine Injury Act, 42 U.S.C. §§ 300aa-1 to 300aa-34 ("Vaccine Act"), alleging that the DTaP vaccination was a substantial cause of each child's SMEI. The evidence submitted to the special master in both cases was largely the same, and much of it—including key testimony for the respondent concerning the SCN1A gene mutation—was presented in a single consolidated hearing. Dr. Marcel Kinsbourne testified for the petitioners. He testified that in both cases the DTaP vaccinations were a substantial contributing cause of the SMEI. He explained his theory of causation as follows: "The DTaP vaccine[s] [received by Amelia and Rachel] caused [each of them] to have a fever; that fever caused a

prolonged seizure classified as a complex febrile seizure; and that seizure damaged [the] brain, lowering [the] level of seizure propensity, thus facilitating further seizures." However, Dr. Kinsbourne agreed that "a trigger doesn't necessarily have to have a further deeper impact," and he admitted that he had simply "inferred" that the children had suffered brain damage from the fact of their initial seizures. He agreed that there was no clinical manifestation of the inferred brain damage in either case.

In support of his theory, Dr. Kinsbourne relied on a series of medical articles, which the special master did not find persuasive. Some of the articles on which Dr. Kinsbourne relied concerned the DTP vaccine, rather than the DTaP vaccine. The special master found those articles unhelpful because neurological reactions to the two different vaccines "do not occur with the same frequency, nor [do they present] the same relative risks." Dr. Kinsbourne also relied on an article by Berkovic et al. to support his theory. The special master, however, found that the Berkovic article supported the respondent's position, not Dr. Kinsbourne's theory, because the authors of that article did not find that vaccines are a "trigger for encephalopathy" as Dr. Kinsbourne argued. Instead, that article concluded that individuals with certain mutations in the SCN1A gene "seem to develop SMEI or SMEB [a related seizure condition] whether or not they are immunized in the first year of life. We do not think that avoiding vaccination, as a potential trigger, would prevent onset of this devastating disorder in patients who already harbour the SCN1A mutation."

In evaluating Dr. Kinsbourne's testimony and qualifications, the special master expressed concern "regarding Dr. Kinsbourne's reliability as an expert witness" due to the fact that Dr. Kinsbourne "has not maintained a hospi-

tal based clinical pediatric neurology practice since 1981." The special master noted that Dr. Kinsbourne's testimony "reflected his lack of recent clinical practice," and that "[h]is testimony was highly generalized and lacked any grounding in practice." He also noted that "Dr. Kinsbourne does not publish, research, teach, counsel, attend meetings or conferences, or have any special training in the field of genetics." The special master concluded that "[t]he fact that for the past twenty-five years Dr. Kinsbourne has not focused his practice, research, or teaching in the field of seizure disorders, and that Dr. Kinsbourne has no expertise in the field of genetics significantly limited his ability to offer reliable, persuasive, and cogent testimony in this case." Although the special master encouraged the petitioners to submit expert testimony from a geneticist, they declined to do so and relied solely on Dr. Kinsbourne.

Three experts testified for the respondent. In Amelia Stone's case, Dr. Michael Kohrman and Dr. Gerald Raymond testified for the respondent. In Rachel Hammitt's case, Dr. Max Wiznitzer and Dr. Raymond testified for the respondent. The special master found the testimony of each of those witnesses to be helpful, but was particularly persuaded by Dr. Raymond, who has a background in both pediatric neurology and genetics. In his opinions in both cases, the special master stated: "Dr. Raymond's knowledge and experience with neurology and clinical genetics is extensive. His essentially unrebutted testimony was very persuasive and was relied upon heavily in deciding this case."

Dr. Raymond testified that the SCN1A gene mutation was the sole cause of SMEI in both Amelia and Rachel. He testified at length as to how he reached that conclusion, beginning with the fact that SMEI is highly corre-

lated with a mutation in the SCN1A gene. All three of the respondent's experts further testified that there was no evidence that either Amelia or Rachel suffered brain damage as a result of their initial febrile seizures. The respondent's experts concluded that there was no evidence that the initial seizures contributed in any way to either child's SMEI.

Dr. Kinsbourne agreed that "SMEI has a genetic bas[is]" that is "very powerful," but he contended that "the pertussis vaccine caused fever, the fever triggered the seizure, [and] the seizure lasted a long time," thereby lowering each child's seizure threshold. As summarized by the special master in the *Stone* case, Dr. Kinsbourne's rebuttal essentially consisted of:

> 1) criticizing the testimony presented by Dr. Raymond regarding the factors a geneticist analyzes in determining a genotype-phenotype relationship; 2) arguing that the SCN1A gene mutation is not a reliable indicator of clinical outcome; 3) arguing that the scientific literature supports an environmental (vaccine role) in causation; 4) arguing that the vaccine was responsible for the first seizure, which was a complex febrile seizure, and complex febrile seizures damage the brain; 5) arguing that the [special master's] prior rulings in [two similar cases] require a finding on behalf of petitioners; and 6) criticizing Dr. Raymond's qualifications.

D

After considering all the evidence, the special master concluded that neither Amelia nor Rachel was entitled to compensation. He determined that the respondent had

demonstrated by a preponderance of the evidence that the SCN1A gene mutation was "more likely than not the 'but for' and 'substantial factor' that caused" the SMEI in both children. *Stone v. Sec'y of Health & Human Servs.* (*Stone I*), No. 04-1041V (Fed. Cl. Spec. Mstr. Apr. 15, 2010); *Hammitt v. Sec'y of Health & Human Servs.* (*Hammitt I*), No. 07-170V (Fed. Cl. Spec. Mstr. Aug. 31, 2010).

The special master noted that the "issue that ultimately must be resolved is whether respondent demonstrated that the mutation is *the* substantial causal factor, or in other words that the vaccine did not also play a substantial causal role in [the children's] SMEI." *Stone I* at 48; *Hammitt I* at 50. As to that question, the special master wrote that "[t]here is simply no evidence that [either child's] initial seizure caused any brain damage, or somehow affected the expression of her genetic mutation in such a way that caused her to develop SMEI or experience further seizures." *Stone I* at 48; *Hammitt I* at 50. Dr. Kinsbourne, the special master found, "was unable to point to any evidence demonstrating that [either child's] vaccination acted as anything more than a trigger to her initial fever-induced seizure." *Stone I* at 48; *Hammitt I* at 50. He was "unable to point to any evidence that [either child's] initial febrile seizure caused her injury, which when combined with her mutation was a substantial cause of her SMEI." *Stone I* at 48; *Hammitt I* at 50. In Rachel's case, the special master stated that he found "compelling" Dr. Raymond's contrary testimony that based on the mutation in her SNC1A gene, she was "going to have [SMEI]," and that "[e]xcept for her having a seizure with fever," the DTaP vaccination "had no significant role in the development of her having [SMEI]." *Hammitt I* at 50. In Amelia's case, the special master stated that the evidence supported Dr. Raymond's opinion "that the initial fever-induced seizure was part of the

normal progression of Amelia's SMEI," which was "completely unrelated to the fact that she had an immunization that day." *Stone I* at 48-49. Accordingly, the special master concluded that in both cases the petitioners had "failed to present evidence that the vaccine-induced seizure caused injury to [the child's] brain," and that the respondent had "met the burden of proving a factor unrelated to the vaccination caused [the children's] SMEI." *Stone I* at 51; *Hammitt I* at 53.

On review in the Court of Federal Claims, both reviewing judges remanded for further findings. The reviewing judge in the *Hammitt* case concluded that the special master had not specifically stated whether the petitioners had presented a prima facie case and, if so, whether the respondent had proved that the SCN1A gene mutation was the "sole substantial factor" in causing Rachel's SMEI. *Hammitt v. Sec'y of Health & Human Servs.*, No. 07-170V (Fed. Cl. Dec. 22, 2010). The reviewing judge in the *Stone* case concluded that the special master had not made an express determination that the genetic mutation was the sole cause of Amelia's SMEI. *Stone v. Sec'y of Health & Human Servs.*, No. 04-1041V (Fed. Cl. Oct. 28, 2010).

On remand, the special master wrote supplemental opinions in which he made specific findings on the issues identified in the remand opinions. In the *Hammitt* case, the special master concluded that the petitioner had not made a prima facie case under the applicable standard, regardless of whether the evidence of the effect of the SNC1A mutation was considered in assessing the prima facie case. He also concluded that, even if the petitioner's evidence were sufficient to make out a prima facie case for compensation, the government had satisfied the requirements of the "factors unrelated" defense of section

13(a)(1)(B) of the Vaccine Act, which provides that compensation will not be awarded if the special master finds that there is "a preponderance of the evidence that the [injury] is due to factors unrelated to the administration of the vaccine." 42 U.S.C. § 300aa-13(a)(1)(B).

In the *Stone* case, the special master wrote:

> Based upon Dr. Raymond's expertise and vastly superior testimony, Dr. Kinsbourne's unfortunately very weak testimony, the presence of genetic factors that when considered cumulatively by a geneticist enable the geneticist to opine to a genetic cause, and the absence of evidence that the complex febrile seizure actually injured the brain, the undersigned is convinced beyond any doubt that respondent proved by a preponderance of the evidence that [the] SCN1A gene mutation was the sole cause and was principally responsible for [the] SMEI.

Stone v. Sec'y of Health & Human Servs. (*Stone II*), No. 04-1041V, at 4 (Fed. Cl. Spec. Mstr. Jan. 20, 2011). The special master made the same finding in the *Hammitt* case, using nearly identical language. *Hammitt v. Sec'y of Health & Human Servs.* (*Hammitt II*), No. 07-170V, at 10 (Fed. Cl. Spec. Mstr. Mar. 4, 2011). The reviewing judges of the Court of Federal Claims affirmed the special master's ruling in both cases. *Hammitt v. Sec'y of Health & Human Servs.*, No. 07-170V (Fed. Cl. June 23, 2011); *Stone v. Sec'y of Health & Human Servs.*, No. 04-1041V (Fed. Cl. May 19, 2011).

The Stones and Mr. Hammitt filed separate appeals. We consider the two appeals together because of the

substantial overlap of the evidence and issues in the two cases.

II

Both the Stones and Mr. Hammitt argue that the special master erred by failing to apply the proper causation principles when analyzing the effect of the DTaP vaccinations in causing the children's SMEI. The petitioners argue that the special master should have applied the doctrine of "superseding cause" set forth in the Second Restatement of Torts and that under that standard, they would have been entitled to compensation.

For cases involving injuries that do not fall within the Vaccine Injury Table, 42 U.S.C. § 300aa-14(a)—the so-called "off-Table" cases—the petitioner has the burden to prove causation by a preponderance of the evidence. 42 U.S.C. § 300aa-13(a)(1)(A); *Moberly v. Sec'y of Health & Human Servs.*, 592 F.3d 1315, 1321-22 (Fed. Cir. 2010); *Althen v. Sec'y of Health & Human Servs.*, 418 F.3d 1274, 1278 (Fed. Cir. 2005). To prove causation, a petitioner must show that the vaccine was "not only a but-for cause of the injury but also a substantial factor in bringing about the injury." *Shyface v. Sec'y of Health & Human Servs.*, 165 F.3d 1344, 1352-53 (Fed. Cir. 1999). We have held that the causation standard in off-Table Vaccine Act cases is to be applied consistently with the principles set forth in the Second Restatement of Torts. *Walther v. Sec'y of Health & Human Servs.*, 485 F.3d 1146, 1151 (Fed. Cir. 2007), citing *Shyface*, 165 F.3d at 1351. As noted, the statute further provides that a petitioner is not entitled to compensation if the special master or the court finds that the injury is "due to factors unrelated to the administration of the vaccine." 42 U.S.C. § 300aa-13(a)(1)(B).

As special masters have observed in this and other cases, *see, e.g.*, *Heinzelman v. Sec'y of Health & Human Servs.*, No 07-01V (Fed. Cl. Spec. Mstr. Dec. 11, 2008), interpretations of the Vaccine Act have given rise to some confusion as to the order of proof regarding causation in off-Table cases. In particular, the question has arisen whether, in assessing whether a prima facie showing of causation has been made in an off-Table case, a special master may consider evidence of other possible causes for the injury in question, or whether evidence of other possible causes may be considered only in connection with the "factors unrelated" defense on which the government has the burden of proof.

Our decisions support the commonsense proposition that evidence 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. *See, e.g.*, *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."); *Pafford v. Sec'y of Health & Human Servs.*, 451 F.3d 1352, 1358-59 (Fed. Cir. 2006) ("[T]he presence of multiple potential causative agents makes it difficult to attribute 'but for' causation to the vaccination. . . . [T]he Special Master properly introduced the presence of the other unrelated contemporaneous events as just as likely to have been the triggering event as the vaccinations."). Indeed, in some cases a sensible assessment of causation cannot be made while ignoring the elephant in the room—the presence of compelling evidence of a different cause for the injury in question. *Walther*, 485 F.3d at 1151 n.4 ("Where multiple causes act in concert to cause the injury,

proof that a particular vaccine was a substantial cause may require the petitioner to establish that the other causes did not overwhelm the causative effect of the vaccine."). Therefore, the special master is entitled to consider the record as a whole in determining causation, especially in a case involving multiple potential causes acting in concert, and no evidence should be embargoed from the special master's consideration simply because it is also relevant to another inquiry under the statute. *See Doe v. Sec'y of Health & Human Servs.*, 601 F.3d 1349, 1356-58 (Fed. Cir. 2010); *De Bazan*, 539 F.3d at 1353; *Shyface*, 165 F.2d at 1352. The two related points that our cases make clear about "factors unrelated" evidence is, first, that a special master may not require the petitioner to shoulder the burden of eliminating all possible alternative causes in order establish a prima facie case, *see Doe*, 601 F.3d at 1356-57; *Walther*, 485 F.3d at 1152, and second, that a special master may find that a factor other than a vaccine caused the injury in question only if that finding is supported by a preponderance of the evidence, *Walther*, 485 F.3d at 1151.

In both of the cases before us, the special master found that the government had satisfied its "preponderance" burden under the "factors unrelated" defense. It is therefore unnecessary for us to address whether the special master was correct in holding, in the *Hammitt* case, that the petitioner failed to make out a prima facie case of causation.

In pressing their legal theory of causation, the petitioners rely on Sections 442 and 451 of the Second Restatement of Torts. Those sections deal with the issue of when intervening events constitute "superseding causes" that have the legal effect of breaking the causal connec-

tion between a defendant's tortious act and a plaintiff's injury. Section 442 reads as follows:

> § 442. Considerations Important In Determining Whether An Intervening Force Is A Superseding Cause
>
> The following considerations are of importance in determining whether an intervening force is a superseding cause of harm to another:
>
> (a) the fact that its intervention brings about harm different in kind from that which would otherwise have resulted from the actor's negligence;
>
> (b) the fact that its operation or the consequences thereof appear after the event to be extraordinary rather than normal in view of the circumstances existing at the time of its operation;
>
> (c) the fact that the intervening force is operating independently of any situation created by the actor's negligence, or, on the other hand, is or is not a normal result of such a situation;
>
> (d) the fact that the operation of the intervening force is due to a third person's act or to his failure to act;
>
> (e) the fact that the intervening force is due to an act of a third person which is wrongful toward the other and as such subjects the third person to liability to him;
>
> (f) the degree of culpability of a wrongful act of a third person which sets the intervening force in motion.

Section 451 reads as follows:

> § 451. Extraordinary Force Of Nature Intervening To Bring About Harm Different From That Threatened By Actor's Negligence
>
> An intervening operation of a force of nature without which the other's harm would not have resulted from the actor's negligent conduct prevents the actor from being liable for the harm, if
>
> (a) the operation of the force of nature is extraordinary, and
>
> (b) the harm resulting from it is of a kind different from that the likelihood of which made the actor's conduct negligent.

The petitioners argue in both cases that the DTaP vaccinations caused the children's injuries and that the SCN1A gene mutation was not a superseding cause of their seizure disorders under the Restatement. They argue that the gene mutation cannot be considered a superseding cause because in each case the DTaP vaccination and the SCN1A gene mutation acted together to cause the SMEI and that the gene mutation brought about harm identical in kind to the harm caused by the DTaP vaccine—an increased propensity or susceptibility to seizures.

The problem with that argument is that the petitioners assume the special master determined that the SCN1A gene mutation was a "superseding cause" of the SMEI. That is not the case, however. To the contrary, the special master determined in both cases that the

SCN1A gene mutation "was the sole, substantial cause, principally responsible for [the] SMEI." *Hammitt II* at 11; *Stone II* at 4 (using substantially identical language). The special master concluded that the DTaP vaccine played no role whatsoever in either child's SMEI. *Stone I* at 48 ("There is simply no evidence that [the] initial seizure caused any brain damage, or somehow affected the expression of [the] genetic mutation in such a way that caused Amelia to develop SMEI or experience further seizures."); *Hammitt I* at 50 (using substantially identical language). Because the special master determined that the gene mutation was the sole cause of the children's SMEI, he did not engage in a superseding cause analysis, nor did he need to. The "superseding cause" analysis presupposes that the first factor was causally related to the injury; the analysis seeks to determine whether that causal relationship should be considered to have been superseded by subsequent events. That analysis has no role to play where, as here, the initial factor is found to have no causal relationship to the ultimate injury.

From their legal challenge, the petitioners move to taking issue with the special master's factual findings that the vaccines played no role in causing either child's SMEI. They contend that the special master should have found, as a factual matter, that in both cases the DTaP vaccine resulted in an increased propensity to have seizures, which made the children more vulnerable to the onset of the seizure condition associated with their SCN1A gene mutations. The problem with that argument is that the special master found that the only harm caused by the DTaP vaccination in each case was the single, isolated, initial febrile seizure, which is not by itself a compensable injury. *Hammitt I* at 53-54; *Stone I* at 52. The special master found that there was "simply no evidence that [the] initial seizure . . . caused [Amelia or

Rachel] to develop SMEI or experience further seizures." *Hammitt I* at 50; *Stone I* at 48. The seizure disorder, the special master found, was triggered by the SCN1A gene mutation alone, and the initial febrile seizures did not result in any brain injury that caused, triggered, or rendered either child more susceptible to developing SMEI. *E.g.*, *Hammitt II* at 11; *Stone II* at 4.

The petitioners' factual argument is unpersuasive in light of the applicable standard of review, which requires us to uphold the findings of the special master unless they are arbitrary or capricious. *See Porter v. Sec'y of Health & Human Servs.*, 663 F.3d 1242, 1249 (Fed. Cir. 2011). The Stones rely on Dr. Kinsbourne's assertion that Amelia suffered brain damage from the initial febrile seizures. His testimony to that effect, however, was not based on any evidence of a clinical manifestation of brain damage resulting from Amelia's initial seizure.[2] The respondent's experts testified that the medical record contains no indication of brain damage or any other continuing effect from Amelia's initial febrile seizures. The special master found the respondent's experts' testimony on that issue to be more reliable than Dr. Kinsbourne's in view of their more extensive and more recent experience in the fields of pediatric neurology and genetics. The Stones point to no clear error of fact committed by the special master, but simply contend that the special master was wrong to disregard the possibility that the initial febrile seizure had an effect on Amelia's susceptibility to seizures in the

[2] In their brief, the Stones argue that an EEG administered the day after Amelia's first seizure showed a vaccine-caused encephalopathy. The evidence, however, showed that the treating physicians characterized the results of the first EEG as "questionable," and the results of a second EEG conducted two days later were reported as normal.

future. The special master's findings on that issue were based on extensive expert evidence and cannot be regarded as arbitrary and capricious.

The Stones argue that the special master should not have credited Dr. Raymond's testimony because (1) Dr. Raymond is not an expert on the SCN1A gene, (2) Amelia's SCN1A variant is novel and unstudied, (3) Dr. Kinsbourne's testimony rebutted Dr. Raymond's theory, and (4) Dr. Raymond's theory employs circular logic. None of those arguments undermines the special master's findings that Amelia's initial febrile seizure did not have continuing effects and did not contribute to, trigger, or make her more susceptible to developing SMEI.

The special master found that Dr. Raymond was extremely well qualified to testify as to the genetic cause of Amelia's SMEI. Dr. Raymond is an associate professor in neurology at Johns Hopkins University and the director of neurogenetics at the Kennedy Kreiger Institute. Dr. Raymond's specialty is neurogenetics, and he is board certified in neurology with a special competence in both pediatric neurology and clinical genetics. Although the petitioners contend that Dr. Raymond is not an expert on the SCN1A gene, the evidence showed that Dr. Raymond is an expert in neurology and genetics. Accordingly, even though Amelia's SCN1A mutation may have been atypical, Dr. Raymond was qualified to testify about her genetic condition generally and the effect of that mutation in particular.

We reject the petitioners' contention that Dr. Raymond's theory of causation was the product of circular logic, i.e., that he reasoned backwards from the fact that Amelia has SMEI to the conclusion that her SNC1A mutation must have caused it. Dr. Raymond addressed in

some detail the reasons he concluded that the SNC1A gene mutation caused SMEI in both Amelia and Rachel. He explained that a number of factors cumulatively demonstrated that the gene mutation was responsible for both children's SMEI: (1) the gene mutation was not inherited but arose de novo, so the absence of SMEI in either parent was not probative; (2) the mutation resulted in a non-conservative amino acid change, i.e., the mutation produced a new amino acid having very different physical properties from the corresponding amino acid found in normal individuals; (3) the mutation affects a functionally important region, a portion of the sodium channel in neurons that is crucial to the normal functioning of the nervous system; (4) the mutation occurs in an area that is well conserved across species, "indicating that changes here are probably not well tolerated"; (5) there is an absence of the mutation in the normal population; (6) medical reports show that a mutation in the same location has been associated with SMEI; and (7) between 80 and 90 percent of patients with SMEI have an SCN1A gene mutation. It was those factors, not circular reasoning, that led Dr. Raymond to conclude that the SCN1A gene mutation was the cause of the SMEI in both children.

We also reject the petitioners' arguments that Dr. Kinsbourne successfully rebutted Dr. Raymond's theory and that the special master's findings should be rejected as arbitrary and capricious for that reason. The petitioners cite several medical articles that Dr. Kinsbourne discussed in his testimony and contend that those articles rebut Dr. Raymond's theory. The special master addressed each article and explained why the articles failed to support Dr. Kinsbourne's theory.

The petitioners note that Dr. Kinsbourne relied on an article by Dr. Christoph Lossin, in which Dr. Lossin wrote that he could not predict a child's clinical condition based on the child's SCN1A gene mutation. However, the special master found that "[p]etitioners simply failed to develop fully this argument." *Stone I* at 34. The special master also pointed out that Dr. Lossin is not a clinical geneticist, and that Dr. Raymond's opinion as a clinical geneticist is that a correlation can be made between a child's clinical condition and the SCN1A gene mutation. *Id.* at 34, 38-39. After considering the Lossin article, the special master credited Dr. Raymond's determination that "a reasonable clinical geneticist if presented with this information that we have in front of us today would come to the same conclusions that I have." *Id.* at 34.

The petitioners also relied on several other articles in support of the proposition that a child's clinical condition cannot be predicted based on the SCN1A gene mutation. However, the special master found that none of those articles offered persuasive rebuttal to Dr. Raymond's reasoned conclusion that Amelia's SMEI was caused by her SCN1A gene mutation. The special master observed that most of the examples of divergent conditions occurred among family members with the same mutation, presumptively an inherited variant that, because it is inherited, does not have devastating effects on the victim. The evidence showed, however, that Amelia's mutation arose de novo and was not inherited, so the evidence from persons with inherited mutations is not especially relevant. *Stone I* at 37. The special master further observed that none of the articles cited by the petitioners discussed mutations involving the amino acid change that resulted from Amelia's mutation, nor did they discuss the particular mutation in Amelia's DNA. The special master therefore concluded that the petitioners' examples were "not

comparable and thus are not persuasive rebuttal of Dr. Raymond's analysis." *Stone I* at 38. After reviewing the literature, the special master concluded that most or all of it supports Dr. Raymond's theory, and that "petitioners' allegation that Dr. Raymond's analysis is not supported by the literature or by objective evidence is simply not accurate." *Id.* at 35. The special master added:

> In addition, it cannot be overstated that petitioners' rebuttal suffered from the lack of credible expert testimony. Dr. Kinsbourne simply was not qualified or able to counter the testimony of Dr. Raymond. Petitioners thus had to rely upon cherry-picked snippets from the medical literature . . . in an effort to undermine Dr. Raymond. That effort failed.

Id.

In sum, because of Dr. Raymond's expert testimony and the considerable evidentiary support for his views in the record, we cannot conclude that the special master's conclusion that the SCN1A gene mutation was solely responsible for Amelia's SMEI was arbitrary or capricious.

III

The petitioners next argue that the special master erred by imposing an inappropriately high burden of proof on them. Specifically, they argue that the special master required direct evidence of brain damage and required them to prove the biological mechanism by which the vaccines caused the children's injuries.

The petitioners are correct that in order to prevail in a vaccine case a petitioner need not provide proof of the

specific biological mechanism leading to the injury at issue. *See Knudsen v. Sec'y of Health & Human Servs.*, 35 F.3d 543, 549 (Fed. Cir. 1994) ("[T]o require identification and proof of specific biological mechanisms would be inconsistent with the purpose and nature of the vaccine compensation program."). The special master, however, did not impose such a burden on the petitioners in these cases. He denied compensation not because the parties failed to show *how* the vaccines caused brain damage, but because they failed to show *that* the vaccines caused any brain damage.

As noted above, Dr. Kinsbourne's theory was that the vaccines contributed to the children's SMEI because they caused fevers, which triggered the initial febrile seizures, which in turn resulted in a reduced seizure threshold due to brain damage caused by the initial seizures. A key component of Dr. Kinsbourne's theory is that the initial seizure caused some form of lasting brain injury that had downstream consequences for both children, specifically a lowered seizure threshold. Accordingly, the special master sought evidence of brain damage resulting from the initial febrile seizures. However, Dr. Kinsbourne was unable to identify any evidence that either child had suffered brain damage as a result of those seizures. When the special master asked Dr. Kinsbourne if there was any clinical manifestation of the brain damage to support his inference of brain damage, Dr. Kinsbourne responded that there was not. The respondent's experts also testified that the records indicated that neither child suffered brain damage as a result of their initial seizures. With respect to both Amelia and Rachel, the special master concluded that "[t]here is simply no evidence that [the] initial seizure caused any brain damage, or somehow affected the expression of [the] genetic mutation in such a way that caused [each child] to develop SMEI or experi-

ence further seizures." *Stone I* at 48; *Hammitt* I at 50. Thus, the special master did not insist on evidence of the biological mechanism by which the brain damage was caused. He merely sought evidence of the existence of brain damage—a key component of Dr. Kinsbourne's theory—and Dr. Kinsbourne was unable to provide any.

In support of their claim that the special master required evidence of the biological mechanism by which the vaccines caused brain damage, the Stones point to the following statement in the special master's first opinion: "As discussed, Dr. Kinsbourne and petitioners failed to demonstrate how Amelia's vaccination or her fever resulting from her vaccination altered the course of her genetically based seizure disorder." *Stone I* at 49. Mr. Hammitt points to the following statement, also from the special master's first opinion: "Nor is there any cogent explanation for how an environmental trigger, specifically a vaccine, significantly contributed to Rachel's SMEI." *Hammitt I* at 51. In context, however, it is clear that those statements do not indicate that the special master required the petitioners to prove the biological mechanism of the injury. The quoted statements were made in the course of the special master's discussion of whether there was any clinical evidence of brain damage, not as a commentary on the absence of any explanation of the mechanism by which the injury may have occurred. It is clear in context that the special master sought evidence *that* brain damage existed, not *how* it was caused.

Finally, we reject the petitioners' argument that the special master improperly disregarded Dr. Kinsbourne's evidence of brain damage because that evidence was circumstantial rather than direct. The special master did not reject the petitioners' evidence of brain damage on the ground that it was circumstantial; rather, he found that

Dr. Kinsbourne's inference of brain damage, in the face of clinical records showing no brain damage, was unpersuasive and that it was therefore insufficient to carry the petitioners' burden on causation.

IV

The final issue is unique to Mr. Hammitt. After the special master's initial decision in the *Hammitt* case, which the Court of Federal Claims remanded to the special master for application of the correct standard of proof, Mr. Hammitt moved to submit additional evidence in the form of a medical journal article, a comment on the article, and a supplemental report from Dr. Kinsbourne. The special master denied the motion. Mr. Hammitt argues that the special master's refusal to supplement the record was an abuse of discretion.

The special master gave several reasons for denying Mr. Hammitt's motion. First, he noted that the case had been remanded for further explanation of the standard of proof, and, more specifically, to address whether the petitioner had presented a prima facie case for compensation and whether the burden of proof had shifted to the respondent. The case was not remanded for further factual development.

Second, the special master found that the petitioner's expert, Dr. Kinsbourne, was "aware of the article and its significance" well before the special master issued his initial opinion in the case. For that reason, the special master explained, the petitioner "had ample opportunity to move for its consideration."

Third, the special master reviewed the new article and concluded that it "does not appear to support peti-

tioner's case." The respondent filed a response to the article, in which Dr. Raymond disputed Dr. Kinsbourne's representations regarding the article and concluded that "[t]here is no evidence that has been submitted to date that any of the variability in outcomes is due to any vaccination received." Full consideration of the submitted information would require further expert testimony, the special master concluded, which likely could not be completed within the remand period.

The petitioner relies on *Vant Erve v. Secretary of Health & Human Services*, 39 Fed. Cl. 607 (1997), in support of his position that the special master abused his discretion in declining to supplement the record. In *Vant Erve*, the case was still pending before the special master in the damages phase when the respondent moved to reopen the record. *Id.* at 610. The Court of Federal Claims found that the special master abused his discretion when he denied respondent's motion, and the court therefore remanded the case to the special master, who ultimately reversed his previous decision on the merits based on the new evidence.

Vant Erve is not helpful to the petitioner. Here, the petitioner waited until after he had appealed the special master's entitlement decision and the case had been remanded on a legal issue before attempting to submit the evidence. The remand order did not contemplate the submission of new evidence, and the special master found that the "new" evidence was known and available to the petitioner prior to the special master's initial decision and could have been submitted in a timely fashion. Moreover, because it was not clear that the article would have strengthened the petitioner's case or affected the special master's decision, the petitioner has not shown that he was prejudiced by the special master's denial of the

motion. The special master therefore did not abuse his discretion by denying the petitioner's motion.

Accordingly, we affirm the judgments in both cases before us.

AFFIRMED