

IN THE UNITED STATES COURT OF FEDERAL CLAIMS

OFFICE OF SPECIAL MASTERS

CHRISTOPHER LOVING and CARLA *
LOVING, parents of Camille Loving, *

No. 02-469V
Special Master Christian J. Moran

Petitioners, *

Filed: October 6, 2008

v. *

entitlement, DTaP, significant
aggravation of infantile spasms

SECRETARY OF THE DEPARTMENT *
OF HEALTH AND HUMAN SERVICES, *

Respondent. *

William Dobreff, Esq., Dobreff & Dobreff, Warren, MI, for petitioners;
Melonie J. McCall, Esq., United States Dep't of Justice, Washington, D.C., for respondent.

PUBLISHED DECISION DENYING ENTITLEMENT*

Christopher Loving and Carla Loving claim that a diphtheria, tetanus and acellular pertussis (“DTaP”) vaccine significantly aggravated a neurological problem suffered by their daughter, Camille Loving. Before Camille received the third dose of the DTaP vaccine on March 27, 2001, she had already experienced infantile spasms. Within minutes of receiving this third dose, Camille began experiencing more infantile spasms.

* Because this published decision contains a reasoned explanation for the special master's action in this case, the special master intends to post it on the website for the United States Court of Federal Claims, in accordance with the E-Government Act of 2002, Pub. L. No. 107-347, 116 Stat. 2899, 2913 (Dec. 17, 2002).

All decisions of the special masters will be made available to the public unless they contain trade secrets or commercial or financial information that is privileged and confidential, or medical or similar information whose disclosure would clearly be an unwarranted invasion of privacy. When such a decision or designated substantive order is filed, the person submitting the information has 14 days to identify and to move to delete such information before the document’s disclosure. If the special master agrees that the identified material fits within the categories listed above, the special master shall redact such material from public access. 42 U.S.C. § 300aa-12(d)(4)(B); Vaccine Rule 18(b).

The Lovings claim that the vaccination caused worsening of Camille's problems, and, pursuant to the National Childhood Vaccine Injury Act, 42 U.S.C. §§ 300aa-1 et seq. (2006), the Lovings seeks compensation for this worsening. A preponderance of the evidence establishes that petitioners are not entitled to compensation because they have not established that the DTaP vaccine could incite an aggravation of infantile spasms in such a short amount of time.

I. Factual History

The basic facts are not disputed. Camille's date of birth is August 2, 2000. She was healthy until January 2001. Exhibit 1 at 1; exhibit 5.

In January 2001, Camille began having infantile spasms. There is no dispute about the accuracy of this diagnosis. To some degree, Camille's condition improved while she was on medication. Tr. 36-40, 456 (Dr. Shuman's testimony). She had fewer seizures. Tr. 459 (Dr. Shuman). For example, during one 23-hour EEG, Camille had one incident that was clearly a seizure. She also had other episodes, which could not be evaluated due to technical limitations of the equipment monitoring her. Exhibit 9B at 234; tr. 294, 535, 545-47. The extent of Camille's improvement and whether the improvement was permanent are disputed strenuously. See tr. 458-59 (Dr. Shuman's testimony), 548, 606 (Dr. Kohrman's testimony); Pet'r Post-Trial Br. at 9, 19, 29-32; Resp't Post-Trial Br. at 4-5, 21-22.

On March 27, 2001, Camille received the third dose of the DTaP vaccine. Within minutes of the vaccination, Camille began experiencing seizures. Exhibits 5A, 3B, 4B at 103, 10B at 237, and exhibit 29B at 345.

After the March 27, 2001 vaccination, Camille had seizures frequently. Eventually, Camille stopped having seizures – the seizures have “burned out.” Tr. 22, 179. Unfortunately, the cumulative effect of these seizures impaired Camille's development. When a hearing was held in this case, Camille's development approximately matched the level of less than a one year old, although chronologically Camille was seven years old. Tr. 241. She is unlikely to advance beyond her current condition.

II. Procedural History

The Lovings filed their petition on May 9, 2002. Attached to the petition were 25 exhibits. At this time, the Lovings acted pro se. Mr. Dobreff became counsel of record in December 2002.

The process of gathering additional medical records and obtaining an expert report took several years. The Lovings filed a report from Dr. Robert M. Shuman on December 23, 2005 and a supplemental report on January 18, 2006.

Respondent reviewed this material and filed his report pursuant to Vaccine Rule 4 on February 27, 2006. Respondent denied that the Lovings were entitled to compensation. Respondent also presented the report and curriculum vitae of Dr. Michael Kohrman. Exhibit A-B. Respondent later filed medical articles on which Dr. Kohrman relied.

A May 9, 2006 order required the Lovings to file any articles on which Dr. Shuman relied by June 9, 2006. With the anticipation that this deadline would be met, a hearing was scheduled for July 28, 2006. Order, filed May 23, 2006.

On June 26, 2006, the Lovings filed more than 50 articles on which Dr. Shuman relied. The submission of this much material so close in time to the start of the hearing prompted a rescheduling of the previously-scheduled hearing.

Pursuant to another order, the Lovings filed a supplemental report from Dr. Shuman, exhibit 90, in which he explained the significance of each article he presented in June. This supplemental report permitted a hearing to be scheduled on November 17, 2006, in Chicago, Illinois. Both parties filed additional material shortly before and during this hearing.

During this hearing, Dr. Shuman testified. However, he did not complete his testimony. His testimony could not be completed, in part, because he presented more material just before the hearing that respondent was not prepared to address. After Dr. Shuman stopped testifying, Dr. Kohrman responded to a portion of Dr. Shuman's testimony. Then, the hearing was suspended.

Following the first session of the hearing, the Lovings filed another supplemental report from Dr. Shuman. Exhibit 90. Respondent then filed a supplemental report from Dr. Kohrman. Exhibit J. With this record, another hearing was held. This one was held on November 14, 2007, approximately one year after the first hearing. During the second hearing, both Dr. Shuman and Dr. Kohrman completed their oral testimony.

The parties were given an opportunity to settle this case and also to file post trial briefs. After the parties submitted briefs after the hearing, the undersigned filed, as exhibit 401, an additional medical article, which had been discussed during the hearing. The parties were given an opportunity to comment upon this article. Order, filed July 29, 2008. Despite this opportunity neither party did so within the time permitted. Thus, the case is ready for adjudication.

III. Analysis

Camille's infantile spasms began in January 2001, before she received the third dose of the DTaP vaccine. Infantile spasms are not listed on the Vaccine injury table. See 42 C.F.R. § 100.3 (2008). Thus, the Lovings cannot take advantage of any presumptions regarding causation established by the Vaccine Act or its corresponding regulations. Thus, Camille's claim alleges significant aggravation of an off-table injury. See Pet'r Post Hearing Br. at 18.

Cases in which petitioners claim significant aggravation of an off-table condition are rare. No appellate court has established the elements for this type of case. See DeRoche v. Sec’y of Health and Human Servs., Fed. Cl. 97-643V, 2002 WL 603087 * 33 (Spec. Mstr. Mar. 28, 2002) (stating “off-Table significant aggravation law is largely uncharted territory.”).¹

Pursuant to the Federal Circuit’s instruction in Althen, a petitioner seeking compensation in a non-table case bears the burden of establishing:

that the vaccination brought about [the] injury by providing: (1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of a proximate temporal relationship between vaccination and injury.

Althen v. Sec’y of Health and Human Servs., 418 F.3d 1274, 1278 (Fed. Cir. 2005). Although the petitioner in Althen sought compensation pursuant to a cause-in-fact theory, the Federal Circuit’s analysis can be transferred to cases, like the Lovings’ case, in which petitioners claim “significant aggravation,” rather than an “injury.”

In all respects, proof of medical certainty is not required; a preponderance of the evidence suffices. Bunting v. Sec’y of Health and Human Servs., 931 F.2d 867, 873 (Fed. Cir. 1991).

In this case, the decisive element is the timing. The Lovings do not challenge the legal proposition that they bear the burden of showing the appropriate temporal relationship between the vaccination and the aggravation of Camille’s infantile spasms. In both their initial brief and in their reply brief, they argue that the evidence supports a finding that they satisfied the appropriate temporal relationship. They do not argue that examining the temporal relationship is wrong as a matter of law. Pet’r Post-Trial Br. at 43; Pet’r Post-Trial Reply at 28.

The Lovings allege that the amount of time between Camille’s receipt of the third DTaP vaccine and the resumption of her seizures is appropriate. However, a preponderance of the evidence demonstrates that the Lovings’ allegation is not persuasive. Therefore, they are not entitled to compensation.

¹ The Lovings observe that the Chief Special Master decided DeRoche before the Federal Circuit decided Althen. Pet’r Reply at 22. However, the Lovings do not propose a legal test to evaluate off-Table significant aggravation claims.

A. A Showing of a Proximate Temporal Relationship Between Vaccination and Aggravation

1. Factual Predicate

The Lovings claim that after Camille received her vaccination, she had a seizure within approximately five minutes. The primary piece of evidence supporting this assertion is Mrs. Loving's journal. An entry for March 27, 2001, states "About 2 mins after shots as I picked her up + dressed her Camille began to make a head dropping gesture that was very similar to a weakened spasm. She did this 5-6 times + then stopped." Exhibit 29 at 345.

Mrs. Loving's journal entry is supported by the history obtained by Camille's pediatric neurologist, Dr. Chugani. On April 10, 2001 (or approximately two weeks after the vaccinations), Camille saw Dr. Chugani. He recorded "when she went to get her six months shots, within minutes of getting the shots, actually within five minutes, she started having clusters of infantile spasms again." Exhibit 11 at 241.

These entries establish, by a preponderance of the evidence, that Camille had a weakened spasm approximately five minutes after receiving the vaccination. See Curcuras v. Sec'y of Health & Human Servs., 993 F.2d 1525, 1528 (Fed. Cir. 1993). Respondent does not challenge this point. Tr. 470 (statement of respondent's counsel); 597-98 (cross-examination of Dr. Kohrman).²

2. Parties' Positions

Although the parties accept the statement that Camille had a spasm within approximately five minutes of the vaccination, the parties differ on the significance of this timing. Dr. Shuman opines that this timing is appropriate. Tr. 449. In contrast, Dr. Kohrman believes that Camille's reaction occurred too quickly to be connected to the vaccine. Tr. 531.

Dr. Shuman proposes a biological explanation for how the vaccine could have caused a resumption in infantile spasms in approximately five minutes. Dr. Shuman believes that Camille had a toxic reaction as opposed to an immune-mediated reaction.³ Certain substances in the

² However, it is odd that the office notes from the pediatrician do not indicate anything about Camille having a seizure. Exhibit 10(b) at 237; tr. 668. Mrs. Loving's journal says that a nurse in the pediatrician's office may have seen the last of the spasms. Exhibit 29 at 345.

³ A fair number of claims in the Vaccine Program are based upon a theory that the recipient's immune system has functioned in an unexpected way. For example, some vaccines are alleged to cause acute disseminated encephalomyelitis (ADEM). Because the immune system is believed to be involved in the development of ADEM, the timing between the vaccination and the onset of problems is expected to be longer than the proposed timing in the

body, known as cytokines, can be activated in only seconds. These cytokines can travel through the blood stream to the brain, where they can cross the blood-brain barrier. Once in the brain, the cytokines permit the development of seizures. Tr. 328-36.

Dr. Shuman also contends that various articles support his explanation. According to Dr. Shuman, the facts as outlined in various reports of cases are consistent with his opinion that the DTaP vaccination can cause a resumption in infantile spasms within approximately five minutes. E.g., tr. 489.

As noted, Dr. Kohrman disagrees with Dr. Shuman's opinion about the temporal relationship. Dr. Kohrman states that a reaction based upon activation of cytokines did not take place because the activation of cytokines necessarily produces a systemic response. Because Camille displayed no evidence of a systemic response, her cytokines were not activated. See tr. 562.

Dr. Kohrman also interprets the literature much differently. Dr. Kohrman argues that any potential response to the pertussis vaccine discussed in the literature occurred in a much longer period of time than five minutes. See tr. 564.

3. Analysis

a. Comparison of the Two Experts

As a preliminary matter, it must be noted that both Dr. Shuman and Dr. Kohrman are well qualified to opine about the appropriate temporal relationship. Each has practiced in the field of pediatric neurology for more than 20 years. Both have written articles that were published in the peer-reviewed journals. Tr. 13-20 (Dr. Shuman's background); exhibit 102 (Dr. Shuman's curriculum vitae) & exhibit B (Dr. Kohrman curriculum vitae).

Additionally, both Dr. Shuman and Dr. Kohrman appeared sincere when they testified. Each seemed to believe genuinely in the validity of the position each was asserting.

Consequently, this case cannot be resolved by looking at the two experts. Neither their appearance on paper (as reflected in their curriculum vitae) nor their appearance at the hearing differentiate Dr. Shuman and Dr. Kohrman in any meaningful sense.

b. Evaluation of the Literature

To determine which expert is more persuasive, the literature on which the expert relied will be considered. On a whole, the literature fails to establish, by a preponderance of the

present case. See tr. 262, 471-72.

evidence, that vaccinations can cause infantile spasms, regardless of whether the infantile spasms are new or a resumption of previously experienced spasms, within five minutes.

An expert is not required to cite any literature supporting his or her theory. Althen v. Sec’y of Health & Human Servs., 418 F.3d 1274, 1281 (Fed. Cir. 2005). However, medical articles may be considered in evaluating an expert’s opinion. Daubert v. Merrell Dow Pharmaceuticals, Inc., 509 U.S. 579, 593-94 (1993); Merck & Co., Inc. v. Teva Pharmaceuticals USA, Inc., 395 F.3d 1364, 1374 (Fed. Cir. 2005); Terran v. Sec’y of Health & Human Servs., 195 F.3d 1302, 1316 (Fed. Cir. 1999) (affirming special master’s use of Daubert in vaccine program cases); Libas v. United States, 193 F.3d 1361, 1366-67 (Fed. Cir. 1999); see also Knight v. Kirby Inland Marine Inc., 482 F.3d 347, 354 (5th Cir. 2007) (stating a lack of textual support may “go to the weight, not the admissibility” of the expert’s testimony); Waleryszak v. Sec’y of Health & Human Servs., 45 Fed. Cl. 573, 578-79 (1999), appeal dismissed, 250 F.3d 753 (Fed. Cir. 2000).

Evaluation of medical articles to determine the appropriate interval of time between the vaccination and onset of symptoms is particularly relevant here. Otherwise, “the vaccination might receive blame for events that occur weeks, months, or years outside of the time in which scientific or epidemiological evidence would expect an onset of harm.” Pafford v. Sec’y of Health & Human Servs., 451 F.3d 1352, 1358 (Fed. Cir. 2006) (emphasis added).

In the context of timing, the experts discussed several articles. These are analyzed below.⁴

(1) Institute of Medicine

Frequently, the Lovings cite a study by the Institute of Medicine (IOM). Tr. 323, 508, 635-37 (cross-examination of Dr. Kohrman). Reports from the IOM are favored, although not dispositive, in the Vaccine Program. Cucuras v. Sec’y of Health & Human Servs., 993 F.2d 1525, 1529 (1993) (finding that special master did not abuse his discretion in determining that a 1991 IOM report was entitled to great weight); Cohen v. Sec’y of Health & Human Servs., Fed. Cl. 94-353V, 1998 WL 408784 *8 (Spec. Mstr. July 1, 1998).

The 1991 IOM report, which is the same report discussed in Cucuras, analyzed whether the pertussis vaccine can cause infantile spasms. The IOM’s ultimate conclusion was that “[t]he evidence does not indicate a causal relation between DPT vaccine or the pertussis component of

⁴ The articles discussed below report on cases involving the whole cell pertussis vaccine. Camille, however, received the acellular pertussis vaccine. The acellular pertussis vaccine is a cleaner and safer vaccine. Tr. 269, 489. The analysis assumes that if the whole cell pertussis vaccine were reported to cause a significant aggravation of infantile spasms in five minutes, then the acellular pertussis vaccine could do so also. See tr. 396-98 (respondent acknowledges that the risk of developing an adverse reaction to the acellular pertussis vaccine is not zero).

DPT and infantile spasms.” Exhibit D (Comm. to Review the Adverse Consequence of Pertussis and Rubella Vaccines, Institute of Medicine, Adverse Effects of Pertussis and Rubella Vaccines (Christopher P. Howson et al., eds. 1991)) at 77. Although Dr. Shuman disputes this conclusion, Dr. Shuman cites to part of the IOM’s analysis in which it states that “[t]he time intervals reported between vaccination and the onset of infantile spasms have been from minutes to weeks.” Id. at 67. The sole authority cited for this interval is the 1971 study by Melchior. (The IOM also cites other studies about pertussis vaccine being associated with infantile spasms. Some of these are discussed below.)

(2) Melchior 1971

The undersigned obtained the 1971 Melchior study and filed it as exhibit 401. Order, filed July 29, 2008. This study does not support a finding that the DTaP vaccine can cause a resumption of infantile spasms within five minutes.

This article examines whether immunizations are related to infantile spasms. Dr. Melchior states that the data he analyzed does not allow any firm conclusion to be drawn. Exhibit 401 (Johannes C. Melchior, Infantile Spasms and Immunisations in the First Year of Life, 3(1) Neuropädiatriae 3 (1971)) at 6.

The data consisted of a review of eight articles, summarized at table II of the article. The shortest amount of time reported between a vaccination and the possible onset of infantile spasms was 20 minutes in the Byers and Moll study. Id. at 5. Dr. Melchior summarized his analysis as showing that the data shows a time interval “from hours to a few days.” Id. at 6.

(3) Byers and Moll 1948

An episode showing the shortest interval between vaccination and the possible onset (or aggravation) of infantile spasms is contained in the article by Byers and Moll. The Lovings filed this article as exhibit 135 during the hearing. Tr. 529. Dr. Shuman’s February 21, 2007 supplemental report contains a summary of the cases reported by Byers and Moll. Exhibit 117 at 1430;⁵ see also tr. 386 (describing chart). (Dr. Shuman reproduced this chart as exhibit 126.) The fifth case reported by Byers and Molls has the shortest amount of time between a vaccination and the possible onset (or aggravation) of infantile spasms. Exhibit 117 at 1430; see also tr. 491-93. But, as reported by Byers and Moll, this incident does not support an opinion that a vaccination can cause the onset of (or aggravation of) infantile spasms within approximately five minutes.

⁵ The Lovings had originally submitted Dr. Shuman’s supplemental report as exhibit 101. However, the Lovings overlooked that they previously submitted other material as exhibit 101. Therefore, Dr. Shuman’s supplemental report was assigned the label exhibit 117. Order, filed March 19, 2007.

Dr. Byers and Dr. Moll wrote in 1948, and they stated that they were the first to report about “severe encephalopathies which have been observed following the prophylactic use of pertussis vaccine in infants.” Exhibit 135 (Randolph K. Byers and Frederic C. Moll, Encephalopathies Following Prophylactic Pertussis Vaccine, 1(4) *Pediatrics* 437 (1948)) at 437. In the general medical usage of 1948, the term “encephalopathy” means “any disease of the brain.” Stedman’s Practical Medical Dictionary (16th Rev. Ed. 1946) at 360. Today, it has essentially the same meaning – “any degenerative disease of the brain.” Dorland’s Illustrated Medical Dictionary (30th ed. 2002) at 610.⁶

This definition of “encephalopathy” captures many conditions, not just infantile spasms. Infantile spasms are just one type of degenerative disease of the brain. Another type is ADEM.

The fifth case reported by Byers and Moll appears not to be a case involving infantile spasms. Byers and Moll reported that an 18-month-old boy “[a]bout 10 to 20 minutes [after receiving the first pertussis vaccination] became drowsy, then unresponsive, rigid and febrile.” Exhibit 135 (Byers and Moll) at 447. The authors did not report that the boy had a seizure and the authors did not report that the child had infantile spasms. Tr. 639-41 (testimony of Dr. Kohrman).

It is more likely than not that the fifth case does not describe an episode of infantile spasms. Infantile spasms are characterized by myoclonic seizures, which are specific movements such as jackknifing. Tr. 24-26. By way of contrast, the subject of Byers and Moll’s fifth case became “drowsy,” which suggests a depressed neurological system. In addition, infantile spasms usually lead to developmental delay. The child in Byers and Moll’s was “fairly competent,” although that analysis was only one month after the initial episode. Exhibit 135 at 447. Thus, a preponderance of the evidence indicates that the child did not have infantile spasms.

Because the child in the report suffered from a condition other than infantile spasms, the report from the fifth case of Byers and Moll’s does not provide information helpful to establishing the minimum amount of time necessary from a vaccination to the onset (or significant aggravation) of infantile spasms. See Pafford, 451 F.3d at 1359 (Fed. Cir. 2006) (affirming special master’s determination that evidence about the temporal relationship for arthralgias in general does not show the temporal relationship for a specific disease).

Byers and Moll also report about other episodes in which the pertussis vaccination may have caused an encephalopathy. However, a detailed review of these other incidents are not necessary because the reported time in those reports is not similar to the time reported in the

⁶ In the table of injuries presumed to be caused by certain vaccines, “encephalopathy” has a more specific meaning. National Vaccine Injury Compensation Program Revision of the Vaccine Injury Table, 60 Fed. Reg. 7678, 7686-88, 7694-95 (Feb. 8, 1995) (codified at 42 C.F.R. § 100.3(b)(2)). The regulatory definition of encephalopathy does not affect the discussion in the text.

incident involving Camille. Other than the fifth reported case, the minimum amount of time in the reported cases is one hour, which is for the second and tenth cases. Exhibit 135 (Byers and Moll) at 439, 444, 452. For purposes of determining whether the interval between vaccination and onset (or aggravation) of symptoms is appropriate, one hour is a much different amount of time from five minutes. In addition, the second and tenth cases appear not to be cases of infantile spasms.

(4) Other Articles

Although they submitted many other articles, the Lovings primarily use the 1991 IOM report, which cited the 1971 Melchior article, and the Byers and Moll article to establish that the temporal relationship is appropriate for Camille's case. The Lovings' briefs do not cite to other articles to support their assertion that five minutes is an appropriate time frame. See Pet'r Post Hearing Br. at 43; Pet'r Post Hearing Reply at 28 & 38-41.

These other articles submitted by the Lovings do not contain examples of situations in which a vaccine was associated with the onset (or significant aggravation) of infantile spasms in an amount of time comparable to five minutes. See tr. 595 (Dr. Kohrman's testimony). Therefore, these other articles do not assist the Lovings in establishing the proposition that it is more likely than not that the DTaP vaccine can cause an aggravation of infantile spasms within approximately five minutes. See Order, filed June 30, 2006 (requiring Dr. Shuman to address literature in his testimony); tr. 9-10 (reminding parties to discuss pertinent literature); see also Guillory v. United States, 59 Fed. Cl. 121, 126 (Fed. Cl. 2003) (stating that "The court is not aware of, and petitioner does not cite to, any requirement that the special master must reference in his decision each item of evidence presented during the proceedings before the special master.")

Dr. Shuman has performed a diligent search of the literature, submitting articles that date as far back as the Byers and Moll study in 1948. Few articles are relatively recent. One reason for the lack of fairly recent articles is that as medical science has learned that vaccines can cause adverse reaction, a standard of practice has developed not to administer an additional dose of a vaccine when an earlier dose of that vaccine may have caused an adverse reaction. This standard of practice is based upon the principle of ethical medicine "First do no harm." Tr. 62. It is also reflected in the warnings (or contraindications) given with the vaccines. Tr. 54, 57-58, 64, 659. (The manufacturer's contraindications, however, are not the same as saying that a causal relationship has been established. Tr. 203.) Refraining from re-vaccinating people who may have experienced an adverse reaction limits the pool of people who could experience a significant aggravation of an underlying disorder. Tr. 94.

It is possible that if the people who were at risk of experiencing a significant aggravation of an underlying problem received the pertussis vaccine, then someone else may have experienced a significant aggravation within approximately five minutes and that this case would have been reported in the medical literature. However, this possibility is entirely speculative.

The collection of medical articles in this case (and the Lovings filed more than 90 articles) does not establish the reliability of Dr. Shuman's theory that the acellular pertussis vaccine can cause a resumption of infantile spasms within five minutes.

Consequently, because the line of evidence based on medical articles is not persuasive, the Lovings' other supporting information will be considered. This alternative approach is based on the biological mechanism.

c. Biological Mechanism

Dr. Shuman attempts to ground his opinion that five minutes is an appropriate amount of time for the resumption of infantile spasms for Camille on more than just medical articles. Dr. Shuman also proposes a biological mechanism to explain how the acellular pertussis vaccine could cause Camille to resume having seizures within five minutes. However, a preponderance of evidence does not support Dr. Shuman's opinion.

Preliminarily, it must be pointed out that the Lovings are not required to establish the "specific biological mechanism[]." Knudsen v. Sec'y of Health & Human Servs., 35 F.3d 543, 549 (Fed. Cir. 1994). However, perhaps in an attempt to make Dr. Shuman's opinion more persuasive, the Lovings elicited testimony from Dr. Shuman to explain how the acellular pertussis vaccine can cause infantile spasms within approximately five minutes. See tr. 329-41. Consequently, this evidence must be considered. 42 U.S.C. § 300aa-13 (requiring special masters to evaluate the record "as a whole").

Dr. Shuman proposes this explanation for what happened after the DTaP vaccine was injected into Camille's deltoid muscle. The DTaP vaccine contained some amount of endotoxin and other components that could, in some dose, have a toxic effect. Tr. 354. Some (or all) of the vaccine is picked up and transported within the circulatory system to the brain. Tr. 470. The circulatory system moves blood throughout the body in approximately one minute. Tr. 329 (testimony of Dr. Shuman) discussing exhibit 129; tr. 646-57 (testimony of Dr. Kohrman) Once in the brain, the endotoxin crosses the blood brain barrier. Tr. 472-73, see also tr. 260 (testimony of Dr. Kohrman describing blood brain barrier), tr. 331-32 (testimony of Dr. Shuman describing blood brain barrier).⁷

According to Dr. Shuman, the presence of endotoxin and other components of the acellular pertussis vaccine caused Camille to activate substances known as cytokines. Tr. 334. Cytokines can be activated within seconds of the body's encountering a foreign substance. Tr. 474-75. The cytokines can travel to the brain and once in the brain, the cytokines permit the development of seizures. Tr. 328-36.

⁷ Camille's previous infantile spasms may have weakened the barrier between her circulatory system and her brain. Tr. 336; but see tr. 649.

Two problems with Dr. Shuman's proposed biological mechanism prevent it from being persuasive. One problem is based on the facts of this case and, therefore, a more powerful criticism. The other problem is more theoretical.

The stronger criticism is that the activation of cytokines causes other generalized effects, such as redness at the injection site or a fever. Tr. 70, 563. Dr. Shuman agreed that the production of cytokines is associated with a "systemic, that is, generalized" reaction. Tr. 669. However, Camille did not display any signs of a systemic reaction after her vaccination. Exhibit 29 at 345 (Camille's mother's journal); exhibit 11 at 241 (report of Dr. Chugani); see also tr. 584 (testimony of Dr. Kohrman), 669 (testimony of Dr. Shuman). Thus, it follows that because she did not have a systemic reaction, she did not activate a large enough quantity of cytokines that would have been associated with some components of the acellular pertussis vaccine permeating her brain.

When Dr. Shuman was asked about this point during the rebuttal phase of the case, Dr. Shuman's response was not persuasive. As Dr. Shuman recognized, his explanation was not based upon any experimental data. Tr. 669-70. Consequently, the failure of Camille to express a systemic reaction precludes a finding that she produced an abundance of cytokines after the DTaP vaccination.

Additionally, there is some question about how quickly components of the DTaP vaccine enter the circulatory system. Dr. Kohrman maintained that parts of the DTaP vaccine, such as endotoxin, could not have reached Camille's brain as quickly as Dr. Shuman proposes. Tr. 243, 260-61. Dr. Kohrman explained that the vaccine also contains an adjuvant, a chemical that keeps the vaccine in place in the body to allow the body to respond to it. Thus, the adjuvant will slow the dispersion of the vaccine into the circulatory system. Tr. 562. This delay would prevent Camille from having a seizure within five minutes of receiving the DTaP vaccine.

Dr. Shuman disagrees with Dr. Kohrman. Dr. Shuman believes that although the adjuvant may increase the amount of time before the vaccine is taken up by the circulatory system, the first portion of the vaccine to be absorbed is the endotoxin because this is a relatively small molecule. Tr. 481-82.

Resolving this particular dispute is not necessary. Even if the theory that the endotoxin disperses more quickly than other parts of the acellular pertussis vaccine were reliable, there has not been a showing that the endotoxin caused Camille to activate the cytokines. Thus, the different contentions about the release of endotoxin are theoretical. In addition, neither Dr. Shuman nor Dr. Kohrman appears to have a specific background in immunology. Thus, opinions about the processes of the immune system may be beyond their expertise.

In sum, the Lovings have not established persuasively a mechanism that explains how the acellular pertussis vaccine could have caused Camille to have an infantile spasm within five minutes of receiving the vaccine. This failure, combined with the Lovings' failure to present any

medical articles supporting Dr. Shuman's opinion regarding timing, means that the Lovings have failed to meet their burden of establishing, by a preponderance of the evidence, the appropriate time interval.

When the evidence demonstrates that an alleged adverse reaction happened too close in time to the vaccination to be medically appropriate, petitioners are not entitled to compensation. Bazan v. Sec'y of Health & Human Servs., No. 2008-5013, 2008 WL 3927499 *3 (Fed. Cir. Aug. 28, 2008).

B. Additional Elements

As explained above, the Lovings failed to establish that the return of Camille's infantile spasms happened at a time that was medically appropriate following the vaccine. Thus, they are not entitled to compensation. Bazan, Pafford v. Sec'y of Health & Human Servs., 451 F.3d 1352, 1358-59 (Fed. Cir. 2006).

Consequently, evaluating the other elements of the Lovings' case is not necessary. A great amount of the evidence, including both medical articles filed as exhibits and testimony from both Dr. Shuman and Dr. Kohrman, concerned whether Dr. Shuman's theory that the acellular pertussis can significantly aggravate infantile spasms is reliable. No determination is being made on this point.

Additionally, it is not decided whether Camille's status after the vaccination reflects the natural course of infantile spasms. Dr. Shuman believes that Camille's improvement on Sabril indicated that it was most likely that she would continue to improve. Dr. Shuman, however, could not predict that Camille would develop normally even if she had not received the vaccine, which Dr. Shuman believes caused her deterioration. In contrast, Dr. Kohrman believes that Camille's infantile spasms were not well-controlled before the vaccination. This lack of control indicated that Camille was not likely to regain normal development.

Both issues (whether DTaP can significantly aggravate infantile spasms and the extent to which Camille would have improved) are extremely difficult to decide. Both parties' presentations were strong. However, because Camille's case is being resolved based upon her failure to prove one element, the necessary temporal relationship, these other elements are not addressed.

IV. Conclusion

The Lovings have not established all the elements of their case. Therefore, they are not entitled to compensation. The Clerk's Office is ordered to enter judgment in accord with this opinion unless a motion for review is filed.

IT IS SO ORDERED.

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