

IN THE UNITED STATES COURT OF FEDERAL CLAIMS

OFFICE OF SPECIAL MASTERS

LOUIS TOSCHES, III, a minor, by and through his parent and natural guardian, LOUIS TOSCHES, II, Petitioner,

No. 06-192 Special Master Christian J. Moran

v.

SECRETARY OF HEALTH AND HUMAN SERVICES, Respondent.

Filed: January 31, 2008 Failure to prove entitlement; DTaP; opsoclonus-myoclonus syndrome; fourth dose of vaccination

Ronald C. Homer, Esq. and Sylvia Chin-Caplan, Esq., Conway, Homer & Chin-Caplan, P.C., Boston, Massachusetts for petitioner; Nathaniel J. McGovern, Esq., United States Department of Justice, Washington, D.C. for respondent.

PUBLISHED DECISION*

Louis Tosches II, on behalf of his son Louis III ("Lou"), filed a petition seeking compensation under the National Vaccine Injury Compensation Program ("the Program"), 42 U.S.C. §§ 300aa-1 et seq. Mr. Tosches alleged that the Diphtheria-Tetanus-acellular Pertussis vaccine ("DTaP"), which Lou received on March 19, 2003, caused him to suffer opsoclonus-myoclonus syndrome ("OMS"). Amended Petition ("Am. Pet.").

* 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 United States Court of Federal Claims's website, in accordance with the E-Government Act of 2002, Pub. L. No. 107-347, 116 Stat. 2899, 2913 (Dec. 17, 2002).

Vaccine Rule 18(b) states that 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, petitioner has 14 days to identify and to move to delete such information before the document's disclosure. If the special master, upon review, agrees that the identified material fits within the banned categories listed above, the special master shall delete such material from public access.

The evidence demonstrates that Mr. Tosches is not entitled to compensation. The Clerk's Office is ordered to enter judgment in favor of respondent if no motion for review is filed within 30 days.

I. Facts

The parties do not dispute the basic chronology, which is set forth in medical records created contemporaneously with the events being described. Instead of disputing what happened, the parties and their experts draw different conclusions from those facts. Thus, an outline of the facts is provided to provide context for the different opinions for the experts.

Lou was born on September 19, 2001. Exhibit 3 at 17. He was healthy, only experiencing normal childhood diseases, until about March 19, 2003. See exhibit 4 (records of Main Street Pediatrics). In his report filed pursuant to Vaccine Rule 4, respondent does not argue that any condition existing before January 2003 caused Lou to suffer cerebral ataxia. Respondent, however, does contend that a viral illness is a more likely cause for the cerebral ataxia. Resp't Rep't at 15.

Respondent's argument about a virus derives from various medical records. First, in January 2003, Lou suffered from otitis media. Otitis media is an inflammation of the middle ear. Dorland's Illustrated Medical Dictionary (30th ed. 2003) at 1339. He was also diagnosed with a viral infection of his upper respiratory tract. Exhibit 4 at 32.

Second, in February 2003, Lou's pediatrician, Dr. Dawn Audi, diagnosed another upper respiratory infection. For this visit, Lou had returned to the pediatrician's office because he was fussy, had a runny nose, had a fever of 103°, was pulling at his ears, and had one episode of vomiting. Exhibit 4 at 34.

Around March 4, 2003, Lou began staying up during the night "screeching." Around March 14, 2003, Lou began having diarrhea. During the next few days, his parents switched to a lactose-free diet and the diarrhea improved but did not disappear. Exhibit 4 at 35; see also tr. 18-19, 39, 137.

On March 19, 2003, Dr. Audi saw Lou for his 18-month check up. During this visit, Lou received his fourth dose of the DTaP vaccine. Exhibit 4 at 2. (Lou also received his third dose of the inactivated polio vaccine and the fourth dose of the hemophilus influenzae type B vaccine. However, the petitioner does not allege that either of these vaccinations caused Lou's cerebral ataxia. Pet'r Posthearing Br. filed Oct. 23, 2007, at 1.)

During this check up, Dr. Audi assessed Lou's development as within the normal range. Lou's abilities included speaking 30 words, following directions, using a spoon and fork, running and climbing. Exhibit 4 at 35.

The night after his 18 month check up, Lou was irritable and had a low-grade fever. Exhibit 11 (affidavit of Louis Tosches, II, dated March 23, 2006) ¶ 2. Lou also had nasal congestion. These problems persisted until March 24, 2003, when Lou saw Dr. Audi again five days after his vaccinations. Dr. Audi diagnosed conjunctivitis and otitis media and prescribed an antibiotic.

On March 29, 2003, ten days after vaccination, Lou began to display clumsiness. He was falling and his hand trembled at least once that an adult observed. A few days later, Lou woke with his head tilted to the left. Since his head remained tilted, Lou's parents brought him to Dr. Audi again. Exhibit 11 ¶ 4.

On April 4, 2003, Dr. Audi recorded a history from the parents consistent with the preceding paragraph. Dr. Audi noted that his otitis media resolved and that he was negative for an upper respiratory infection. Dr. Audi scheduled an MRI. Exhibit 4 at 38.

Events after this date do not need to be stated in detail because they have little effect, if any, on the question of whether the March 19, 2003 vaccinations caused Lou to develop problems. It is sufficient to say that Lou's neurologic system deteriorated. After a slow progression of symptoms, Lou's treating doctors diagnosed him with opsoclonus-myoclonus syndrome. Exhibit 7 at 3 (report of Dr. Michael Pranzatelli, dated January 14, 2004). The neurologists retained by the parties in this case agree with the diagnosis of OMS.

OMS is a rare neurologic disorder. It is "a syndrome of movements of the eye (opsoclonus) and trunk (myoclonus), occurring in conjunction with a number of conditions." Dorland's at 1827. Doctors have not identified the cause of OMS. About one-half the cases are associated with a neuroblastoma, which is a type of tumor. About one-half the cases are associated with an infection, usually a viral infection. A small number of cases, perhaps one percent, are not preceded by either an identified neuroblastoma or an identified infection. OMS usually appears between ages of nine months and two years. Tr. 9-11, 20.

For purposes of determining whether the vaccinations caused Lou's OMS, remarks of two treating physicians are notable. Dr. Lori Jordan, a neurologist at Johns Hopkins Hospital, noted that two weeks before his Lou's problems were noticed, he received a set of vaccinations. Exhibit 6 at 52 (report, dated April 15, 2003).

Similarly, Dr. Michael Pranzatelli recounted the history that Lou's neurologic problems began after Lou received the DTaP vaccine. Exhibit 7 at 3 (report, dated January 14, 2004).

Presently, Lou suffers from developmental delay. Exhibit 11 at 5. The parties agree that Lou's developmental delay was caused by the OMS. Exhibit 17 at 5-6 (report of Marcel Kinsbourne, neurologist); Exhibit C (supplemental report of John MacDonald, neurologist).

Thus, the question is whether Mr. Tosches has met his burden of establishing that the fourth DTaP vaccination caused Lou's OMS. To establish this point, Mr. Tosches presented the opinion testimony of Dr. Marcel Kinsbourne, a neurologist. Respondent, in turn, presented the opinion testimony of Dr. Christine McCusker, an immunologist, and Dr. John MacDonald, a pediatric neurologist. All three doctors testified, in person, at a hearing on February 12, 2007. Both parties submitted medical literature.

After the initial hearing, Mr. Tosches requested an opportunity to challenge the testimony of Dr. McCusker. Because of the importance of Dr. McCusker's opinion, Mr. Tosches was allowed to present additional evidence. Mr. Tosches presented an opinion from Dr. Vera Byers and several medical articles. Both Dr. Byers and Dr. McCusker testified at a second hearing on July 23, 2007.

Each party submitted a post trial brief. Respondent was ordered to submit a supplemental brief to which no response was required. Thus, the matter is ready for adjudication.

II. Analysis

A. Introduction

1. Summary Of Expert Opinions

To receive compensation for Lou's condition under the Program, Mr. Tosches must prove either: (1) that Lou suffered a "Table Injury"--*i.e.*, an injury falling within the Vaccine Injury Table – corresponding to one of his vaccinations, or (2) that Lou suffered an injury that was actually caused by a vaccine. See 42 U.S.C. §§ 300aa-13(a)(1)(A) and 300aa-11(c)(1); Capizzano v. Sec'y of Health and Human Servs., 440 F.3d 1317, 1320 (Fed. Cir. 2006). Here, Mr. Tosches does not claim that Lou suffered a table injury. Pet'r Posthearing Br. filed Oct. 23, 2007, at 23. Thus, he must prove causation in fact.

A petitioner may not be given a Program award based solely on the petitioner's claims alone. Rather, the petition must be supported by either medical records or by the opinion of a competent physician. 42 U.S.C. § 300aa-13(a)(1). In determining whether a petitioner is entitled to compensation, the special master shall consider all material contained in the record. 42 U.S.C. § 300aa-13(b)(1). This universe necessarily includes "any . . . conclusion, [or] medical judgment . . . which is contained in the record regarding . . . causation . . . of the petitioner's illness." 42 U.S.C. § 300aa-13(b)(1)(A). Here, because the medical records do not seem to support Mr. Tosches's claim, a medical opinion must be offered in support of the claim. Mr. Tosches, consequently, has offered the opinion of Dr. Kinsbourne, as supplemented by Dr. Byers.

Dr. Kinsbourne believes that the fourth DTaP vaccine substantially contributed to Lou's contraction of OMS. However, Dr. Kinsbourne does not disregard the effect of a possible virus.

Dr. Kinsbourne believes that even if Lou had a virus, the virus and the vaccine acted together to cause the OMS. Tr. 21-22; exhibit 17 at 5.

To respond to Dr. McCusker, Mr. Tosches also presented Dr. Byers, an immunologist. The scope of her opinion was relatively narrow: whether it was possible to react adversely to the fourth dose of a vaccine if the first three doses of that vaccine did not produce an adverse reaction. Dr. Byers believes this is possible due a phenomenon known as “epitope spreading,” which is described in more detail below. Tr. 307; exhibit 20 (report of Dr. Byers).

In opposition to Dr. Kinsbourne and Dr. Byers, respondent presented Dr. John MacDonald, a pediatric neurologist, and Dr. Christine McCusker, a pediatric immunologist. Dr. MacDonald challenged Dr. Kinsbourne’s theory that a vaccine caused Lou’s OMS. Dr. MacDonald believes that no evidence shows that the vaccine caused the disease. Exhibit A (report of Dr. MacDonald) at 2; tr. 183.

Dr. McCusker also testified on behalf of respondent. She believes that the fourth dose of a vaccine cannot cause an adverse reaction that was not caused by the first three doses. Exhibit G (report of Dr. McCusker) at 6; exhibit V (supplemental report of Dr. McCusker) at 5; tr. 82-84, 150, 388. Because Dr. McCusker opines that it is “virtually impossible” for the fourth dose of the DTaP vaccine to have caused Lou’s OMS, tr. 134; her opinion is broader and, in a sense, more powerful than the opinion of Dr. MacDonald, whose opinion focuses on the lack of supporting evidence to show causation.

In this case, the evidence includes conflicting opinions from each side’s experts. The persuasiveness of the experts must be evaluated, and the testimony of one side’s expert may be rejected when a reasonable basis supports such a rejection. Burns v. Sec’y of Health & Human Servs., 3 F.3d 415, 417 (Fed. Cir. 1993). A decision about the persuasiveness of an expert is virtually not reviewable on appeal. Bradley v. Sec’y of Health & Human Servs., 991 F.2d 1570, 1575 (Fed. Cir. 1993).

In the Vaccine Program, an expert’s opinion may be evaluated according to the factors identified by the United States Supreme Court in Daubert v. Merrell Dow Pharmaceuticals, Inc., 509 U.S. 579 (1993). Terran v. Sec’y of Health & Human Servs., 195 F.3d 1302, 1316 (Fed. Cir. 1999). As recognized in Terran, the Daubert factors for analyzing the reliability of testimony are:

- (1) whether a theory or technique can be (and has been) tested;
- (2) whether the theory or technique has been subjected to peer review and publication;
- (3) whether there is a known or potential rate of error and whether there are standards for controlling the error; and,
- (4) whether the theory or technique enjoys general acceptance within a relevant scientific community

Terran, 195 F.3d at 1316 n.2, citing Daubert, 509 U.S. at 592-95.

Here, the evidence presented in this case fails to show that the fourth dose of the DTaP vaccine could have caused an adverse reaction not caused by the first three doses. Dr. Byers's testimony on this point was much less persuasive than Dr. McCusker's competing testimony. Dr. Byers seemed often to wander from the topic and had much less command of her subject area than Dr. McCusker. Significantly, the literature that Dr. Byers submitted to support her opinion did not, in fact, support her point. This discrepancy significantly reduced the value of Dr. Byers's opinion.

2. Immune System

Both Dr. Byers and Dr. McCusker rest their competing theories on how the immune system responds to the introduction of a foreign substance, such as an immunization. The medical community refers to the foreign material as an "antigen." Tr. 77. The first response to an antigen is mounted by the innate immune system. Tr. 244, 249, 252. When the innate immune system fails to remove the antigen, another response is required. This additional response is known as the adaptive immune system. Id.

The adaptive immune system is divided into two different strands, known as T cells and B cells, also known as a humoral response. Tr. 80. The introduction of the DTaP vaccine provokes a response mostly from the B cell side of the adaptive immune system because the DTaP vaccine does not contain a live virus. Tr. 85-88, 98-99, 431; see also tr. 320-22 (testimony of Dr. Byers recognizing that the B cell aspect of the adaptive immune system plays a "central role," assisted by the T cell aspect). The humoral aspect of the immune system produces antibodies that attack the invading antigen. Tr. 81.

The first time an antigen enters the body, it encounters pre-existing antibodies that are not specifically matched to the antigen. Tr. 81-82. These antibodies, after receiving assistance from a cell known as a T helper cell, begin to divide. The newly formed cells, known as daughter cells, have a greater affinity for the antigen. Tr. 82-83; exhibit G at 3-4; exhibit V at 2 and 5. An antibody called immunoglobulin G ("IgG") is usually produced in detectable amounts after approximately five days. IgG has a strong affinity for the antigen. Tr. 262-63. For a first exposure to an antigen, the antibodies usually clear the antigen within approximately 12 days. See exhibit 38, slide 4.

Toward the end of the response from the immune system, the B cells create memory cells. Memory cells have learned how to respond to a specific antigen. Thus, when the body sees the same antigen a second time, the immune system responds more quickly and more strongly because the existing B cells have a greater affinity for the antigen. Tr. 83-84, 268.

To remove the antigen, the antibodies form a bound with the antigen. Antigens, like other substances, consist of proteins. Proteins, in turn, are made of up chains of amino acids. A series of amino acids to which an antigen can bind is known as an epitope or peptide. Each

protein contains an immunodominant epitope, the epitope to which antibodies usually bind, and several other epitopes. Tr. 238, 291, 303-04. The effect of these other epitopes is a disputed point, discussed below.

Both Dr. McCusker and Dr. Byers agree about this basic summary of how the immune system operates. For example, in her report, Dr. Byers states “with each vaccination to the same thing, the specificity of the antibodies generates get[s] better.” Exhibit 20 at 2. However, at this point, the two experts diverge.

Dr. McCusker advances a concept known as affinity maturation. In affinity maturation, repeated exposure to the same antigen produces another generation of daughter cells that are more strongly attracted to the antigen. Dr. McCusker proposes the model of an upside down pyramid in which each generation of antibodies becomes more narrow than the previous generation. Tr. 82, 158.

This more focused response has two effects. First, there is little danger that the immune system would deviate from its previous response. If the immune system cleared the antigen, such as the DTaP vaccine, the first time it was exposed to the antigen without any adverse consequences, the immune system will do the same each time. Actually, Dr. McCusker opines that a new adverse reaction would be “virtually impossible.” Tr. 135.

The second effect is the time necessary to eliminate the antigen. According to Dr. McCusker, the body will eliminate a previously seen antigen much more quickly, perhaps within three days. Two factors contribute to this rapid response. First, some previously produced antibodies remain circulating in the body. These existing antibodies can react to and can destroy the antigen as soon as it reenters the body. Second, the existing memory cells create antibodies with strong affinity to the antigen. Using Dr. McCusker’s image, the response to a previously seen antigen starts several tiers down the upside-down pyramid.

This model underlies Dr. McCusker’s opinion that the fourth dose of the DTaP vaccine could not have caused Lou’s OMS. Dr. McCusker emphasizes that Lou’s three earlier exposures to the DTaP vaccine had sharpened his immune system. Therefore, Lou’s immune system knew not to attack parts of Lou’s own brain. Tr. 96, 100, 124, 425.

Dr. McCusker draws supplemental support from the interval between Lou’s vaccination and the onset of his OMS, which was 12 days. Dr. McCusker believes that Lou responded to and eliminated the DTaP vaccine within three days. After he removed this antigen, Lou’s immune system turned itself off and stopped creating antibodies. Thus, according to Dr. McCusker, there were no antibodies circulating in Lou’s brain to cause the OMS, starting 12 days later. Tr. 170.

Dr. Byers presents a contrasting opinion.¹ While recognizing that subsequent vaccinations produce a stronger response from the immune system, Dr. Byers does not believe that this response is targeted. Instead, Dr. Byers believes the immune system “degenerates” and becomes more diffuse. Tr. 344, 440; exhibit 20. This concept is known as epitope spreading. Exhibit 20 at 2-3 (report of Dr. Byers). Dr. Byers compares this process to a pyramid in which the first exposure produces a small reaction and repeated exposures produce greater reactions. Repeated exposures to the same antigen produce antibodies that react to more and more proteins. Exhibit 20 at 2, 5; tr. 344.

Epitope spreading is based upon how antibodies interact with antigens after the antibody binds to the antigen. As the body reacts to the antigen, the antibody unravels the coiled strands of proteins that comprise the antigen. This uncoiling exposes other epitopes of the antigen to the body. Because the body has not seen this precise epitope before, the body responds by sending out a new sequence of antibodies. See tr. 271-73.

According to Dr. Byers, these new antibodies could mistake part of the self for an invading antigen. When the antibody makes this mistake and attacks the self, an autoimmune disease results. See tr. 251, 269.

Under a theory of epitope spreading, damage is more likely to occur with each exposure to an antigen. For example, the fourth dose of the DTaP vaccine is more likely to produce an adverse reaction than the first dose. Tr. 344. Thus, Dr. Byers supports Dr. Kinsbourne’s theory that the fourth dose of the DTaP vaccine was a substantial factor in causing Lou’s OMS. Tr. 342.

3. Evaluation Of Experts’ Opinions

As set forth above, Dr. Byers’s opinion differs dramatically from the opinion of Dr. McCusker. Determining which opinion is more persuasive determines the outcome of the claim for compensation because if Dr. McCusker’s opinion is accepted, then petitioner’s sequence of proof fails. For the three reasons explained below, Dr. McCusker’s opinion is found to be more persuasive than Dr. Byers’s opinion.

a. Supporting Examples

First, Dr. McCusker points out, with relative simplicity, that a stronger and more precise response to different antigens is the way bodies work. Dr. McCusker illustrates her theory with a common (and therefore, easily understood) example – children and sicknesses. Dr. McCusker notes that when children are young, they get many infections. As they mature in adults, they

¹ Respondent criticizes Dr. Byers for not discussing Lou’s case specifically. Resp’t Posthearing Br. at 16-17. This criticism is misguided because Mr. Tosches submitted Dr. Byers’s opinion to supplement and to strengthen Dr. Kinsbourne’s opinion. Because Dr. Kinsbourne opined about Lou specifically, it was not necessary for Dr. Byers to address Lou.

become sick less frequently. A reason for this improved health is that over the course of time, people's immune systems see different antigens, such as viruses, and learn how to respond to them. Tr. 104; see also exhibit 40 (American Academy of Allergy, Asthma & Immunology, Tips to Remember: Recurrent or Unusually Severe Infections, printed from <http://www.aaaai.org/patients/publicedmat/tips/recurrentinfections.stm>) at 1.

Mr. Tosches attempted to counter this argument with two points. Mr. Tosches contested Dr. McCusker's illustration of how bodies usually respond by raising, during cross-examination, the concept known as challenge-rechallenge and by questioning Dr. McCusker about the evolution of allergies. Additionally, Mr. Tosches argued that Lou's immune system was impaired before the fourth DTaP. Therefore, he could not and did not respond like a normal person. All points are not persuasive.

Dr. McCusker readily addressed the paradigm known as challenge-rechallenge. "A rechallenge event occurs when a patient who had an adverse reaction to a vaccine suffers worsened symptoms after an additional injection of the vaccine." Capizzano, 440 F.3d at 1322. Rechallenge is completely consistent with Dr. McCusker's theory that the fourth dose of a vaccine is unlikely to cause an adverse reaction that was not previously experienced. In a rechallenge case, the recipient experiences the same reaction. Tr. 124-25, 160.

Dr. McCusker also explained why the fact that some people develop allergies to food that they have been consuming all their lives does not contradict her theory. Digesting food implicates a part of the immune system known as the mucosal immune system, which includes the gastrointestinal system. The B cells within this system produce a different type of antibody, called immunoglobulin E. In contrast, a vaccine is processed by the systemic immune system and B cells producing IgM and IgG. Tr. 127-130, 160-164. Thus, the development of allergies does not contradict Dr. McCusker's opinion that the immune system produces a stronger and more narrowly focused response.

Dr. McCusker testified about challenge-rechallenge and food allergies during the first hearing. Afterwards, Mr. Tosches was permitted to produce evidence to contest Dr. McCusker's opinion and this supplemental material led to a second hearing during which Dr. Byers testified. Dr. Byers did not attempt to rebut Dr. McCusker's analysis of challenge-rechallenge and food allergies in any way. Dr. Byers, however, did express an opinion that Lou's immune system was deficient before he received the fourth dose of the DTaP vaccine. Tr. 325-26.

Lou responded normally to first three doses of the DTaP. Tr. 37-38. Nevertheless, Dr. Byers grounds part of her opinion upon a belief that Lou was not healthy because he experienced an unusually high number of colds or infections (11) during his first 18 months. Tr. 325-36. In contrast, Dr. McCusker believes that a "normal" 18 month old child could have as many as 15 infections. Tr. 387; 427-29.

The literature confirms Dr. McCusker's assessment, which was informed by her practice as a pediatrician. An article submitted by Mr. Tosches states "[t]he average young child between 1 and 3 years of age may get up to 12 colds a year." Exhibit 40 at 2. An article filed by respondent uses a similar estimate. Exhibit Y (David L. Goldman, Recurrent Infections, in Primary Pediatric Care (4th ed. 2001)) at 1235 (stating "up to 15 infections per year can still be considered within the normal range.").

Because Dr. McCusker's opinions about childhood illnesses are supported in articles prepared outside of the litigation context, they are entitled to more weight. Dr. Byers's testimony, which appears in conflict with these external sources, is less persuasive.

b. Medical Literature

A second and very strong reason for rejecting Dr. Byers's theory is the lack of support in peer reviewed journals. A fact finder may consider whether peer reviewed journals support an expert's theory. Merck & Co., Inc. v. Teva Pharmaceuticals USA, Inc., 395 F.3d 1364, 1374 (Fed. Cir. 2005); 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).

Mr. Tosches and Dr. Byers were given several opportunities to submit literature undermining Dr. McCusker's theory. Order, filed March 8, 2007. On March 29, 2007, and April 2, 2007, Mr. Tosches filed seven medical articles (exhibits 22-28) and Dr. Byers's initial report. After receiving a supplemental expert report from Dr. McCusker, Mr. Tosches filed eight more articles (exhibits 30 thru 37). Due to the complexity of the articles, the parties were advised to elicit testimony from their experts about any article that the party believed supported its case. Order, dated July 17, 2007. Mr. Tosches asked Dr. Byers to discuss only exhibit 30 (tr. 317), exhibit 32 (tr. 311), exhibit 33 (tr. 292, 305), exhibit 34 (tr. 286), exhibit 35 (tr. 288, 322), exhibit 36 (tr. 308), and exhibit 37 (tr. 285). In addition, respondent asked Dr. Byers to discuss exhibit 23 during cross-examination. Tr. 349.²

While each article is discussed in some detail below, the general failing of the set of articles is easily stated: the articles do not contradict Dr. McCusker's theory that a normal person's immune system responds more specifically and more forcefully to repeated exposures to an antigen. Tr. 390. Remarkably, Dr. Byers, herself, recognized that the articles are based in

² Before the hearing, the parties were ordered to raise any articles during the experts' testimony. Order, filed July 17, 2007. Nevertheless, Mr. Tosches did not elicit any testimony regarding articles filed as exhibits 22-28 and exhibit 31. Thus, although these exhibits have been considered, they are not discussed in this decision.

unusual situations. Tr. 439. Thus, Dr. Byers's submissions of articles provide very little assistance in determining what happened to Lou.

The title of Exhibit 30 alone demonstrates the mismatch. Exhibit 30 (Mary L. Disis, et al., Humoral Epitope-Spreading Following Immunizations with a HER-2/neu Peptide Based Vaccine in Cancer Patients, 24 J Clinical Immunology 571 (2004)). Cancer differs from autoimmune diseases because the cancerous cells are part of the bodies own self. Therefore, the body must be tricked into attacking itself. In contrast, with autoimmune diseases, the problem is that the body is attacking itself. Tr. 351-53, 404-05. Dr. Byers contends that this article shows that epitope spreading occurs with antibodies. Tr. 318. However, the context of epitope spreading in a treatment for cancer is so far removed from this case that the article is not useful. Tr. 391 (describing cancer treatments).

Exhibit 32 reports on a study of rabbits. Exhibit 32 (Judith A. James et al., Immunoglobulin Epitope Spreading and Autoimmune Disease after Peptide Immunization: Sm B/B'-derived PPPGMRPP and PPPGIRPGP Induced Spliceosome Autoimmunity, 181 J Experimental Medicine 453 (1995)). Dr. Byers reports that this article shows antibody epitope spreading. Tr. 313-14. Dr. McCusker, however, explained that this study is based upon injecting the rabbits with an epitope that is usually part of the rabbit's constitution and then stimulating an immune response. Under these conditions, the rabbits develop antibodies to a protein sequence contained in their bodies. But, the circumstances in the rabbit study are different from what happened to Lou because the components of the DTaP vaccine are not normally found in the body. Thus exhibit 32 does not show how a foreign substance leads to an attack on self. Tr. 390-91.

Exhibit 33 is, by Dr. Byers's characterization, a "very confusing article." Tr. 305. At several places, Dr. Byers appeared to have a less than thorough understanding of the article. Tr. 300. In contrast, Dr. McCusker was well prepared to explain it. The article describes the results of a study of heart disease. Researchers investigated how rats responded as a disease progressed from myocarditis (an inflammation of a heart muscle) to cardiomyopathy, in which the functioning of the heart muscle is impaired. To do this, the investigators presented a protein from the heart muscle with an adjuvant. An adjuvant is a "nonspecific stimulator of the immune system." Dorland's at 32. Initially, the rats developed antibodies to the whole protein. Later testing revealed antibodies to some epitopes comprising the whole protein. Exhibit 33 (Yoh Matsumoto, B-Cell Epitope Spreading Is A Critical Step for the Switch from C-Protein Induced Myocarditis to Dilated Cardiomyopathy, 170 Am. J of Pathology 43 (2007)); tr. 293, 30-06, 394-97.

Dr. Byers interpreted exhibit 33 as showing epitope spreading because as time elapsed, more antibodies to more parts (epitopes) of the protein were detected. Tr. 306-06.

Dr. Byers's point overlooked at least two facts about the study from exhibit 33 that make it distinguishable from what happens in a typical vaccination. First, the investigators stimulated

the rats' immune system, causing the rats to attack part of their own heart muscle. Because the heart muscle exists within their own body, the rats could never eliminate the offending antigen. The heart muscle stimulated an extended immune reaction. The rats' response differs because in a vaccination, the body eventually removes the invading antigen entirely. Tr. 396.

Second and relatedly, the constant exposure to the antigen (or heart muscle) allowed the rats to develop more and more antibodies to the individual epitopes. Exhibit 33 at 49 (figure 4). Dr. McCusker explained, persuasively, that the antibodies to the epitopes were not detectable initially because the antibodies were present in such a small quantity that they were not detectable. As the rats' immune systems continued to generate more antibodies, the antibodies accumulated and eventually achieved a detectable level. Tr. 395, 399-402.

Exhibit 34 is an excerpt from a handbook providing instructions in how to develop antisera. Antisera are serums that contain an antibody or antibodies. Dorland's at 108. Dr. Byers discussed this exhibit briefly. Tr. 286-87, and Dr. McCusker not at all. Dr. Byers did not explain how this article supports her theory of epitope spreading.

Like exhibit 33, exhibit 35 is based on a study in which the invading antigen is not cleared from the body. Dr. Byers cites this article to demonstrate that both the T cell side and the B cell side of the immune system can have epitope spreading. Tr. 288-89, 322. Again, there is some superficial support for this proposition. Dr. Byers emphasizes a section of the article with the heading "Determinant spreading." Id., citing exhibit 35 (Yang D. Dai, George Carayanniotis and Eli Sercraz, Antigen Processing by Autoreactive B Cells Promotes Determinant Spreading, 2 Cellular and Molecular Immunology 169 (2005) at 170.

Dr. McCusker correctly raises an important distinction. The "determinant spreading" observed by the authors arises "[i]f the immunodominant response fails to clear the targets at first." Exhibit 35 at 170. Thus, the article is premised on the perpetual presence of the antigen stimulating an immune response. This chronic condition does not happen in a typical vaccination. Tr. 421, 432. Therefore, this article does not explain what happened to Lou.

In exhibit 36, the researchers examined how a different autoimmune disease, type I diabetes, progressed. Children develop an antibody to a substance known as glutamic acid decarboxylase ("GAD") approximately two years before they develop symptoms of type I diabetes. Because they help diagnose the disease, the antibodies are "pathopneumonic." However, these antibodies do not cause the disease, meaning they are not "pathogenic." Tr. 308-11, 355. In the study reported in exhibit 36, researchers determined that during the two-year latent period, the children developed antibodies to different epitopes of GAD. Exhibit 36 (Ezio Bonafactio et al., Maturation of the Humoral Autoimmune Response to Epitopes of GAD in Preclinical Childhood Type 1 Diabetes, 49 Diabetes 202 (2000)).

Dr. McCusker succinctly identifies the flaw in relying upon this study. The study examines the progression of an autoimmune disease. It does not examine how the autoimmune

disease is caused and it does not appear to be predicated upon a vaccination. Tr. 432. Thus, exhibit 36 provides little, if any, support for a theory that the fourth dose of a vaccine can provoke an adverse reaction that was not previously experienced.

Exhibit 37 is an article whose value is mostly historical. It is an article by Gregory W. Siskind and Baruj Benacerraf titled “Cell Selection by Antigen in the Immune Response.” According to Dr. Byers, this article first established the not widely-held proposition that the first time an animal sees a pathogen, the immune response is immature. Tr. 267. Later exposures prompt a more effective immune response. Tr. 285, 377. As such, this article actually supports Dr. McCusker’s theory. Moreover, Dr. Byers recognizes that the Siskind and Benacerraf article does not discuss epitope spreading. Tr. 285. Consequently, this article does not advance Dr. Byers’s opinion.

Dr. Byers did not rebut Dr. McCusker’s points about the literature that was discussed. When Dr. Byers was recalled at the court’s request to answer Dr. McCusker’s analysis, Dr. Byers essentially confirmed that the articles represented atypical responses. At best, Dr. Byers offered to present articles in the context of a normal response. Tr. 440-41. If such articles exist, Dr. Byers’s failure to present them is perplexing. Dr. Byers is an experienced expert witness whose frequent appearances in Vaccine Program cases began as early as 1999. See Lawson v. Sec’y of Health & Human Servs., Fed. Cl. No. 90-2455V, 1999 WL 603693 (Spec. Mstr. May 28, 1999), vacated on non-relevant grounds, 45 Fed. Cl. 236 (1999). Through Mr. Tosches, Dr. Byers submitted more than a dozen articles on two different occasions. Given both the opportunity to file relevant literatures and the experience to determine what constitutes a relevant article, the literature on which Dr. Byers relies is wholly deficient.

c. Demeanor

Third, Dr. McCusker testified more credibly than Dr. Byers. Their appearances in court allowed their demeanor to be observed. Evaluations of credibility by fact-finders who observe testimony are accorded “great deference.” Pafford v. Sec’y of Health & Human Servs., 451 F.3d 1352, 1359 (Fed. Cir. 2006); cert. denied, ___ U.S. ___, 127 S. Ct. 2909 (2007); accord Energy Capital Corp. v. United States, 302 F.3d 1314, 1329 (Fed. Cir. 2002).

Determinations about which witness is more credible or more persuasive “are by nature impressionistic.” Tweten v. Sec’y of Health & Human Servs., 26 Cl. Ct. 405, 410 (1991). Nevertheless, the following observations are the basis for the finding regarding credibility.

Dr. McCusker presented her opinions with confidence. She explained immunology and her theories in a way that was easily understood. Her knowledge of the articles cited by Dr. Byers was thorough. Even though Mr. Tosches filed a group of articles only a few days before the hearing, Dr. McCusker analyzed them and was prepared to discuss them at the hearing. Tr. 233.

Although Dr. McCusker's theory that the fourth dose of a vaccine cannot cause adverse effects not previously experienced is a bold statement, Dr. McCusker's views about vaccines and diseases are also nuanced. For example, Dr. McCusker admitted that if Lou had suffered the same adverse reaction after the first dose of the DTaP vaccine, then her opinion would adjust. She could not state with as much certainty that it was impossible (or virtually impossible) for a second dose of a vaccine not to cause an adverse effect. Tr. 157-58. She also recognized that a second dose of a vaccine might cause an adverse effect. Tr. 150-51. In addition, Dr. McCusker has diagnosed a patient with developing cerebellitis due to the flu vaccine. Tr. 157, 176-78. Dr. McCusker's openness to the possibility that vaccines, in rare cases, cause adverse events strengthens her overall credibility.

These traits contributed to the very positive impression made by Dr. McCusker. While Dr. Byers was generally knowledgeable about immunology, her presentation suffered when compared with Dr. McCusker's.

While Dr. Byers testified with a demeanor suggesting that she believed in the theories that she was expressing, the force of Dr. Byers's testimony was blunted because her testimony was occasionally wandering. In addition, Dr. Byers struggled at times to explain the basis for her confidence. Part of the problem may be attributable to Dr. Byers's long history of working in the field of immunology. Her expertise may have impeded her attempts to explain concepts during the hearing. See, e.g., tr. 296-97.

Dr. Byers's relative unfamiliarity with the literature that she, herself, provided is not as easily explained and is a factor in finding her less persuasive than Dr. McCusker. Dr. Byers did not have many of the details about the studies at her fingertips. This lack of depth was especially evident when Dr. Byers discussed exhibit 33. Her initial attempts to explain the study were, at best, unclear, and may have been misleading unintentionally. Tr. 292-302, 305-7; see also tr. 395. Additionally, as discussed at length above, the articles selected by Dr. Byers provide very little, if any, support for the proposition that she was trying to establish. This mismatch diminishes the overall impression of Dr. Byers.

Furthermore, there is also a dichotomy in the professional activities of Dr. McCusker and Dr. Byers. Dr. McCusker is a fellow in the Royal College of Physicians & Surgeons in two practice areas: pediatrics and immunology. Exhibit B (curriculum vitae); tr. 70-71, 384-85. She spends approximately half her time treating patients, almost all of whom are children. Tr. 71. Her practice requires her to advise her patient's parents about how immunizations may affect their children. Tr. 73.

Rather than treating patients, Dr. Byers is using her knowledge of immunology in other ways. Her primary activity is to assist pharmaceutical companies developing clinical trials to test products. Tr. 245-46, 373-74. Dr. Byers currently sees patients only in the context of litigation. Tr. 374-75. She last practiced allergy and immunology in approximately 1999 when her practice,

which was in San Francisco, focused on treating people with AIDS. Tr. 241, 335-36, 364. Dr. Byers is also not board certified in immunology. Tr. 365; exhibit W.

In sum, numerous discrete points combine to form an overall picture that Dr. McCusker was more persuasive than Dr. Byers. No factor was decisive; all points support rejecting Dr. Byers's theory. See Burns, 3 F.3d at 417 (affirming special master's decision to credit one expert rather than another). When this analysis of Dr. Byers and Dr. McCusker is applied to the elements of Mr. Tosches's case, it is clear that Mr. Tosches cannot meet these criteria.

B. Elements Of Petitioner's Case

To prove causation in fact, a petitioner must establish at least three elements. The petitioner's

burden is to show by preponderant evidence 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). 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).

1. A Medical Theory Causally Connecting the Vaccination and the Injury

Relying upon the opinion of Dr. Kinsbourne, the opinion of Dr. Byers, and the submitted medical articles, Mr. Tosches asserts that vaccines can cause OMS. Pet'r Posthearing Br. at 33 n.13. His theory, broadly stated, is that an aberrant immune system response, either bystander activation or epitope spreading, caused Lou's body to attack itself. Id. at 27.

Respondent's experts did not challenge the proposition that immunizations could play a role in causing OMS. Tr. 195 (testimony of Dr. MacDonald); exhibit A at 2 (report of Dr. MacDonald). Instead, respondent implicitly narrowed the theory. Respondent emphasizes that the body first response to an antigen differs from a subsequent response to the same antigen. Resp't Posthearing Br. at 7.

Although respondent's attempt to modify petitioner's theory could be analyzed within the first prong of Althen to fit Lou's case more exactly, a better course is to consider the facts about Lou within the second prong of Althen. Therefore, Mr. Tosches is credited with fulfilling the first prong of Althen.

2. Logical Sequence of Cause and Effect Showing that the Vaccination Was The Reason for The Injury

Even if Mr. Tosches's broadly stated theory were accepted, a preponderance of the evidence fails to show a "logical sequence of cause and effect showing that the vaccination was the reason for the injury." The facts of Lou's case, especially his history of not responding adversely to the three previous DTaP vaccinations, do not show that he suffered an adverse reaction. Furthermore, the treating doctors do not support a finding of causation.

Mr. Tosches's argument about the second Althen prong posits that a petitioner prevails when he or she shows that "a generally healthy person receives a vaccine, sustains an injury that can be caused by the vaccine, with symptoms occurring at an expected time after the vaccine, and if no other cause exists." Pet'r Posthearing Br. at 37. Mr. Tosches brief cites no case for this proposition. Id. However, at another place in the same portion of his brief, Mr. Tosches cites Grant v. Sec'y of Health & Human Servs., 956 F.2d 1144, 1148 (Fed. Cir. 1992). Pet'r Posthearing Br. at 35.

Grant indicates that special masters should consider "relevant scientific and medical evidence about the particular nature of Quadrigen [the vaccine at issue in Grant]." Grant, 956 F.2d at 1149. The particular vaccine at issue for Lou is the fourth dose of DTaP.

As explained in section III.A.3 above, the fact that Lou is alleged to have responded adversely to his fourth dose is critical. Dr. McCusker explained persuasively why Lou did not react adversely to the fourth dose of the DTaP vaccine. Evidence about how a petitioner responded to a previous administration of the same vaccine is relevant to determining whether the petitioner had an adverse reaction. See Capizzano, 440 F.3d at 1320, 1322 (discussing rechallenge). Although Mr. Tosches was given a generous opportunity to introduce evidence to contradict Dr. McCusker, he did not do so effectively. Mr. Tosches's posthearing brief is similarly sparse in analyzing Dr. McCusker's opinion.

Rather than attempt to address the strengths of Dr. McCusker's opinion, Mr. Tosches relies upon three statements from treating doctors. Pet'r Posthearing Br. at 29-33. Opinions of treating doctors must be considered. Capizzano, 440 F.3d at 1326. However, Mr. Tosches draws unfounded inferences from their reports. Mr. Tosches argues "When Lou's treating physicians associated his vaccine with his injury, they were simply attempting to identify the nature and cause of his symptoms so they could treat him and make him healthier." Pet'r Posthearing Br. at 31 (emphasis added).³ Undoubtedly, some treating physicians "associated" Lou's OMS with the

³ Similarly, Mr. Tosches argues that:

His treating physicians, through their statements in the medical records, establish that Lou: (1) was prone to develop OMS because he was suffering from diarrhea at the time of his vaccination; (2) had a reaction to

vaccine in the sense that they recognize that the vaccination preceded the onset of the OMS. However, the treating physicians' statements do not take the next step – saying that the vaccine “caused” the OMS.

Chronologically, the first relevant statement from a treating doctor is from the emergency room of the hospital where Lou was seen for problems with his gait. This report states, in part, that approximately two weeks earlier, Lou received his 18 month vaccinations. Exhibit 6 at 710 (report, dated April 5, 2003). Given that Lou was not diagnosed with OMS until at least one year later, the emergency room doctor did not state that the vaccinations caused Lou's OMS.

Mr. Tosches also cites the report of Dr. Jordan, who works at the same hospital. Dr. Jordan also states that Lou's problems began two weeks before he was admitted to the hospital, he was vaccinated. Exhibit 6 at 52 (report dated April 15, 2003). This statement is not the same as saying that the vaccinations caused the reason for his admission. Moreover, Mr. Tosches ignores another report from Dr. Jordan in which she says that “a viral illness is the [likely] etiology.” Id. at 35 (dated Jan. 20, 2004).

Finally, Mr. Tosches identifies a report from Dr. Michael Pranzatelli. Dr. Pranzatelli is an expert in OMS, and was the doctor who diagnosed Lou as afflicted with that condition. Dr. Pranzatelli authored an article about OMS on which Dr. Kinsbourne relies. In this article, Dr. Pranzatelli stated that OMS may be an autoimmune condition. Dr. Pranzatelli suggested that “[e]nvironmental factors are likely to be very important in OMS, including infecting agents such as virus or bacteria and immunizations or vaccinations.” Exhibit 17 (Michael R. Pranzatelli, The Immunopharmacology of the Opsoclonus-Myoclonus Syndrome, 18 Clinical Neuropharmacology 1 (1996)) at 18. Given Dr. Pranzatelli's expertise in this area, his opinions about Lou's case are especially important. (Through Dr. Kinsbourne, Mr. Tosches requested that Dr. Pranzatelli participate in this case. However, Dr. Pranzatelli declined.)

Dr. Pranzatelli does not state that the vaccinations caused Lou's OMS. Dr. Pranzatelli's report says Lou's “neurological problems began at the age of 18 months, following a DTaP /HIV [sic, should be HIB] / polio immunization.” Exhibit 7 at 3. This statement accurately sets out the fact that Lou was vaccinated, then his OMS began. It does not, however, state a causal relationship.

his DTaP vaccine; (3) had an appropriate temporal relationship between the vaccine and his injury; and (4) continues to suffer symptoms of OMS. They also establish: (5) that his physicians believed his OMS was associated with his vaccination; and (6) that there was no likely alternate cause.

Pet'r Posthearing Br. at 32. There is no support for these statements.

An unwillingness to name vaccines as the cause of OMS is consistent with Dr. Pranzatelli's article: "[a]ssessments of the potential effects of immunizations on the onset of OMS is not simple." Exhibit 17 at 18.

Collectively, these reports from treating doctors do not assist Mr. Tosches in proving, by a preponderance of the evidence, that Lou's fourth DTaP vaccine caused his OMS. Dr. Jordan and Dr. Pranzatelli were aware that the vaccinations preceded the onset of OMS. However, neither Dr. Jordan nor Dr. Pranzatelli said that the antecedent event (the vaccination) caused the following event (the onset of OMS).

Therefore, Mr. Tosches has not established, by a preponderance of the evidence, a logical sequence of cause and effect that Lou's vaccination was the cause of his OMS. This failure of proof means that Mr. Tosches is not entitled to compensation. Nevertheless, for sake of completeness, the third factor is also addressed below.

3. A Showing of a Proximate Temporal Relationship Between Vaccination and Injury

The time between Lou's vaccination on March 19, 2003, and the onset of symptoms associated with OMS on April 1, 2003, is 13 days. Respondent was conceded that this number of days is an appropriate temporal relationship. Resp't Response to Special Master's Order, filed Nov. 16, 2007, at 2. However, this concession does not alter the outcome. For the reasons explained above, Mr. Tosches has not met his burden of establishing the second prong of Althen.

C. Summary

At best, Mr. Tosches has fulfilled the first and third prongs of Althen. However, his evidence on the second prong was not persuasive at all. In such a case, a petitioner is not entitled to compensation. Capizzano, 440 F.3d at 1327 (stating "[t]he second prong of the Althen III test is not without meaning").

In regard to showing, by a preponderance of the evidence, that the fourth DTaP vaccine "was the reason for the injury," Althen, 418 F.3d at 1278; Mr. Tosches's evidence is not persuasive. Dr. Byers did not match the persuasiveness of Dr. McCusker. Conceivably, another immunologist could present different information to support the theory of epitope spreading. But, in this case, Mr. Tosches's evidence fell well-short of being a preponderance of the evidence. See Althen, 418 F.3d at 1281 (stating the "special master's role is to assist the courts by judging the merits of individual claims on a case-by-case basis.")

III. Conclusion

Mr. Tosches has failed to demonstrate that he is entitled to compensation. Absent a motion for review, the Clerk's Office is ordered to enter judgment in favor of respondent.

S/ Christian J. Moran

Christian J. Moran
Special Master