OFFICE OF SPECIAL MASTERS

No. 01-0060V

(Filed: October 23, 2003)

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TAMMY KUPERUS, as Natural Parent of PHILLIP KUPERUS, a minor,	*	
Petitioner,	*	
	*	To be Published
v.	*	
SECRETARY OF THE DEPARTMENT OF HEALTH AND HUMAN SERVICES,	*	
Respondent.	*	
* *		

William Dobreff , Esq., Warren, Michigan, for Petitioner.

Althea W. Davis, Esq., United States Department of Justice, Washington, D.C., for Respondent.

ENTITLEMENT DECISION

ABELL, Special Master:

I. ISSUE

The case presents two issues before this Court. The first issue is whether Phillip Kuperus suffered an acute disseminated encephalomyelitis (ADEM). The second issue is, if Phillip indeed did suffer ADEM, did the DTaP vaccination he received on 15 April 1998 cause it. The Court finds that it is more likely than not that Phillip did suffer ADEM and such was more likely than not the result of the DTaP vaccination at issue.

II. PROCEDURAL BACKGROUND

On 30 January2001, Petitioner filed a claim under the National Childhood Vaccine Injury Compensation Act (Vaccine Act or Act)[1] alleging a vaccine-related injury to her son Phillip Kuperus. Petitioner claims that as a result of receiving a DTaP vaccination on 15 April 1998, Phillip suffered ADEM . Pet. Pre-Hearing Memo at 25.

Petitioner has satisfied the requirements for a *prima facie* case pursuant to § 300aa-11(b) and (c) by showing that: (1) Petitioner is a valid legal representative; (2) the vaccine at issue, DTaP, is a vaccine set forth in the Vaccine Injury Table; (3) the DTaP vaccination was administered to Phillip in the United States; (4) no one has previously collected an award or settlement of a civil action for damages arising from the alleged vaccine injury; and, (5) no previous civil action has been filed in this matter. Additionally, the § 300aa-16(a) requirement that the petition be timely filed has been met.

On 25 September 2002, the Court conducted an evidentiary hearing in this matter. The Court heard testimony from Petitioner's medical expert, Dr. Robert H. Shuman,[2] and Respondent's medical expert, Dr. Subramaniam Sriram.[3] The hearing transcript was filed on 25 October 2002.

Thereafter, the parties filed post-hearing briefs. On 1 April 2003, Petitioner filed her post-hearing brief. On 27 May 2003, Respondent filed a post-hearing brief. Petitioner filed her *sur-response* on 16 July 2003. Thus, the record is complete and ripe for decision.

III. FACTS

Phillip Kuperus ("Phillip") was born on 8 February 1997 weighing ten pounds, two ounces. Pet. Ex. 1 at 6. His APGAR[4] scores were seven and nine at one and five minutes respectively. *Id*. at 9. He

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[1] The statutory provisions governing the Vaccine Act are found at 42 U.S.C. §§ 300aa-1 to 300aa-34 (1991 & Supp. 2002). Hereinafter, for ease of citation, all references will be to the relevant subsection of 42 U.S.C. § 300aa.

[2] Robert H. Shuman, M.D. is board certified in neurology with special competence in child neurology, board certified in pathology with special competence in neuropathology, and is board certified in neuroimaging (MRI). He is a 1968 graduate of Stanford Medical School and has been a practicing physician for over thirty five years. Dr. Shuman owns Child Neurology, Inc. in South Bend, Indiana, a pediatric neurology practice that addresses children's neurological conditions.

[3] Subramanian Sriram, M.D. is board certified in neurology and internal medicine. He is a 1973 graduate of the University of Madras, in Madras, India where he received an M.B. and B.S. He is currently the William Weaver Professor of Neurology at Vanderbilt University.

[4] An acronym that stands for "appearance (color), pulse (heart rate), grimace (reflex irritability), activity (muscle tone), and respiration (score reflecting condition of newborn)." Neil M. Davis, MEDICAL ABBREVIATIONS:

was discharged on 10 February 1997. *Id*. On 21 February 1997, Phillip first saw Dr. Janet Johns, his pediatrician, and no problems were noted at that visit. Pet. Ex. 4 at 43. Phillip next saw Dr. Johns on 15 March 1997 for a febrile illness, which the history records as a 101 degree temperature. Pet. Ex. Pet. Ex. 3 at 42. Phillip was referred to Butterworth Hospital for an evaluation for sepsis, *Id*., and a history from the Butterworth Hospital records notes a four day history of rhinorrhea without cough, nasea, vomiting, or diarrhea. *Id*. at 30. Phillip was prescribed antibiotics, his condition improved and he was discharged without definitive diagnosis on 17 March 1997. *Id*. at 36. Phillip was next seen by Dr. Johns on 8 April 1997 for mild congestion and some regurgitation. Pet. Ex. 4 at 43. Dr. Johns recommended that Phillip be propped up if the regurgitation continues and that cereal should be added to his feedings. *Id*. As of the date of this visit, Phillip had yet to receive any vaccinations.

On 15 April 1998, Phillip saw Dr. Thomas A. Stevenson for a twelve month well care visit. Pet. Ex. 5 at 50. Dr. Stevenson assessed Phillip as a well child, *Id*., and, at the request of Phillip's parents, administered a DTaP[5] shot. *Id*. Dr. Stevenson also administered a neurological examination and found "No cerebellar signs or ataxia." *Id*. Additionally, Phillip started to walk in April 1998. Pet. Ex. 4 at 43.

In mid May 1998,[6] Mrs. Kuperus, Phillip's mother, noticed that Phillip was having trouble walking and he was clumsy. Trans. at 21. He had trouble grasping toys, had some slight tremoring and was running into things. *Id*. She described that his hands were shaking intermittently "like he was an old person." *Id.* at 22. He began having difficulty feeding himself, began to fall more, and walked "as if he was drunk." Petitioner's Petition (hereinafter "Pet.) at 1-2. Mrs. Kuperus stated that she was not alarmed at first because she thought the problems would go away. Trans. at 22. Mrs. Kuperus stated that Phillip's problems became more evident over time and that by June of 1998 other people began to notice as well. *Id*. at 23.

At the recommendation of her father, Mrs. Kuperus took Phillip to see a Eric W. Seif, D.C., a chiropractor. Dr. Seif treated Phillip on 3 August 1998, 21 September 1998, and 28 October 1998. Pet. Ex. 24. Dr. Seif observed that Phillip was more than "just clumsy," that he "appeared to struggle to maintain his balance, to walk without falling or avoid bumping into things." *Id*. Dr. Seif's treatments were unsuccessful and he recommended that Phillip consult a pediatric neurologist. *Id.*

On 1 October 1998, Phillip visited Dr. Johns. Pet. Ex. 4 at 43. This was six and a half months after his DTaP shot and five and half months subsequent to the onset of his problems. In her remarks, Dr. Johns

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8600 CONVENIENCES AT THE EXPENSE OF COMMUNICATIONS AND SAFETY (6th ed. 1993).

[5] Because they are dairy farmers, Phillip's parents originally requested a tetanus shot only. However, the only vaccine that Dr. Stevenson had available with the tetanus toxoid was DTaP. Phillip's parents agreed to have the DTaP administered. Pet. Ex. 5 at 50.

[6] Mrs. Kuperus testified that it was mid May when she began to notice Phillip's problems. In her affidavit, she stated it was four to six weeks after the 15 April 1998 DTaP vaccination. Pet. Ex. 34 at 601.

noted that Phillip was "'still unsteady' walking." *Id*. During the visit, Dr. Johns observed that Phillip's grasp was normal "but even sitting he appears to have truncal instability, seems to 'catch' himself . . . just looks mildly unsteady walking, even sitting." *Id*. at 42. From Mrs. Kuperus telling her that "Phillip is slower to put circles over toy pegs, etc.," *Id*., Dr. Johns proposed that Phillip may have "occasional mild choreiform movement of either hand." *Id*. As a result of the visit, Dr. Johns referred Phillip to Dr. David H. Van Dyke, a neurologist, for evaluation of ataxia. *Id*.

On 23 November 1998, Phillip visited Dr. David Van Dyke with the chief complaint of "[s]ome ataxia and incoordination." Pet. Ex. 6 at 52. Mrs. Kuperus told Dr. Van Dyke that Phillip always seemed "unsteady on his feet," that ever since he started to walk in April of 1998 "he has had a rather clumsy gait," and that she has always been concerned that Phillip has been "'a bit behind.'" *Id*. Dr. Van Dyke noted that Mrs. Kuperus felt as though Phillip was not getting any better. *Id*. Mrs. Kuperus told Dr. Van Dyke that Phillip was having trouble grasping. *Id*. Dr. Van Dyke noted that Phillip "does have tremors in his hands" and has developed "some unusual head movements." *Id*. Dr. Van Dyke's impression as a result of his evaluation stated that Phillip had ataxia that was "probably non-progressive." *Id*. In his report to Dr. Johns, Dr. Van Dyke was concerned about Phillip's "significant ataxia, tremors, and choreoathetosis." Pet. Ex. 6 at 54. Dr. Van Dyke informed Dr. Johns that Phillip needed to see him again for further evaluation and he scheduled numerous tests, including an MRI. *Id*. Dr. Van Dyke noted that Phillip had not been immunized. *Id*. at 52[7]

The MRI, which was performed on 13 January 1999, revealed several "tiny foci of T2 hyperintensity in the frontal lobe white matter. At least three lesions are present on the right and one is present on the left." Pet. Ex. 7. The radiologist reading the MRI, Bradford W. Beltz, M.D., found that MRI findings were "suspicious for areas of gliosis[8] or demyelination[9], such as from acute disseminated encephalomyelitis." *Id*. On 1 February 1999, in a letter to Dr. Johns, Dr. Van Dyke stated that he had yet to have a diagnosis in Phillip's case but posited that it could be a "non-progressive process with a post infectious etiology based on the MRI findings but note those are subtle and non-progressive." Pet. Ex. 19 at 488. On 13 April 1999, Dr. Van Dyke performed an EEG based on reports that Phillip had begun to experience episodes "in which his eyes would roll up and he would be unaware of his surroundings." *Id*. at 486. The EEG was "markedly abnormal because of diffusely slowed background, the presence of bilateral spike wave discharges with slow spike and wave predominating, and with some discharges of high voltage occipital spikes." Pet. Ex. 6 at 56. Dr. Van Dyke noted that this type of EEG results can be seen

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[7] Dr. Van Dyke must not have been informed that Phillip had received a DTaP shot on 15 April 1998. Pet. Ex. 5 at 50.

[8] "An excess of astroglia in damaged areas of the central nervous system." DORLAND'S ILLUSTRATED MEDICAL DICTIONARY 699 (27th ed. 1988). Astroglia: "neurological cell(s) of ectodermal origin, characterized by fibrous, protoplasmic, or plasmatofibrous processes. *Id*. at 160.

[9] "Destruction, removal, or loss of the myelin sheath of a nerve or nerves." DORLAND'S ILLUSTRATED MEDICAL DICTIONARY 443 (27th ed. 1988).

in degenerative neurologic conditions. *Id*.

From 14-19 April 1999, Phillip was seen by several specialists at the Mayo Clinic. Pet. Ex. 9. The specialists at the Mayo Clinic reported final diagnoses of primary generalized nonconvulsive seizures and developmental arrest with ataxia. *Id*. at 95. On 14 September 1999, Phillip was evaluated at the University of Michigan's Mott Children's Hospital by Dr. Katherine Holland and Dr. Mamdouh Abdulrazzak. Pet. Ex. 10. The two doctors concluded that Phillip's "seizure [symptomology], EEG findings, and the poor response to treatment so far are most consistent with generalized epilepsy which has so far been refractory to treatment. So far, his extensive workup has failed to define a clear etiology to his neurologic syndrome." *Id*. at 117.

In November 1999, Dr. Van Dyke referred Phillip to pediatric neurologist Dr. Robert Shuman for "evaluation, suitability, and induction of ketogenic diet.[10]" Pet. Ex. 12. As a result of his physically examining Phillip, Dr. Shuman noted that "[h]e is extraordinarily tremulous and his tremors interfere with everything. He also has developed trunkal and head titubation,[11] and it interferes with walk and station." *Id*. at 124. Dr. Shuman's impression from his evaluation and the parental history was: 1) "Primary Generalized Epilepsy, intractable" and, 2) "Post vaccinal encephalomyolopathy is possible, presenting as tremor and ataxia 6 weeks after exposure. My supposition is that he developed seizures with the vaccination, either coincidently or ideogentically, and the seizures are what produced the ataxia. The seizures didn't present themselves clinically until March 1999." *Id.* A 30 November 1999 MRI, ordered by Dr. Shuman, revealed "a few tiny areas of high signal in the subcortical white matter" which had reduced in size since the 13 January 1999 MRI. Pet. Ex. 8 at 70. The radiologist reading the MRI, Dr. Jerrold A. Van Dyke, opined that the findings may represent the sequela of an ADEM. *Id*. Dr. Jerrold A. Van Dyke read the MRI with a history that Phillip "is presumed to have a post vaccination acute disseminated encephalomyelitis." *Id*.

Dr. Shuman placed Phillip on a ketogenic diet on 29 December 1999 and by April 2000 an EEG performed on Phillip was "absolutely normal." Pet. Ex. 12 at 128. As the result of a 4 April 2000 follow-up evaluation, Dr. Shuman noted under his impressions that Phillip's post vaccinal encephalomyelitis has been arrested, his tremulousness has now improved to herky-jerky spasticity[12], and Phillip's cognitive

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[10] "The ketogenic diet is a special diet used to treat seizures. It was initially studied in the 1920's as a treatment option for those with intractable epilepsy. Since then, medications have replaced the diet, but there is now a resurgence of interest in the Ketogenic diet. The diet is high in fat, and low in carbohydrate and protein, which results in ketosis. In addition, fluids are limited, which helps contribute to the diet's success. This ketotic state exerts an anti-epileptic effect, though its precise mechanism of action is not completely understood." http://www.stanford.edu/group/ketodiet/FAQ.html#Heading2

[11] "The act of staggering or reeling; a staggering or stumbling gait with shaking of the trunk and head, commonly seen in cerebellar disease." DORLAND'S ILLUSTRATED MEDICAL DICTIONARY 1726 (27th ed. 1988).

[12] "A state of hypertonicity, or increase over the normal tone of muscle, with heightened deep tendon reflexes." DORLAND'S ILLUSTRATED MEDICAL DICTIONARY 1552 (27th ed. 1988).

decline has now reversed with a sense of normal development. *Id*. at 129. In August 2000, Phillip's seizures were completely controlled with the ketogenic diet and discontinuance of the sole anticonvulsant medication that Phillip was taking was considered. *Id.* at 132. Phillip continued to have marked tremors that had a "quality of chorea to them." *Id.* In October 2000, Phillip had another normal EEG, despite the continuance of the anticonvulsant medication. *Id* at 135. However, on 9 October 2000, Phillip began to have seizures again and in February 2001, Phillip had his first grand mal seizure. Pet. Ex. 16 at 186. Anticonvulsant medications were reintroduced in February 2001.

IV. DISCUSSION AND ANALYSIS

1. Does Phillip have Acute Demyelinating Encephalomyelitis (ADEM)?

"ADEM is an immunologically mediated inflammatory demyelinating disease of the central nervous system principally effecting the white matter. It is usually preceded by a viral infection or vaccination and has a wide clinical spectrum, ranging from episodes diagnosed incidently by brain magnetic resonance imaging (MRI) showing multi-focal white-matter lesions, to a rapidly fulminating rapidly progressing course with seizures and coma." Pet. Ex. 53 at 1539.[13] "The most common presenting symptom of ADEM is ataxia." *Id.* at 1539, 1541. "Brain [MRI] showing bilateral symmetrical hyperintense lesions of the same age in the . . . subcortical white matter is a mainstay of diagnosing ADEM." *Id.* at 1539. "[ADEM] is characterized pathologically by diffuse foci of perivenular inflammation and demyelination most prominent in the white matter of the brain." Pet. Ex. 89 at 1469.[14]

"Although regarded as a monophasic condition, a characteristic feature of ADEM is the evolution of symptoms and signs over time. . . . Ataxia [is] usually present at the outset and [does] not develop later in the illness." Pet. Ex. 53 at 950-51.[15] "Patients may recover completely or be left with residual symptoms, which may be mild or severe. There may be only slight motor disturbances . . . . In children, recovery from the acute stage is sometimes followed by permanent disorder of behavior, mental retardation or *epilepsy*." Pet. Ex. 38 at 704.[16]

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[13] R. Arul Apak, M.D. et al., Acute Disseminated Encephalomyelitis in Childhood: Report of 10 Cases, 14 JOURNAL OF CHILD NEUROLOGY 198 (March 1999).

[14] INSTITUTE OF MEDICINE, ADVERSE EVENTS ASSOCIATED WITH CHILDHOOD VACCINES: EVIDENCE BEARING ON CAUSALITY 83 (1994).

[15] J. L. Hynson et al., Clinical and neurological features of acute disseminated encephalomyelitis in children, 56 NEUROLOGY 1308, 1310-11 (May 2001).

[16] Raymond D. Adams, M.D. & Charles S Kubik, M.D., The Morbid Anatomy of the Demyelinative Disease, AMERICAN JOURNAL OF MEDICINE 510, 530 (May 1952) (emphasis added).

a. Ataxia[17]

Mrs. Kuperus testified that in mid May 1998 Phillip started "having trouble walking, he was clumsy. He was having trouble grasping toys. He would run into things, furniture, some slight tremoring." Trans. at 21. His hands would "intermittent[ly]" shake "like he was an old person." *Id.* at 22. She stated that Phillip's condition gradually got worse and that by June other people noticed as well. *Id.* at 23; Pet. Ex 34 at 602. Mrs. Kuperus first heard Phillip's shakiness and hand tremors called ataxia when she took him to Dr. Janet Johns on 1 October 1998. *Id.* at 30.

Dr. Janet Johns observed that Phillip looked "mildly unsteady walking, even sitting"and wanted to refer Phillip for possible ataxia. Pet. Ex. 4 at 42. Dr. David Van Dyke, after examining Phillip on 23 November 1998, noted that Phillip had ataxia that was "probably non-progressive." Pet. Ex. 6 at 53. Dr. Shuman, Phillip's treating neurologist, definitively testified that Phillip has ataxia, Trans. at 116, as well as choreoathetosis[18] and tremor.[19] *Id.* The Court observed Phillip prior to the hearing demonstrate these movements by walking "down the hall with his feet more widely spaced apart than usual and the sudden loss, seeming loss of balance and leaning to the left or leaning to the right or leaning backward." *Id*. at 116-17. The Court also observed Phillip putting a cap on a pen with some difficulty because his hands were shaking and the pen was moving left to right. *Id*. at 27.

According to Mrs. Kuperus, Phillip's ataxia developed gradually approximately four to six weeks after the 15 April 1998 vaccination date. Pet. Ex. 34 at 1. During his 15 April 1998 doctor's visit, Dr. Stevenson did a neurological examination of Phillip and specifically noted "No . . . ataxia." Pet. Ex. 5 at 50. Although certain records indicate that Mrs. Kuperus was worried that Phillip had always been clumsy since he started walking and she felt he had been "a bit behind," Pet. Ex. 6 at 52, Dr. Stevenson's conclusion from his neurologic exam of Phillip on 15 April 1998 was that there was no ataxia. Thus, the Court must conclude that the ataxia developed subsequent to the vaccination at issue and more likely than not within the four to six week time frame Mrs. Kuperus has stated.

b. Multi-focal White-Matter Lesions

"An MRI of the brain revealed the presence of several tiny foci on T-12 weighed image in the front lobe right matter bilaterally. The findings were considered to reflect areas of demyelination gliosis, and were consistent with a diagnosis of acute disseminated encephalomyelitis. Pet. Ex. 95 at 1524. As stated

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[17] "Failure of muscular coordination; irregularity of muscular action." DORLAND'S ILLUSTRATED MEDICAL DICTIONARY 160-61 (27th ed. 1988).

[18] "Choreoathetosis is a combination of the quick, flick jerks and slow sensuous movements that the patient didn't intend and give the patient a herky-jerky appearance, and Phillip has that." Trans. at 116.

[19] "Tremor is that fine low aptitude movement at rest or during intention, which interferes with executive movement." Trans. at 116.

supra, bilateral lesions of the white matter is a "mainstay" in the diagnosis of ADEM. Respondent's expert, Dr. Sriam agreed that a typical finding of ADEM is bilateral lesions in the brain's white matter. Trans. at 336.

c. Monophasic

One reason that Dr. Sriram contests the diagnosis of ADEM is that he claims that Phillip's cascade of symptoms manifested over six months. Trans. at 327. Dr. Sriram asserted that ADEM is a full-blown disease that progresses fairly rapidly. *Id*. Dr. Sriram posits that if the acute stage of Phillip's ADEM occurred in May 1998, evidenced by the onset of his ataxia, then Phillip's choreoathetoid movements would not have first manifested in November 1998. *Id*. at 329. However, when on cross examination, Dr. Sriram did agree that a characteristic feature of ADEM is the evolution of symptoms and signs over time. *Id*. at 335. Additionally, he agreed with Petitioners' expert, Dr. Shumer, that relapse can occur in those with ADEM when the underlying cause has not run its course. *Id.* at 122; 335-36.

Dr. Shumer stated that because Phillip was not treated with steroids during the acute phase he was more susceptible to relapse. *Id*. at 123. Dr. Sriram agreed that steroids are the recommended treatment for ADEM. *Id.* at 295.

The MRIs of Phillip and the successive regression of the demyelination evidenced the monophasic nature of the attack. The first MRI, obtained 13 January 1999, "shows perivascular demyelination of the cerebral white matter." Pet. Ex. 35 at 651; *see also* Pet. Ex. 7 at 68. The second MRI, obtained 30 November 1999, ten months after the first MRI, "shows some pattern of perivascular demyelination but to a *lesser severity*." *Id.* (emphasis added). Dr. Shuman testified that because no new abnormalities appear on the second MRI and the existing abnormalities have decreased in size prove the acute onset and subsequent regression of the injury, thus, pointing to its one phase nature. Trans. at 127.

Dr. Sriram had reservations about the successive MRI results because the films were not taken at the same facility and the type of machine used may have been different. Dr. Sriram opined that "if the MRI scan was not done at the same MRI machine, it was not done with the same processes to make sure that the head is in the same place, then you are not getting the same cuts of the MRI from one time to another" and the conclusions drawn could be wrong. *Id*. at 305-06. However, Dr. Sriram did state that Dr. Shuman, who read all of Phillip's successive MRI's, "was extremely well qualified to read an MRI." *Id.* at 321.

d. Epilepsy

As stated *supra,* recovery from the acute stage of ADEM is sometimes followed by epilepsy. Pet. Ex. 38 at 704. Dr. Shuman states that the appearance of epilepsy is "common in ADEM." Pet. Ex. 35 at 660. Phillip developed intractable epilepsy within ten months of the onset of his ataxia, which Petitioner alleges was the acute phase of the ADEM. *Id*.

e. Independent Diagnosis of ADEM

As indicated *supra*, Phillip's first MRI was performed on 13 January 1999. The reading physician, Bradford Betz, M.D., a radiologist, recorded under "Findings" that bilateral lesions present in the frontal lobe white matter "are suspicious for areas of gliosis or demyelination, such as from acute disseminated demyelination [ADEM]." Pet. Ex. 7 at 68. Jerrold A. Van Dyke, M.D., the radiologist who read Phillip's 30 November 1999 MRI, compared it to the previous one and opined that the regression of the findings "may represent the sequela ADEM." Pet. Ex. 8 at 70. Dr. Sriram testified that he was a bit cynical of Dr. Jerrold Van Dykes opinion because "a history was told to him as a child with ADEM." Trans. at 320. However, when pressed on his cynicism, Dr. Sriram admitted that Dr. Van Dyke's findings were at least consistent with the history and did not rule out ADEM. *Id.* It is of note that Dr. Betz only had a history of ataxia to inform his opinion when reading the initial MRI. Pet. Ex. 7 at 68. Dr. Sriram conceded that two physicians looking at the MRI's at different times drew the same conclusion and that their conclusions were consistent with Dr. Shuman's diagnosis of ADEM. Trans. at 321. However, Dr. Sriram pointed out that the University of Michigan and the Mayo Clinic doctors did not diagnose ADEM. *Id.*

f. Conclusion on Diagnosis of ADEM

Phillip developed ataxia in mid May 1998, which is the most common presenting symptom of ADEM. Phillip's successive MRI's revealed bilateral lesions of the white matter which is a "mainstay" in the diagnosis of ADEM. Although, Dr. Sriram contends that the onset of Phillip's symptomology belies the monophasic nature of the injury, Dr. Sriram did agree that a characteristic feature of ADEM is the evolution of symptoms and signs over time. Phillip developed epilepsy, which sometimes follows the recovery from the acute onset of ADEM. Finally, two other doctors independently asserted that Phillip's symptoms were consistent with ADEM and were in agreement with Petitioner's expert, Dr. Shuman. Thus, considering the preceding facts, the Court finds that it is more likely than not that Phillip did indeed suffer an acute disseminated encephalomyelitis.

2. Was the 15 April 1998 DTaP vaccination the cause of Phillip's ADEM?

Petitioner can prove she is entitled to compensation under the Program in one of two ways. She can prove entitlement through a statutorily prescribed presumption of causation or, by proving causation-in-fact. First, Petitioner may prove that Phillip suffered an injury or condition listed in the Vaccine Injury Table within the statutorily prescribed time period. § 11(c)(1)(C)(i). If Petitioner establishes that Phillip suffered such injury by a preponderance of the evidence, Petitioner is entitled to a presumption of causation. § 13(a)(1)(A). If Phillip qualifies under this presumption, she will be said to have suffered a "Table injury." The burden would then shift to the Respondent to prove that the injury or condition "is due to factors unrelated to the administration of the vaccine described in the petition." § 13(a)(1)(B).

If Petitioner fails to satisfy the requirements under the Act for demonstrating a Table injury,

Petitioner may prove by a preponderance of the evidence that the vaccination in question, more likely than not, caused the alleged injury. §§ 11(c)(1)(C)(ii)(I) and (II). This causation-in-fact standard, according to the Federal Circuit, requires proof of a "logical sequence of cause and effect showing that the vaccination was the reason for the injury." *Grant v. Secretary of HHS*, 956 F.2d 1144, 1148 (Fed. Cir. 1992). Once again, if Petitioner is successful in that showing, the burden shifts to Respondent to prove that the injury or condition "is due to factors unrelated to the administration of the vaccine described in the petition." § 13(a)(1)(B).

In the present case, Petitioner does not allege that Phillip suffered a Table injury. Petitioner alleges that the onset of Phillip's ADEM was the result of the DTaP vaccine he received 15 April 1998. Pet. at 2. The Table does not list ADEM as a recognized adverse event that warrants presumption, thus, Petitioner's claim is one of causation-in-fact.[20]

a. Causation-In-Fact

In order to demonstrate entitlement to compensation in a causation-in-fact claim, a petitioner must affirmatively demonstrate by a preponderance of the evidence that the vaccination in question *more likely than not* caused the injury alleged. *See* 11(c)(1)(C)(ii)(I) and (II); *Grant v. Secretary of HHS*, 956 F.2d 1144 (Fed. Cir. 1992); *Strother v. Secretary of HHS*, 21 Cl. Ct. 365, 369-70 (1990), *aff'd*, 950 F.2d 731 (Fed. Cir. 1991). The Federal Circuit, which summarized the legal criteria required to prove causation-in-fact under the Vaccine Act, requires that every petitioner:

> show a medical theory causally connecting the vaccination and the injury. Causation in fact requires proof of a logical sequence of cause and effect showing that the vaccination was the reason for the injury. A reputable medical or scientific explanation must support this logical sequence of cause and effect.

Grant, 956 F.2d at 1148 (citations omitted); *see also Strother*, 21 Cl. Ct. at 370.

This Court has organized the legal criteria in *Grant* by means of a two-part test. *First*, a petitioner must provide a reputable medical theory causally connecting the vaccination and the injury. In fine, can DTaP cause the type of injury alleged? *Second*, a petitioner must also prove that the vaccine actually caused the alleged symptoms in her particular case.

Under the first prong, a petitioner must demonstrate the biologic plausibility of their theory. This may be accomplished in a number of ways. First, a petitioner must proffer a scientific pathogenesis underlying the alleged causal relationship. Reliability and plausibility are found by providing evidence that at least a sufficient minority of physicians have accepted the theory. In addition, epidemiological studies

[20] 42 C.F.R. § 100.3(a).

and an expert's experience, while not dispositive,[21] lend significant credence to the claim of plausibility. Articles published in respected medical journals, which have been subjected to peer review, are also persuasive.

The second prong of the causation-in-fact test is difficult but not impossible. A petitioner must show, by a preponderance of the evidence--as this special master is wont to say, a test based on 50% and a feather--that the vaccine caused the symptoms that manifested in this case. A petitioner does not meet this affirmative obligation by merely showing a temporal association between the vaccination and the injury. Rather, a petitioner must explain *how* and *why* the injury occurred. *Strother*, 21 Cl. Ct. at 370; *see also Hasler v. United States*, 718 F.2d 202, 205 (6th Cir. 1993), *cert. denied*, 469 U.S. 817 (1984) (inoculation is not the cause of every event that occurs within a ten day period following it).

b. Applicability of the Two Part test in Phillip Kuperus' Case

In Phillip's case, the Court follows the two pronged causation in fact analysis tailored as: (i) Is it biologically plausible that DTaP, as a whole or in its individual components, can cause ADEM?; and, (ii) Did Phillip's DTaP vaccination result in his ADEM?

(i) ***Is it biologically plausible that DTaP, as a whole or in its individual components, can cause ADEM?***

Petitioner's medical expert, Dr. Shuman, posits a convincing theory of biologic plausibility based on the immunological challenge presented by the DTaP vaccination. In his "Opus Kuperus,"[22] Dr. Shuman stated that ADEM is an immune-mediated attack on the central nervous system (CNS) and can be stimulated by any one of the antigens[23] in the DTaP vaccine. Pet. Ex. 35 at 656. The immunological attack is a side effect of the antigens stimulating the immunological response. *Id*. This produces a result of injury to the CNS and immunity to diphtheria, tetanus and pertussis. *Id*. Dr. Shuman states that combining

[21] This first prong of the Court's test meets easily with cases where epidemiological or case study reports are already available. Beginning with this prong is practical when there is epidemiological evidence, for it avoids the tautalogical reasoning that would result when one attempts to answer *Can It?* without having reports and studies that previously would have answered *Did It?*

[22] Dr. Shuman referred to his report concerning the cause of Phillip's ADEM as his "Opus Kuperus." Trans at 112. The report was filed as Petitioner's Exhibit 35.

[23] Antigen: "any substance which is capable, under appropriate conditions, of inducing a specific immune response, and of reacting with the products of that response, that is, with specific antibody or specifically sensitized T-lymphocytes, or both. Antigens may be soluble substances, such as toxins and foreign proteins, or particulate, such as bacteria and tissue cells . . . ." DORLAND'S ILLUSTRATED MEDICAL DICTIONARY 100 (27th ed. 1988).

vaccines, as is the case with DTaP, increases the number of immunogens.[24] *Id.* Accordingly, if one or more of the immunogens in the vaccine resembles one of the proteins in the myelin sheath, ADEM may result. *Id.* In layman terms, Dr. Shuman posits that the mechanism that causes ADEM is the body attacking itself because a component of the myelin resembles an antigen introduced by the vaccine. The antigen was introduced to produce an immunological response, making the body immune to future introductions. However, because a component of the myelin sheath resembles the antigen, "[i]mmunological war breaks out" and the myelin is attacked. *Id* at 657.

Respondent's medical expert, Dr. Sriram, added a small measure of credibility to Dr. Shuman's theory of biologic plausibility. On cross-examination, Dr. Sriram agreed that when searching for a cause of ADEM a doctor will look for a prior immunological challenge. Trans. at 286. Dr. Srirarm also agreed that the administration of the vaccines for diphtheria, tetanus, and acellular pertussis constitutes an immunological challenge. *Id*. at 287. However, Dr. Sriram stated that Dr. Shuman's hypothesis had never been proven and that studies that tried to mimic Dr. Shuman's theory failed to get the expected results. *Id*. at 270-71.

The Institute of Medicine (IOM)[25] has written extensively on the relationships between vaccines and specific adverse events. Respondent usually relies on the IOM's publications to confirm Respondent's own positions, generally that there is a lack of causation between a particular vaccine and an alleged injury. Concerning the relationship between ADEM and the diphtheria and tetanus toxoids, the IOM concluded that "[t]he evidence is inadequate to accept or reject a causal relation between tetanus toxoid, DT, or Td and demyelinating diseases of the CNS [such as ADEM]." Pet. Ex. 89 at 1471.[26] However, the IOM did state that "it *is biologically plausible* that injection of an inactivated virus, bacterium, or live attenuated

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[24] Immunogen: a substance capable of inducing an immune response, in most contexts synonymous with antigen. DORLAND'S ILLUSTRATED MEDICAL DICTIONARY 821 (27th ed. 1988).

[25] The National Childhood Vaccine Injury Compensation Act established a committee at the Institute of Medicine (IOM) — a prestigious medical research organization funded by Congress to provide objective, timely, authoritative information and advice concerning health to government, the corporate sector, the professions, and the public — to review the medical literature on health problems or injuries occurring after vaccination. This Court, created by the same legislation, gives great deference to the committee's findings. "The principal purpose of the committee's work was to describe as precisely as possible, on the basis of all available evidence, the relationship between vaccines under study and specific adverse events. This led the committee to ask with each vaccine-adverse event pair, 'Can administration of the vaccine cause the adverse event.' All available sources of information were analyzed, from epidemiologic studies to unpublished case reports. Final decisions on causality were made by consensus after group discussion of all of the available evidence. In pursuing its conclusions, the committee adopted a neutral stance and maintained that stance consistently through each step in the process, assuming neither presence nor the absence of causal relation between the vaccines and the adverse events until the evidence indicated otherwise." INSTITUTE OF MEDICINE, ADVERSE EVENTS ASSOCIATED WITH CHILDHOOD VACCINES: EVIDENCE BEARING CAUSALITY (1994).

[26] INSTITUTE OF MEDICINE, ADVERSE EVENTS ASSOCIATED WITH CHILDHOOD VACCINES: EVIDENCE BEARING CAUSALITY, 86 (1994).

virus might induce an autoimmune response, by nonspecific activation of T cells directed against myelin proteins . . . ." *Id.* at 84 (emphasis added). Both the diphtheria toxoid and tetanus toxoid vaccines are inactivated bacterium.[27] Additionally, the IOM's conclusion dovetails nicely with Dr. Shuman's proposed mechanism.

Petitioner submitted numerous articles espousing a connection between the onset of demyelinating disorders and vaccines. In one such article,[28] the authors state that ADEM is usually preceded by a viral infection or vaccination, Pet. Ex. 97 at 1539, and that a preceding viral infection or vaccination also supports the diagnosis of ADEM. *Id.* at 1541. Other literature explains that ADEM is regarded as an immunologically mediated form of myelin destruction, Pet. Ex 56 at 971,[29] and non-viral organisms such as diphtheria toxin and tetanus toxin have been implicated in such. Pet. Ex. 55at 964.[30] Additionally, ADEM has been observed after vaccination with pertussis. Pet. Ex. 82 at 1316.[31]

Dr. Shuman's explanation of "immunological warfare" as set forth *supra*, is the scientific pathogenesis he alleges that caused Phillip's onset of ADEM. Taking into account Dr. Shuman's obvious expertise and comprehensive research in the subject, the Court accepts Dr. Shuman's explanation of biologic plausibility. Additionally, objective evidence in the form of numerous medical articles also support Dr. Shuman's theory. Thus, the Court finds that it is indeed biologically plausible that the DTaP vaccine can result in ADEM.[32]

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[27] Toxoid: "a modified or inactivated *bacterial* exotoxin that has lost toxicity but retains the properties of combining with, or stimulating the formation of, antitoxin." DORLAND'S ILLUSTRATED MEDICAL DICTIONARY 1736 (27th ed. 1988) (emphasis added).

[28] R. Arul Apak. M.D. et al., Acute Disseminated Encephalomyelitis in Childhood: Report of 10 Cases, 14 Journal of Child Neurology 198 (March 1999).

[29] John J. Kepes. M.D., Large Focal Tumor-like Demyelinating Lesions of the Brain: Intermediate Entity Between Multiple Scelrosis and Acute Disseminated Encephalomyelitis? A Study of 31 Patients, 33 Annals of Neurology 18 (Jan. 1993).

[30] 2 KENNETH F. SWAIMAN, M.D. & STEPHEN ASHWAL, M.D., PEDIATRIC NEUROLOGY PRINCIPLES & PRACTICE 849 (3d ed. 1999)

[31] Richard A. Rudick, Chapt. 483: Central Nervous System Complications of Viral Infections and Vaccines, CECIL TEXTBOOK OF MEDICINE (2000).

[32] Although not binding, the Office of the Special Masters has reached this conclusion in other cases. *Corder v. Sec'y Dep't of Health and Human Services*, 1999 WL 476256, at 7 (Fed. Cl. 1999) (the Chief Special Master found that "DPT vaccination can cause ADEM.") and *Johnson v. Sec'y Dep't of Health and Human Services*, 2000 WL 1141582, at 11 (Fed. Cl. 2000) (finding that the Td vaccine was a substantial factor in causing ADEM); *see also Althen v. Sec'y Dep't of Health and Human Services*, 2003 WL 21439669, at 11 (Fed. Cl. 2003) , *rev'd*, 00-0170V, slip op. at 20 (Fed. Cl. Sep. 30, 2003) (on appeal, Judge Braden found that not only was it biologically plausible that tetanus toxoid could cause ADEM, but also found that the tetanus toxoid caused the ADEM).

(ii) Did the 15 April 1998 DTaP vaccination caused Phillip's ADEM?

Dr. Shuman has concluded that "Phillip had an acute monophasic inflammatory reaction damaging his myelin as a result of his exposure to the DPT [sic]." Trans. at 144. Dr. Shuman agreed that ADEM can be viewed as an autoimmune disease. *Id.* at 129, however, he stated that a more apt description would be a "post-antigenic exposure disease." *Id*. In the case of Phillip's ADEM, Dr. Shuman stated that exposure to antigens from the DTaP caused the initial inflammatory response. *Id*. The monophasic nature of the response was due to the one time introduction of the antigens in the DTaP shot.[33] *Id.*

Dr. Shuman asserts that the manifestation of symptomology of ADEM typically occurs in five days to six weeks after exposure, with the most common time of presentation being at approximately six weeks. Pet. Ex. 35 at 8[34]; *Id*. at 141-42. The IOM concludes that ADEM "generally occurs after an interval of 5 days to six weeks following infection (not clinical disease) or injection of antigen." Pet. Ex. 89 at 1451.[35] Here, Mrs. Kuperus noticed that Phillip had become more clumsy and stopped progressing about four to six weeks subsequent to the 18 April 1998 DTaP shot. Trans. at 74. The medical records describe Phillip's clumsiness as "shakiness, tremor, and ataxia" six weeks after exposure to the DTaP. Pet. Ex. 10 at 116; Pet. Ex. 11 at 123.

Respondent disagrees with Dr. Shuman's assertion that onset typically occurs from five days to six weeks, citing another special master's decison in *Johnson ex rel. Johnson v. Sec'y of Dept. of Health and Human Services*, 2000 WL 1141582 (Fed. Cl. 2000). Res. Post Hrng. Memo at 21. In that decision, the special master found that onset between ten and twenty one days to be very important in her awarding entitlement. *Johnson*, at 6, 10. However, in *Johnson*, the injured party's ADEM effected her spinal cord, not her brain, as is the case with Phillip. *Id*. at 1. In his "Opus Kuperus," the data that Dr. Shuman presents agrees with *Johnson* in that the onset of the spinal cord form of ADEM does manifest within approximately ten to twenty one days. Pet. Ex. 35 at 657. However, that same data indicates that the occurrence of ADEM that attacks the myelin sheath in the brain manifests between five days to six weeks, with the largest proportion occurring closer to six weeks. *Id*. Additionally, as noted *supra*, the IOM concludes that onset is within five days to six weeks of the introduction of an antigen.

ADEM is usually preceded by a viral infection or vaccination. Pet. Ex. 53 at 1539. When looking for a cause of ADEM, one issue to be addressed is any prior immunological challenge that may have

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[33] Dr. Shuman stated that by reintroducing the same antigens that caused the initial inflammatory response would cause a reoccurrence or relapse. Trans. at 130.

[34] H. Shakari & S Otani, The Latent Period of Rabies Post-Vaccinal Encephalomyelitis In Man 71, fig. 4 (1959).

[35] INSTITUTE OF MEDICINE, ADVERSE EVENTS ASSOCIATED WITH CHILDHOOD VACCINES: EVIDENCE BEARING ON CAUSALITY 47 (1994).

occurred within the requisite time frame. Trans. at 287. Here, the only immunological challenge evident in the medical records is the DTaP vaccination. Dr. Sriram stated that children acquire a lot of infections that go undetected, however, he admits to no evidence of such in this case. *Id*.

Physicians found no other cause of Phillip's ADEM despite a focused effort to do so. After conducting numerous tests, Dr. David H. Van Dyke could find no "specific trend toward making a specific metabolic diagnosis." Pet. Ex 6 at 55. Dr. Pamela Kernes, a geneticist in the Mayo Clinic's Department of Medical Genetics, found that all of the studies undertaken at Phillip's genetic consultation were negative and she was unable to find a genetic or biochemical cause for Phillip's disorder. Pet. Ex. 9 at 88; Res. Rpt. at 5-6. Dr. Patterson performed an extensive work-up that showed no results on the potential cause of Phillip's injury. Pet. Ex. 9 at 73. An extensive evaluation by Dr. Katherine Holland and Dr. Mamdouh Abdulrazzak of Michigan University's Mott Children's Hospital, failed to define any clear etiology for Phillip's neurologic disorder. Pet. Ex. 10 at 117.

Petitioner provides a medically plausible mechanism, an autoimmune response, for Phillip's ADEM. The onset of his injuries was within the relevant time frame for such and was temporal to the administration of the DTaP vaccine. The 18 April 1998 DTaP shot was the only known immunological challenge introduced into Phillip's system at that time. The medical records indicate that doctors searched for other causes for Phillip's injuries but found none. Although both medical experts are eminently qualified, Dr. Shuman, Petitioner's expert, is board certified in neurology with special competence in child neurology, board certified in pathology with special competence in neuropathology, and board certified in neuro imaging. Dr. Shuman has diagnosed and treated numerous children with ADEM. Trans. at 99. Dr. Sriram is not a pediatric neurologist and is not involved in the diagnosis or treatment of children with ADEM. *Id.* at 298. Dr. Sriram describes his role in such cases as a consultant offering treatment recommendations. *Id*. Additionally, Dr. Sriram defers to Dr. Shuman's expertise in reading an MRI. *Id.* at 321. Thus, the Court finds that Petitioner has proven by a preponderance of the evidence that the DTaP vaccine that Phillip received on 15 April 1998 was more likely than not the cause of his ADEM.

V. FURTHER PROCEEDINGS

For the reasons stated above, the Court finds that the Petitioner is entitled to an award under the Vaccine Act for the acute disseminated encephalomyelitis that Phillip suffered as a result of the DTaP vaccination he received on 15 April 1998. The Court strongly encourages the parties to come to a meeting of the minds in determining the amount of the award. Thus, the Court requests Petitioner's counsel to initiate efforts in this regard. Petitioner's counsel is also requested to contact this Court to schedule a status conference and to initiate the process for the composition of a life-care-plan for Phillip.

IT IS SO ORDERED.

Richard B. Abell
Special Master