

PROCEDURAL BACKGROUND

On October 5, 1995, respondent filed a report in this matter recommending compensation be denied since contemporaneous medical documentation did not support petitioners' claim. Respondent's Report, filed October 5, 1995. An evidentiary hearing was held in this matter on October 14, 1997, in Washington, D.C. Petitioners presented the testimony of Belinda and Joseph Jenkins, Wesley's parents, and Dr. Mark Geier. Dr. Arnold Gale testified on respondent's behalf.

II.

FACTUAL BACKGROUND

The following evidence is contained in the record in this matter:⁽²⁾

Wesley was born on December 23, 1979, following an uncomplicated pregnancy. Tr. at 6. His APGAR⁽³⁾ scores were 8 and 9 at one and five minutes respectively. *Id.* at 7; P. Ex. 3 at 1. Other than some slight jaundice at birth, Wesley was a healthy baby who developed normally. Tr. at 8, 35. On January 2, 1980, Wesley received his two-week check-up and was found to be a well child. *Id.* at 8; P. Ex. 4 at 3. Mr. and Mrs. Jenkins described Wesley as a "healthy, happy, responsive baby" who developed normally. Tr. at 8, 35.

On March 11, 1980, Mr. and Mrs. Jenkins took Wesley to his pediatrician for a well-baby visit. Wesley was assessed as normal and received his first DPT vaccination at that time. Tr. at 9, 36; P. Ex. 4 at 3. Mrs. Jenkins testified that following his vaccination Wesley was slightly fussy and irritable with a low-grade temperature. Tr. at 10. Mr. Jenkins recalled that Wesley was lethargic and sleepy. *Id.* at 37. Wesley's fever subsided shortly thereafter and Mrs. Jenkins stated that her son experienced no further problems at that time. *Id.* at 10.

Mrs. Jenkins testified that on March 16, 1980, she put Wesley down for a nap in the late afternoon. *Id.* When Mrs. Jenkins later checked on Wesley, she found him lying on his stomach with jerking movements in both of his upper extremities and his head. *Id.* Mrs. Jenkins observed the jerking for approximately two to five minutes during which time Wesley's eyes remained in a fixed stare. *Id.* at 11; P. Ex. 18 at 99. Following the incident, Wesley's left arm was limp for approximately thirty minutes to an hour.⁽⁴⁾ Tr. at 11-12, 14; P. Ex. 18 at 99. With the help of her neighbor, Mrs. Jenkins contacted her husband. Tr. at 11, 12. When Mr. Jenkins arrived home, Wesley seemed fine. *Id.* at 12, 37. Wesley's parents, however, decided to take him to the emergency room. *Id.* at 12. The record from the emergency room states: "Jerking [left] side. Mother noticed baby jerky on left side as she woke [him] up from nap. Not sure if the boy had arm underneath his head. When seen in clinic, boy looked active, alert, happy & pleasant."⁽⁵⁾ P. Ex. 9 at 75. No tests other than a clinical examination were conducted. Tr. at 15; P. Ex. 18 at 99. After arriving home from the hospital, Wesley ate and slept well that evening. *Id.*

On the following day, March 17, 1980, Wesley was fine until early afternoon when Mrs. Jenkins went to check on him while he was napping. Tr. at 15. Mrs. Jenkins again found Wesley lying on his stomach with jerking movements of his upper extremities and head. *Id.* Wesley's eyes were fixed and deviated to the right. *Id.* The observed jerking episode lasted a maximum of five minutes. *Id.*; P. Ex. 18 at 99. Mrs. Jenkins subsequently took Wesley to the pediatric clinic to see the same pediatrician he had seen in the emergency room the previous night. Tr. at 16; P. Ex. 9 at 75. Wesley's physical exam was again within normal limits, but the doctor explained that Wesley could have experienced a seizure

and would need an EEG scheduled. *Id.*

Mrs. Jenkins testified that Wesley seemed fine for several days following this second incident. Tr. at 18. He was afebrile and continued to eat and sleep well. *Id.*; P. Ex. 6 at 5; P. Ex. 18 at 99. Thereafter, however, Wesley's parents began to notice him experiencing some slight jerking and deviated fixed eyes. Tr. at 18, 39. On the evening of March 19, Mr. Jenkins witnessed Wesley suffer a more pronounced seizure which resulted in mild cyanosis. *Id.* at 18, 40. Afterwards, Mr. Jenkins spoke to his commanding officer who arranged for Wesley to have an EEG immediately at Portsmouth Hospital. *Id.* at 18-19, 41; P. Ex. 9 at 74.

Wesley was admitted to Portsmouth Hospital on March 21, 1980, and remained there until March 25, 1980. Tr. at 21; P. Ex. 6 at 5. An EEG performed during this hospitalization showed an area of electrical abnormality in the right parietal area. P. Ex. 18 at 100. On March 25, 1980, Wesley was discharged on Phenobarbital with a diagnosis of idiopathic seizure disorder with an area of electrical abnormality in the right parietal area. Tr. at 21, 42; P. Ex. 6 at 7. His prognosis was considered excellent. P. Ex. 6 at 7. Following Wesley's discharge, Mrs. Jenkins recalled that her son was "drug[ged] down, sleepy, lethargic . . . he continued to eat but [was] just excessively sleepy and nonresponsive as far as stimulation, noise, [and] voices." Tr. at 22. Wesley continued to have seizures despite preventative medication. *Id.*

On April 22, 1980, Wesley received his second DPT and polio vaccinations. P. Ex. 9 at 73. During this visit, the doctor noted that Wesley was not experiencing any developmental lag and his head control was good. *Id.* On August 16, 1980, Wesley again saw his pediatrician at which time it was recorded that Wesley had not suffered any seizures since his original episode, but that Mrs. Jenkins was concerned about Wesley's neurological development. *Id.* at 71.

On October 8, 1980, a health record indicated that Wesley's seizures were "taking on an 'infantile spasm' character." *Id.* at 67. Wesley was admitted to the hospital the following day, on October 9, 1980. The admission record contains the following history of Wesley's condition:

The patient did well until about one month prior to admission when he began having head dropping and arm stiffening times one or two episodes. . . Seizures were then decreased in frequency and intensity times about one week. Two weeks prior to admission he again had arm stiffening and head dropping; also had an episode of body stiffening with eyes deviated downward to the right times 10 to 20 seconds. Two days prior to admission he had two episodes of generalized jerking of the extremities and staring times 15 seconds, associated with mild circumoral cyanosis. On the day of admission he had two more episodes of mild jerking of the extremities and staring which would last a few seconds. The patient smiles and laughs, rolls back to front at 3 to 4 months of age and rolled front to back shortly thereafter; no grasping of objects; no sitting; no transfer of objects; no repetitive syllables. Normal growth and development, development essentially stopped at about 3 to 4 months of age level.

P. Ex. 6 at 2. The physician noted "some head lag in sitting position." *Id.* During his stay, Wesley had an EEG which showed a hypsarrhythmic pattern consistent with infantile spasm syndrome. *Id.* at 2-3; Tr. at 26. Wesley was discharged on October 10, 1980, with a diagnosis of infantile spasms. P. Ex. 6 at 1, 3; P. Ex. 13 at 65.

Wesley's subsequent medical history is relevant in the following respects. A record from October 21, 1980, reflects that Wesley suffered psychomotor delays. P. Ex. 9 at 62. On November 25, 1980, Wesley's pediatrician assessed his

development at the level of a four to six month old. *Id.* at 61. In February 1981, Wesley underwent a developmental evaluation which indicated significant developmental delays. P. Ex. 7 at 19, 22. On April 1, 1982, Wesley was hospitalized for hepatitis; he was also diagnosed with static encephalopathy at this time. P. Ex. 12 at 47, 51, 54. Over the years, Wesley has received several diagnoses for his seizure disorder including cerebral palsy, seizures, encephalopathy, and infantile spasms. Tr. at 30; P. Ex. 13 at 5.

Several records address the etiology of Wesley's seizure disorder and psychomotor retardation; however, those most contemporaneous to the onset of his seizures in March 1980 make no connection to the DPT. For instance, the cause of his first seizure on March 16, 1980, was considered unknown. P. Ex. 9 at 75. In addition, the physicians considered numerous causes during his March 21, 1980, hospitalization and evaluation: central nervous system degenerative disease, metabolic, infection, neoplastic, toxic, congenital, and idiopathic; but discharged Wesley on March 25, 1980, with a diagnosis of an idiopathic seizure disorder. P. Ex. 6 at 7; P. Ex. 13 at 19. In February 1981, the etiology of his condition was still considered unknown. P. Ex. 9 at 47. A June 1982 genetics report suggested a possible relationship between Wesley's seizure disorder and heredity. P. Ex. 12 at 27. The etiology of Wesley's encephalopathy remained uncertain in April 1985, three years after he was first diagnosed. *Id.* at 9. Other records, again none contemporaneous, suggest a possible connection to the vaccination. A June 2, 1982, psychological report indicates Wesley was diagnosed in March 1980 with a seizure disorder possibly due to his DPT vaccination; however, this seems to be an inaccurate read of the records since the reports from 1980 do not suggest the association. P. Ex. 7 at 11. In September 1985, a screening clinic record notes Wesley's seizure disorder since infancy and states "? related to DPT immunization." P. Ex. 9 at 22. An August 1988 psychological report notes a "history of psycho-motor delay and seizures secondary to DPT injection in infancy." P. Ex. 7 at 1. Finally, a May 1990 record questions the etiology of Wesley's condition in terms of the temporal relationship to his DPT. P. Ex. 9 at 2.

Throughout his seizure disorder, Wesley has experienced head-drop, dive-type, absence, petit mal and grand mal seizures.⁽⁶⁾ Tr. at 22, 42. His diving-type seizures began when he was approximately 8-9 months old and involved head dropping. *Id.* at 32. His grand mal seizures consisted of his body becoming very rigid, with his arms and legs up and his eyes fixed and usually deviated down. *Id.* at 22. Afterwards, Wesley would be very sleepy. *Id.* at 22-23. Mr. Jenkins testified that in January 1996, Wesley's seizures became severe with projectile vomiting and extended periods of cyanosis. *Id.* at 23-24, 43. Mrs. Jenkins further testified that Wesley's seizures have never been under control. *Id.* at 21, 42. The longest Wesley has gone without a seizure has been approximately one month. *Id.* at 21. He has been on several types of medications and as of October 1997 was taking Oxcarbazepine, an experimental medication, which seemed to control his convulsions although, at the time of the hearing, Wesley had begun experiencing breakthrough seizures. *Id.* at 23, 24, 43.

III.

THE VACCINE ACT

The issue in this case is whether the injuries Wesley allegedly suffered, an acute encephalopathy and/or seizure

disorder, were caused by his March 11, 1980, DPT vaccination.⁽⁷⁾ Causation in Vaccine Act cases can be established in one of two ways: either through the statutorily prescribed presumption of causation, or by proving causation-in-fact. Petitioners must prove one or the other in order to recover under the Act.⁽⁸⁾ § 11(c). The Vaccine Injury Table lists certain injuries and conditions which, if found to occur within a prescribed time period, create a rebuttable presumption that the vaccine caused the injury or condition. § 14(a). The Table lists encephalopathy and residual seizure disorder as compensable injuries which create such a presumption if the onset of either occurs within 72 hours of the administration of the vaccine in question.⁽⁹⁾ *Id.* The presumption may be overcome by an affirmative showing that the injury was caused by a factor unrelated to the administration of the vaccine. § 13(a)(1)(B).

Since the onset of Wesley's seizures occurred more than 72 hours after his DPT vaccination and, as will be discussed, there's no proof petitioners demonstrated a Table encephalopathy, petitioners must prove that the vaccination caused-in-fact Wesley's injuries, commonly referred to as an off-Table case. In order to demonstrate entitlement in an off-Table case, petitioners must affirmatively demonstrate by a preponderance of the evidence that the vaccination in question more likely than not caused the injuries alleged. §§ 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, 369-370 (1990), *aff'd without opinion*, 950 F.2d 731 (Fed. Cir. 1991). This requires that petitioner show "that the vaccine was not only a but-for cause of the injury but also a substantial factor in bringing about the injury." *Shyface v. Secretary of HHS*, 165 F.3d 1344, 1352-1353 (Fed. Cir. 1999); *see also Grant*, 956 F.2d at 1148. Petitioners do not meet this affirmative obligation by merely showing a temporal association between the vaccination and the injury. Rather, petitioners 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 the ten day period [following the vaccination] . . . Without more, this proximate temporal relationship will not support a finding of causation"). If petitioners place "singular reliance on the temporal relationship between the administration of the vaccine and the onset of symptoms," the claim must fail. *Thibaudeau v. Secretary of HHS*, 24 Cl. Ct. 400, 403 (1991). Nor may petitioners meet their burden by eliminating other potential causes of the injury. *Grant*, 956 F.2d at 1149-1150.

In addition, petitioners' theory "must be supported by a sound and reliable medical or scientific explanation." *Knudsen v. Secretary of HHS*, 35 F.3d 543, 548 (Fed. Cir. 1994). "[E]vidence in the form of scientific studies or expert medical testimony is necessary to demonstrate causation" for a petitioner seeking to prove causation-in-fact. H.R. Rep. No. 990908, 99th Cong. 2d Sess., pt. 1 at 15 (Sept. 26, 1986), *reprinted in* 1986 U.S. Code Cong. and Admin. News 8344, 8356. Under *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 113 S.Ct. 2786, 2795 (1993), an expert's testimony based on scientific, technical or other specialized knowledge must be supported by more than "subjective belief or unsupported speculation" and "derived by the scientific method." *Daubert*, 113 S.Ct. at 2795. This requires that the proponent demonstrate that there is "some objective, independent validation of the expert's methodology." *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 43 F.3d 1311, 1316 (9th Cir. 1995) (Kozinski, J.), *on remand from* 113 S.Ct. 2786 (1993). The overall touchstone is "whether the analysis undergirding the experts' testimony falls within the range of accepted standards governing how scientists conduct their research and reach their conclusions." *Id.* at 1316.

IV.

PERTINENT MEDICAL LITERATURE⁽¹⁰⁾

Petitioners pursuing a causation-in-fact theory of recovery that the DPT vaccine actually caused the injuries alleged have often relied on epidemiological studies and other pertinent medical reports to substantiate their

claim. Petitioners here rely heavily on the National Childhood Encephalopathy Study ("NCES") and the Institute of Medicine ("IOM") reports to demonstrate not only that the vaccine can cause an encephalopathy, seizure disorder, and permanent neurological damage, but that the DPT did cause these injuries in Wesley's case. A general overview of the NCES and IOM reports follows; the particulars of the study and reports that petitioners rely on will be more thoroughly discussed in the expert testimony and discussion portions of this decision.⁽¹¹⁾

National Childhood Encephalopathy Study: The NCES was initiated in 1976 "to assess the risks of certain serious neurological disorders associated with immunization in early childhood." R. Ex. C at 80. The researchers set out to confirm their hypothesis that there exists a causal link between pertussis and serious neurological illnesses by showing that the serious neurological "disorders occurred in immunized children, at specified time intervals after immunization, more often than expected by chance in an appropriate control group." *Id.* at 96. The researchers advanced a case-control approach to test this hypothesis.⁽¹²⁾ *Id.* at 97. The approach called for the identification of all cases of specifically enumerated acute neurological illnesses leading to hospital admissions in children ages 2-36 months over a three year period from July 1, 1976, to June 30, 1979. *Id.* at 101. Treating physicians were asked to report all incidences of acute or subacute encephalitis/encephalomyelitis, encephalopathy; unexplained loss of consciousness; convulsions with a total duration of more than about ½ hour; convulsions followed by coma lasting two hours or more; convulsions followed by paralysis or other neurological signs not previously present lasting 24 hours or more; infantile spasms (West's syndrome); and/or Reye's syndrome (acute encephalopathy with abnormal liver function tests). *Id.* at 155-157. After matching the identified case children by age, sex, and area of residence with appropriate control children, the investigators conducted in-depth examinations of every study participant, gathering a history of the child's immunizations, previous infections, clinical course (in case children), family medical and social background, and other risk factors. *Id.* at 101. After determining the date of onset of the acute illness for each case child and placing the participant in one of three categories which corresponded with the child's previous and subsequent neurological medical history, the investigators undertook an evaluation of the risks associated with the pertussis vaccine. *Id.* at 102-104, 107-108, 146-147.

Institute of Medicine, Committee to Review the Adverse Consequences of Pertussis and Rubella Vaccines, 1991 Report: In November 1989, in response to the Vaccine's Act's summons for a review of the scientific literature (including the NCES) and other information regarding the possible adverse consequences of pertussis, the IOM created the Committee to Review the Adverse Consequences of Pertussis and Rubella Vaccines. The committee was charged with several duties, among them to:

identify and review all available medical and scientific literature on the nature, circumstance, and extent of the relationship, if any, between vaccines containing pertussis (including whole cells, extracts, and specific antigens) and the following illnesses and conditions: hemolytic anemia, hypersarrhythmia, infantile spasms, Reye syndrome, peripheral mononeuropathy, deaths classified as sudden infant death syndrome (SIDS), aseptic meningitis, juvenile diabetes, autism, learning disabilities, hyperactivity, and other illnesses as recommended by the committee or the Advisory Commission on Childhood Vaccines.

Christopher P. Howson, et al. at vi.⁽¹³⁾ The committee also agreed in May 1990 to review the relationship between the pertussis vaccine and "anaphylaxis; erythema multiforme or other rashes; Guillain-Barré syndrome (polyneuropathy); protracted inconsolable crying or screaming; thrombocytopenia; and shock and 'unusual shock-like state' with hypotonicity, hyporesponsiveness, and short-lived convulsions (usually febrile)." *Id.* Lastly, the committee assessed the causal relation between the pertussis vaccine and permanent neurologic damage. *Id.* Composed of experts in "infectious diseases, pediatrics, internal medicine, neurology, epidemiology, biostatistics, decision analysis, biologic mechanisms of vaccines, immunology, and public health," the committee reviewed various information sources "including case series and individual case reports published in peer-reviewed journals and reported by vaccine manufacturers; unpublished case reports from physicians, parents, and other concerned persons; epidemiologic studies; studies in animals; . . . other laboratory studies[;]. . . conference and symposium proceedings[;] legal judgments[;] and academic dissertations." *Id.* at vi-vii. The committee published its comprehensive findings in 1991.

Institute of Medicine, Committee to Study New Research on Vaccines, 1994 Report: Beginning in December 1993, the IOM's Committee to Study New Research on Vaccines revisited the issue of adverse events associated with DPT vaccination, specifically reevaluating the causal relation between the vaccine and permanent neurological damage. R. Ex. F at 5. This reevaluation was prompted solely by the 1993 publication of the ten-year follow-up report to the National Childhood Encephalopathy Study. *Id.* at 4; *see also* R. Ex. E. This committee was composed of six individuals experienced in pediatrics, neurology, and epidemiology who had served on either the Vaccine Safety Committee, the Committee to Review the Adverse Consequences of Pertussis and Rubella Vaccines, or both. R. Ex. F at 5-6. This committee published its findings in 1994.

V.

EXPERT TESTIMONY

Dr. Mark Geier

Petitioners presented the testimony of Dr Mark Geier.⁽¹⁴⁾ Dr. Geier believes to a reasonable

degree of medical certainty that it is more likely than not that Wesley's seizures and mental retardation were caused by his DPT vaccination. Tr. at 49, 64; P. Ex. 19 at 3, 23-24. Dr. Geier bases this opinion in part on three criteria.⁽¹⁵⁾ First, Wesley was a healthy, normal child prior to his vaccination. Tr. at 48, 75; P. Ex. 19 at 4, 10, 11, 23. Second, Wesley developed an obvious, significant neurological reaction, *i.e.*, seizures and encephalopathy, five days after his vaccination. Tr. at 48, 75; P. Ex. 19 at 11, 12, 23, 24. Third, no alternative cause was ever found for Wesley's seizures despite an extensive work-up.⁽¹⁶⁾ Tr. at 49, 75; P. Ex. 19 at 11, 12, 22, 23. As support for this three-criteria approach, Dr. Geier relies on the NCES, the IOM's 1994 report, and other medical literature which states that DPT vaccinations can cause permanent neurological damage in otherwise apparently normal children who suffer a serious acute neurological injury within seven days of the inoculation. Tr. at 49; P. Ex. 19 at 12-20. Dr. Geier testified that the key to the NCES and IOM report is the time window between the DPT vaccination and the onset of the neurological illness; Dr. Geier relies heavily on this temporal association. Tr. at 93-94, 114. However, Dr. Geier agreed on cross-examination that a reaction is less likely to be DPT-related if it occurs more than 72 hours after the inoculation. *Id.* at 87-88.

Dr. Geier further substantiated his causation opinion with a probability calculation taken from the IOM's (1991) data. *Id.* at 50, 53, 58-60, 76-77; P. Ex. 19 at 20-21. Dr. Geier explained that the IOM calculated the probability that a child will develop an encephalopathy in a two-day period following a DPT vaccination in the first year of life; he also testified the IOM estimated the probability that the encephalopathy is vaccine-related. Tr. at 50, 58; P. Ex. 19 at 20-21. From this data, Dr. Geier calculated that there is an 83.8 percent probability that Wesley's encephalopathy was a result of his DPT vaccination administered five days earlier and did not occur by random association.⁽¹⁷⁾ Tr. at 53, 58-59; P. Ex. 19 at 22-23. The remaining 16.2 percent, Dr. Geier testified, is made up of many different possible disorders which could explain Wesley's seizures. Tr. at 55. Dr. Geier further concluded that *in any case* where an encephalopathy occurs within five days of the vaccination, more likely than not the injury is DPT-related. P. Ex. 19 at 22. However, Dr. Geier also admitted there is no test or biological marker to determine if the vaccination or other etiology caused the neurological insult, nor can one differentiate, based on the three criteria, between cases that occur by chance and those that are DPT-related. Tr. at 76, 77-78. Instead, only a probability of causation can be offered, and there *is* a percentage of neurological injuries within the seven days following vaccination which are random occurrences. *Id.* at 76, 77, 89.

Dr. Geier also believes Wesley would have been admitted into the NCES since he was sick enough to have been hospitalized because of his seizures. *Id.* at 62, 115. Dr. Geier further opined that Wesley experienced an encephalopathy five days after his vaccination. *Id.* at 62; P. Ex. 19 at 11, 12, 24. He elaborated: "If you look up encephalopathy in the medical dictionary it means damage to the brain. In the general sense, clearly this child had encephalopathy. It was a child that had no seizures and ended up with an intractable seizure disorder and that change occurred in the brain. So, clearly, this child had an encephalopathy." Tr. at 62. Dr. Geier also believes Wesley's infantile spasms would have prompted notification to the NCES since the study did not require, for reporting purposes, that the infantile spasms begin within a certain time frame following vaccination. *Id.* at 115-116.

Dr. Arnold Gale

Dr. Gale, respondent's expert, opined to a reasonable degree of medical certainty that Wesley's seizures five days after his first DPT were not caused by the vaccination.⁽¹⁸⁾ Tr. at 97. Dr. Gale bases his opinion on the fact that there is no known biological or historical marker, physical sign or symptom, or laboratory results to substantiate that the vaccine, versus another etiology, caused Wesley's seizures.⁽¹⁹⁾ *Id.* at 98, 125; R. Ex. A at 4. Dr. Gale also opined that epidemiological studies alone fail to provide "the kind of data that would permit us to say, within a [reasonable] degree of medical probability that any one child during the seven days following vaccination had seizures that were attributable to the shot."⁽²⁰⁾ Tr. at 98. Nevertheless, Dr. Gale agreed the DPT vaccine can cause permanent neurological injury in a previously normal child who suffers a neurological symptom within seven days of the inoculation, although he also reported the causal relation between serious acute neurological illnesses and the DPT is unclear and, at the very least, rare.⁽²¹⁾ *Id.* at 110-111; R. Ex. A at 4.

Dr. Gale also opined that Wesley, who appeared alert and happy following his first seizure, did not experience an acute encephalopathy or illness when his seizures began.⁽²²⁾ Tr. at 103; R. Ex. A at 3. Instead, he related Wesley's encephalopathic condition to "an epileptic or postepileptic encephalopathy as most of the youngsters who have infantile spasms at some point during their lives develop."⁽²³⁾ *Id.* Dr. Gale further posited that Wesley would not have been included in the NCES study. Tr. at 104-106. He explained Wesley initially suffered an afebrile seizure, without coma or significant paralysis.⁽²⁴⁾ *Id.* at 105. Dr. Gale also rejected the notion that Wesley would have been reported to the study for his infantile spasms. He believes the NCES only admitted cases where infantile spasms represented the presenting epilepsy. *Id.* at 128. He noted Wesley's infantile spasms developed later in his course and were not classic infantile spasms: "[h]e has myoclonic seizures that began in the middle of having [an] epilepsy. It's not the same thing as having infantile spasms, and I'm fairly confident of that."⁽²⁵⁾ *Id.* at 106, 124. Dr. Gale also noted the 1991 IOM report found no causal relation between DPT and afebrile seizures or infantile spasms. R. Ex. A at 4.

Dr. Gale rejected Dr. Geier's attempt to apply the IOM data to this case to prove the DPT caused Wesley's seizures; he believes the DPT's role in individual cases is speculative. *Id.*; Tr. at 106-108. He asserted that "the use of the statistics from the study cited in [the IOM] report are in clear contradistinction to the intentions of the authors who wrote those reports . . . they never intended the data as they assembled them and analyzed them to be used in that fashion." Tr. at

99, 100. Dr. Gale agreed the IOM itself generated a statistical finding from published and processed data of studies, but emphasized the authors "warned that they would not ascribe an individual case to the vaccine based on the data that they have examined" and they cautioned others against doing so.⁽²⁶⁾ *Id.* at 100, 109. Dr. Gale posited that no epidemiologist would use the data in this manner and he was unsure how a *clinician* would draw conclusions from the data to apply to individual cases. *Id.* at 99.

VI.

DISCUSSION

Since the primary issue in this case is whether Wesley's March 11, 1980, DPT vaccination caused-in-fact the injuries alleged, the resolution of this issue involves a two-prong analysis: 1) *can* the DPT vaccination cause the injuries alleged?; and 2) *did* the DPT vaccination actually cause Wesley's injuries in this case? *Guy v. Secretary of HHS*, No. 92-779V, 1995 WL 103348 (Fed. Cl. Spec. Mstr. Feb. 21, 1995) (two-step causation-in-fact analysis used); *Alberding v. Secretary of HHS*, No. 90-3177V, 1994 WL 110736 (Fed. Cl. Spec. Mstr. Mar. 18, 1994) (two-step causation-in-fact analysis used).⁽²⁷⁾ After a thorough review of the record, I conclude that the DPT can cause the injuries Wesley suffered and that petitioners have thus satisfied the first prong of the causation-in-fact analysis. However, petitioners have failed to prove actual causation in this case. While I find that Wesley would likely have been reported to the NCES researchers based solely on his October 1980 infantile spasms diagnosis, it is this same diagnosis which excludes him from ultimately meeting the NCES criteria. As the IOM concluded in its 1991 report, there is no causal relation between the DPT and infantile spasms. I have also determined that Wesley did not suffer an acute encephalopathy within five days of the inoculation. Therefore, any relative or attributable risk estimates utilized by Dr. Geier to assess actual causation in Wesley's case are irrelevant. Given these findings and for the reasons explained below, petitioners have failed to prove causation-in-fact and are not entitled to compensation.

1) Can the DPT vaccination cause the injuries alleged?

Petitioners allege Wesley suffered two injuries as a result of his vaccination: acute encephalopathy and seizure disorder. Thus, the first prong of the causation-in-fact analysis must address separately whether the DPT vaccination can cause each injury alleged.

(a) Can the DPT vaccination cause an acute encephalopathy?

A review of the evidence provides a reasonable basis for finding that the pertussis component of the DPT vaccine can cause an acute encephalopathy in children under certain circumstances.

NCES: In evaluating the risks associated with the DPT vaccine, the NCES researchers immediately recognized the potential difficulty in ascribing causation to the pertussis component since acute encephalopathic conditions are not only extremely rare in children, but can have many causes or, alternatively, no identifiable cause.⁽²⁸⁾ R. Ex. C at 95. In addition, acute encephalopathic or convulsive conditions postulated to be DPT-related may be clinically similar to other illnesses with a different etiology. *Id.* at 95, 96. Nevertheless, the investigators pursued their hypothesis. In seeking reports of encephalopathic injuries, the researchers defined the illnesses as follows:

The term "encephalitis" is taken to indicate any infective or inflammatory cerebral disorder. The more general term "encephalopathy" is used when the cause of the cerebral disorder is not immediately obvious.

The Clinical features of both types of illness may include: altered level of consciousness, confusion, irritability, changes in behaviour, screaming attacks, neck stiffness, convulsions, visual, auditory and speech disturbances, motor and sensory deficit.

Id. at 157. After analyzing 1,000 case children and their matched controls, the researchers concluded that:

(a) Most cases of acute and potentially damaging neurological illness in early childhood are attributable to causes other than immunization. (b) Such illnesses occur more frequently within 7 days, and particularly within 72 hours, after DTP vaccine . . . than would be expected by chance. Most affected children made a complete recovery . . .

Id. at 149. The researchers reported various relative risks, with and without reference to a specific illness, based on the dates of admission and onset and dependent on when the immunization was administered.⁽²⁹⁾ *Id.* at 118, 129. The researchers concluded, based on the relative risks, that the vaccine "probably can cause acute neurological reactions." *Id.* at 141. The study further noted that "the onset of these serious neurological illnesses has been shown to 'cluster' at particular time intervals after [the DPT immunization], which supports a causal association . . . The possibility that causal associations exist between immunization with pertussis . . . and the development of serious neurological disorders is widely regarded as biologically plausible." *Id.* at 142.

Institute of Medicine 1991 Report: In 1991, the IOM's Committee to Review the Adverse Consequences of Pertussis and Rubella Vaccines concluded that the NCES results "suggest that DPT immunization is associated with an increased risk, within seven days, of seizures and encephalopathy." R. Ex. D at 101. The IOM determined that the relative risk for an encephalopathic injury within seven days of the vaccine was 3.1 (in the NCES, of the 904 children suffering acute neurological events, excluding infantile spasms, only 389 suffered an encephalopathy and only 12 of the 389 had the onset within the seven days following the vaccination). *Id.* The IOM further concluded that "[t]he evidence is consistent with a causal relation between DPT vaccine and acute encephalopathy, defined in the controlled studies reviewed as encephalopathy, encephalitis, or encephalomyelitis . . . The range of excess risk of acute encephalopathy following DPT immunization is consistent with that estimated for the NCES: 0.0 to 10.5 per million immunizations." *Id.* at 118 (footnote omitted).

Expert Testimony: Both experts agreed the DPT can cause an acute encephalopathy. Dr. Geier couched this plausibility in terms of a probability calculation, while Dr. Gale conservatively agreed the causal relationship occurs rarely. However, Dr. Gale also questioned attributing cause, even generally, to the DPT shot where no biological marker exists to distinguish the illness from non-DPT related diseases. Nevertheless, he accepted that the DPT can cause permanent neurological injury in a previously normal child *who had neurological symptoms within seven days of the vaccination.*

In light of the evidence discussed above, I conclude that the DPT vaccine can cause an acute encephalopathy (as defined by the NCES) in children within seven days after the administration of a DPT vaccine.

(b) Can the DPT vaccination cause seizures/seizure disorder?⁽³⁰⁾

A review of the evidence provides a reasonable basis for finding that the pertussis component of the DPT vaccine can cause the onset of certain types of seizures, which then progress to seizure disorders, within seven days of the vaccination.

NCES: As mentioned, treating physicians were asked to apprise the NCES researchers of any children admitted for convulsions (i) with a total duration of more than about ½ hour, or (ii) followed by coma lasting two hours or more, or (iii) followed by paralysis or other neurological signs not previously present lasting 24 hours or more. R. Ex. C at 157. Physicians were also asked to communicate any cases of infantile spasms (West's syndrome). *Id.* Again, the NCES researchers concluded generally that "[m]ost cases of acute and potentially damaging neurological illness [including those seizures meeting the reporting criteria] in early childhood are attributable to causes other than immunization[, and] [s]uch illnesses occur more frequently within 7 days, and particularly within 72 hours, after DTP vaccine . . . than would be expected by chance. Most affected children made a complete recovery." *Id.* at 149. They also reported that "the onset of these serious neurological illnesses has been shown to 'cluster' at particular time intervals after these two immunizations, which supports a causal association . . . The possibility that causal associations exist between immunization with pertussis . . . and the development of serious neurological disorders is widely regarded as biologically plausible."⁽³¹⁾ *Id.* at 142.

Institute of Medicine 1991 Report: The committee concluded that the NCES results "suggest that DPT immunization is associated with an increased risk, within seven days, of seizures and encephalopathy." R. Ex. D at 101, 107. The IOM determined that the relative risk for convulsions within seven days of the vaccine was 3.3; this calculation took into consideration that only 515 of the 904 children experiencing an acute neurological event (excluding infantile spasms children) had convulsions and only 18 of the 515 had a seizure within seven days of the vaccination. *Id.* at 101. In examining the pertussis vaccine's relationship with seizure types particularly, the reviewers found a causal relation between the vaccine and febrile seizures,⁽³²⁾ but insufficient evidence to indicate such a relation with epilepsy. *Id.* at 118. The committee also determined that "the available data provides no evidence of a statistically significant increase in the risk of afebrile seizures following DPT vaccinations" and consequently "the evidence does not indicate a causal relation between DPT vaccine and afebrile seizures." *Id.* at 115, 118. More importantly for our purposes here, the IOM's 1991 report found "[t]he evidence does not indicate a causal relation between DPT vaccine or the pertussis component of DPT and infantile spasms." *Id.* at 77.

Expert Testimony: Dr. Geier again couched his discussion of the causal relation between seizures and the DPT in terms of the alleged related encephalopathy. Dr. Gale again questioned the causal relationship generally, as stated above. However, Dr. Gale also specifically rejected that epidemiological studies alone could provide the data from which one could opine that a seizure was attributable to the DPT inoculation. Tr. at 97.

In light of the evidence discussed above, I conclude generally that the DPT vaccine can cause seizures, which then progress to seizure disorders, in children within seven days of the vaccination.

Incidentally, petitioners must not only demonstrate that the vaccine caused the alleged injuries, but that Wesley "suffered the residual effects or complications of such illness, disability, injury, or condition for more than 6 months after the administration of the vaccine." § 11(c)(1)(D)(i). Since Wesley suffered numerous seizures in the six months following the vaccination and continued to experience convulsive activity thereafter and to this day, petitioners have met their burden on this prerequisite element. Whether Wesley's current condition of mental retardation is related to his alleged vaccine-related injuries is an inquiry appropriate in the damages phase, but one which has been routinely

assessed by the special masters in the entitlement stage for reasons of judicial economy.⁽³³⁾

In this case, the experts agreed, based on the IOM's 1994 report, that the DPT vaccine can cause permanent neurological injury in children who suffer serious neurological illnesses, as defined by the NCES, within seven days of the inoculation.⁽³⁴⁾ The IOM determined in 1994, following the completion of the NCES ten-year follow up study, that "the *balance of evidence is consistent with* a causal relation between DPT and the forms of chronic nervous system dysfunction described in the NCES in those children who experience a serious acute neurologic illness within 7 days after receiving DPT vaccine."⁽³⁵⁾ R. Ex. F at 2.

The 1993 follow-up report was based on twelve of 367 case children (who were reviewed on follow-up, had no previous neurologic injury, and suffered death or some dysfunction) who had received the vaccination within seven days of their acute illness. R. Ex. E at 4; *see also* R. Ex. F at 10. The follow-up study assessed six areas of dysfunction: neurological, motor, sensory, educational, behavioral, and self-care. R. Ex. E at 3. Cases of infantile spasms and those with neurologic defects prior to the onset of the acute illness were excluded from the relative risk estimates of death or long-term dysfunction. *Id.*; *see also* R. Ex. F at 10. The study revealed that "[c]ase children who had received DPT within 7 days prior to the acute event were no more or less likely to have died or experienced dysfunction at the 10-year follow-up (66.7%) than case children who had not been vaccinated with DPT within 7 days prior to the acute event (61.6%)." R. Ex. F at 10; *see also* R. Ex. E at 4. The NCES authors could not determine whether the outcome was different based on the initial diagnosis, nor could they assess whether the dysfunction was different in nature between those children who were and were not immunized prior to the acute illness. R. Ex. E at 4; *see also* R. Ex. F at 11. Nevertheless, the IOM concluded that the evidence was consistent with the causal relation between the vaccine and permanent neurological damage in prescribed circumstances.

Petitioners' burden of proof in demonstrating that the current condition is related to the vaccine-related injury "is not a difficult burden, and requires far less than medical certainty" but it does demand "some logical, direct causal link" between the injury and the areas of impairment. *Hossack v. Secretary of HHS*, 32 Fed. Cl. 769 (1995). Based on the NCES and IOM's findings, I accept that mental retardation may be the sequela of a vaccine-related, NCES-defined acute neurological injury which occurs in a previously neurologically normal child.⁽³⁶⁾

Given that the DPT vaccine can cause an acute encephalopathy, seizures, and permanent neurological damage, albeit often in prescribed circumstances, petitioners have satisfied the first prong of the causation-in-fact analysis.⁽³⁷⁾

2) Did the DPT vaccination actually cause the injuries in this case?

Given that the NCES is the most significant study conducted to date on the effects of the pertussis immunization, special masters have frequently analyzed this second prong in a two-part inquiry which utilizes the methods and conclusions of the study's investigators. The first inquiry asks whether a petitioner would have been notified to and included in the study. Assuming an affirmative finding for the first inquiry, the second inquiry then requires an analysis of whether and how the conclusions and statistical calculations performed by the researchers assist in determining if a particular petitioner's injuries were more likely than not caused by the DPT vaccine.⁽³⁸⁾

(a) Would Wesley have met the NCES's criteria for notification and inclusion?

In an attempt to identify all relevant cases of children admitted for acute neurological illnesses, the NCES researchers devised a notification scheme outlining which illnesses should and should not be reported to the researchers. Placing Wesley in the context of the study, his physicians should have reported him to the NCES for any of the five neurological illnesses previously outlined.

Acute or subacute encephalitis/encephalomyelitis; encephalopathy: After a review of the record and NCES criteria, I find that Wesley did not suffer an acute or subacute encephalopathy or encephalitis/encephalomyelitis compelling notification. As previously stated, physicians were asked to notify the NCES researchers of these encephalopathic events regardless of the temporal relationship of such illnesses with the administration of a vaccine. These injuries were specifically defined:

The term 'encephalitis' is taken to indicate any infective or inflammatory cerebral disorder. The more general term 'encephalopathy' is used when the cause of the cerebral disorder is not immediately obvious.

The Clinical features of both types of illness may include: altered level of consciousness, confusion, irritability, changes in behaviour, screaming attacks, neck stiffness, convulsions, visual, auditory and speech disturbances, motor and sensory deficit."⁽³⁹⁾

R. Ex. C at 157. Although I find Dr. Geier qualified to render an opinion based upon his review of the medical records and his knowledge of the DPT literature, he is not a pediatric neurologist, and his opinion that Wesley suffered an encephalopathy within five days of his DPT vaccination is not persuasive absent supporting documentation.⁽⁴⁰⁾ In my view, Dr. Gale, a pediatric neurologist, is more qualified to opine whether Wesley experienced an acute encephalopathic injury. I find persuasive Dr. Gale's testimony that Wesley developed a chronic encephalopathy *as a result of his subsequent seizure disorder*, but was not encephalopathic when his seizures began five days following his DPT vaccination. Dr. Gale's opinion is supported by the medical records which reflect Wesley was not diagnosed with an encephalopathy until April 1982, two years after the onset of his seizures. The records also show that Wesley's March 16, 1980, examination was within normal limits; he appeared alert and active with a flat, soft anterior fontanelle. Moreover, Wesley's parents described a relatively normal child following the vaccination. While Wesley experienced lethargy, slight fussiness, and a short-lived low-grade fever immediately after the inoculation, no other problems were noticed until his first seizure. After his initial seizure, Wesley was "fine" and "relatively normal" by the time Mr. Jenkins returned home from work; the child then ate and slept on the evening of March 16. A clinical examination following his second seizure on March 17, 1980, was considered normal. In the days following March 17, Wesley was deemed afebrile and "okay," he ate and slept well. In late March, despite being diagnosed with a seizure disorder, his prognosis was excellent. In April 1980, almost 1½ months after the vaccination, Wesley suffered "no developmental lag" and maintained good head control. On July 2, 1980, Wesley was considered a "well baby" and received his second DPT. P. Ex. 4 at 4. Finally, no contemporaneous records specifically diagnose an acute encephalopathy. I conclude, therefore, that Wesley did not suffer from an acute or subacute encephalitis/encephalomyelitis or encephalopathy which would have necessitated notification to the NCES researchers.⁽⁴¹⁾

Unexplained loss of consciousness: Neither Mr. nor Mrs. Jenkins testified that Wesley was at any time

unconscious following his DPT vaccination, nor do the medical records support such an incident. Thus, Wesley would not have been reported for an unexplained loss of consciousness.

Convulsions: Wesley's parents testified they observed seizures lasting no more than five minutes. The medical records do not support that Wesley experienced any seizures over 30 minutes, or at least any before his hospitalization in October 1980. It is also apparent from Wesley's parents' testimony and the medical records that he did not experience a coma or sustain paralysis or neurological signs which lasted 24 hours or more following his convulsive activity. Instead, according to Mr. and Mrs. Jenkins' testimony and the medical records, Wesley appeared "fine" after his seizure incidents, and at most, experienced lethargy and limpness for thirty minutes to an hour following his first seizure. Thus, Wesley's seizure activity failed to meet this reporting criterion established by the NCES investigators.

Infantile spasms (West's syndrome): Wesley was diagnosed with infantile spasms in October 1980, seven months after his DPT vaccination.⁽⁴²⁾ Dr. Geier opined that Wesley's infantile spasms would have prompted notification since the study did not require, for reporting purposes, that the infantile spasms begin within a certain time frame following vaccination. In contrast, Dr. Gale testified Wesley's infantile spasms were not a part of his acute illness following his vaccination, but developed much later in his seizure course; thus, he would not have been reported to the NCES researchers.⁽⁴³⁾ Dr. Gale believed, based on a lecture presented by Dr. Marty Feldman, a pediatrician, that inclusion in the study required that the infantile spasms be the presenting epilepsy. Dr. Gale also testified Wesley did not suffer "classic" infantile spasms and, therefore, would not have been included in the study. I am unconvinced by Dr. Gale's understanding of the study's treatment of infantile spasm cases; there simply is nothing in the NCES itself which states that the infantile spasm must be the presenting epilepsy to be reported to or included in the study. Instead, physicians were asked to report any children admitted for any of the conditions defined in the notification table; the NCES stated and the IOM verified that the children could be reported with confirmed or possible diagnoses. R. Ex. C at 155, 157; R. Ex. D at 100. This manner of reporting seems to be further supported by the IOM's (1991) criticism that the study was limited with respect to its infantile spasms cases, since no uniform definition was used "in that children were considered infantile spasms cases if they were so designated by the admitting physician." R. Ex. D at 74 (citation omitted). Of the 1,000 cases reviewed, 269 children were admitted with diagnoses of infantile spasms.⁽⁴⁴⁾ *Id.* at 73. Of these, it appears 212 were diagnosed with infantile spasms at fifteen days after admission or on discharge. R. Ex. C at 117. In 96 of the 212 infantile spasms cases (*i.e.*, 46%), the child was deemed to have been previously neurologically *abnormal* (*i.e.*, Category II) which suggests that the infantile spasms may not have been the presenting epilepsy in some cases.⁽⁴⁵⁾ *Id.* A thorough review of the NCES notification criteria and the researchers' specific handling of infantile spasms suggests to me that Wesley *would have been reported* to the NCES investigators based solely on his infantile spasm activity and related October 1980 admission and diagnosis.⁽⁴⁶⁾

Since I have determined that Wesley's infantile spasms would likely have prompted *notification* to the study, the next step is to determine how his case would have been treated. Once the NCES investigators were satisfied that all those reported met the notification criteria, in-depth examinations of each study participant (case and control children) were conducted. R. Ex. C at 101. This involved gathering the history of the child's immunizations, previous infections, clinical course, family medical and social background, and other risk factors. *Id.* Following this examination, the investigators then determined the *date of onset of the acute neurological illness* for all case participants regardless of their respective vaccination histories. *Id.* at 102. The investigators based this determination on a comprehensive review of all information provided by the physicians and parents.⁽⁴⁷⁾ *Id.* The "date of onset" was defined as "the date on which acute neurological symptoms or signs related to the current illness first developed."⁽⁴⁸⁾ *Id.*; *see also Id.* at 146-147. However, given the inability at times to establish an accurate date of onset using this measure, the researchers also analyzed the data based on the date of the hospital admission,⁽⁴⁹⁾ which was typically undisputed. *Id.* at 102, 103.

In subsequent examination of the cases, the researchers recognized the limits of their analysis which was arbitrarily

confined to a review of those cases in which the vaccine was administered within 28 days of the admission or onset of the acute illness. *Id.* at 146. For instance, a child may have suffered minor convulsions prior to their hospital admission for a major seizure. While the major seizure may have prompted notification, the previous brief seizure activity would not have been considered under their initial review process, which could have resulted in the exclusion of possible vaccine-associated cases.⁽⁵⁰⁾ *Id.* In addition, the researchers were concerned with whether the vaccination triggered events which resulted in a later, more serious convulsions. *Id.* Therefore, in hopes of recognizing all potential vaccine-associated cases, the researchers revised their analysis and reviewed every case for previous seizure activity. *Id.* at 147. In convulsion cases, a negative answer to whether the child suffered any earlier convulsions established the date of onset as the date of the major convulsion for which the child was admitted. *Id.* In those cases where prior seizure activity occurred, a further inquiry was conducted into whether the convulsions were part of a "single pathological process," *i.e.*, an "obvious and continuing underlying clinical or pathological explanation."⁽⁵¹⁾ *Id.* Where no single pathological process existed to relate the major convulsion with the earlier seizure activity, the date of onset of the acute illness was determined to be the date of the convulsion for which the child was admitted and notified to the study. *Id.* In such cases, the previous seizures were then considered to be part of the past medical history and children in this group were omitted from the count of possible vaccine-associated cases.⁽⁵²⁾ *Id.* In these instances, the researchers believed "that the thread of causality linking the initial immunization and later serious convulsions is at its most tenuous." *Id.* Cases in which the major convulsions were related via a single pathological process to earlier, even minor, convulsions were given the date of onset of the first convulsion and were included "amongst [their] count of 'vaccine-associated' cases[.]" *i.e.*, had the potential to be one of the vaccine-associated cases.⁽⁵³⁾ *Id.*

A somewhat similar analysis was conducted in infantile spasms cases with the hopes of better identifying the onset of the infantile spasms.⁽⁵⁴⁾ Following notification to the study for a diagnosis of infantile spasms, the investigators obtained the child's full clinical history from the child's parents or guardian with the hopes of assessing *when* the infantile spasms began; this presumably entailed an assessment of what prior convulsive or other activity related to the definitive infantile spasms diagnosis. *Id.* In assessing the date of onset in such cases, the investigators noted:

In many cases this history revealed that the first of the infantile spasms occurred some time *before* the child's admission to the hospital and, therefore, its notification to the Study. This date of onset was used in the analysis of "vaccine-associated" cases of infantile spasm, and for this diagnostic group the analysis of immunization in the 28 days before onset of the illness is more reliable than that using the 28 days before the date of admission to hospital.

Id.

Given Wesley's medical history as outlined in the medical records, it appears his date of onset would have been analyzed in two ways. Clearly, one date of onset would be October 9, 1980, the date of the hospital admission which would have prompted notification of his infantile spasms activity, although, as mentioned, this appears to be the less reliable date. A second but less obvious onset date would be the date of the first convulsion or other neurological symptom which is deemed to have been the onset or first manifestation of Wesley's infantile spasms. In this second instance, depending on the evidence provided through the medical records or expert testimony, the date may or may not be March 16, 1980, when Wesley experienced his first seizure five days after his DPT vaccination.⁽⁵⁵⁾ It is of importance that Wesley was admitted to the hospital in October 1980 following a month of ever-changing convulsive activity; on October 8, 1980, a health record indicated that Wesley's seizures were "taking on an 'infantile spasm' character." Unfortunately, neither party reviewed petitioners' claim in the detailed manner outlined above so it is not clear *when* his infantile spasms began and whether the date of onset fell within the 28 days following immunization. Dr. Gale only offered that Wesley's infantile spasms were not part of his acute illness.

Nevertheless, it is immaterial that the date of onset of Wesley's infantile spasms activity is uncertain because the IOM's 1991 report determined that "[t]he evidence does not indicate a causal relation between DPT vaccine or the pertussis component of DPT and infantile spasms." R. Ex. D at 77. In rejecting the causal relationship, the committee noted: "The fact that nearly identical results were observed for children who received the DPT and DT vaccines suggests that exposure to the pertussis component of the DPT vaccine does not increase the risk of infantile spasms." *Id.* at 74. The committee recognized that "[g]iven the insidious onset of infantile spasms, the temporal relation of immunization and onset is difficult to establish with certainty." *Id.* at 76. Previous studies demonstrated inconsistent and insignificant (statistically) risk estimates. *Id.* The committee believed two Denmark controlled studies offered the strongest evidence of the causal relation, but the results "argue[d] against an excess risk of infantile spasms attributable to the pertussis component of the vaccine." *Id.* The IOM reiterated that "[g]iven the insidious onset of infantile spasms, it is difficult to establish a temporal sequence with certainty, and there are no other aspects of the clinical presentation that suggest a relation to DPT immunization. Considerations of the specificity of the association are not relevant since a causal relation is not suggested by the evidence. There are no data bearing on mechanisms or biologic plausibility." *Id.* at 77. Therefore, although Wesley would have been notified and possibly even included within a statistically significant time period following the vaccination, current available medical evidence does not appear to substantiate a conclusion that the DPT can cause infantile spasms.⁽⁵⁶⁾ Thus, in this case, the NCES criteria and conclusions provide no support for petitioners' claim.⁽⁵⁷⁾ The only symptom that would have possibly included Wesley in the NCES, his infantile spasms which were diagnosed seven months after the initial onset of his seizure disorder, would exclude him under the IOM's 1991 report. Therefore, petitioners have failed to prove causation-in-fact.⁽⁵⁸⁾

I also reject for lack of foundation Dr. Geier's statement that his three-criteria approach establishes more likely than not that the DPT caused the injuries alleged. While Dr. Geier conceded on cross-examination that his overall causation theory is rooted in the three-criteria approach *and* his statistical calculations, he nevertheless maintained his opinion that satisfaction of the three criteria demonstrates causation by a preponderance of the evidence.⁽⁵⁹⁾ I find this opinion in itself without merit. Petitioners, in essence, are attempting to create a new Table injury. To accept such a theory suggests that *in any case* where a previously normal child suffers, for example, an encephalopathy or a seizure, however defined, within seven days of the vaccination, the DPT is more likely than not the cause (absent a finding of an alternative cause) of the acute and chronic injury. This reasoning seriously misrepresents the NCES and IOM findings.⁽⁶⁰⁾ First, unlike in Dr. Geier's theory, the NCES specifically defined which acute neurological injuries qualified a child for inclusion in the study and the IOM's conclusions in its 1994 report are based only on these children. Dr. Geier's theory impermissibly and without sufficient support broadens this inclusion base.⁽⁶¹⁾ Second, the NCES researchers recognized, through their assessment of whether seizures were related via a single pathological process, that not all *acute* events had to actually occur within the seven days following vaccination. That is, a later major event could have been related to a minor event occurring in the week following the inoculation; Dr. Geier's theory excludes these cases. Third, accepting this theory would contrast sharply with the NCES and IOM findings that the causal relationship is a rare event; under Dr. Geier's theory, many petitioners submitting DPT causation-in-fact claims before this Program would meet the three criteria and prevail. Fourth, as the IOM determined in 1991, not all types of seizures can be causally related to the DPT vaccine. Fifth, this theory would bestow entitlement even where a petitioner only suffered one serious seizure, and no sequela, within the seven days following vaccination; however, petitioners must demonstrate pursuant to the statutory scheme that they suffered the residual effects of their injuries for more than six months. Finally, embracing this theory logically implies that no statistical analysis is ever needed.⁽⁶²⁾

A more precise evaluation of Dr. Geier's overall causation opinion requires a review of his statistical calculation. After all, Dr. Geier's opinion is ultimately rooted in the *reliability* of his probability estimates. This, however, assumes his formula's application and conclusions are accurate and acceptable within the scientific community. I am not convinced they are since the parties laid an insufficient foundation in this respect. Regardless, since Wesley essentially does not meet the NCES criteria allowing inclusion in the study, the risk estimates calculated by the NCES researchers are irrelevant here.

(b) Do the statistical calculations and conclusions performed by the NCES researchers and IOM assist in determining whether Wesley's injuries were more likely than not caused by the DPT vaccine?

Given the findings above, I need not address whether the statistical analyses and conclusions performed by the NCES and IOM assist in calculating the probability that Wesley's injuries were more likely than not caused by the DPT vaccine. However, I should note that Dr. Geier's calculation that there is an 83.8 percent likelihood that Wesley's acute illness was caused by his DPT vaccination is based solely on relative risk assessments for an acute encephalopathic injury. He provides no similar calculations for relative risks associated solely with seizure activity or for infantile spasms specifically. Since I have determined that Wesley did not suffer an acute encephalopathy, Dr. Geier's percentages are useless. In addition, the IOM (1991) explained the *limited purpose* of its informal meta-analysis, upon which Dr. Geier bases his encephalopathy calculations: "The committee felt that a formal meta-analysis . . . was not appropriate for the data on encephalopathy because of the relatively few cases recorded in studies other than the NCES. The committee did, however, make the [informal meta-analysis] calculations *to assess the consistency of data on encephalopathy from the other studies with those from the NCES.*"⁽⁶³⁾ Christopher P. Howson, et al. at 344 (emphasis supplied). Although the IOM preceded to estimate the background rates to determine the relative and attributable risk of encephalopathic injuries following the DPT, the IOM gave various risk estimates depending on the studies relied upon. *Id.* at 344-345. The IOM did not explain if or how these calculations could be used to assess the probability of causality in individual cases where the onset of the acute illness occurred five days after the inoculation, nor is the formula Dr. Geier applied so outlined.⁽⁶⁴⁾ Tr. at 60.

In addition, courts have objected to using statistical analysis in individual cases to demonstrate actual causation except in certain instances. *See Sharpnack v. Secretary of HHS*, 27 Fed. Cl. 457, 461 (1993), *aff'd*, 17 F.3d 1442 (Fed. Cir. 1994)("Probability analysis does not have direct application in any particular case"); *Knudsen v. Secretary of HHS*, 35 F.3d 543, 550 (Fed. Cir. 1994)("bare statistical fact[s]" provide insufficient evidence to demonstrate actual causation); *but see Daubert*, 43 F.3d at 1321, citing *DeLuca v. Merrell Dow Pharmaceuticals, Inc.*, 911 F.2d 941, 958 (3rd Cir. 1990)("For an epidemiological study to show causation under a preponderance standard, 'the relative risk of . . . [the defect or injury] arising from the epidemiological data . . . will, at a minimum, have to exceed '2'").⁽⁶⁵⁾ It is also unclear whether Dr. Geier's formula using the IOM's informal meta-analysis calculations even meets the standards for expert testimony or theory set forth, *supra*, in *Grant* and *Daubert*.

More importantly, the NCES original and follow-up reports expressed concern regarding the appropriateness of using statistical calculations to determine causation in a specific case. The NCES concluded that "attribution of a cause in individual cases is precarious" and the estimates of attributable risk calculated "should be interpreted with considerable caution."⁽⁶⁶⁾ R. Ex. C at 99, 149; *see also Id.* at 141, 143. The investigators elaborated:

The demonstration of a statistically significant association between two independent variables does not mean that one event necessarily causes the other. In this Study, for a relative risk to be regarded as statistically significant, the convention adopted was that the lower limit of the 95 per cent confidence interval for the risk should exceed unity. This is helpful in interpreting the calculated risks but does not in itself imply that any association which reaches this level of significance must be causal. It simply means that it is very unlikely to have arisen by chance and, therefore, must be taken seriously, preferably in conjunction with other evidence. Other evidence that would support a causal relationship between immunization and serious neurological disorders includes whether or not the illnesses are clinically distinctive, how far they are restricted to immunized children, the closeness of their time relationship to immunization, and whether the suspected association seems biologically plausible. Finally, the absence of any alternative explanation for the illnesses would further strengthen suspicion.

Id. at 141-142; *see also Id.* at 143("[T]he [statistically significant] results of the NCES . . . suggest but do not prove that immunization with DTP vaccine does cause the development of serious neurological disorders in a small number of children who were previously apparently neurologically normal as well as in some children who were not neurologically normal and in whom the vaccine is sometimes held to be contraindicated").

The authors of the 1993 NCES follow-up report also expressed caution: "[T]he number of affected children who had been immunised recently was extremely small; the relative risk estimates therefore have wide confidence intervals. The potential effects of other limitations of the study, including the possibility of errors or bias in the data collection and unknown confounding factors, remain uncertain and call for caution in the interpretation of the results." R. Ex. E at 4. The authors suggested further prudence: "[T]his does not prove that the vaccine was the sole or even the prime cause of either the illnesses or the adverse outcomes *in these cases*. It remains an open question as to whether or not such illnesses occur related to diphtheria, tetanus, and pertussis vaccine in children whose brains are structurally and functionally normal and in the absence of concomitant factors. *Certainly, attribution of a cause in individual cases must be speculative.*" *Id.* at 5 (emphasis supplied).

Given that Dr. Geier presented a probability estimate based on an illness which I find Wesley did not suffer within five days of his vaccination, coupled with jurisprudence and the repeated cautions of using statistical analysis to prove causation in specific cases, I find the statistical evidence *presented in this case* is insufficient to demonstrate that Wesley's seizures were caused-in-fact by his DPT vaccination.⁽⁶⁷⁾

Considering all of the above, petitioners have *not* met their burden of proving, by a preponderance of the evidence, that the DPT vaccination actually caused Wesley's seizure disorder.

VII.

FINDINGS OF FACT

1. As parents and natural guardians of Wesley, petitioners have the requisite capacity to bring this action. § 11(b)(1)(A); Pet. at 1.

2. Petitioners have not previously collected an award or settlement of a civil action in connection with any alleged injury sustained by Wesley due to the administration of the DPT vaccine in question. § 11(c)(1)(E); Pet. at 2-3.

3. Wesley was administered a vaccine listed in the Vaccine Injury Table.

§ 11(c)(A); Pet. at 1.

4. Said vaccine was administered in the United States, in Jacksonville, North Carolina. § 11(c)(1)(B)(i)(I); Pet. at 1-2.

5. There is not a preponderance of the evidence that Wesley suffered an acute encephalopathy following his DPT vaccination on March 11, 1980.

6. There is not a preponderance of the evidence that Wesley's neurological problems were in-fact caused by his DPT vaccination on March 11, 1980.

7. There is not a preponderance of the evidence that petitioners expended in excess of \$1000 in unreimbursed medical expenses as a result of a vaccine-related injury.⁽⁶⁸⁾

VIII.

CONCLUSION

Based on the foregoing, the undersigned finds, after considering the entire record in this case, that petitioners are *not* entitled to compensation in this case under the Vaccine Act.⁽⁶⁹⁾ In the absence of a motion for review filed pursuant to RCFC Appendix J, the clerk of the court is directed to enter judgment in accordance herewith.

IT IS SO ORDERED.

Elizabeth E. Wright

Special Master

1. The National Vaccine Injury Compensation Program comprises Part 2 of the National Childhood Vaccine Injury Act of 1986, Pub. L. No. 99-660, 100 Stat. 3755 (codified as amended at 42 U.S.C.A. §§ 300aa-1 through -34 (West 1991 & Supp. 1998)). References shall be to the relevant subsection of 42 U.S.C.A. § 300aa.
2. The evidence in the record consists primarily of exhibits submitted as part of the petition filed in this case ("P. Ex. ____"), respondent's exhibits filed in this matter ("R. Ex. ____"), plus evidence taken at the evidentiary hearing in this matter ("Tr. at ____").
3. An APGAR test measures heart rate, respiration, muscle tone, responsiveness to stimulation, and skin color. Generally, two tests are performed at exactly one and five minutes after birth. The maximum score is ten. *The Merck Manual* 1858 (15th ed. 1987). The score taken at one minute is an index of asphyxia, while the five minute score is an index of the likelihood of death or neurological residua. *Nelson Textbook of Pediatrics* 362 (13th ed. 1983). The accuracy of the score for the prediction of long-term outcome, however, is inconsistent. R. Summitt, *Comprehensive Pediatrics* 370 (1990).
4. At Wesley's April 22, 1980, check-up, the physician recorded a history of generalized seizures and Todd's paralysis of the left arm. P. Ex. 9 at 73.
5. Mrs. Jenkins contested the accuracy of this medical record because Wesley was jerking his head and both his arms. Tr. at 13; P. Ex. 6 at 2.
6. Mr. Jenkins described Wesley's initial seizures as involving tonic-clonic type movements with a postictal state. Tr. at 40. He stated: "first he would be rigid in the tonic phase and then he would become clonic mostly with his upper body. Now, the rigidity seemed to be his whole body and then he started shaking his head and arms and then he would relax and then just be a dish rag for sometimes 30 minutes to an hour, and slowly come too, almost like coming too." *Id.*
7. While petitioners alleged only a seizure disorder and mental retardation in the petition, petitioners' expert, Dr. Geier, testified Wesley also suffered an acute encephalopathy following his DPT vaccination.
8. Petitioners must prove their case by a preponderance of the evidence, which requires that the trier of fact "believe that the existence of a fact is more probable than its nonexistence before [the special master] may find in favor of the party who has the burden to persuade the [special master] of the fact's existence." *In re Winship*, 397 U.S. 358, 372-373 (1970) (Harlan, J., concurring), quoting F. James, *Civil Procedure* 250-251 (1965). Mere conjecture or speculation will not establish a probability. *Snowbank Enter. v. United States*, 6 Cl. Ct. 476, 486 (Cl. Ct. 1984).
9. Effective March 10, 1995, the Vaccine Injury Table was amended to exclude residual disease disorder as a presumptively vaccine-related illness under the DPT, pertussis, DT, tetanus-diphtheria toxoid, and tetanus toxoid vaccines. See 60 Fed. Reg. 7678-7696 (February 8, 1995), codified at 42 C.F.R. 100.1-100.3. This amendment does not apply to petitioners' claim since their petition for compensation was filed prior to this Table change.
10. See R. Ex. C (R. Alderslade, et al., Department of Health and Social Security, In: Whooping Cough: Reports from the Committee on the Safety of Medicines and the Joint Committee on Vaccination and Immunisation, The National Childhood Encephalopathy Study: a report on 1000 cases of serious neurological disorders in infants and young children from the NCES research team (1981)); R. Ex. D (Christopher P. Howson, et al., Institute of Medicine, Adverse Effects of Pertussis and Rubella Vaccines (1991)); R. Ex. E (D.L. Miller et al., *Pertussis immunisation and serious acute neurological illnesses in children*. 307 Brit. Med. J. 1171-1176 (1993)); R. Ex. F (Kathleen R. Stratton, et al., Institute of Medicine, DPT Vaccine and Chronic Nervous System Dysfunction: A New Analysis (1994)).

11. Petitioners submitted various medical articles in support of Dr. Geier's opinions. However, most of the literature was published before the 1991 and 1994 IOM reports and, for the most part, fails to provide any additional relevant information especially since I have concluded the vaccine *can cause* the injuries alleged. To the extent Dr. Geier relies on the literature to bolster his opinion that the DPT, as the causative agent, is *more probable than possible in certain instances*, I find the literature immaterial. That is, since I have concluded that the IOM's 1991 report essentially makes the NCES inapplicable in Wesley's case, there is no need to discuss in further detail whether the vaccine caused Wesley's injuries more probably than not.

12. According to the NCES, "[t]he case-control approach involves the collection of a series of individuals with a particular disease and comparing their history of exposure to the suspected agent with that of an appropriately selected group of individuals who do not have the disease . . . Controls must be selected from among individuals who are at similar risk of exposure to the risk factor (in this case immunization) but who are not affected by the disease in question (in this case serious neurological disorder)." R. Ex. C at 97.

13. Respondent's submission of the 1991 committee's report, at Respondent's Exhibit D, only covers pages 65-123.

14. Dr. Geier holds an M.D. and Ph.D. (in genetics) from George Washington University. Tr. at 45. He has practiced obstetrical genetics since 1980. *Id.*; P. Ex. 19 at 1-2. He is not board certified in pediatrics or epidemiology, nor does he have formal training or an expertise in pediatric neurology. Tr. at 74, 75. However, Dr. Geier is involved in the work-up and diagnosis of pediatric neurology problems as they relate to his genetics review and consult duties, although he does not treat children with neurological conditions. *Id.* at 45, 74, 75. He also uses epidemiology in his genetics practice and in assessing DPT causation. *Id.* at 75. Dr. Geier has performed research at the National Institutes of Health ("NIH") on the effect of prokaryotic molecules on eukaryotes which Dr. Geier states is what occurs with a DPT vaccination. *Id.* at 45. While at the NIH, Dr. Geier worked with others addressing problems of vaccine contamination. *Id.* at 46. Dr. Geier has extensively reviewed and compiled literature and testimony on the DPT vaccine. *Id.* at 46; P. Ex. 19 at 2. Dr. Geier has also published numerous articles on the various problems associated with inoculations. Tr. at 46.

15. Dr. Geier apparently advances this three-criteria approach in every DPT causation-in-fact case in which he testifies; satisfaction of these criteria, he opines, establishes causation more probably than not. Tr. at 48-49, 75; P. Ex. 19 at 23. In addition to these three criteria, Dr. Geier relies on statistical calculations to opine causation. Tr. at 76-77

16. Dr. Geier also relies on several records from Wesley's medical providers, which, as Dr. Geier interprets them, state that the DPT "probably" caused Wesley's condition. P. Ex. 19 at 7-10, 12. However, none of the records cited were contemporaneous to the onset of Wesley's seizures or noted a "probable" connection with the possible exception of an August 1988 psychological report which records a "history of psycho-motor delay and seizures secondary to DPT injection in infancy." P. Ex. 7 at 1; *see also* those records outlined in the Factual Background portion of this decision.

17. Dr. Geier figured into his calculation his belief that the cause of an encephalopathy can be identified in 50% of cases. Tr. at 59; P. Ex. 19 at 22.

18. Dr. Gale is a neurology consultant and Associate Clinical Professor of Pediatrics and Neurology at Stanford University School of Medicine and University of California's San Francisco School of Medicine. Tr. at 95; R. Ex. B at 2, 3. He is board certified in pediatrics and board eligible in neurology with special competence in child neurology. Tr. at 95-96. Dr. Gale has treated children with seizure disorders, developmental delay, and acquired encephalopathies. *Id.* at 97.

19. Dr. Gale stated ardently that "[y]ou can't demonstrate that a person more likely than not has a particular disease for which there is no biological marker." Tr. at 126.

20. For example, Dr. Gale opined that seizures associated with Lennox-Gastaut syndrome are more common than post-immunization seizures. Tr. at 98.

21. Dr. Gale also stated that the IOM's 1994 report found insufficient evidence to show whether or not the shot increases the overall risk of chronic nervous system dysfunction in children. R. Ex. A at 4.

22. Dr. Gale noted that subsequent exams, including one July 2, 1980, showed a normal, "well" baby. R. Ex. A at 3.

23. Dr. Gale opined that with this type of seizure course, the hypersarrhythmia usually resolves and evolves into something else, which is "typically associated with multiple, difficult to manage or intractable seizures, diminished intellectual function, poor motor function and coordination." Tr. at 103-04. Dr. Gale related Wesley's profound mental retardation, motor disability, and behavioral problems to the infantile spasms and intractable epilepsy; he found no evidence this permanent damage was caused or significantly aggravated by the DPT vaccine. *Id.* at 110; R. Ex. A at 3, 4.

24. Dr. Gale believes Wesley likely experienced Todd's paralysis in his left arm following the first seizure, but the parents testified this lasted no more than one hour. Tr. at 12, 101.

25. Dr. Gale testified several times that Wesley developed infantile spasms. Tr. at 103, 111. However, Dr. Gale also believes Wesley suffers from one seizure disorder with multiple seizure types. *Id.* at 102. He testified Wesley's "seizures began either with generalized tonic clonic seizures or, more likely, with focal seizures that became quickly secondarily generalized." *Id.* at 101. He elaborated: "Within weeks to months, he was having more than one seizure type. They were not focal. They were generalized, but they weren't just tonic clonic. They were not purely motor seizures. He had seizures that involved his brain stem as well, and that was demonstrated by extensor or flexor spasms where his head would come down, his shoulders would protract, his arms would flex and then he would come back." *Id.* at 102. Dr. Gale indicated this is common with intractable complicated epilepsy where multiple parts of the brain are involved. *Id.*

26. Dr. Gale noted the 1994 IOM report is based on only 12 cases, an insufficient number from which to extract significant statistics for individual case causation purposes. Tr. at 100-101; R. Ex. A at 3-4. He reported that the NCES follow-up authors noted:

the numbers of cases associated with vaccine are too small to reach any firm conclusions . . . The potential effects of other limitations of the study, including the possibility of errors or bias in the data collection and unknown confounding factors, remain uncertain and call for caution in the interpretation of the results . . . the role of pertussis vaccine as a prime or concomitant factor in the etiology of these illnesses cannot be determined in any individual case . . . certainly attribution of a cause in individual cases must be speculative.

R. Ex. A at 4; *see also* R. Ex. E at 4, 5.

27. The special masters and the parties practicing before them have routinely relied on the NCES and subsequent IOM reports to assess the risk of neurological sequela following a pertussis immunization. Several vaccine cases have found the NCES to be reliable and reputable, offering the best statistically significant estimates of risk of neurological injury following a DPT vaccination. *See Sumrall v. Secretary of HHS*, 23 Cl. Ct. 1, 5 (1991); *Sharpnack v. Secretary of HHS*, No. 90-983V, 1992 WL 167255, at *2, *5 (Cl. Ct. Spec. Mstr. June 29, 1992), *aff'd*, 27 Fed. Cl. 457, 460-461 (1993), *aff'd*, 17 F.3d 1442 (Fed. Cir. 1994); *Wolf v. Secretary of HHS*, No. 90-3137V, 1994 WL 142295, at *6 (Fed. Cl. Spec. Mstr. Apr. 7, 1994). However, it appears that in these and other DPT causation-in-fact cases the parties presented limited evidence on the specifics of the NCES's notification and inclusion criteria, thus preventing as thorough a review of the issues as I have undertaken here.

28. The NCES investigators noted "the absence of any alternative explanation does not prove that the illness is due to pertussis vaccine." R. Ex. C at 95.

29. Relative risk "is the *ratio* of the incidence of a defined condition in those *exposed* to a suspected causal agent in a population to the incidence of the same condition in those who are *not exposed* (in this case, the ratio of the incidence of serious neurological illnesses in immunized children to that in unimmunized children)." R. Ex. C at 98. According to the 1991 IOM report, the NCES researchers reported a statistically significant relative risk of encephalopathy in the early postimmunization period (*i.e.*, onset within 7 days of the vaccination) of 3.1 (the attributable risk was 2.7 per million immunizations). R. Ex. D at 101, 104, 117.

30. One option in analyzing the first prong of the causation-in-fact case is to inquire from the start whether the DPT

can cause the *specific* seizure disorder alleged, e.g., infantile spasms, afebrile seizure disorder, febrile seizure disorder, epilepsy, etc. Dr. Geier testified that in this case, the initial inquiry is not whether the vaccine can cause infantile spasms, but whether it can cause "a generalized encephalopathy seizure disorder type syndrome." Tr. at 63. Dr. Geier noted that children in various studies assessing DPT causation were often multiply labeled and the analyses were not specific to the type of seizure disorder suffered. *Id.* While this may be true with the NCES to some extent, the IOM (1991) specifically reviewed the causal relationship between the vaccine and particular seizures and concluded that "the evidence does not indicate a causal relation between DPT vaccine and afebrile seizures" and there is "insufficient evidence to indicate a causal relation between DPT vaccine and epilepsy." R. Ex. D at 118.

31. Of the 904 NCES case children who suffered an acute encephalopathic injury or convulsions (non-infantile spasms), 515 suffered seizures. R. Ex. D at 101; R. Ex. F at 8. Two-thirds of these seizure cases involved febrile convulsions while one-third involved seizures of other types. R. Ex. F at 8. The NCES researchers did not distinguish between those children with febrile or afebrile seizures in their final statistical analysis. However, they did provide the percentages of those with a past history of afebrile and febrile seizures (children who previously suffered afebrile seizures were placed in Category II) and noted the outcome of those in the vaccine-associated group which suffered "simple/febrile seizures" and "prolonged/febrile seizures." R. Ex. C at 103, 133-134.

32. The 1991 IOM committee also noted the data suggests that "febrile seizures following administration of DPT vaccine occur during the ages when children are most likely to experience these seizures related to other febrile events" and the "DPT vaccine may cause a doubling or tripling of the febrile seizure rate in the first few days following immunization." R. Ex. D at 108 (citations omitted), 118.

33. While the IOM recognized that permanent neurological damage may result from acute neurological illnesses occurring within seven days of a DPT vaccine, it also noted that "it is important to recognize that a serious neurologic illness may or may not result in permanent brain damage." R. Ex. D at 87. In addition, some illnesses may not be linked to a particular sequela. For example, the NCES researchers noted that "[f]ebrile convulsions, which are sometimes reported after immunization, also occur for many other known and unknown reasons during the first few years of life and *usually do no lasting harm.*" R. Ex. C at 91 (emphasis supplied).

34. The NCES investigators and the IOM initially questioned the relationship between DPT and permanent neurological damage. The early data provided only limited information on the permanent sequela of those acute neurological illnesses assessed in the NCES. The investigators first concluded that "[t]aking account of possible alternative explanations of the clinical findings in cases associated with DTP and of the fact that similar cases occur after DT vaccine, it seems likely that permanent damage as a result of pertussis immunization is a very rare event and attribution of a cause in individual cases is precarious." R. Ex. C at 149. The IOM determined in 1991 that the evidence was "insufficient . . . to indicate a causal relation between DPT vaccine and permanent neurologic damage." R. Ex. D at 104-106, 118.

35. The IOM committee also reported that "children who experience a serious acute neurologic illness are at increased risk for death or dysfunction 10 years later," but "the *evidence is insufficient to indicate* whether or not DPT increases the overall risk in children of chronic nervous system dysfunction." R. Ex. F at 2, 13.

36. Petitioners' burden in such cases is not to demonstrate that the vaccine caused the current condition, but to prove, first, that the vaccine caused the acute injury and, second, that the sequela or current condition flows from that vaccine-related acute injury. Both the experts and the NCES use language which suggests that the vaccine is the cause of the permanent damage, but implicit in this is the understanding that the sequela is related to the injury. As the follow-up report concluded: "Diphtheria, tetanus, and pertussis vaccine may on rare occasions be associated with the development of *severe acute neurological illnesses that can have serious sequelae.*" R. Ex. E at 1 (emphasis supplied).

37. The NCES researchers stated: "The possibility that causal associations exist between immunization with pertussis . . . and the development of serious neurological disorders *is widely regarded as being biologically plausible.*" R. Ex. C at 142 (emphasis supplied).

38. Whether this two-part inquiry is the only way to address the second-prong of the causation-in-fact analysis is unclear. It is, however, the process testified to by the experts in this case. Moreover, the extent to which epidemiological studies may be used to assess causation in individual cases is also unclear, and perhaps is the ultimate issue regardless of whether a petitioner may have been reported and subsequently included in the NCES. Nevertheless,

I have chosen to assess petitioners' claim in the stated fashion to address fully the issues raised and since my resolution of this case precludes the necessity of a statistical analysis.

39. Simply because the NCES researchers noted that irritability and seizures, which Wesley suffered, may be signs or symptoms of an encephalopathy does not then lead me to conclude Wesley suffered an acute encephalopathy in this case. Without supporting medical records or credible expert testimony demonstrating Wesley suffered this injury within five days of his vaccination, I have no basis to conclude that he did.

40. Dr. Geier bases his opinion that Wesley developed an encephalopathy on the simple fact that Wesley suffered a seizure for which he was hospitalized and then developed a seizure disorder. The IOM stated that "[s]eizures in themselves are not sufficient to constitute a diagnosis of encephalopathy and, in fact, most seizures occur without encephalopathy." R. Ex. D at 87. The NCES researchers also recognized the possible distinctive nature of seizures and acute encephalopathy, as they listed these two illnesses separately for notification purposes. On the other hand, I have accepted, along with other special masters, that seizures may be broadly recognized as manifestations of an encephalopathy. See *Fuller v. Secretary of HHS*, No. 90-3709V, 1996 WL 65734 (Fed. Cl. Spec. Mstr. Jan. 31, 1996); *Cepeda v. Secretary of HHS*, No. 90-2664V, 1994 WL 390352 (Fed. Cl. Spec. Mstr. July 12, 1994); *Queli v. Secretary of HHS*, No. 90-2561V, 1993 WL 536638 (Fed. Cl. Spec. Mstr. Dec. 8, 1993). However, the test here is whether the injury meets the NCES's definition of encephalopathy, not Dr. Geier's, and more importantly whether the diagnosis is supported by the medical records or qualified medical testimony, both absent here.

41. Since notification was required regardless of the vaccination date, it is unclear whether the static encephalopathy diagnosis rendered in 1982 would have compelled notification to the study. I am unclear as to the acute or subacute nature of the illness and the diagnosis was rendered at the time of Wesley's hospitalization for a hepatic coma. Even if the diagnosis would have compelled reporting, it is reasonable to conclude the researchers would have excluded Wesley's case since the encephalopathy had its onset outside the 28 day time frame utilized by the researchers. R. Ex. C at 146. Further inquiry into this point is unnecessary since I have determined that Wesley would likely have been notified to the researchers before the encephalopathy diagnosis for his infantile spasms in October 1980. Incidentally, there is also some evidence to suggest Wesley's April 1982 encephalopathy diagnosis was noted with increased liver function tests, although he was not diagnosed with Reye's syndrome. P. Ex. 12 at 52. Nevertheless, I find that Wesley did not suffer an acute or subacute encephalitis/encephalomyelitis or encephalopathy or Reye's syndrome (an acute encephalopathy with abnormal liver function tests) which would have met the notification criteria.

42. According to the NCES, infantile spasms are a type of epileptic disorder. When the spasms are seen "in combination with an electroencephalogram (EEG) pattern of hypsarrhythmia and psychomotor retardation or regression, [the condition] is referred to as West Syndrome." R. Ex. D at 65.

43. The experts' testimony in this case exemplifies a common misinterpretation of the NCES notification methods. While the study's final results attach significance to events occurring within the seven day period following vaccination, physicians were asked for notification purposes to make reports based on the occurrence of specifically listed acute neurological illnesses without reference to the patient's vaccination history. Determining whether a child would have been reported is the very first hurdle which any petitioner must overcome. Success in this inquiry then opens the door to a later examination of whether the child would have remained included as a study participant and, if so, in what capacity and with what significance.

44. The IOM (1991) gives a slightly different figure: of the 1,167 cases of acute neurological disease, 263 were infantile spasms. R. Ex. D at 101.

45. In addition, of the 212 infantile spasms cases, 48 (10%) were in Category IA (Normal-Normal) and 68 (22%) were in Category IB (Normal-Abnormal). R. Ex. C at 117. Of the 35 DPT-associated cases, upon which the relative risks are based, six were diagnosed with infantile spasms (three in Category IA and three in Category IB). *Id.* at 133-134.

46. It is important to distinguish a child's being *reported* to the study from one being *included*. Obviously, a child must first be notified to the study before inclusion, or continued participation, is possible. Some children may be notified but subsequently excluded from the researchers' analysis for various reasons; these children would then not be included in the study. When experts opine that a child would have been included in the study, they usually mean the child would have been one of the cases from which significant statistical findings are extracted. For purposes of this case, notification occurs when a treating physician reports a child for any of the listed acute neurological illnesses. Inclusion

occurs if the child is not excluded from the study and remains a study participant, and of course, of interest is whether the child ultimately falls in line with the statistically significant cases.

47. The investigators initiated a thorough review to establish the correct date of onset since, in some cases, hospital admissions may have been delayed (*e.g.*, in infantile spasms cases, children may not have been admitted or admitted some considerable time after the onset of their illness). R. Ex. C at 102. The investigators also felt it important to consider the significance of minor prodromal events and their relationship to the onset of the acute illness. *Id.*

48. Presumably, the "current illness" refers to the neurological illness which prompted notification.

49. In this instance, of importance is the date the child was admitted to the hospital *for the acute neurological event which prompted notification*. This interpretation seems reasonable in light of the fact that the physicians were asked to report an admission only if the child suffered one of the five acute neurological illnesses outlined in the notification chart. It is also important to recognize that the "date of admission" may be different from the "date of the onset of the acute neurological event for which the child was admitted."

50. In the final statistical analysis, the vaccine-associated cases refer to those which fall within the statistically significant time period following vaccination. In the study, this group is the 35 children who were immunized with the DPT within seven days before the onset of their illness. R. Ex. C at 132. Of course, before the final analysis was completed, every case had the *potential* to be in the vaccine-associated group; only upon the final statistical analysis could the investigators learn which cases were deemed vaccine-associated and which were not.

51. The researchers suggested that progressive mental deterioration might indicate the existence of a single pathological process; however, what other indicators may signify such a process is unclear. The NCES is also rather vague on what may constitute an acceptable single pathological process (*e.g.*, do seizures related via a single pathological process to a prenatal injury qualify?) and when the process must commence (*e.g.*, must the process either commence or be active during the time or in relation to the date of the notifying event?). *See also* R. Ex. C at 143 (wherein the researchers did not exclude cases which *may have been* caused by another etiology); *Id.* at 142, 143, 146 (wherein the researchers were concerned with whether the vaccine could *trigger* an acute event).

52. Even though the researchers revised their methods for determining the date of onset of the acute illness in some cases by considering the previous seizure history and assessing whether a single pathological process existed, once the date of onset was finally ascertained, the investigators excluded from the count of potentially vaccine-associated cases those in which the determined date of onset was beyond 28 days after the vaccination; this was an arbitrary cut-off date established by the investigators which seems to have applied to all cases, regardless of the initial diagnosis. R. Ex. C at 146-147. Only those cases regarded in the final analysis to be vaccine-associated (*i.e.*, vaccination within seven days of the onset of the acute illness) or having the immunization within seven days of the admission were statistically analyzed in terms of the relative risks. *Id.* at 119-121, 129.

53. Following the date of onset determination and assuming a case was not excluded in this analysis, each participant was placed in one of three categories which corresponded with the child's previous and subsequent neurological status or medical history. The investigators then undertook an evaluation of the risks associated with the pertussis vaccine. R. Ex. C at 102-104, 107-108. It is unclear, in cases where earlier seizures were related to later seizures, which subsequent history was utilized for category placement. It is also unclear if being in a specific category makes a difference statistically. It certainly seems to matter in those cases where a child was deemed previously normal (Category IA or IB) since some of the study's relative risks are based on children in this category. *Id.* at 120, 121, 129.

54. It is not clear whether the investigators applied the "single pathological process" analysis, as specifically defined in the study, to infantile spasms. What is clear is that the investigators reviewed infantile spasms cases to determine when this particular condition first manifested or developed, *i.e.*, when it had its onset. This may have entailed some discussion between the investigators of the pathological or clinical process connecting the seizures or other neurological events to the ultimate diagnosis, but the NCES is simply unclear on this point. *See* R. Ex. C at 146-147.

55. The NCES researchers recognized the difficulty in assigning a date of onset in infantile spasms cases since the initial manifestations may be subtle. R. Ex. C at 147; R. Ex. D at 64.

56. According to the IOM's 1994 report, the NCES researchers "did not include cases with infantile spasms in the

calculations regarding DPT on the basis of post-hoc analyses showing no association between infantile spasms and earlier DPT immunizations." R. Ex. F at 8. This seems to conflict with the NCES results which show six infantile spasms cases in the 35 vaccine-associated cases. In any event, any discrepancy is irrelevant since the IOM found no causal relation between the vaccine and infantile spasms. Moreover, it is clear that the 10 year follow-up report assessing DPT-related permanent damage, upon which the 1994 IOM report is based, also excluded infantile spasms cases from their analysis based on the lack of a causal relation. R. Ex. E at 3.

57. This finding is in line with other Program cases. See *Jackson v. Secretary of HHS*, No. 90-1903V, 1995 WL 120210 (Fed. Cl. Spec. Mstr. Mar. 3, 1995); *Woodcock v. Secretary of HHS*, No. 90-1030V, 1992 WL 92169 (Cl. Ct. Spec. Mstr. Apr. 10, 1992); *Shelley v. Secretary of HHS*, No. 90-604V, 1991 WL 239093 (Cl. Ct. Spec. Mstr. Oct. 29, 1991).

58. If Wesley were not reported to the researchers for the infantile spasms, no notification, and thus inclusion, would likely occur, and petitioners' case would fail. Assuming, *arguendo*, that at some point Wesley would have been reported for complicated seizure activity, such as a 30 minute or more seizure, his seizure disorder seems to have been afebrile. The IOM concluded in 1991 that "the evidence does not indicate a causal relation between DPT vaccine and afebrile seizures." R. Ex. D at 118; see also *Terran v. Secretary of HHS*, No. 95-451V, 1998 WL 55290 (Fed. Cl. Spec. Mstr. Jan. 23, 1998), *aff'd*, 41 Fed. Cl. 330 (1998), *appeal docketed (on other issues)*, No. 98-5161 (Fed. Cir. Sept. 4, 1998). The IOM also found "insufficient evidence to indicate a causal relation between DPT vaccine and epilepsy." R. Ex. D at 118. Thus, regardless of the characterization of Wesley's seizure activity, petitioners' claim fails.

59. Dr. Geier agreed on cross-examination that it is the *combination* of the three criteria with the probability estimate which "take[s] you over that line, that takes you into the realm of this is cause and fact versus a chance[, an] association." Tr. at 76-77; see also *Id.* at 85.

60. I note here that the Court in *Sumrall v. Secretary of HHS*, 23 Cl. Ct. 1 (1991), involving a child's seizures five days after a DPT vaccination, held that Dr. Geier's three criteria, when "viewed together, and in light of the NCES . . . are sound criteria upon which to base a finding of causation." *Sumrall*, 23 Cl. Ct. at 6. See also *Sharpnack v. Secretary of HHS*, 27 Fed. Cl. 457, 458-459 (1993), *aff'd*, 17 F.3d 1442 (Fed. Cir. 1994); *Estep v. Secretary of HHS*, 28 Fed. Cl. 664, 668-669 (1993). However, Special Master Hastings recently rejected what he called "Dr. Geier's own personal theory of when one can deem a case of chronic neurologic dysfunction to have been caused by a pertussis vaccination." *Lewis v. Secretary of HHS*, No. 95-728V, slip op. at 8-10, 1999 WL ____ (Fed. Cl. Spec. Mstr. June 14, 1999). In that case, as similarly presented here, Dr. Geier opined, "When a neurologically sound individual receives the whole-cell pertussis vaccine, manifests a significant neurologic symptom within seven days thereafter, goes on to develop a chronic neurologic abnormality, and a thorough medical work-up fails to identify a cause for the chronic abnormality, it is reasonable to conclude that it is 'more probable than not' that the chronic abnormality was caused by the vaccine." *Id.* at 8. In rejecting his theory, Special Master Hastings noted that the NCES considered vaccine-caused, serious neurologic injuries to be "*at most an extremely rare event.*" *Id.* at 9 (citations omitted). He also believed Dr. Geier failed to support with medical literature how causation can be attributed more probably than not in a *particular* case. *Id.* Lastly, he deferred to respondent's expert that the vaccine could only cause chronic neurologic injury where such was preceded by a "significant, dramatic episode of neurologic injury" which was a more stringent requirement than that outlined in Dr. Geier's criteria. *Id.* at 9-10. Special Master Hastings found that the vaccinee did not suffer a serious, acute neurological illness and specifically withheld any opinion as to whether Dr. Geier's theory would be acceptable if the child instead had suffered an NCES-qualifying neurological event. *Id.* at 5-8, 11.

61. In petitioners' case, it is not entirely clear what satisfies Dr. Geier's definition of an "obvious, significant neurological reaction," which is the second of his three criteria. Although Dr. Geier's reliance on the NCES and IOM implies that his approach requires an NCES-qualifying neurological event, Dr. Geier never directly declares this. For the reasons stated, I reject Dr. Geier's three-criteria approach in so far as it accepts a significant neurological reaction which does not qualify under the NCES's notification and inclusion measures. However, I make no determination here whether it is possible to demonstrate more probably than not that the vaccine caused the neurological injury when that injury meets the NCES's definition for a serious, acute neurological illness (and there is no known alternative cause for the illness) and is suffered within seven days of the vaccination by a previously neurologically intact child.

62. Dr. Geier's three-criteria approach also rejects, at least in assessing whether a petitioner meets the NCES inclusion criteria, those children apparently previously abnormal. Yet, in the NCES, three of the 35 vaccine-associated cases upon which the significant statistical findings are based were previously abnormal. R. Ex. C at 132. However, the IOM (1994) only assessed the causal relation between the vaccine and permanent damage in previously normal or

neurologically intact children who suffered a NCES-defined serious, acute neurological illness within seven days of the vaccination.

63. A portion of the IOM's 1991 report which was not submitted by the parties but emphasizes the limits of the meta-analysis conducted by the IOM states:

After considering whether meta-analysis could be used to estimate the risk of a number of adverse events following pertussis or rubella vaccination, the committee decided that data adequate to justify a meta-analysis were available for four adverse events following pertussis immunization: febrile seizures, afebrile seizures, SIDS, and hypotonic, hyporesponsive episodes . . . *The committee was not able to use meta-analysis data for other adverse events, primarily because a sufficient number of comparable studies were not available . . .* There were four controlled epidemiologic studies of encephalopathy reviewed . . . , but these are dominated in size by a single study, the NCES . . . the NCES includes 389 children with encephalopathy, whereas the other available studies include a total of 29 cases of encephalopathy. *Any pooled estimate based on these studies would clearly be dominated by the NCES results, so the committee judged that meta-analysis [for encephalopathy] would not yield useful information.*

Christopher P. Howson, et al. at 52 (emphasis supplied).

64. Dr. Geier did, however, make three interesting points. First, that the Act's existence presumes that causality can be attributed in individual cases; second, that many experts testifying before the special masters have related the vaccine to individual cases; and third, that the IOM and others conducted statistical analyses involving specific cases. Tr. at 60, 113, 120. However, weighing these points with the whole of the evidence, I am not persuaded by Dr. Geier's probability theory. Simply put, it is petitioners' burden to demonstrate their case. Although jurisprudence permits proof of a relative risk greater than two to show causation, I would still have to find that the methods employed by the experts to show that causal relationships are reliable and independently validated. Such proof is lacking here.

65. If it is the case that a DPT-related illness cannot be demonstrated clinically, biologically, or pathologically, it may be that the only possible avenue of proof is through epidemiological evidence, which courts have forbidden except in certain circumstances not applicable here. Having noted this, I make no determination of whether epidemiology alone can prove causation-in-fact in such cases, and if so, under what circumstances; I have simply not been afforded the necessary information on this issue and the probability estimates offered by Dr. Geier are inapplicable in Wesley's case.

66. Attributable risk, for our purposes, is "the incidence of serious neurological illnesses in young children attributable to pertussis vaccine." R. Ex. C at 97-98.

67. Dr. Gale, while a respected neurologist, is not an epidemiologist. The undersigned would have benefitted from a detailed primer from qualified experts from both sides on the usefulness and reliability of statistical evidence generally and the NCES's and IOM's utilization of statistics particularly. In any DPT causation-in-fact case which intends to rely on statistical probabilities to prove actual causation, detailed discussion is warranted.

68. Since I conclude that no vaccine-related injury occurred, I cannot find that any expenses incurred on Wesley's behalf were vaccine-related.

69. I do find, however, that this case was brought in good faith and with a reasonable basis. Petitioners are therefore entitled to reasonable attorney's fees and costs.