OFFICE OF SPECIAL MASTERS

No. 96-0412 V

Filed: January 5, 2000

LORENA ALMEIDA, by Her Mother and Next Friend, MARIBEL ALVARADO,	*	
Petitioners,	*	**TO BE PUBLISHED**
v.	*	
SECRETARY OF HEALTH AND HUMAN SERVICES,	*	
Respondent.	*	

Ronald C. Homer, Boston, Massachusetts for petitioner.

David L. Terzian, United States Department of Justice, Washington, D.C. for Respondent.

DECISION

French, Special Master.

This matter arises under 42 U.S.C. §§ 300aa-1 et seq. (West 1991 and Supp. 1998), the National Childhood Vaccine Injury Act of 1986. On July 12, 1996, Mrs. Maribel Alvarado filed this claim on behalf of her daughter, Lorena Almeida, alleging that as the result of a Diphtheria-Pertussis-Tetanus (DPT) vaccination administered on July 15, 1993, Lorena sustained a significant aggravation of a preexisting neurological condition. Respondent defends by arguing that any change in Lorena's condition was not vaccine-related, but merely reflects the expected evolution of a preexisting seizure disorder.

PROCEDURAL BACKGROUND

On September 23, 1997, a hearing was held in Boston Massachusetts. Petitioner presented the testimony of Dr. Marcel Kinsbourne, a pediatric neurologist. Respondent presented the testimony of Dr. Joel Herskowitz, also a pediatric neurologist. Petitioner

presented no fact witnesses, but relied on affidavits and medical records as evidence of the facts.

FACTUAL FINDINGS

The following facts are documented in the medical records. Lorena Almeida was born by cesarean section on January 19, 1993, the product of an uncomplicated pregnancy and delivery. Her APGAR scores were nine and nine at one and five minutes, respectively. Petitioner's Exhibit (hereinafter P. Ex.) 2 at 5. Lorena's development appeared normal and she had no illnesses of note. P. Ex. 3 at 3-13. She was given DPT shots on March 18, 1993 and May 21, 1993 with no apparent adverse effects. On July 15, 1993, three days before her six-month anniversary, Lorena visited her doctor's office for a routine well-baby examination. The pediatrician's notation for July 15, 1993 states that Lorena was asymptomatic, had good tone, was smiling and playful, had good eye contact, and had symmetrical reflexes. Her development seemed up to date; she was rolling over, vocalizing, and attempting to sit. P. Ex. 3 at 14. The doctor found her to be a well child, and he ordered her third DPT shot which was given that same day. Id. at 14.

That evening, Lorena suffered an afebrile tonic-clonic seizure of approximately 45-minutes duration. Rescue workers were unable to stop the seizure with Valium, and she was rushed in an apneic condition to Miami Children's Hospital where intubation was attempted without success. Eventually, however, the child began to breathe on her own. A lumbar puncture, an EEG, a CT scan of the brain, and cultures for infection were all negative. Lorena showed some improvement over the next two days, but on July 18, 1993, Lorena had episodes of unresponsiveness interpreted by her doctors as seizure activity. The neurologist on call confirmed the episodes as seizure activity.[1] P. Ex. 3 at 17. The neurologist, Dr. Danilo Duenas, diagnosed her condition as a generalized seizure disorder of unknown etiology "precipitated by vaccinations." P. Ex. 5 at 1. She remained hospitalized for a period of nine days. Her doctors ordered the elimination of the pertussis component from future shots. Thereafter, DT, only, was given. P. Ex. 13.

According to the medical records, the next seizure, a second tonic-clonic seizure of 30-minutes duration, occurred on August 6, 1993, approximately one month after the

[1] Respondent's expert, Dr. Herskowitz, challenges the doctor's diagnosis of seizure activity on that particular day because an EEG did not show epileptiform tracings, although later EEGs, indeed, showed abnormalities. The court takes note of Respondent's reservations as to the character of the episodes, but places greater weight upon the opinions of the treating physicians who were in a better position to make that determination at the time. Moreover, medical literature indicates that an EEG may not always identify epilepsy in early stages. In one report of such findings by respected expert, Dr. Jean Aicardi, a study of a series of 20 cases of pertussis vaccine complications following DPT revealed that EEGs were initially normal in 75% of such cases but tended to deteriorate thereafter. P. Ex. 21 (b) at 18.

July 15, 1993 event. The medical record for that event notes that Lorena was admitted to Miami Children's Hospital with a "four-day history of tremors in both hands lasting between five and ten seconds." P. Ex. 4 at 6. Both admitting and discharge summaries confirmed that Lorena was suffering from a seizure disorder. She remained in the hospital for three days on this occasion and was discharged on August 9, 1993.

Seizures continued to occur thereafter, including episodes of status epilepticus (seizures lasting 30 minutes or more) requiring hospitalizations on the following dates: August 31, 1993; September 28, 1993; October 17, 1993; November 3, 1993; and January 24, 1994, on which occasion a particularly explosive seizure occurred, persisting for at least two hours. On February 7, 1994, another lengthy seizure occurred that was followed by a non-verbal period. P. Ex. 4. After the devastating January 24 and February 7, 1994 episodes, Lorena began to demonstrate other neurological complications including hypotonia, developmental delay in both fine and gross motor skills, and, subsequently, speech and language disorder. At the time of this writing, Lorena is 6 years and nine months old. Her seizures are intractable despite the fact that she takes three different anticonvulsant medications.

ADDITIONAL FACTUAL ISSUE

The foregoing facts are documented and are so found. One factual issue remains for the court's determination. The physician who admitted Lorena at the July 15, 1993 hospitalization recorded that Lorena had "no prior history of seizures." P. Ex. 10 at 1. Both parties admit the inaccuracy of that statement. Subsequent histories, those recorded after July 15, 1993, reveal that Lorena, in fact, had a brief seizure prior to July 15, 1993. (Respondent argues that the medical records suggest the possibility of two or even three episodes that could very well have been seizures.) The number of prior seizure events is material in this case in determining whether Lorena's post-vaccination condition meets the criteria for a significant aggravation. To determine whether Lorena had one, two, or three seizure events prior to July 15, 1993 the court has interpreted the following medical records:

Medical History of July 18, 1993: According to the doctor's notes recorded on July 18, 1993 (three days after the child's first hospital admission), Lorena's father told the doctor that--

> [A] similar episode occurred at two and one-half months of age . . . movements to the right arm, eyes rolling back. The episode lasted for [only] minutes then stopped, followed by a post-ictal state with limp right arm for hours.

P. Ex. 3 at 17.

Medical History of August 9, 1993: Lorena was hospitalized for a 30-minute seizure on August 6, 1993. Prior to her discharge three days later, Dr. Lopez transcribed the following history:

> History of present illness: This is a 7 [month old] [white Latino female] brought to MCH [(Miami Children's Hospital)] due to sz [(seizure)] of 30 min. duration. This is 2nd episode that child seizes. First time was July 93 [after] immunization and was hospitalized. During above mention [sic] sz child was [undecipherable] tonic/clonic episode, eyes did not roll back, lost consciousness approx 30 min. Didn't have BM [(bowel movement)].

P. Ex. 4 at 9.

Following the doctor's notation, seven lines are left blank. On the eighth line, just above the words "Past history", the following reference is made concerning an earlier event: "Pt. [(patient)] also had a similar episode of sz [(seizure)] at age 2 mo. As per Mother's hx [(history)]."

Id.

Medical History of September 29, 1993: On September 29, 1993, during yet another hospital admission, Lorena's mother describes the prior event again: "[A]t age three [months] of 'clutch hands' [sic] and body stiffness [lasting] a few seconds." P. Ex. at 4.

Respondent argues that the medical histories cited above suggest the occurrence of not one, but three separate incidents. Dr. Herskowitz, Respondent's expert, believes the history recorded by Dr. Lopez on August 9, 1993 should be interpreted as proof of two 30-minute seizures, one on August 6, 1993 for which Lorena was then being hospitalized, and a 30-minute seizure at age two months, because the mother reported the earlier seizure as "a similar" episode. P. Ex. 4 at 9. The court disagrees with Respondent's interpretation for two reasons. First, the gap in spacing clearly relates the "30-minute" notation to the seizure for which the child was being hospitalized. True, this history seems to combine present and past episodes in a less than clear manner, but only by a stretch of the imagination could one construe the words "similar episode" to describe the earlier episode as also of 30-minutes duration. Second, other medical histories refer consistently to a single brief incident of mild symptoms at about three months of age. See for example: P. Ex. 5 at 1 ("Child had short seizure at 3 months of age."); P. Ex. 5 at 6; ("Lorena is now seven months of age . . . and had some clinical paroxysmal event at about 3 months of age."); P. Ex. 15 at 4 ("First episode [(of seizure)] at age 3 [months] according to mother had an episode of clutch [sic] hand and body stiffness for few seconds.") (Emphasis supplied).

One other consideration leads the court to conclude that the medical histories of July, August, and September, set forth above, are three versions of the same event. On May 12, 1993, prior to the dates those histories were recorded, Lorena was taken to the Pasteur Clinic with a complaint of "pain in the right arm since that morning" and the child was unable to move her arm. P. Ex. 3 at 11. By the time a doctor examined her, Lorena was back to normal, moving her arm without pain, and in no distress. The doctor, who was not a neurologist, diagnosed the incident as a possible subluxation of the right arm.[2] Id.

The experts for both parties suspect that the May 12, 1993 incident may have been the post-ictal state of a seizure that occurred prior to Lorena's arrival at the clinic. Petitioner's counsel presented the following interpretation of the May 12, 1993 event:

> Petitioner probably suffered a seizure on May 12, 1993, approximately 2 months prior [to] her third DPT vaccination. The probable seizure was retrospectively described as eyes rolling back and involuntary movements in the right arm [that] lasted for minutes, then stopping with a post-ictal pain [in] the right arm lasting for hours.

P. Pre-Hearing Memorandum at 3-4.

Respondent's expert, Dr. Herskowitz, is convinced that the incident represents a missed diagnosis of a seizure. Dr. Kinsbourne, for Petitioner, is also of the opinion that this notation probably constitutes a reliable documentation, incompletely described, of the first [and probably only] manifestation of the onset of Lorena's seizure disorder.

The court is inclined to agree with the experts about the May 12, 1993 incident. The court is not convinced that the medical histories should be interpreted to represent multiple seizures prior to vaccination. The court finds that more likely than not, histories placing the first brief incident variously at two months, two and one-half months, three months, (or on May 12, 1993), although described somewhat differently at different times, are inexact histories of the same event. Dr. Kinsbourne stated "I think that's just the typical inaccuracy of trying to remember when something happened." Tr. at 68. The court agrees. All medical records that discuss the earlier event refer to a single brief event although not necessarily described in the same way. Lorena's mother may have been imprecise in her descriptions of the infant's age at the time, but neither parent varied, when relating Lorena's history to her doctors, and insisted consistently that there had been a single prior event.

Further Finding of Fact

[2] Subluxation is described as "an incomplete or partial dislocation." Dorland's Pocket Medical Dictionary, 565 (24th ed. 1982).

The medical records support a finding that Lorena had a single, brief, mild seizure prior to the major event that occurred on July 15, 1993, and the court so finds.

STATUTORY PROVISIONS AND RELEVANT JURISPRUDENCE

Table Case Method of Proof: A petitioner who files a claim under the Vaccine Act may establish causation in one of two ways. Petitioner may establish a Table case by proving that the individual sustained an injury set forth in the Vaccine Injury Table (§14 of the Act) or sustained a significant aggravation of a preexisting injury set forth in the Table, and that the first manifestation or onset of symptoms of that Table injury or the significant aggravation of a preexisting injury occurred within a prescribed time period-- in the case of DPT vaccine--72 hours. If successful, a petitioner enjoys a rebuttable presumption that the injury or significant aggravation was caused by the vaccine.

Causation-in-Fact Method of Proof: If petitioner is unable to establish a Table case, for example, if the claimed injury is not listed in the Vaccine Injury Table, or if the onset did not occur within the 72-hour Table time, an alternative method is available. Petitioner may pursue an off-Table claim by establishing that the vaccine "in fact" caused the injury. This method, commonly referred to as "actual causation" or "causation-in-fact," is analogous to the method of proving traditional tort claims.

Prior to March 10, 1995, the court's factual findings would have constituted probative evidence of an on-Table significant aggravation of a preexisting neurological condition. Both the injury itself and the time of onset were consistent with the requirements set forth in the Vaccine Injury Table found in section 14 of the Act prior to the date of March 10, 1995. Unless Respondent succeeded in rebutting Petitioner's claim by establishing that the child's injuries, more likely than not were caused by a factor unrelated to the vaccine, Petitioner would have benefited from a statutory presumption of causation. That possibility is no longer available to this Petitioner.

Petitioner, here, may not avail herself of the on-Table Case method, with its attendant presumption of causation, for the reason that a change in the law removed Residual Seizure Disorders from the list of Table injuries. All cases filed after March 10, 1995, are subject to this change in the Table. Petitioner filed her claim on July 12, 1996. The amended Table, therefore, applies. Lorena Almeida's alleged injury, a residual seizure disorder, must be proved by establishing that the DPT vaccine was in fact the cause of her seizures and of any sequelae claimed.

Proving Causation-in-Fact

The court in Grant v. Secretary of HHS, 956 F.2d 1144 (Fed. Cir. 1992) provides that a reputable or scientific explanation or theory causally connecting the vaccination and the injury (or aggravation of a preexisting injury) is required to support a causation-in-fact-case. Such theory should offer a logical sequence of cause and effect showing that the vaccination was the reason for the injury or aggravation. As in tort claims, the standard of proof is a simple preponderance of the evidence--demonstrating that it is more likely that the vaccine rather than any other factor, caused the injury or aggravation. Williams v. Secretary of HHS, No. 90-301V, 1998 WL 156967 (Fed. Cl. Spec. Mstr. March 18, 1998), citing Wagner v. Secretary of HHS, No. 90-2208V, 1997 WL 617035 (Fed. Cl. Spec. Mstr. Sept. 22, 1997)(dec. on remand). In causation-in-fact cases, the burden of proof never shifts to respondent to prove alternative cause. Id. The burden of affirmative proof rests with the petitioner.

The Significant Aggravation Claim:

The Act provides compensation for the significant aggravation of a preexisting condition. §11(c)(1)(C)(I)(ii)(I). Section 33 (4) of the Act,("Definitions") defines the term "significant aggravation" as "any change for the worse in a preexisting condition which results in markedly greater disability, pain, or illness accompanied by a substantial deterioration of health." [3] In an off-Table claim, unlike an on-Table claim, the fact that the prior injury is not an injury named in the Table itself is irrelevant.[4]

With the exception of the brief description in the legislative history of what constitutes a significant aggravation set forth in footnote 3 of this decision, guidelines for proving a significant aggravation were not spelled out in any specificity in the statute. The Federal Circuit, however, set forth a three-part analysis that is useful to the court and will be followed here. The Court of Appeals for the Federal Circuit in Whitecotton v. Secretary of HHS, 81 F.3d 1099 (Fed. Cir. 1996), describes the process of establishing a significant aggravation claim by requiring petitioner to prove that the onset of the significant

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[3] The legislative history explains the significant aggravation provision as follows:

> This provision does not include compensation for conditions which might legitimately be described as pre-existing (e.g., a child with monthly seizures who, after vaccination, has seizures every three and a half weeks), but is meant to encompass serious deterioration (e.g. a child with monthly seizures who, after vaccination, has seizures on a daily basis).

H.R. Rep. No. 908, 99th Cong., 2nd Sess. 1986, 1986 U.S.C.C.A.N.

[4] Following the March 10, 1995 amendments, on-Table injuries for DPT consist of two only--Anaphylaxis or (anaphylactic shock), and Encephalopathy (or encephalitis). The parties agree that insufficient evidence exists to establish either of these on-Table injuries within Table-time frame.

worsening began within the relevant Table time (72 hours) following DPT vaccination, and that the individual's current condition is substantially worse than her pre-vaccination condition. That analysis requires the court to: 1) assess the individual's condition prior to the administration of the vaccine; 2) assess the person's current condition; and 3) determine if the person's current condition is significantly worse than the individual's condition prior to the vaccination.

Ample evidence exists in the present case to show that petitioner's neurological condition was dramatically worse after the July 5, 1993 vaccination. Dr. Kinsbourne, for Petitioner, summarizes the facts:

> [I]n the first six months of the child's life, we have one event. . . . We now have status epilepticus. We have a litany of seizures following this, breaking through treatment. There is no comparison between this child's state before and after that six-month date.

Tr. at 98.

Dr. Kinsbourne testified further that Lorena's seizures were more severe, more prolonged, more resistant to control, and by age one year, had resulted in permanent brain damage. She made some gains after the initial onset, but the severity of continual status epilepticus seizures took its toll, and after the particularly explosive event of January 24, 1994 (two hours duration) and another lengthy seizure on February 7, 1994, other neurological deficits began to surface:

> Up to this time, Lorena's mental and motor development had been within normal limits, but from then onward, she fell progressively behind her peers. Her epilepsy continued in spite of the use of numerous antiepileptic drugs.

P. Ex. 18 at 2.

The facts set forth by Dr. Kinsbourne have been so found by this court to be a reliable account of Lorena's clinical course and persuade the court that her condition had changed dramatically as compared with her prior condition. Based on the evidence documented in the medical records, the court finds that following the July 15, 1993 episode of status epilepticus, Lorena's condition was much worse. The cause of this change, of course, is the subject of the ensuing inquiry.

Method of Proof

Petitioner bears the onerous burden of proving affirmatively that the DPT vaccine caused a significant aggravation of her neurological condition. The analysis to be applied is two-fold: (1) Can the DPT vaccine cause the particular injury claimed, (in this case, a

seizure of major proportions followed by other seizures, many of which were explosive in nature), and her chronic brain damage subsequently manifested by severe and permanent neurological deficits? And (2) did the DPT vaccination in fact cause the injury and significant aggravation in this particular child? See 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. March 18, 1994) (two-step causation-in-fact analysis used).

THE ISSUE

As Respondent argues, the occurrence of a prior seizure unrelated temporally to any DPT shot, however brief it may have been, suggests the possibility that Lorena had an underlying neurological condition of undetermined origin prior to the July 15,1993 vaccination. Respondent argues two positions: First, that in an off-Table claim, Petitioner has the burden of affirmative proof, and has failed to establish her case by the relevant standards; and Second: the change in her condition, more likely than not, was simply the natural evolution of her prior condition,

THE EXPERT TESTIMONY

Testimony of Dr. Marcel Kinsbourne for Petitioner:

Dr. Kinsbourne attributes Lorena's seizure disorder and her present neurological deficits to the vaccine administered on July 15, 1993. The onset of her sudden post-vaccinal neurological event, an unusual explosive seizure in excess of 45 minute duration, occurred within eight to ten hours after vaccination. A seizure of this character qualifies as "status epilepticus." Dr. Kinsbourne believes firmly that the event was caused by the vaccination she had just received. She was apparently in stable condition prior to vaccination, and demonstrated an immediate and permanent change in health within hours of the DPT shot. Although the event was uncommonly severe, Dr. Kinsbourne acknowledges that it cannot be characterized as an encephalopathy, because the symptoms did not meet the "current" definition for on-Table injuries required by the March 1995 revisions to § 14 of the statute, the Vaccine Injury Table. The event would have qualified as an encephalopathy prior to the March 10, 1995 revisions. Dr. Kinsbourne maintains, instead, that the vaccine, in fact, caused the seizure, exacerbated her condition and worsened her disorder. Her seizures became intractable and more frequent, and ultimately culminated in a devastating condition that is now acknowledged as a chronic encephalopathy. Lorena presently demonstrates not only seizures, but also severe developmental delay and other neurological dysfunctions.

Testimony of Dr. Joel Herskowitz for Respondent:

Dr. Joel Herskowitz appeared in person and testified for Respondent. Dr. Herskowitz acknowledges that the character of Lorena's July 15, 1993 episode of status epilepticus, because of its length and severity, would qualify as a "serious acute neurological injury" as that condition is defined in the National Childhood Encephalopathic Study (NCES).[5] He argues however, that such injuries are not "a tight correlation" and that not everyone who has such an injury will demonstrate [permanent] brain damage thereafter. Tr. at 134. He considers Lorena's symptoms insufficiently severe to have caused her subsequent neurological deficits. He acknowledges that she was deemed sufficiently severe as to merit hospitalization. But he notes that although she regressed in certain skills, and lost some milestones after the relevant DPT shot, she continued to demonstrate limited progress, albeit at a slower pace. Dr. Herskowitz, would not be willing to accept a causal relationship between the vaccine and the injury unless the initial event had been accompanied by evidence of an encephalopathy as that term is now defined in the revised Vaccine Injury Table guidelines--a far more stringent definition. He holds that opinion in spite of the fact that the revised definition does not apply in causation -in-fact cases.[6] Dr. Herskowitz is not convinced that Lorena's condition was significantly aggravated. Although slowed thereafter, her development did not cease altogether. Her

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[5] The NCES will be addressed in greater detail hereafter. The National Childhood Encephalopathy Study (NCES) was a major epidemiological study of the incidence of neurological injury following the administration of the DPT vaccine. Children who demonstrated an acute serious neurological event were included in the study of such cases between 1976 and 1979. The study was conducted throughout England, Scotland and Wales.

[6] The 1995 revisions of the Vaccine Table, included significant amendments to both the table and relevant regulations. These changes were instigated by the Department of Health and Human Services (the Respondent in all vaccine cases) pursuant to its statutory authority to do so. Removal of Residual Seizure Disorder from the Table has been already addressed. The second change relevant to this case was a major change in the definition of "'encephalopathy" to be applied in all on-Table claims. Prior to the amendments, an encephalopathy was defined as "any significant acquired abnormality of, or injury to, or impairment of function of the brain," and convulsions were considered to be among the frequent manifestations of encephalopathy or abnormal function of the brain. Such neurological manifestations, under the old guidelines, according to the statute, might prove to be "temporary with complete recovery, or may result in various degrees of permanent impairment." Id. Proof of an encephalopathy that meets the new guidelines for on-Table cases, is far more difficult than formerly and is confined to cases that demonstrate only the most catastrophic of symptoms. In this court's experience, few Petitioners have been able to meet the new criteria for proof of encephalopathy.

Dr. Herskowitz would require Petitioners to meet the more stringent criteria in both off-and on-Table cases. It is sufficient to say that Lorena did not meet the criteria for an on-Table injury and, therefore, is pursuing a causation-in-fact case. Her claim is that irrespective of the more stringent guidelines her injuries, in fact, were caused by the vaccine.

small gains suggest in his mind, a return to a normal state. Medical Report of Joel Herskowitz, M.D., filed March 20, 1997 at 14-17.

Testimony of Dr. Robert J. Baumann, for Respondent.

The court was not satisfied that the issues had been fully addressed at the initial hearing. A second hearing was scheduled, but it was ultimately decided that additional expert testimony in the form of written reports would suffice. On December 8, 1998, Respondent filed supplemental evidence in the form of a report by Dr. Robert J. Baumann, a pediatric neurologist. He did not appear in person as a witness. Dr. Baumann's report presents the following reasons for concluding that the vaccine was not responsible for the child's injuries. First: Dr. Baumann believes that if the DPT had in fact injured Lorena's brain in such a manner as to cause the obvious severity of her subsequent deficits, her acute injury would have shown signs of encephalopathy. Dr. Baumann argues that she did not demonstrate signs and symptoms of encephalopathy consistent with the requirements in the 1995 revisions for on-Table cases. He argues further that if injury to the brain had occurred, evidence of injury would be evident on MRI, developmental lags would have been identified immediately, and one would expect lags in head growth. Medical Expert report of Dr. Robert J. Baumann at 1,2. Second: Dr. Baumann alleges "that seizures [themselves] do not produce neurologic impairment, but rather, may be markers of those children with underlying neurologic disease." Id. Third: It is his opinion that one can never identify a pertussis-related cause of injury for the reason that although data indicate that DPT immunization has the potential for causing an acute neurological injury, one can never prove such cause in an individual child because DPT injury produces no unique markers or patterns of injury. Finally, Dr. Baumann believes one cannot rely upon epidemiological studies, such as the NCES, as guidance for diagnosing the cause of injury in an individual child. Id. at 5. He summarizes:

> [T]he [epidemiological] data indicate that DPT immunization has the potential for causing an acute neurological injury that can give chronic neurologic disability. Nevertheless the [data] does not provide guidance for diagnosing an individual child. Since neurological damage from DPT immunization does not produce a unique pattern of injury, the diagnosis of this form of injury should follow the standard rules of neurologic diagnosis, requiring evidence of significant acute neurologic injury before postulating the possibility of persisting and chronic neurologic handicap.

Medical Expert Report of Dr. Baumann at 5.

DISCUSSION

The first question: "Can the DPT cause acute neurological injury?" has been answered in the affirmative by all three experts, Drs. Herskowitz and Baumann, for

Respondent, and Dr. Kinsbourne, for Petitioner. The second question: "Did it do so in this case?" is the remaining issue. An answer to the second question depends on the court's evaluation of the nature and sufficiency of evidence required to prove an off-Table, causation-in-fact, significant aggravation case.

Both parties acknowledge that Lorena did not exhibit evidence of an immediate encephalopathy as that term is now defined. Respondent's view, according to the testimony, is that in an individual case, unless evidence of encephalopathy accompanies a seizure disorder, it is impossible for one to ascribe a causal relationship between the vaccine and the injury that followed. Respondent does not argue that the vaccine cannot cause seizures. Respondent generally acknowledges that seizures following DPT may be attributed to fever that frequently accompanies DPT shots. But seizures have been removed from the Table of injuries, thus removing presumption of causation. And because medical science has not yet found a way to identify markers or footprints unique to a vaccine-related injury, one can identify the presence of neurological injury, but one cannot invariably identify its etiology. The experts agree generally that no pathognomonic sign of a pertussis vaccine injury exists. This fact, Dr. Baumann argues, makes it impossible for any petitioner to provide a legally sufficient proof.

The argument goes like this: Other causes of seizure disorders exist; some causes remain unidentifiable. But absence of any other identifiable cause of injury will not advance Petitioner's case because in proving causation in fact, Petitioner's duty is to affirmatively establish the cause; and cannot rely on the fact that other causes have been ruled out. Absent affirmative proof, one must conclude that Petitioner's seizure disorder constituted the natural and expected progression of her underlying neurological condition, or that her injury was merely a coincidence and that the etiology is simply unknown.

If the court accepts Respondent's argument, one would never be able to prevail in an off-Table claim of a seizure disorder or of a Significant Aggravation of a seizure disorder unless the seizure had been accompanied by an on-Table encephalopathy. In other words, unless a Petitioner can prove an on-Table case, with its presumption of causation, a Petitioner could never prove that a vaccine had a significant role as a primary or concomitant factor in the etiology of a neurological illness. This court considers that conclusion to be unnecessarily harsh and contrary to the intents and expectations of the Vaccine Act.

The basic premise of the Vaccine Act is that the pertussis vaccine can cause injuries such as petitioner claims. As early as 1981, experts and researchers suspected that aggregated clinical case material "gave a very strong impression that the vaccine is often responsible for the neurological events which followed." [7] In consideration of

[7] A Report of an advisory panel on The Data Relating to Pertussis Vaccine: A Report by the Committee on Safety of Medicines to the Secretary of State for Social Services on the data submitted

Respondent's arguments, and in consequence of the amended Vaccine Injury Table, how can one establish causation? The court proposes that evidence from the following sources may suffice in some cases once the factual matters have been successfully established.

EXPERT OPINION

Persuasive, rational, relevant and well supported expert opinion is probative. The credentials and expertise of the experts in this case are relatively equal, and their experience more or less comparable as well. Opposing opinions have been well and reasonably stated for the most part. In evaluating the relative weight to be accorded to each expert's testimony, the court finds the testimony of Dr. Kinsbourne superior in this case, more persuasive and rational. In spite of the absence of immediate signs of the more stringent criteria for encephalopathy, the court is convinced that the vaccine did in fact aggravate Petitioner's underlying seizure disorder.[8] As Dr. Kinsbourne explains, subsequent escalating episodes of status epilepticus further damaged the brain resulting eventually in "static" (permanent) encephalopathy. A preponderance of evidence convinces the court that Lorena's pre-vaccination condition, from all indications, was that of a relatively benign nature; the factual evidence of a dramatic change after the vaccination is much stronger than Respondent's alleged evidence of a return to normal. Dr. Kinsbourne's explanation is more consistent with the facts and the evidence. It is more likely than not, so finds the court, that the vaccine not only triggered the initial explosive seizure of July 15, 1993 but also must be considered responsible for its aftermath--the further damage caused by her intractable seizure disorder.[9] The following is a detailed discussion of the relative weight and persuasiveness of the parties' arguments.

Are signs of acute injury always immediately apparent ?

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by the Association of Parents of Vaccine-Damaged Children: Preface to the Report entitled Whooping Cough. One of a series of six Reports included in the NCES Report by the Committee on Safety of Medicines and the Joint Committee on Vaccination and Immunisation [sic], Department of Health and Social Security [United Kingdom]. London, Her Majesty's Stationery Office (1981) at 3.

[8] To characterize Lorena's prior seizure as an underlying disorder, may be misleading. According to a follow up study of the NCES, (the NCES is an epidemiological study to be discussed hereafter), "Brief uncomplicated convulsions are usually benign and hence not important so far as the child's later development is concerned. Complicated and/or prolonged seizures of this type, however, may have greater significance." The National Childhood Encephalopathy Study: A 10-year follow-up, Madge, Diamond, Miller, Ross, McManus, Wadsworth, and Yule. "Background to the Study" at 1. (Emphasis supplied.)

[9] "Intractable" is defined as "resistant to cure, relief, or control." Dorland's Illustrated Medical Dictionary, 848 (27th ed. 1988).

Dr. Baumann, for Respondent, insists that if in fact Lorena's massive seizure after the DPT shot had damaged her brain, one would have identified immediate signs of acute neurological injury, and its sequelae (for example, developmental delay) would be apparent immediately and could be documented by imaging tests. He insists that even a prolonged seizure is not adequate evidence that at the time of seizure, the young child's brain sustained a significant injury. Medical Expert Report of Dr. Baumann at 1-2.

Dr. Kinsbourne disagrees; he acknowledges that such is sometimes the case, but "often is not." Citing three medical articles, Dr. Kinsbourne explains why the evidence may not be immediately apparent. "Severe seizure is known to be capable of causing brain damage that facilitates further seizures without generating clinically apparent signs of acute encephalopathy or immediate signs of interrupted development." P. Ex. 26 at 1. Not every prolonged seizure, he says, causes significant brain damage, but such damage has been amply documented not only in older, but also in recent publications. Id. In cases of vaccine injury, particularly in seizure disorders, the MRI will be negative--more often than not, nothing will appear in the early MRI. Tr. at 104. He repeats his position for emphasis. In cases of severe seizure disorders, the initial MRI is more commonly negative than it is positive, regardless of the cause of the disorder. In vaccine injury, both MRI's and CT scans will be normal initially. Over the years, one might expect to observe cerebral atrophy, but one would not observe it right away. Tr. at 103-105. Customarily, one will observe no immediate markers to identify a DPT injury other than its clinical course. If the condition continues, pathology can be later identified, as in this case, but would not indicate what caused the injuries. Footprints to indicate a DPT injury as opposed to some other cause, simply do not exist. Tr. at 106-108. In other words, the outcomes, more often than not, do not indicate what caused those outcomes. [10] Tr. at 107.

Nor should one expect head circumference to fall off under these circumstances. Id. Diminished cognitive functions, speech and language deficits, and Lorena's subsequent motor deficits were the result of her worsening seizures that further damaged the brain. Tr. at 78.

> When the severity of a seizure disorder is of the level of Lorena's then the sequelae of diminishing rate of acquisition of mental skills is not uncommonly seen and there is no need to find a further separate explanation or to diagnose some independent disease causing it. . . . [M]ost

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[10] The Institute of Medicine (IOM)confirms: [There are] "no special characteristics associated with the acute or chronic nervous system illnesses linked to DPT exposure." 1994 Report of the IOM at 1. Dr. Herskowitz's testimony for Respondent is more consistent with Dr. Kinsbourne's explanation. He acknowledges that the literature supports the possibility that given a serious acute neurologic injury, the evidence of chronic brain damage may be evidenced at a later time. Tr. at 133. Dr. Herskowitz cites the well-known National Childhood Encephalopathy Study as his source. (Emphasis supplied.)

> people in the field would accept . . . the concept [that] severe seizures themselves can bring out the kind of damage that results in speech, language, motor and cognitive delays. It happened in this case. Tr. at 77-78.

He explains further. A baby has all the neurons that he or she is going to have for the rest of [the baby's] life, but isn't using them all, as yet. As maturation progresses, more and more of the neurons already in place become functional, in other words, generate behaviors that one can observe. If the damaging event has attacked neurons the baby is currently using, then right after that event, the baby is different. This can be detected by neurological examination . . . often detected by the parents. The baby isn't attending anymore. The baby isn't alert. The baby is paralyzed on one side, or a variety of quite detectable observations. However, it's also believed that some damaging events can damage neurons which are, as yet not functional, but are programmed to come into action weeks later, months later, years later. . . . Speech and language is a prime example of this. Frequently, he continues, injuries in utero or at birth are not observed until the child matures and deficits in the development emerge only gradually. In other words, evidence of brain injury does not always become immediately apparent. The court finds Dr. Kinsbourne's rebuttal to be persuasive and consistent with evidence found in the literature and heard from other experts.

Can Seizures cause further brain damage?

As to the cause of Lorena's present condition, Dr. Baumann has proposed that, seizures themselves, no matter how severe, "do not produce neurologic impairment, but rather, may be markers of those children with underlying neurologic disease." Medical Expert Report of Dr. Baumann at 2. Dr. Baumann's argument is contrary to a large body of medical literature. A number of other experts apparently disagree as will be elaborated hereafter, including Respondent's own expert in this case, Dr. Herskowitz. Tr. at 122. Dr. Kinsbourne acknowledges that the outcome of convulsive status epilepticus may vary. Status epilepticus does not cause permanent damage invariably in every instance, but the prognosis is always guarded. He explains what happens when a seizure lasts for such a long period of time:

> First, it does represent a highly abnormal pattern of brain functioning and. . . . the neurons, which each should be doing their own thing in the complex building up of a mental state, instead are beating together in insensate fashion, causing the musculature to beat accordingly. The length of the seizure, in a sense, indicates the severity of the seizure disorder . . . One would look [also] at the frequency of seizures. . . . Tr. at 41.
>
> I think that child neurologists would agree that repeated status epilepticus can have, and often does have, a cumulatively harmful effect on mental development.

That proposition was voiced by a former President of the World Congress of Child Neurology, Dr. Jean Aicardi. Tr. at 56.

This court discussed in detail the same issue in another case. In Lurtz v. Secretary of HHS, No. 90-1703V, 1998 WL 321926 at 7-8 (Fed. Cl. Spec. Mstr. June 4, 1998) the court cited the following respected experts:

> A series of studies by epileptologist, Dr. Jean Aicardi, found a high incidence of mental deficits following status epilepticus. Dr. Aicardi notes that studies by Fukuyama, et al. found similar results, finding mental and/or neurological sequelae in 40 of 79 children that had seizures lasting one hour or more, and a high incidence of motor damage as well. In the Aicardi series, seizures occurring after status epilepticus were mainly of a type usually associated with brain damage. Aicardi concluded:
>
> Convulsive seizure may end in death or may leave severe mental and/or neurological sequelae that appear to result, at least in part, from the convulsive activity itself, irrespective of its causes. . . . and poor prognosis is often associated with early age of onset.

Jean Aicardi, Epilepsy in Children, Raven Press, N.Y. at 6, 36, 52, and 160, 243, 251, and 258 (1986). See also the following:

> 1) Dr. Aicardi, Epilepsy in Children: Chapter 16, "Status Epilepticus," 1986 ("[Status epilepticus is] a major emergency because of its life-threatening character and the high incidence of its sequelae.") at 251 and 258;
>
> 2) Dr. Jerome Engle, Jr., Seizures and Epilepsy, "Epileptic Brain Damage," (1989)([T]here is incontrovertible evidence that epilepsy itself can cause structural damage in the brain . . . . The mechanism of action [is not confined] to hypoxia, ischemia, or hypothermia. . . . Most recent evidence indicates that the endogenous excitatory amino acids, particularly glutamate, mediate damage and [other chemicals] activate proteases and lipases and lead to mitochondrial dysfunction.) at 276;
>
> 3) Dr. Eric Lothman, "The Biochemical Basis and Pathophysiology of Status Epilepticus," 40 Neurology, at 19 (May 1990);
>
> 4) Dr. Claude G. Wasterlain, et al., "Pathophysiological Mechanisms of Brain Damage from Status Epilepticus," 34 Epilepsia, at 37 (1993) ("[T]he degree of brain damage can increase with the duration of the seizure;" and "Convulsive, tonic-clonic SE [(status epilepticus)] rapidly leads to severe brain damage.") at 39;

5) Editor's Note, 10 Emergency Medicine Reports, at 65 (April 24,1989) ("[T]ime is brain . . . and in some high-risk patients, seizure activity must be aborted . . . to prevent mortality and excessive morbidity.")

Lurtz, No. 90-1703V, 1998 WL 321926, at 7-8 (Fed. Cl. Spec. Mstr. June 4, 1998).

Over the years, this court has learned that some seizure disorders are relatively benign. But many types of seizure disorders are not. At the far range, are disorders that bear an ominous prognosis, as in this case. Lorena's disorder is one of those that does not bode well, as time has confirmed. The court is convinced that Dr. Kinsbourne's opinion is more in line with the medical realities of the dangers of prolonged seizures than Dr. Baumann acknowledges. Again, Dr. Herskowitz, tends to disagree with Dr. Baumann's theory:

> I will cut to the quick a little bit on this, as far as is possible. Yes, she had status epilepticus. Yes, that can be injurious to the brain because of poisonous toxic chemicals that can be generated as byproducts. Tr. at 122.

Dr. Herskowitz, of course, does not believe Lorena sustained such damage for reasons stated earlier, one of which is his hypothesis that "she bounced back." Id. (The court did not so find.)

The Mechanism of Injury

According to the Federal Circuit Court of Appeals, to support a causation in fact case, Petitioner must provide a logical sequence of cause and effect showing that the vaccine was the reason for the injury. Grant v. Secretary of HHS, 956 F. 2d 1144, 1148 (Fed. Cir. 1992.) According to Knudsen v. Secretary of HHS, Petitioner must support the logical sequence of cause and effect with sound and reliable medical or scientific explanation. Knudsen 35 F. 3d 543, 548 (Fed. Cir. 1994). Dr. Kinsbourne states that because it is consensual that DPT can cause seizures, logically, there has to be a way by which it can do that. There is not yet a general agreement as to the particular way or mechanism that causes seizures. The toxins and endotoxin in the pertussis vaccine have been studied chemically and it is known what they can potentially do in the body. Dr. Kinsbourne believes that the antigens in the vaccine breach the blood-brain barrier, attack brain cells, and affect neuronal metabolism. He acknowledges that these processes are yet to be demonstrated, a fact that is not surprising inasmuch as confirmation would require scientific research on a live individual. The literature, demonstrates that these antigens can damage cells. Regardless of the details of its mechanism, the biological plausibility of acute brain damage caused by pertussis vaccine is beyond doubt. P. Ex. 26 at 1 (citing Alderslade et. al., Institute of Medicine, 1991).

He acknowledges that this is a theory held by many experienced professionals, including himself, but that it remains a minority view. Dr. Kinsbourne's explanation has never been discredited, but he acknowledges that many of his colleagues hold the simple point of view that "we just don't know how this works. " Dr. Kinsbourne considers that to be a "tenable position" also. Regardless of the details of its mechanism, the biological plausibility of acute brain damage caused by pertussis vaccine, according to Dr. Kinsbourne, is beyond doubt. P. Ex. 26 at 1 citing generally, Alderslade et. al., NCES;(1981); Report of the Institute Of Medicine, 1991). Tr. at 25.

Respondent considers that theory to be pure speculation. Dr. Kinsbourne is not alone, however, in suspecting that particular mechanism. That theory was presented to a number of respected experts chosen for their experience and distinction in the field at a 1989 "Workshop on Neurological Complications of Pertussis and Pertussis Vaccination." An abstract of the discussion was prepared by Dr. John Menkes and Dr. Kinsbourne, it was accepted and published by The Journal of Neuropediatrics and filed in this case as P. Ex 21. Prior to publication, it was circulated and reviewed by all participants to make sure that what it contained represented their opinions.

In its own brief review of medical notes the court found two items in which the concept of injury to the brain by breach of the blood-brain barrier was discussed. An article published in Scientific American, "Breaching the Blood-Brain Barrier," by author, Elaine Tuomanen, M.D.,[11] purports to reveal how bacterial cell-wall "debris" penetrates the barrier to disturb the nerve cells and damage the brain. Parenthetically, the author discovered one particularly interesting bacterium, in bordetella pertussis, the agent of whooping cough [as a potential invader].

A reference from the Internet identified as 1998 WL 16782236, 11/13/98 Hous. Chron. 21(Health briefs, Houston Chronical News Services) (Publication page references are not available for this document), discloses that scientists recently found infection of a person's brain cells by a type of bacteria commonly found in the sinuses and lungs. The presence of the bacterium was unexpected because it meant the germ had to penetrate the protective blood-brain barrier.

The court presents this information, not for proof of Dr. Kinsbourne's proposed mechanism of injury, but to suggest that the proposed sequence of cause and effect meets the requirements of Knudsen v. Secretary of HHS, 35F.3d 543, 548 (Fed. Cir. 1994), citing Jay v. Secretary of HHS, 998 F.2d 979,984 (Fed. Cir. 1993). It is logical and based on a "sound and reliable medical or scientific explanation." The court's analysis of the basis for Dr. Kinsbourne's opinion, leads the court to the opinion that it falls within the range of accepted standards governing medical or scientific research required by Daubert v.

[11] Scientific American, February 1993 at 80. Dr. Tuomanen is head of the laboratory of molecular infectious disease at the Rockefeller University.

Merrell Dow Pharmaceuticals, Inc., 43 F.3d 1311, 1316 (9th Cir.1995) , and should not be cavalierly dismissed. His theory of the mechanism of injury neither persuaded me nor dissuaded me from my ultimate decision. The Federal Circuit has held in Knudsen that the precise details of the mechanics of injury are not needed for Petitioner's case to succeed. According to Knudsen, a "detailed medical and scientific exposition on the biological mechanisms," of an injury, is not necessary. Knudsen, at 548. The Federal Circuit held further:

> The determination of causation in fact under the Vaccine Act involves ascertaining whether a sequence of cause and effect is "logical" and legally probable, not medically or scientifically certain. See Bunting v. Secretary of HHS, 931 F.2d 867, 873 (Fed. Cir. 1991) (Scientific certainty is not the standard of proof); (citing Hodges v. Secretary of HHS, 9 F.3d 958, 966-68 (Fed. Cir. 1993) (Newman, J., dissenting). . . . [Causation can be found in vaccine cases based on epidemiological evidence and the clinical picture regarding the particular child without detailed medical and scientific exposition on the biological mechanisms. E.g., Jay, 998 F.2d. at 984. Furthermore, to require identification and proof of specific biological mechanisms would be inconsistent with the purpose and nature of the vaccine compensation program. The Vaccine Act does not contemplate full blown tort litigation in the Court of Federal Claims. Id. at 549.

EPIDEMIOLOGICAL EVIDENCE

Whether Petitioner may rely upon epidemiological evidence to support her claim has been a vexing issue in this case. Respondent challenges the usefulness of epidemiological evidence for several reasons: First, Respondent argues that epidemiological data identifies trends in the population, but does not provide evidence of causation when applied to an individual case; Second, Respondent argues that present epidemiolological information applies only to individuals who were neurologically intact prior to receiving the vaccine for the reason that the National Childhood Encephalopathy Study (NCES) did not address the issue of whether the DPT can cause an exacerbation of a preexisting neurological condition; Third, Respondent takes the position that the authors of the NCES suggest "extreme caution" in drawing conclusions, such as attributing causation in an individual patient; Finally, Respondent considers the NCES a "flawed" study. These issues will be addressed in requisite detail, but, in short, the court finds Respondent's arguments unconvincing. The court does not agree that epidemiological findings must be rendered useless in Petitioner's case.

Epidemiology is defined as --

> [T]he science of studying factors determining and influencing the frequency and distribution of disease, and other health-related events and their causes in a

> defined human population for the purpose of establishing programs to prevent and control their development and spread. Also, the sum of knowledge gained in such a study. (Emphasis supplied.)

Dorland's Illustrated Medical Dictionary, 27th Ed. at 566 (1988).

According to the courts, reliance upon epidemiological studies as evidence of causation in individual cases is not misplaced. Such information has been considered valuable as scientific evidence in many cases where there is no direct evidence of causation: Brock v. Merrell Dow Pharmaceuticals, Inc, 874 F. 2d 307, 311 (5th Cir. 1989) (Epidemiology attempts to define a relationship between a disease and a factor suspected of causing it.) (An odds ratio or relative risk greater than two can demonstrate a causal relationship); Deluca v. Merrell Dow Pharmaceuticals, Inc., 911 F.2d 941, 959 (3rd Cir. 1990) (A relative risk greater than "2" means that the disease more likely than not was caused by the event.); In re Joint Eastern and Southern District Asbestos Litigation, 52 F.3d 1124, 1138 (2nd Cir. 1995) (Without "direct proof of causation," the preponderance of epidemiological evidence standard can be met where the relative risk exceeds two); See also, Manko v. U.S., F.Supp. 1419, 1434 (W.D. Mo. 1986); Marder v. G.D. Searle & Co., 630 F. Supp. 1087,1092 (D. Md. 1986) aff'd 814 F.2d 655 (4th Cir. 1987) (In epidemiological terms, a two-fold increased risk is an important showing for plaintiffs to make because it is the equivalent of the required legal burden of proof--a showing of causation by the preponderance of evidence or in other words, a probability greater than 50%).

As stated earlier, in Knudsen v. Secretary of HHS, 35 F.3d 543 (Fed. Cir. 1994), the U.S. Court of Appeals for the Federal Circuit held that although bare statistical facts alone are insufficient to establish causation in a particular case, causation may be found in vaccine cases based on epidemiological evidence and the clinical picture regarding the particular child.[12]

The National Childhood Encephalopathy Study (NCES)

For many years, medical science struggled with the probability that the DPT vaccine contains reactogenic properties. Since the early 1930's, the medical literature has reported instances in which neurological injury followed DPT vaccinations in close temporal relationship. Such adverse reactions were rare, but their persistence suggested a possible cause and effect relationship. In 1981, the now famous National Childhood Encephalopathy Study was published. The NCES is considered the only epidemiological study of sufficient scope and design to study adequately the adverse effects of pertussis vaccine. The NCES definitively addresses the incidence of what most believe to be a rare

[12] Knudsen, at 549-550. See also, Grant v. Secretary of HHS, 956 F.2d 1144, 1148.

event, namely brain damage caused by the pertussis component of the vaccine. Tr. at 26. Based on the study of two million doses of vaccine administered in England, Scotland, and Wales between 1976 and 1979, the NCES found a statistically significant increased risk of serious neurological injury within seven days of DPT vaccination, the highest rate of incidence of injury occurring within the first 72 hours in individuals who fit within certain criteria specified by the NCES. P. Ex. 21(a). Those criteria specified that a child must have demonstrated at least one of the conditions defined as a "serious acute neurologic illness." "A serious acute neurological illness" included acute encephalopathy; or a minimum of 30 minutes of seizure activity within seven days of vaccination; or a complicated seizure characterized by coma lasting two hours or more; or seizures followed by paralysis or other neurological signs not previously present lasting 24 hours or more.[13]

The NCES is generally acknowledged as the largest, most comprehensive study available. The original NCES evaluations and conclusions were considerably bolstered by a ten-year follow-up study published in 1993 that led the Institute of Medicine (IOM) to reconsider and change its previously tentative position as to whether the vaccine could cause permanent damage.[14]

The 1976-1979 NCES study suggested caution in attributing causation in individual cases. The 1993 follow-up study, however, provided more secure evidence in support of NCES findings of risk of acute neurological illness. Its authors concluded that detailed exploration of the larger body of data on all acute neurological events failed to find evidence of significant system error or bias in the original study in either direction. In fact, none of the interim challenges to the NCES assessment of risk were found to require modification of the NCES' conclusions relating to acute neurological events. Id. at 1174. In other words, the follow-up study confirmed the original study as a valid estimate of risk of neurological injury in excess of random occurrence.

The 1993 follow-up study concluded also that although evidence of a causal relation between DPT and permanent damage had heretofore been uncertain, the follow-up study offered "a more robust assessment of the outcome of such illnesses" than had been available in the earlier study and more secure evidence of long term consequences. (Id. at 1175). According to the NCES authors:

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[13] The uncommon length of her April 15, 1993 seizure would have qualified Lorena for inclusion in the study.

[14] The National Childhood Encephalopathy Study ([NCES]): A 10-Year Follow-up, Madge, Miller, Ross, Wadsworth, and Diamond, Published as "Pertussis immunisation and serious acute neurological illness in children," Brit. Med. J., vol. 307, at 1171-1176 (6 November 1993); P. Ex. E.

> Our results provide good evidence that illnesses such as those studied in the NCES study, including a variety of encephalopathies and severe convulsions, both febrile and afebrile, can have a lasting effect as measured by various indices of brain function. (Emphasis supplied). Id.

Based on medical literature, case reports, the NCES, and the NCES ten-year follow-up report, the Institute of Medicine (IOM) published in 1994 its own report of the Committee to Study New Research on Vaccines, Division of Health Promotion and Disease Prevention which concluded:

> [T]he balance of evidence is consistent with a causal relation between DPT and forms of chronic nervous system dysfunction described in the NCES in those children who experience a serious acute neurologic illness within seven days after receiving DPT.

Stratton, Howe, & Johnson, Eds., Division of Health Promotion and Disease Prevention: Institute of Medicine: DPT Vaccine & Chronic Nervous System Dysfunction: A New Analysis, National Academy Press, Washington, D.C. 1994 (hereinafter "1994 IOM Report") at 2-3; P. Ex. 21 at 2-3.

Relative risk was calculated in the original NCES study as approximately three times greater than would be expected in the background rate of those who were not vaccinated. The relative risk would be even higher in those with reactions occurring in the first 72 hours, as in this case.

Does the NCES analysis of Relative Risk apply in this case?

Respondent insists that the NCES does not apply in this case. Respondent alleges that although epidemiological data exists to establish that the vaccine can cause permanent injury in previously neurologically intact individuals, no such data is available that establishes that it can cause an exacerbation of a preexisting neurological condition. That issue, Respondent argues, was not studied by the NCES. Furthermore, Petitioner's acute neurological event was unaccompanied by fever, and, Respondent alleges, no evidence exists that the DPT can cause "afebrile" seizures.[15] Petitioner's symptoms, Respondent suggests, are more likely attributable to the natural evolution of her underlying disorder.

The court rejects both arguments as untenable. The NCES itself appears to refute Respondent's allegation that no evidence supports a finding that DPT can cause afebrile seizures. Contrary to Respondent's claim, the NCES did not distinguish between febrile

[15] Respondent generally acknowledges that febrile seizures following DPT may be attributed to fever that frequently accompanies DPT shots.

and afebrile seizures in its analysis of relative risk. Both were included in the NCES conclusions. The NCES conclusions suggest instead that those with convulsions "other" than febrile were apparently at even greater risk. The ten-year follow-up analysis noted that those with febrile seizures had less chance of death or dysfunction than those with "other" complicated severe convulsions:

> Cases in all clinical categories were more likely than controls to have died or to show some form of dysfunction. Those with prolonged or complicated febrile convulsions were less likely to have died [3%died] or to show dysfunction in any area [41% dysfunction] as compared with those with encephalopathies or "other" severe convulsions [33% had died and 52% had dysfunction]. P. Ex. E at 1173-1174.
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> . . . . . .
>
> Our results provide good evidence that illnesses such as those studied in the NCES study, including a variety of encephalopathies and severe convulsions, both febrile and afebrile can have a lasting effect as measured by various indices of brain function. P. Ex. E at 1171-1176. (Emphasis supplied).

Respondent claims that NCES assessments of rates of risk apply only to individuals who were neurologically intact prior to vaccination. Dr. Kinsbourne considers that argument invalid and the court is similarly so persuaded. The fact that Petitioner had a brief seizure prior to vaccination does not necessarily eliminate her from NCES rate of risk conclusions. The ten-year NCES follow-up study in 1993, indeed, did not include children with prior neurological events, but not for purposes of negating the applicability of NCES rates of risk to children with prior neurological conditions. The follow-up study, Dr. Kinsbourne explains, excluded such cases because the sample was not large enough for separate statistical treatment. (The sample was small because if a child was known to have had seizures, administration of the pertussis component was contraindicated.) The "more robust" follow-up study statistics would not apply to Petitioner, but the original NCES statistical conclusions would apply. The 1976-1979 study would have included Petitioner in a separate category II, and would have included her in the overall analysis that found a relative risk of acute neurological illness of 3-to-1. In other words, there was no difference in the distribution of neurological abnormality in children in the two categories I and II. There is no reason, therefore, to expect a difference between the two categories of the proportion of children who sustained neurological harm in association with the DPT. Dr. Kinsbourne concludes: "I do not know of any mechanism which would preclude children with prior injuries from sustaining further damage to the brain." P. Ex. 26 at 2.

Dr. Kinsbourne's opinion is consistent with the following evidence in that regard. Among treating physicians, the standard protocol has been to withhold the pertussis component of the DPT vaccine if infants or children were known to have had a prior history of seizure activity. Such cautionary procedures have existed for many years for the reason

that doctors believe that the vaccine poses a risk of causing or triggering further seizures. Such children were administered DT vaccine, but not the pertussis. The additional fact that the NCES included lengthy seizures in their definition of "serious acute neurological events" is significant to this particular discussion as well.[16] The NCES did not distinguish between febrile and afebrile seizures in their relative capacity to injure nor did they exclude neurologically compromised children from their conclusions.

Two remaining arguments must be addressed. Dr. Baumann believes that epidemiology has no place in diagnosis of causation in individual cases. As discussed earlier, the courts have held otherwise. In rebuttal, Dr. Kinsbourne argues that Dr. Baumann's position ignores the significantly increased relative risk of injury within the first 72 hours identified by the epidemiological study, and, he emphasizes, prolonged seizures are included among those injuries. This, he argues, was the main finding of the study and has been endorsed by the Institute of Medicine in their 1991 and 1994 Reports.

> For instance, a relative risk of three (found within 72 hours) would mean that children with post-DPT acute neurological illnesses bear a 75% probability of association to DPT. Such a level of probability would offer a sound basis for a causation opinion to a reasonable medical certainty. P. Ex. 26 at 2.

As an example, medical science found that subclinical lead poisoning was a cause of developmental deficits, based solely on epidemiological evidence. Similarly, injuries have been attributed to the Swine Flu vaccine based on epidemiological evidence. Dr. Kinsbourne suggests that in the absence of evidence of any other cause, one may refer to the relative risk. The NCES, he argues, was performed for the very purpose of ruling out coincidence, finding an approximate 3-to-1 relative risk of a neurological event within seven days of a DPT shot, and an even greater risk of about 4-to-1 ratio within 72 hours. NCES Report at 121. The Institute of Medicine concurred in those findings which leads Dr. Kinsbourne to attribute cause in this case to a reasonable medical certainty (50%+), although, he admits, not to proof beyond 95% certainty.[17] As cited earlier, the courts permit such attribution of causation in similar situations based on epidemiological findings.

Respondent's final claim concerning the relevance of epidemiological evidence is that the NCES is a flawed study. This court is not convinced of the validity of that allegation. In another case, this court addressed the same allegation in a detailed analysis

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[16] In light of this fact, the court finds it curious that Respondent, unilaterally chose to exclude such seizures from the Vaccine Injury Table and now challenges such seizures as irrelevant in this case. To some experts, removal of residual seizure disorder from the Vaccine Injury Table is inconsistent with scientific and epidemiological evidence. Dr. Kinsbourne is of that opinion.

[17] 95% certainty constitutes the laboratorian's standard of proof.

of five areas of criticism cited frequently about the NCES. The court will not duplicate here its holdings which are set forth in full in Sharpnack v. Secretary of HHS, No. 90-983V, 1992 WL 167255 (Cl. Ct. Spec. Mstr. July 28, 1992), at pages 3 through 9. To summarize, based on the ten-year follow-up study and other medical literature responding to criticisms of the NCES, the so-called flaws were not borne out as likely, and the methodology was found fully appropriate and consistent with scientific standards. No evidence of significant system error or bias was found in either direction and no modifications were required in the conclusions of the original study. The NCES authors themselves had concluded from their follow-up study, that their original conclusions of risk were not only sound, but made more firm. This court concluded, based on the evidence submitted in Sharpnack, that a significant percentage of the medical community considers the NCES to be a valid study and the most reliable estimate of relative risk available. In the opinion of this court, no credible evidence has succeeded in discrediting the study, and many neurologists appearing before the undersigned, consider it valid. Indeed, Dr. Herskowitz, Respondent's expert, referred to the NCES on several occasions during oral testimony.

To the present time, there has been no comparable study to support or to refute the findings of the NCES. In the United States a relatively small study was undertaken using methods closely modeled on those of the NCES. The numbers of cases and controls were considered too small to provide a satisfactory answer in light of the fact that vaccine injuries are rare events. The U.S. study, however, demonstrated a positive association between DPT and severe acute neurological illnesses defined in the same way as in the original NCES. The odds ratio did not reach statistical significance, although it was of "similar magnitude to that found in the NCES." Miller, Madge, et al. "Pertussis immunization and serious acute neurological illnesses in children," Abstract , Brit. Med. Journal, 1993, at 1174. [18]

THE INSTITUTE OF MEDICINE

Finally, the court finds support for its decision in this case in the report of the Institute of Medicine, (hereinafter IOM). In its 1994 Report, the IOM found that children with an underlying brain abnormality may experience a DPT-triggered acute neurologic illness and subsequent chronic dysfunction. Based on the NCES, on case reports, and

[18] Similar issues concerning epidemiological evidence were addressed by another special master in Clements v. Secretary of HHS, No. 95-484V, 1998 WL 481881 (Fed. Cl. Spec. Mstr. July 30, 1998) with a contrary outcome. The special master in Clements criticized the epidemiological evidence presented in that case as faulty. This court is not bound by that decision, and I respectfully disagree with my colleague in Clements for reasons set forth in this decision and also in my 1992 decision in Sharpnack referenced in this decision. Clements, however can be distinguished from the instant case. In Clements, the special master was dissatisfied with the evidence provided by the medical expert. In the instant case, I found the epidemiological evidence and opinion testimony relating to the NCES more complete, more persuasive, and supportive of Petitioner's claim.

other medical literature that included the ten-year follow-up NCES report, the IOM published its report which concluded:

> [The] balance of evidence is consistent with a causal relation between DPT and chronic nervous system dysfunction described in the NCES in those children who experience a serious acute neurologic illness within seven days after receiving DPT.

But the IOM had also the following to say on the issue of a significant aggravation of a preexisting neurological condition:

> The NCES data also are consistent with the possibility that some children with underlying brain or metabolic abnormalities (emphasis supplied) (which foster a "triggering" by DPT of an acute neurologic illness) might go on to develop chronic nervous system dysfunction due to a DPT-triggered acute illness. Therefore, the committee concludes 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. (Emphasis in the original.)

Stratton, Howe, & Johnson, Eds., Division of Health Promotion and Disease prevention: Institute of Medicine: DPT Vaccine & Chronic Nervous System Dysfunction: A New Analysis, National Academy Press, Washington, D.C. 1994 IOM Report. P. Ex. 21 at 3-4 and 2-3 respectively. [19]

The Institute of Medicine addressed the issue of how DPT may cause damage to the central nervous system by proposing three scenarios: acute neurological illness and subsequent chronic dysfunction might be caused by the vaccine, or might trigger such injury (and thereby be an immediate proximate cause, but nevertheless is still a cause) (emphasis supplied), or may cause an acute illness in a child with an underlying abnormality. DPT Vaccine and Chronic Nervous System Dysfunction: A New Analysis, IOM Committee to Study New Research on Vaccines, National Academy Press, Washington, D.C. 1994, Executive Summary at 2.

To date, medical science is unable to determine which scenario applies in any given case. Identification of the precise scenario, however, is unnecessary because all three implicate the reactogenic properties in the vaccine as the proximate cause. The court

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[19] The IOM is an independent non-governmental body associated with the National Academy of Sciences. The mission of the IOM is to advance and disseminate scientific knowledge to improve human health. The Institute provides objective, timely, authoritative information and advice concerning health and science policy to the government, the corporate sector, the professions, and the public.

considers this evidence probative in Petitioner's claim.[20] The undersigned considers the IOM statement supportive of the proposition that a significant aggravation of a prior, relatively benign, neurological condition is indeed possible if that aggravation meets the criteria of a serious acute event within the relevant time frame and if chronic dysfunction persists thereafter. Lorena had a mild condition consisting of a brief mild seizure. The subsequent administration of the vaccine caused "or triggered" a serious neurological event of unwonted severity within the relevant time frame, that thereafter changed for the worse the course of her condition.

Respondent's experts appear to hold Petitioner to a much higher standard of proof than necessary. As stated by the Federal Circuit Court of Appeals:

> The findings of the Court [in vaccine cases] need not meet the standards of the laboratorian. Bunting v. Secretary of HHS, 931 F.2d 867 (Fed. Cir. 1991) (citing Tinnerholm).

I have considered carefully Dr. Herskowitz' testimony that the evolution of Lorena's seizure disorder may have been the same with or without the administration of the DPT shot. He speculates that she may have had an unidentifiable metabolic disorder, or "a propensity" to develop multiple seizure types over time, and if her present level of seizure activity had not been triggered by the DPT shot, it could have been triggered by something else-- [e.g.] "Gastroenteritis contracted from a day care center," or by a relatively trivial head trauma . . . [or] with a febrile illness. "It would have been something" to cause her latent predisposition to surface. Tr. at 130-132. Dr. Herskowitz is speculating, of course; nothing in the record exists to suggest that Lorena's condition was triggered by anything other than the DPT vaccine.[21] Moreover, consistent with the Institute of Medicine 1994 Report, this court does not distinguish between "cause" and "trigger."

The court is persuaded that although a modicum of controversy over causation in DPT cases still exists, the evidence supports a conclusion that the DPT can and did cause seizures and permanent damage to Petitioner's central nervous system and that the vaccine caused an exacerbation of Petitioner's underlying neurological condition.

The court's decision in this case is based on the weight that the special master accords to each expert's testimony and the basis proffered for each opinion. Dr. Kinsbourne successfully and persuasively responded to each and every allegation proposed by Respondent in defense of Petitioner's case. His testimony was overwhelmingly credible, superior in all aspects to Respondent's experts' narrow

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[20] But see, footnote 22 on page 29 of this decision.

[21] Tests for other etiologies have been negative. Tr. at 177.

interpretation of the evidence, and in my opinion is fully sufficient to meet the requisite standard by which such evidence must be evaluated. The Court of Federal Claims holds that a petitioner's proof "needs only to 'tip the scale' by the slightest of evidentiary margins." McClendon v. Secretary of HHS, 24 Cl. Ct. 329, 333 (1991), although "mere conjecture or speculation" will not meet the preponderance of evidence standard. Snowbank Enter. V. United States, 6 Cl. Ct. 476, 486 (198); Centmehaiey v. Secretary of HHS, 32 Fed. Cl. 612 (1995), aff'd, 73 F.3d 381 (1995). Dr. Kinsbourne's explanations concerning the relationship between the vaccine and Petitioner's injuries were plain, logical, and coherent. His reasons for testifying that the vaccine can cause further injury in persons who have demonstrated a prior neurological condition are supported by the medical literature and precedence in clinical practice. He gave a rational explanation why formal review and publication of his theory of injury may not meet the laboratorian's standard of scientific certainty due to the present state of the science available. The Supreme Court acknowledged in Daubert that "in some instances, innovative theories will not have been published. . . . Some propositions, moreover, are too particular, too new, or of too limited interest to be published." Daubert v. Merrell Dow Pharmaceuticals, Inc., 43 F.3d 13111, 1316 (9th Cir. 1995) 509 U.S. at 593. According to Knudsen "a detailed medical and scientific exposition on the biological mechanisms" of an injury is not necessary. Knudsen, at 549. The court is required to analyze the logic of the proposed cause and effect, whether a sound medical or scientific explanation exists, and whether the explanation falls "within the range of accepted standards" of research. Dr. Kinsbourne's hypothesis is logical and is accepted by other experts as well as himself. The court finds that hypothesis to be based on good science and may be considered in this case. In other words, it meets the guidelines required by the courts for establishing "a logical sequence of cause and effect [with] a sound and reliable medical or scientific explanation[,] showing that the vaccine was the reason for the injury." Knudsen, citing Jay v. Secretary of HHS, 998 F.2d 979, 984 (Fed. Cir. 1993).

I found Dr. Kinsbourne in these and all other matters to be better informed, his opinions better supported by the medical literature, (as an example, the literature appears to contradict Dr. Baumann's argument that severe seizures themselves cannot cause further neurological damage) and his responses to each challenge raised by the Respondent to be logical and consistent with the weight of opinions offered before this special master over many years of hearing vaccine cases.

I am not persuaded that the NCES is a flawed study or that its conclusions are irrelevant to the general question of causation. It is not my intent to "diagnose" a vaccine-related injury in this particular case. As the U.S. Court of Appeals for the Federal Circuit held, it is not up to special masters to determine "how and why DPT vaccines sometimes destroy the health and lives of certain children." As noted by a colleague in Gall v. Secretary of HHS, (Fed. Cl. Spec. Mstr. Oct. 30, 1998) "a petitioner must support the logical sequence of cause and effect with a 'sound and reliable medical or scientific

explanation.' " Knudsen, 35 F.3d at 549, citing Bunting v. Sec. of HHS , 931 F.2d 867 (Fed Cir. 1991) Petitioner has provided such evidence. [22]

CONCLUSIONS

"Attribution of a cause in individual cases must be speculative." So cautions one of the authors of the NCES.[23] That statement is true of course. No identifiable markers

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[22] In finding that there exists a causal relation between the DPT vaccine and afebrile seizures, I respectfully disagree with my colleague's contrary opinion in Salmond v. Secretary of HHS, No. 91-123V, 1999 WL 778528 (Fed. Cl. Spec. Mstr. Sept. 16, 1999). In that case, the special master concluded, based on the insufficiency of the evidence, that the DPT vaccine could not cause the vaccinee's post-immunization afebrile seizures. Id. at *5. In so finding, the Salmond court relied on the IOM's 1991 report, supporting case law, and administrative changes to the Vaccine Injury Table. Id. More importantly, the court in Salmond rejected the petitioner's claim "principally on petitioners' failure to provide persuasive support for their actual causation claim." Id. at *10. The special master in that case was not persuaded by petitioners' expert's arguments that the 1994 IOM report revised its 1991 IOM's findings on afebrile seizures. Id. at *8. However, in determining that petitioners were not entitled to compensation, the special master in Salmond noted: "This decision should not be read to bar future similar claims . . . it is conceivable that further discussions regarding the causal relationship of DPT and afebrile seizures could produce a different result." Id. at *10.

This court's contrary opinion rests on several factors. First, unlike in Salmond, I find petitioner's expert's testimony to be credible, persuasive, cogent, and sufficient. Second, not only were children with febrile and afebrile seizures included in the NCES, but the study makes no distinction in its ultimate conclusions between those children suffering febrile and afebrile convulsions. The court in Salmond recognized this as well. Third, the NCES authors concluded during their follow up review, *which was two years after the IOM's 1991 report*, that their original conclusions of risk were not only sound, but made more firm. Fourth, the IOM concluded in 1994 that permanent damage could occur in children suffering those illnesses studied in the NCES study, *including afebrile convulsions*--a curious finding were the IOM standing by its earlier contrary determination on afebrile seizures. Finally, the 1991 IOM's conclusion on afebrile convulsions is premised on a pooling of statistical information from only three studies which admittedly "had limited statistical power to detect risks unless they were on the order of 2.4 or larger," and in the case of the SONIC study (Gale et al. 1990), "had limited statistical power to detect changes in risk associated with DPT exposure within strata defined by specific types of acute neurologic illnesses." 1991 Report of the IOM at 113, 118. For these reasons, I reject in this case the controlling nature of the IOM's 1991 opinion that "the evidence does not indicate a causal relation between DPT vaccine and afebrile seizures." Id. at 118. I do not find the IOM's findings on afebrile seizures well supported or persuasive.

[23] Miller, Madge, et al. "Pertussis Immunisation and serious acute neurological illnesses in children," Abstract, Brit. Med. J. (1993) at 1171.

or other means exist for proving causation at the level of scientific certainty. . The possibility of some other, unknown, unidentifiable exists in every vaccine case. Scientific certainty, however, is not required. The requisite standard requires a reasonable degree of medical certainty.

Epidemiological evidence, however, such as a high level of excess risk, as acknowledged by the courts, provides a basis for tipping the scales. The court concludes that Petitioner here has established her case. This decision is based on the following evidence and considerations: Evidence that the NCES has not been successfully invalidated; the NCES study did not distinguish between febrile and afebrile seizures and therefore does not disqualify Lorena Almeida from its risk ratios; that precedence exists that administration of pertussis vaccine is contraindicated in a compromised individual as a further potential risk of provoking additional seizures; on the sound and persuasive testimony of Petitioner's expert; and Respondent's failure to identify or establish a factor unrelated to the vaccine as a more likely cause; the court concludes that Lorena's neurological condition has been significantly aggravated and that her present condition is the sequela of that injury.

The parties are directed to enter into discussions concerning the appropriate amount of compensation required to care for Petitioner's vaccine-related injuries.

IT IS SO ORDERED.

E. LaVon French
Special Master