OFFICE OF THE SPECIAL MASTERS

No. 90-484V

(Filed: July 30, 1998)

* *		
ANDREW M. CLEMENTS, by his Parents, MICHELLE CLEMENTS and MALCOLM CLEMENTS,	*	
Petitioners,	*	**TO BE PUBLISHED**
v.	*	
SECRETARY OF HEALTH AND HUMAN SERVICES,	*	
Respondent.	*	
* *		

Victor C. Harding, Milwaukee, WI, for petitioners.

Claudia Barnes Gangi, Washington, DC, for respondent.

DECISION AND ORDER

MILLMAN, Special Master

On July 28, 1995, Michelle and Malcolm Clements, on behalf of their son, Andrew M. Clements (hereinafter "Andrew"), filed a petition for compensation under the National Childhood Vaccine Injury Act of 1986[(1)] (hereinafter the "Vaccine Act" or the "Act"). Pursuant to 42 U.S.C. § 300aa-11(c), petitioners have satisfied the requirements that: (1) they have not previously collected an award or settlement of a civil action for damages arising from the alleged vaccine injury, (2) DPT vaccination was administered to Andrew in the United States, and (3) they have incurred $1,000.00 in unreimbursable medical expenses prior to filing the petition.

Petitioners allege a causation-in-fact seizure disorder and encephalopathy following DPT. (The petition does not allege a specific injury. However, petitioners' counsel framed the issue as causation-in-fact seizure disorder while petitioners' expert, Dr. John H. Menkes, opined that Andrew had an encephalopathy after the vaccination which counsel further clarified as a causation-in-fact encephalopathy.) 42 U.S.C. § 300aa-11(c)(1)(C)(ii)(I).[(2)] Respondent denies that DPT caused in fact Andrew's onset of seizures or encephalopathy and denies that he had acute encephalopathy after his DPT vaccination.

The court held a hearing in this case on March 19 and 20, 1998. Testifying for petitioners were Mrs. Michelle Clements and Dr. John H. Menkes. Testifying for respondent was Dr. Robert J. Baumann.

FACTS

Andrew was born on January 31, 1992. He received his first DPT vaccination on April 4, 1992 at the age of two and one-quarter months. He received his second DPT vaccination on June 3, 1992 at the age of five months. Med. recs. at 225, 227, 240. He received his third DPT vaccination on August 6, 1992 at the age of six and one-quarter months.

Mr. Clements called an ambulance at 1:16 a.m. on August 7, 1992. P. Ex. 14. The EMTs found Andrew with his father. The Milwaukee Fire Department was dispatched at 1:21 a.m. They found Andrew's temperature to be warm, and his skin normal in moisture and color, but he was tachycardic. P. Ex. 14. The paramedics wrote that they found Andrew in active seizures in care of Engine Co. 9. Mrs. Clements told them that he was found in that condition approximately twenty minutes before. The seizures were clonic-tonic in nature and full-bodied. Mrs. Clements stated that Andrew was very healthy with no history of any problem. He had had his DPT, HIV, and polio vaccinations earlier at 10:45 a.m. Andrew's seizures continued despite administration of Valium. P. Ex. 14.

Andrew was taken to St. Michael's emergency room and transferred to Children's Hospital of Wisconsin on August 7, 1992 where he stayed two days. Dr. Tim Schum[(3)] wrote a history that Andrew received DPT in Dr. Seidl's office on August 6, 1992. That night, his arms shook rhythmically and his eyes stared straight ahead. Mr. Clements could not talk with him. The seizures persisted and the paramedics were called. The seizures stopped at St. Michael's emergency room. Andrew was somewhat postictal. There had been rattling in his chest on and off for several months.

On physical examination, Andrew was initially asleep, but awakened easily. He was looking around and

cooing. He was not toxic-looking, but somewhat subdued. His anterior fontanelle was soft. His temperature was 38.5 degrees centigrade. His lungs showed coarse respiratory breath sounds. He had increased tone in his lower extremities with sustained clonus of five to ten beats on the right and three to four beats on the left. Med. recs. at 474-75.

On the next day, he was completely normalized. The initial assessment was prolonged seizure associated with fever probably secondary to DPT but perhaps due to a viral respiratory infection. He had bronchospasm and several watery loose stools. His neurological examination was completely normal forty-eight hours after admission. His temperature was 39 degrees centigrade even about forty hours post-admission. Andrew's discharge diagnosis was atypical febrile convulsion; viral illness with gastroenteritis and respiratory symptoms; reactive airway disease; temporally associated with DPT but Dr. Schum appended the statement: "I don't believe DPT was the cause of this and there was no sepsis." Med. recs. at 475.

Andrew saw Dr. Seidl on August 10, 1992 for a follow-up. He was still having rattling sounds while breathing and difficulty breathing. His temperature was 100.1 degrees Fahrenheit. Med. recs. at 243. On August 17, 1992, he returned to Dr. Seidl. He was hyperactive with a slight rattle from his chest. Mrs. Clements asked about Andrew's having a possible allergy, saying it ran in her family. Andrew was alert without abnormal breath sounds. He had slight hoarseness. His mucous membranes were not swollen or inflamed. His upper respiratory infection was improved and he ate normally. His sleep was getting back to normal. Med. recs. at 244.

On August 31, 1992, Andrew had an EEG, which was normal. Med. recs. at 244. On November 16, 1992, he went to Dr. Seidl for a follow-up after going to the emergency room for a two- to three-minute seizure. During the prior week, he had been exposed to chickenpox. Andrew was alert, smiling, and walking normally. Med. recs. at 246. On December 10, 1992, he had a seizure without apparent fever. He had good head control. Med. recs. at 247.

From January 11 to 13, 1993, Andrew was at Children's Hospital of Wisconsin. He had a seizure with fever. This was his fourth episode of seizure activity since the age of six months. Apparently, the first episode related to his six-month DPT. His last seizure was in December 1992 and was not related to fever. He had cold symptoms for two days and felt warm. Med. recs. at 479. Andrew had an EEG on January 12, 1993 which was normal. Med. recs. at 332.

From January 17 to 21, 1993, he was at the same hospital for an hour-long generalized tonic-clonic seizure. Med. recs. at 483. On Wednesday, March 24, 1993, he went to Children's Hospital Health Systems. He had received MMR on Thursday, March 18th, and had a seizure on Monday, March 22, 1993. Med. recs. at 498.

From May 13 to 14, 1994, Andrew was at Children's Hospital of Wisconsin with a sixty-minute seizure. He was developmentally normal and otherwise healthy. Med. recs. at 524.

From September 8 to December 23, 1995, Andrew was at Children's Hospital of Wisconsin, having suffered severe anoxic encephalopathy secondary to prolonged status epilepticus. He had multiorgan failure with disseminated intravascular coagulation secondary to streptococcus viridans sepsis. He was in a persistent coma with severe spasticity and hypertension. Med. recs. at 1319.99.

He returned to the same hospital from January 26 to February 14, 1996 with peritonitis and a disrupted gastrostomy tube site. He had anoxic encephalopathy with spastic quadriparesis, cortical blindness, and hypercalcemia. Med. recs. at 2911.

A Milwaukee Public Schools Multidisciplinary Team Report, dated February 9, 1996, records a history that Andrew had 75 seizures between the time he was six months old and September 8, 1995. Mrs. Clements described the seizures as grand mal, tonic-clonic, focal, and petit mal/absence. They lasted from less than 30 seconds to 15 minutes each. He had attention deficit hyperactivity disorder. On September 8, 1995, Andrew's temperature was 108 degrees Fahrenheit. He was in shock and had sepsis due to streptococcal viridans bacteria. He had multi- organ failure and hypoxic encephalopathy. He was taken to the hospital because of seizing, intubated, and ventilated. The seizure stopped. He had respiratory distress syndrome. A CT scan showed massive cerebral edema. Andrew was extubated on October 3, 1995 and discharged on December 23, 1995. He was nonverbal and profoundly retarded. He had anoxic encephalopathy secondary to prolonged status epilepticus, and was in a comatose state. The prolonged status epilepticus reduced him to a newborn level of functioning in gross motor skills. Med. recs. at 582-84, 597, 600.

TESTIMONY

Mrs. Michelle Clements testified first for petitioners. She is thirty years old and has been married for nine years. She has two children: Michael, who is 11 years old, and Andrew, who is 6 years old. Tr. at 11. Michael is normal. He had a slight reaction to his DPT with a sore vaccine site. Tr. at 12. No one in the family has neurological problems besides Andrew. Tr. at 12-13. Andrew was a little irritable after his second DPT and Mrs. Clements gave him Tylenol every four hours as a precaution. Tr. at 14.

On August 6, 1992, Mr. Clements took Andrew in for his third DPT vaccination between 10:00 and 11:00 a.m. Tr. at 15. Andrew always sounded like he had a little rattle, but she would take him into the doctor's office and the doctor would say he was fine. Tr. at 15.

Mrs. Clements is a grocery cashier and Mr. Clements makes pizza. Tr. at 16-17. Mrs. Clements came home from 4:00 to 5:00 p.m. Mr. Clements came home at 11:30 p.m. Tr. at 17-18.

After Andrew's third DPT, he was a little more tired, but okay. Tr. at 15. He took a nap, which was unusual, but he was "pretty fine." Tr. at 17. They ate dinner at 5:30 p.m. which was a normal time. Andrew did not have a temperature. Mrs. Clements put him to bed from 9:30 to 10:00 p.m. Tr. at 18-19. She went to bed from 10:30 to 11:00 p.m., but watched television. Tr. at 19. Andrew and Michael were in the same room. Id.

Mr. Clements came home at 11:30 p.m. and went to check on the boys after eating, reading the paper, and showering. Everything was fine. Tr. at 20. Between 12:30 a.m. to 1:00 a.m., Mr. Clements heard Andrew make a noise and went in. There was drool on the bed and Andrew was wet by his shoulder. Mr. Clements called for Mrs. Clements and handed Andrew to her. Mr. Clements called the ambulance. Tr. at 21. Andrew looked pale, as if he were not breathing. Tr. at 22. They did not see Andrew seize, but he seemed postictal because he was limp. They drove to St. Michael's Hospital, but the ambulance waited at their home because Andrew was seizing. Tr. at 22-23. It took ten to fifteen minutes to get the seizure under control. Andrew was sleeping from 2:00 to 3:00 a.m. Tr. at 25.

They woke up in Andrew's hospital room on August 7, 1992 at 7:00 a.m., but Andrew was still sleeping. He was not himself. He did not focus and was in and out of sleep. He was lethargic and not doing

anything. Tr. at 25-26. They transferred Andrew to Children's Hospital from 5:00 to 6:00 a.m. Tr. at 28.

On August 8, 1992, he slept a lot and was just starting to come around. He progressed toward evening, but he was not pulling up as he normally would. He was pretty much normal on discharge, but still throwing up. (He had thrown up a couple of times in the hospital.) Tr. at 29-30.

Andrew afterward seemed to be progressing normally. Tr. at 32. He had his next seizure in November. He had a low-grade temperature. Tr. at 32-33. He slept for most of the day and then woke up later in the evening and was himself again. Tr. at 33, 55. Afterwards, he seemed normal except he seized periodically. Tr. at 35. Andrew had about 80 seizures. Tr. at 36. He was put on anticonvulsants. Id.

Andrew developed normally except for seizing until he was three years old in 1995. Tr. at 37, 55. Between Sunday, September 3, 1995 and Monday, September 4, 1995, Andrew started running a fever. She took Andrew to the doctor on Tuesday, September 5, 1995, and she gave him medicine every two hours. Tr. at 37. The doctor said Andrew had the flu. He had a short seizure on September 5, 1995. Id. On Wednesday and Thursday, September 6 and 7, 1995, he was awake and alert. Tr. at 39.

At 5:00 a.m. on Friday, September 8, 1995, she woke up to give Andrew medication because if it wore off, his temperature went from 100 to 102 degrees Fahrenheit. Tr. at 38. He was really hot. Mrs. Clements called the doctor because he was not swallowing saliva. The doctor checked Andrew's throat and said it was okay. Id. He was home for one to one and one-half hours on September 8, 1995 but, by 6:00 p.m., he started choking, and turned pale. He was still perky, but his voice was scratchy. Tr. at 38-39. As long as he was not lying down, his breathing was fine. Tr. at 56.

She took Andrew to Children's Hospital emergency room. She laid him back and he choked on his saliva and had a fifteen-minute seizure. Tr. at 40. The hospital decided at 10:00 or 10:30 p.m. to keep Andrew for twenty-four hours to do blood tests. Id. She sat in a room. Andrew went into a seizure and came out of it. Then he went into a second, third, and fourth seizure, each lasting thirty seconds. Tr. at 41. The nurse and doctor saw this. The seizure started at 11:07 p.m., September 8, 1995, and ended at 3:30 a.m., September 9, 1995. Tr. at 42.

When he went into the last one and stayed in it for a half-hour, a doctor asked if Andrew had ever seized that long and she said he had one that lasted about an hour. The doctor asked what they gave him and it was Dilantin, so they got Dilantin for him but it did not stop the seizure. She then told the doctor Andrew had once seized for an hour and one-half. She mentioned another drug and they gave that one to him. But Andrew continued to seize. The doctors then used oxygen. That did not work so they took him to the operating room and put a tube into him. Tr. at 43.

Finally, the doctors administered a paralyzing medication which stopped the seizure. Tr. at 44. At 3:00 a.m., his temperature reached 108.8 degrees Fahrenheit. Tr. at 45, 46. Andrew tripled in size due to the fluid he was administered. Tr. at 46. Twenty-four hours after admitting Andrew to the hospital, his parents learned that he had strep A. Tr. at 59. Andrew is no longer seizing. Tr. at 48.

Dr. John H. Menkes, a pediatric neurologist, testified next for petitioners. His opinion is that Andrew had post-pertussis encephalopathy[(4)] that DPT caused based on the time interval between the DPT and Andrew's first seizure, his normal development up until then, and the exclusion of all other causes. Dr. Menkes testified that Andrew would have been part of the National Childhood Encephalopathy Study (NCES)[(5)] because he had a prolonged seizure within fifteen hours of receiving DPT, resulting in hospitalization. Dr. Menkes posited his diagnosis of post-pertussis vaccine encephalopathy on Andrew's acute change in consciousness and on his having a seizure. He had a forty-five minute seizure and was

lethargic through the next day. He had bilateral sustained clonus (meaning his nervous system was irritable),[(6)] and dorsiflexion of the ankle (repeated contraction, which is pathological). Andrew's nervous system was altered.

The duration of Andrew's encephalopathy is of no significance to Dr. Menkes. He testified that Andrew would have participated in the NCES. According to Dr. Menkes, the NCES shows a sevenfold increased relative risk of a seizure disorder due to DPT, with a confidence interval between 1.9 and 40.9. Tr. at 73, 76. Five percent of vaccinees will have a bad reaction after DPT. Tr. at. 78. The NCES would also have recorded children with bad "reactions" unrelated to DPT. Tr. at 80.

Andrew's first seizure was not a febrile convulsion, which requires documentation of a temperature of 101.5 degrees or higher. Tr. at 82. DPT can cause a seizure with or without a fever. In Dr. Menkes' mind, a forty-five minute seizure is alone sufficient to diagnose encephalopathy. Andrew had increased tone and an acute illness of his brain. It is unusual to have as a first seizure a forty-five minute seizure. Andrew's cold or upper respiratory infection at the time on August 7, 1992 could well have had relevancy to his seizure but he could not prove it. Tr. at 83. Dr. Menkes stated he would be very concerned about the status of Andrew's brain, that he had some brain disease irrespective of DPT vaccination, for him to have a 45-minute seizure at low temperature. Tr. at 86.

When asked for an explanation of how DPT caused Andrew's encephalopathy, Dr. Menkes testified that pertussis toxin alters the seizure threshold of certain groups of neurons by mixing up the messages that the neurons receive and transmit. Id. This has been studied in animals. A group of proteins carry messages called the G proteins and pertussis toxin alters the function of these G proteins. Tr. at 86-87. Pertussis toxin enhances the effect of an excitatory transmitter and reverses the effect of an inhibitory transmitter. It would be like stepping on the accelerator when one meant to step on the brake. Tr. at 87. It is unknown why the blood-brain barrier is breached. Studies suggest that endotoxin alters the blood-brain barrier so that pertussis toxin can cross into the brain and bind to it. This has been done in experimental animals. Tr. at 88. Not the entire brain is affected and the child might not show any symptoms such as screaming. Tr. at 89.

The batches of pertussis vaccine have extreme variability in the amount of endotoxin each lot has. Tr. at 97. The pertussis toxin may or may not swell the brain. Tr. at 104. The brain itself does not have pain sensation. When the blood-brain barrier is breached, the blood vessels inside the brain get leaky. Id. After a child seizes, particularly after he seizes a long time, he spikes a fever. Tr. at 108. A child can start afebrile but, by the time he finishes his seizure, he would be febrile. Id. At 2:20 a.m. on August 7, 1992, Andrew's temperature was 101.7 degrees rectally. Id. It does not make any difference to Dr. Menkes' opinion that DPT caused this seizure whether Andrew was febrile or afebrile. Tr. at 109.

On September 8, 1995, Andrew had probably a streptococcal infection, went to the emergency room, and had a generalized seizure lasting ninety seconds. Tr. at 110-11. He came in at 4:18 p.m. At 11:06 p.m., he had a generalized tonic-clonic seizure and poor air exchange. His saturations dropped and the seizure continued. He became acidotic. The ongoing seizure disorder was due to the pertussis vaccine. He had a lower seizure threshold. Andrew got the strep resulting in one brief seizure and then a long seizure. As he became desaturated, Andrew got streptococcal septicemia with DIC,[(7)] multiorgan failure, and shock. Tr. at 111.

In Dr. Menkes' opinion, Andrew's sepsis did not evolve until 1:00 or 2:00 a.m. because that is when his blood culture was indeed positive for elevated band cells. Tr. at 113. The prolonged status epilepticus lowered Andrew's resistance so that he developed streptococcal sepsis. Id. Andrew's brain was using up more glucose and oxygen than was available to it by 1:35 a.m., meaning he was severely acidotic. Tr. at

113-14. Dr. Menkes thinks that Andrew would have been brain-damaged with or without sepsis, but he would not be as severely brain-damaged if he had only had sepsis without a seizure disorder. Tr. at 115. The prolonged seizure produced acidosis and hyperthermia (elevated temperature to 108 degrees Fahrenheit). Tr. at 116.

Dr. Menkes did not know to what to attribute the excessive length of Andrew's seizures, which at three and one-half hours exceeded any of his prior seizures. Tr. at 117. Dr. Menkes would not be surprised if Andrew had a strep throat before his status epilepticus when he had fever for five days and was choking on his saliva. Tr. at 117-18. He thinks the infection triggered the seizure, but the seizure "fed upon itself," and the hypoxia and acidosis induced the sepsis. Tr. at 118. But if Andrew had not had a prior seizure disorder, the effect of the strep infection on him would not have been as serious. Tr. at 119.

The NCES concluded that chronic nervous system dysfunction can possibly occur in rare instances following DPT immunization, but one should not apply their conclusion to an individual case. Tr. at 131. However, Dr. Menkes would still apply it to this case. Tr. at 131-32. On cross-examination, he admitted that there is no clinical way to determine if the blood-brain barrier is breached. Tr. at 134.

After Andrew's first seizure, which was forty-five minutes long, he was administered eight milligrams of Valium. Dr. Menkes agreed it was the Valium that caused Andrew to be listless for twenty-four hours afterward. Tr. at 134-35. But because Valium would not induce the clonus or increased tone Andrew had, he still thought this was encephalopathy, not a postictal state. Tr. at 136.

Dr. Robert J. Baumann testified for respondent. He is the head of pediatric neurology at the University of Kentucky, a tertiary care hospital. He treats patients with intractable epilepsy. Tr. at 156. His opinion is that Andrew's seizure disorder is unrelated to his third DPT vaccination. The basis for his opinion is that Andrew was not acutely encephalopathic after his third DPT. Andrew's post-seizure sleepiness after being taken to the hospital was a result of the eight milligrams of Valium that he received, an amount that exceeds the recommended dosage. Tr. at 157.

Andrew did not manifest an increase in intracranial pressure or any acute encephalopathic behavioral disturbances after his third DPT vaccination. Id. His clonus and increased tone were manifestations of Todd's paresis, a postictal phenomenon that is well-known. Tr. at 158. That Andrew seized for forty-five minutes does not mean he was acutely encephalopathic. Tr. at 159. He would not assume that Andrew had just had a seizure and was postictal the night after his third DPT vaccination when his father found him drooling, sweaty, and wet, since that is a relatively common event with little children. Tr. at 160. Until September 1995, Andrew was never encephalopathic. Id. In addition, he was not febrile at the time of his first seizure. Tr. at 161.

Although a forty-five minute seizure is uncommon, Dr. Baumann has patients with seizures just like this. Id. Andrew's EEG was initially normal, but became abnormal gradually. On October 6, 1994, Andrew's EEG showed polyspike wave discharges. This is a well-recognized pattern. Id. Some refer to this as severe myoclonic epilepsy of infancy. This condition is notorious for not responding to medicine. Tr. at 161-62. However, Andrew was normal intellectually, which is how these children are. Tr. at 162.. His anticonvulsant medication caused transient abnormalities. Id. If Andrew had had acute encephalopathy severe enough to give him a seizure disorder, he would have had an abnormal EEG shortly afterwards as well as an abnormal CT scan. Tr. at 163.

Andrew's EEG was eventually abnormal because of the epilepsy, not because of acute encephalopathy. Polyspike and waves are an abnormality often seen in primary generalized seizure disorders. Id. Andrew's first seizure was a grand mal. Id. He had a generalized clonic seizure. Tr. at 164. If DPT had

caused this seizure, it would have made him acutely encephalopathic. He would have had increased intracranial pressure and acute behavioral changes such as irritability, lack of contact with his environment, inconsolability, high-pitched crying, and an abnormal EEG. Others are deeply unconscious. Andrew did not show any of this. Tr. at 164-65.

Most doctors agree that an event could not cause that level of injury, i.e., a seizure disorder, without having an acute encephalopathy. Tr. at 166-67. The October 6, 1994 EEG does not indicate brain damage even though it reflects an abnormal brain. Tr. at 167. Dr. Baumann criticized some of the literature upon which Dr. Menkes relied in supporting his opinion of causation. The Menkes abstract and Aicardi study are collections of cases, not evidence, because they are merely anecdotal. Tr. at 168. Dr. Cherry's article (Dr. Cody is the first author) did not have any controls. Tr. at 168-69. The NCES dealt with design problems in these studies. Tr. at 169.

Dr. Baumann does not think fever is a crucial issue. What is crucial to him is whether the child has an acute encephalopathy. Id. However, when young children have illnesses that give them acute encephalopathy, they tend to run fevers. Tr. at 170.

As for the proposed mechanism of breach of the blood-brain barrier, Dr. Baumann does not find it persuasive. In animal tests, the toxin is applied in its active form directly to tissue. No animal model is reasonably parallel to the immunization of children. Tr. at 171. A child's having difficult-to-control seizures is unrelated to whether a vaccination preceded their onset. Tr. at 172.

Dr. Baumann testified that the NCES is a very well-done epidemiologic study and provides valuable data that DPT and chronic encephalopathy are related in some children. But the authors of the NCES cautioned against using the study to prove causation in an individual case. Tr. at 172. One cannot use relative risk from the NCES to make a diagnosis. Tr. at 173. Andrew would have been in the NCES study because of the duration of his seizure (longer than thirty minutes). He would not have needed encephalopathy to be part of the study. Tr. at 178-79. But the NCES study had wide confidence limits because it involved a very small group of children who seized or were seriously ill after vaccination with DPT. Tr. at 179.

Moving on to the events in September 1995, Dr. Baumann testified that Andrew had a persistent fever and his doctors thought he had a viral infection. Tr. at 183-84. Something changed in Andrew on September 8, 1995. He started having respiratory problems, stopped swallowing, and breathed rapidly. Doctors looked for an airway obstruction, but did not find one. He had tonsillar hypertrophy, which was not serious. Tr. at 184. On September 9, 1995, at 6:30 a.m., a lung x-ray showed consolidated changes in his left lung, indicating a touch of pneumonia. But Andrew's problem was not pneumonia or pulmonary collapse. Tr. at 185-86.

Andrew's problem was a very severe form of sepsis in which chemical mediators injured epithelial cells so that they stopped allowing oxygenated blood to enter tissues and stopped allowing blood from the tissues containing acidotic waste products to go back into the bloodstream. Tr. at 186. These tissues became oxygen-starved. Id. When cells become injured, eight hours to three days can pass before the injury is detected in blood tests, CT scans, and x-rays. Tr. at 186-87.

The small infiltrate in Andrew's lung was coincidental to his sepsis. Tr. at 187. He had a block in his capillaries so that he was not exchanging oxygen well, causing shortness of breath. He was not swallowing because he felt he was having trouble getting air. Id.

On September 8, 1995, Andrew was septic. Dr. Nelson said Andrew had pulmonary involvement in the

ICU. Tr. at 188. Andrew had classic multiorgan function syndrome. Tr. at 189. When he was transferred to the operating room for intubation, his oxygen saturation was 98 percent on one hundred percent oxygen. His arterial blood gas on September 9, 1995 at 1:35 a.m. had a ph of 7.01, and his PO was 214 (the normal being 100). Andrew received a lot of oxygen. But Andrew had anoxic or hypoxic encephalopathy because the oxygen was not going from his capillaries to his organs due to the septic injury to his epithelial cells. Tr. at 190-91.

Andrew seized for four hours because he had inadequate oxygen to his brain because of the septic effect on the ability of his capillaries to deliver oxygen to his brain. Tr. at 191. That is why this set of seizures was clearly different from all his other seizures and was not treatable. Tr. at 191-92. Even if Andrew had not had a prior seizure disorder, he would have seized for this amount of time due to the septic effect on his epithelial cells and the resulting damage to his brain. Tr. at 192. Dr. Baumann testified that Andrew's sepsis and its consequences were unrelated to his prior seizure disorder. Id.

Andrew's arterial pH was 7.01. He had a venal pH of 7.16 at the same time. He had previously (on January 17, 1993) had a lower pH of 6.92, but did not suffer brain damage then even though he was more acidotic than in September 1995. Dr. Baumann brought this up to show that Andrew's current condition is the consequence of his sepsis rather than his prior seizure disorder. Tr. at 193. As for finding meaning in the number of Andrew's bands (a band is an immature white cell newly released from the bone marrow), Dr. Baumann stated that one of the medications Andrew received, Epinephrine, releases bands. Therefore, it is hard to find any significance in the number of bands he had. Tr. at 194. A child with an infection and a high temperature should have a high white blood cell count, but if he does not, he is not fighting the infection. Id. A positive blood culture for strep veridans is unequivocal support for concluding Andrew had strep. Tr. at 196. Dr. Baumann testified that Andrew had strep veridans infection in his blood on September 8, 1995 prior to seizing. Tr. at 196-97. Mrs. Clements was quite clear that Andrew's illness changed on September 8th. A viral infection preceded the sepsis. It is well-known in pediatrics that viral infections make children more susceptible to bacterial infections. Tr. at 197. Strep entered Andrew's blood stream through the mouth, but Dr. Baumann does not know how. Tr. at 198. A febrile illness is a risk factor for sepsis, but epilepsy is not a risk factor for sepsis. Tr. at 199.

A child in the early stages of sepsis can be alert and active, but Andrew was not septic before September 8, 1995. Tr. at 204. Andrew's blood oxygen was good, but his tissue oxygen was not good. Tr. at 221-22. Acidotic chemicals were in his tissues and to a lesser extent in his blood. Tr. at 222. Those acidotic tissues included the brain. Tr. at 223. Hypoxic injury is not only lack of oxygen but also accumulation of acid products. The acidosis poisons the chemical reactions in the cells. Eventually the cells misfunction and die. Tr. at 223-24. This caused Andrew's brain to experience edema and death of brain cells. Tr. at 224.

Of all of the handful of Dr. Baumann's patients with severe myoclonic epilepsy of infancy, he does not know the cause in any of their cases. Tr. at 259. No one else knows the cause either. Tr. at 260. There is no convincing evidence that DPT can cause a seizure without a fever. Tr. at 280, 284. Andrew's lack of a fever before his initial seizure is part of the basis for his opinion that DPT did not cause Andrew to seize. Tr. at 293. The NCES did not break out febrile or afebrile seizures in its analysis. Tr. at 243, 323. Most of the children listed as having convulsions in the NECS had febrile seizures with encephalopathy. Tr. at 323. The authors of the NCES did not break them out because the numbers would have been too small. Tr. at 324. Dr. Baumann would not say that an epileptic has encephalopathy. Tr. at 243. He would expect an acute encephalopathy to accompany a seizure disorder before he would opine that DPT caused it. Tr. at 292.

Dr. Baumann does not believe that exotoxin breaches the blood-brain barrier in the context of immunization. Tr. at 312. He stated that nothing acute happened to explain Andrew's seizure disorder.

Tr. at 322.

Dr. Menkes mentioned that more senior neurologists believe DPT has adverse effects than younger neurologists do, and he is correct. They have had very different experiences because of an enormous drop in serious, acute illness and death in young children and, because diagnostic processes are better today, younger doctors can make diagnoses that older doctors could not. Tr. at 329-30. A lot of the reports in older medical literature discuss what Dr. Baumann views as chance associations between DPT and illness. Tr. at 330.

DISCUSSION

Encephalopathy Petitioners allege that Andrew suffered an acute encephalopathy which DPT caused in fact. To satisfy their burden of proving causation in fact, petitioners must offer "proof of a logical sequence of cause and effect showing that the vaccination was the reason for the injury. A reputable medical or scientific explanation must support this logical sequence of cause and effect." See Grant v. Secretary, HHS, 956 F.2d 1144, 1148 (Fed. Cir. 1992); Agarwsal v. Secretary, HHS, 33 Fed. Cl. 482, 487 (1995); see also Knudsen v. Secretary, HHS, 35 F.3d 543, 548 (Fed. Cir. 1994); Daubert v. Merrell Dow Pharmaceuticals, Inc., 509 U.S. 579 (1993).

"[E]vidence showing an absence of other causes does not meet petitioners' affirmative duty to show actual or legal causation." Grant, supra, 956 F.2d at 1149. Mere temporal association between vaccination and injury is insufficient to establish causation. Hasler v. United States, 718 F.2d 202, 205 (6th Cir. 1983), cert. denied, 469 U.S. 817 (1984). The court must determine that the evidence makes causation in fact "legally probable, not medically or scientifically certain." Knudsen, supra, at 548-49. The Federal Circuit in Knudsen gave as an example of finding causation in vaccine cases if epidemiological evidence and the particular vaccinee's clinical picture substantiate that conclusion "without detailed medical and scientific exposition on the biological mechanisms." Id., at 549.

Dr. Menkes pins his diagnosis of encephalopathy mostly on the forty-five minute length of Andrew's first seizure. He and petitioners are asking the undersigned to accept that the mere occurrence of a lengthy seizure equals an encephalopathy. Dr. Baumann disagreed, stating there needs to be something more than a seizure to justify a conclusion that Andrew had an acute encephalopathy as well. Important to Dr. Baumann in determining whether or not Andrew had an acute encephalopathy at the time of his first seizure was whether he had an alteration in consciousness. In addition, if Andrew had been acutely encephalopathic, his first EEG would have been abnormal. Dispositive for Dr. Baumann was Andrew's apparently normal clinical signs before his seizure and his normal initial EEG.

Although Dr. Baumann agreed that a first seizure of that length is unusual, it does occur in the diagnostic entity called severe myoclonic epilepsy of infancy. It does not mean that the child has an acute encephalopathy. Andrew's developing normally for three years in the context of 75-80 seizures of varying duration, both febrile and afebrile, fits within that category of disease describing a number of Dr. Baumann's patients. Dr. Baumann does not know the cause of severe myoclonic epilepsy of infancy, and testified that no one else does either.

Dr. Menkes ignores the medical records of Children's Hospital of Wisconsin from August 7 to August 9, 1992 which describe Andrew as awakening easily, looking around, cooing, and not toxic-looking. The lack of Andrew's being more lively (the record says he was "somewhat subdued") both Dr. Menkes and Dr. Baumann attributed to the overdose of Valium he received to stop his seizures. By the day after admission, according to the record, Andrew was completely normal. Moreover, the neurological examination that Andrew's doctors performed two days after admission was completely normal. Petitioners cannot make a credible case for encephalopathy when Andrew's neurological examination was completely normal.

Moreover, Dr. Menkes also did not put Andrew's 45-minute seizure in the context of his other seizures, of which there were 75-80 over three years, some lasting seconds, and others lasting an hour to an hour and one-half. Yet Andrew was developing normally over those three years. He did not truly becoming acutely encephalopathic until the tragedy that occurred on September 8, 1995.

This court does not find Dr. Menkes' testimony as credible as Dr. Baumann's because Dr. Menkes based his opinion on only a portion of the facts in evidence (omitting the significance of the initial EEG's being normal, and Andrew's continuing normal development) and because Dr. Baumann is actively engaged in treating epileptic patients of whom he has a number with the same disease entity that Andrew manifested from 1992-95. Moreover, the twenty-four alteration in Andrew's behavior is explainable not only by his excess dosage of Valium, but also by the postictal state that occurs after a lengthy seizure. Andrew did not manifest any clinical sign of neurologic abnormality before his first seizure. The only sign of difference is that he napped and seemed a little more tired the afternoon of the vaccination, a difference the court does not find to be clinically significant.

Based on the foregoing, petitioners have not satisfied their burden of proving that Andrew had an acute encephalopathy at the time of his first seizure. Therefore, petitioners have failed to satisfy their burden of proving that DPT caused in fact Andrew to have encephalopathy.

Seizure Disorder

Petitioners also allege that Andrew's DPT vaccination caused in fact his seizure disorder.

This court has previously held that DPT vaccine can cause a fever which in turn causes the onset of a seizure disorder. McMurry v. Secretary, HHS, No. 95-682V, 1997 WL 402407 (Fed. Cl. Spec. Mstr. July 27, 1997). In McMurry, the vaccinee had a high fever and seized for fifty or more minutes following her DPT. Id. at *1-2. In addition, she was unresponsive and in status epilepticus. Id. Based on the occurrence of the fever as well as the onset of severe seizures, the court held for petitioners. McMurry, supra, at *8-9.

McMurry and this case are distinguishable based on the vaccinees' symptomatology and subsequent courses. In this case, Mrs. Clements testified that Andrew did not have a fever prior to his initial seizure. Rather, he had a fever only after he had been brought to the hospital (101 degrees at 2:00 a.m.). The first documentation the court has of Andrew's fever is after hospitalization (although the paramedics recorded he was warm; this may have reflected a seizure occurring before Mr. Clements found Andrew). Both Dr. Menkes and Dr. Baumann testified that a seizure may precipitate a fever. The court holds that the

temperature that Children's Hospital of Wisconsin recorded occurred after Andrew's seizure, not before.

The undersigned sees no difference (except for the length of the initial seizure) between this case and a similar case of "post-regulation change" seizure disorder following DPT in O'Connell v. Secretary, HHS, No. 96-63V, 1998 U.S. Claims LEXIS 28 (Fed. Cl. Spec. Mstr., Feb. 2, 1998), aff'd, 40 Fed. Cl. 891 (1998), appeal docketed (Fed. Cir. July 6, 1998) (afebrile seizure one day post-vaccination), and Terran v. Secretary, HHS, No. 95-451, 1998 U.S. Claims LEXIS 21 (Fed. Cl. Spec. Mstr., Jan. 23, 1998), aff'd, 1998 U.S. Claims LEXIS 151 (Fed. Cl., July 10, 1998) (afebrile seizure one day post-vaccination), in which petitioners did not prevail. Notably Dr. Menkes testified for petitioners and Dr. Baumann for respondent in Terran. Although different experts testified in O'Connell, reference was also made to the blood-brain barrier theory and to the NCES.

Dr. Menkes posited a logical sequence of cause and effect, which relied partly on temporal association, and partly on a biologically plausible theory to support his opinion that DPT caused Andrew's seizure, i.e., the breaching of the blood-brain barrier.[(8)] While he opined that there would be no clinical symptoms of such an immunological affront to the system, the court has previously held that post-DPT symptoms of extreme irritability, anorexia, and insomnia, followed by lethargy and death, are evidence of a Table encephalopathy (before the regulation change) causing death in a vaccinee. Misenko v. Secretary, HHS, No. 92-0013V, 1995 WL 761436, at *14-15 (Fed. Cl. Spec. Mstr. Dec. 7, 1995). However, Andrew did not experience any of these symptoms after receiving DPT and before his seizure.

Mrs. Clements testified that after Andrew's third DPT, he was a little more tired, but "okay." Although he napped, which was unusual, in her words, he was "pretty fine." He ate dinner at a normal time. He went to bed at a normal time and presumably slept because, when Mr. Clements checked on Andrew and his brother Michael at 11:30 p.m., everything was fine.

It would be extraordinary to conclude that Andrew, at this time, was experiencing a breach of his blood-brain barrier, with a consequent lowering of blood sugar (hypoglycemia) and blood pressure (hypovolemia), as the undersigned held Lynette Misenko experienced when she refused to sleep or eat and was screaming, inconsolable, and ultimately lethargic before her death two days after DPT vaccination. Their symptoms are in no way comparable.

Petitioners in Misenko prevailed in explaining how Lynette proceeded from a Table encephalopathy to death on the same theory of breach of the blood-brain barrier because both sides' experts agreed that endotoxin could lower blood sugar and blood pressure, and that endotoxin was in the vaccine. Lynette's clinical symptoms were consistent with these processes leading to her death. Moreover, the vaccine lot that Lynette received was a "hot lot," that is, a lot for which a higher than usual number of adverse reactions was reported (17 reactions compared to the average of 3.2). Id., at *8.

The undersigned held that petitioners had presented a logical sequence of cause and effect between the Table injury of encephalopathy and Lynette's death based on her symptoms and petitioners' expert's interpretation of them. Andrew did not have any of the symptoms that Lynette had. Moreover, petitioners herein have not presented any evidence that the lot of vaccine he received was "hot."

In the instant case, petitioners rely heavily on animal studies, but not on Andrew's clinical signs because he did not manifest any significant clinical signs before his first seizure. Dr. Menkes opined that breach of the blood-brain barrier would not cause clinical signs. This seems testimony tailored to the facts of the case (no signs) rather than to a credible linking of theory to actuality (the effects of lowered glucose and blood pressure on the individual experiencing them). It is worth noting that Lynette never had a provable seizure. Herein, Andrew never had a provable encephalopathy before his first seizure. This

court has never held that breach of the blood-brain barrier is a sufficient explanation for a seizure disorder and has held only in one case that it led to encephalopathy (a Table encephalopathy) and subsequent death, relying in part on respondent's expert's agreement that the ingredients of DPT vaccine could lower glucose and decrease blood volume, having marked encephalopathic effects and causing injury.

It is important to note that mere temporal association with the vaccination, though attractive to the layman's eye as a target for causation, does not legally prove causation. Hasler, supra. When Dr. Baumann was asked if he knew the cause of severe myoclonic epilepsy of infancy in the patients who have it whom he treats, he replied that he did not know the cause in any of their cases. Moreover, he said that no doctor knows the cause.

In the instant case, petitioners have submitted animal studies to support their theory that endotoxin breached Andrew's blood-brain barrier, permitting pertussis toxin (exotoxin) to damage his brain, causing his seizure. However, petitioners have not shown how these animal studies are applicable to Andrew because he had no sign of injury after the vaccination except for his seizure. Although petitioners are faced with the quandary of establishing a plausible nexus between vaccination and injury, the mere positing of a theory applicable to someone with symptoms other than this vaccinee is not legally sufficient. That a biologic process may cause injury is not dispositive of the question whether it did cause injury in this case. Knudsen, supra, at 550. This is not to say that petitioners have to provide proof of specific biological mechanisms (id., at 549), but their theory of causation must at least be applicable to the facts of this case. The court cannot engage in speculation as a basis for holding that petitioners have satisfied their burden of proving causation in fact scientifically. See Daubert, supra (although describing admissibility rather than weight of evidence, offers guidelines for assessing scientific evidence).

The undersigned has previously rejected use of animal testing as proof of encephalopathy or residual seizure disorder because of methodological deficiencies or lack of neurologic deficits in the animals inoculated with endotoxin. Haim v. Secretary, HHS, No. 90-1031V, 1993 WL 346392 (Fed. Cl. Spec. Mstr., Aug. 27, 1993); Braccio v. Secretary, HHS, No. 90-1318V, 1993 WL 59266 (Fed. Cl. Spec. Mstr., Feb. 19, 1993). Interestingly, one of the documents petitioners have submitted in evidence voices doubt about the applicability of animal studies to the inducing of neurologic illness in vaccinees.[(9)]

In the instant case, Dr. Menkes would have the undersigned hold that Andrew experienced a breach of his blood-brain barrier *in vacuo*, that is, without the appearance of any symptom to indicate lessened blood sugar and blood pressure. A child who naps which is unusual for him, but seems "okay "or "really fine," who eats supper at a normal time, goes to bed at a normal time, and sleeps is not, to this court's mind, experiencing the breach of his blood-brain barrier.

There is another leg upon which petitioners' case stands in the attempt to prove DPT caused in fact Andrew's seizure disorder: the NCES study (P. Doc. 232), as well as other epidemiologic literature. But as the undersigned held in Haim, supra, in which the issue was whether DPT caused in fact a seizure disorder whose onset was five days post-vaccination, the NCES authors themselves cautioned that their study should not be used to show DPT caused a neurologic injury in an individual case. Their confidence limits were too wide to yield reliable results and their derivation of attributable risk suffered from the fact that they performed a case-control study rather than a cohort study.[(10)]

In addition, the NCES authors included cases in which there might be etiologies other than DPT vaccine, which would increase or overestimate the risk from the vaccine.[(11)] The authors criticized their own study design because it was one that would not normally allow for calculation of attributable risk.

(12) Because the NCES authors' concern to find neurologic illness after DPT vaccine was known to clinicians, there may have been bias in the selective reporting of children who were vaccinees compared to reporting of children who were non-vaccinees. That would show DPT vaccine to be more neurotoxic than it is.(13)

Two of the authors of the NCES participated in a symposium and contributed to an article stating that the NCES evaluated only a "very small" number of ill vaccinees and the NCES's conclusions, therefore, must be treated with extreme caution.(14)

A further NCES follow-up in 1993 concluded that the children, whether vaccinated or not, with acute neurologic illness whom they studied may have had an underlying condition making them more susceptible to external insults like viruses or immunization. Thus, the authors state they did not prove in the NCES that DPT "was the sole or even the prime cause of either the illnesses or the adverse outcomes in these cases"; "attribution of a cause in individual cases must be speculative."(15)

The U.S. Court of Appeals for the Federal Circuit has warned against relying on bare statistical facts in drawing conclusions about causation. Knudsen, supra, at 550. That the NCES concluded that a sevenfold relative risk occurred in a small population of DPT vaccinees, among whom were those with seizures not identified as febrile or afebrile as well as those who had encephalopathy, is insufficient by itself to conclude that in the instant action, DPT caused in fact Andrew's seizure disorder. The Federal Circuit stated causation may be found based on epidemiological evidence and the clinical picture regarding the particular child (id., at 549), but as the undersigned has already discussed, the epidemiological evidence is faulty and the clinical picture of Andrew is lacking in significant medical manifestations prior to his first seizure.

Petitioners' reliance on animal studies and epidemiologic data in the absence of clinical signs to support a causal relationship is insufficient to substantiate their allegations, regardless of the validity of the studies and data. Petitioners have not satisfied their burden of proving that DPT caused in fact Andrew's seizure disorder. Because petitioners have failed to make a prima facie case of DPT causing in fact Andrew's seizure disorder, the issue of whether or not his status epilepticus in September 1995 was due to his sepsis or his prior seizure disorder is moot.

CONCLUSION

This case is indeed tragic, principally for the effects on Andrew of his illness in September 1995. The undersigned sympathizes with the Clements family for their situation and was very favorably impressed with Mrs. Clements as both a witness and a mother. However, petitioners may prevail solely on the evidence they present, not on the sympathy they engender. Petitioners' evidence herein does not enable them to prevail. This case is dismissed with prejudice. 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.

DATE: _____ _____

Laura D. Millman

Special Master

1. [1] The statutory provisions governing the Vaccine Act are found in 42 U.S.C.A. § 300aa-1 et seq. (West 1991). The National Vaccine Injury Compensation Program comprises Part 2 of the Vaccine Act. For convenience, further reference will be to the relevant subsection of 42 U.S.C. § 300aa.

2. [2] Under a change in the regulations, effective March 10, 1995, residual seizure disorder is no longer considered a Table injury. See 42 C.F.R. §100.1-100.3. In addition, the definition of encephalopathy as a Table injury changed in such a way that Andrew's symptomatology would not satisfy the new regulations. Id. Since petitioners filed their petition after the effective date of the regulations, they proceeded under a theory of causation in fact with respect to both the seizure disorder and encephalopathy. The undersigned discussed with counsel the question of whether there was a "separation of powers" argument concerning the regulatory change, i.e., whether Congress could legitimately delegate to the Secretary, part of the executive branch, the power to alter the statute so markedly that individuals such as Andrew could no longer make a prima facie case as he could under the statute as originally passed (Andrew would have had a prima facie residual seizure disorder). However, this issue is not for the undersigned, but for a U.S. Circuit Court of Appeals to decide. O'Connell v. Secretary, HHS, 40 Fed. Cl. 891, 893-95 (1998), appeal docketed (Fed. Cir. July 6, 1998); 42 U.S.C. §300aa-32.

3. According to a Vaccine Adverse Event Reporting System (VAERS) form, dated August 26, 1992, that Dr. Schum filled out, on August 7, 1992 at 12:15 a.m., Andrew had a prolonged generalized seizure. This was about fifteen hours after receiving DPT. He was febrile at the hospital and had a fever forty hours after injection. He had had a cold at the time of vaccination. Andrew had bronchospasms and Dr. Schum suspected a viral illness, associated fever, and febrile seizures. P. Ex. 13.

4. Petitioners' counsel clarified that petitioners are not alleging what would be an on-Table encephalopathy as of the date they filed their petition. Tr. at 72, lines 8-13.

5. See Alderslade, R., et al., "The National Childhood Encephalopathy Study, Whooping Cough: Reports from the Committee on Safety of Medicines and the Joint Committee on Vaccination and Immunisation," 79-184 (London 1981). P. Doc. 232.

6. Clonus was present for a day and then disappeared.

7. DIC is disseminated intravascular coagulation.

8. This theory suggests that pertussis toxin and endotoxin, which are both present in DPT, breach the blood-brain barrier, permitting interference with the firing of neutrons.

9. "Since there is no consistent clinical syndrome of neurologic events temporally associated with pertussis vaccine administration and no histopathologic pattern has been demonstrated..., it is difficult, if

not impossible, to validate any response in animals as a model for the hypothetical phenomenon." E.L. Hewlett and J.L. Cowell, "Evaluation of the Mouse Model for Study of Encephalopathy in Pertussis Vaccine Recipients," 57 Infection and Immunity 3:661-63, 663 (1989). P. Doc. 2152.

10. NCES, pp. 98-99 (P. Doc. 232). See also, "Pertussis immunization and serious acute neurological illness in children," by D.L. Miller, E.M. Ross, R. Alderslade, M.H. Bellman, and N.S.B. Rawson, 282 Brit. Med. J. 1595-9, esp. 1595-96 (1981) (P. Doc. 72). The authors, who are the same as the ones writing the NCES, state that they chose case-control, despite the disadvantage that unknown factors affecting the selection of controls might influence their chance of recent immunization, because they could not acquire the extremely large numbers of immunized and unimmunized children to do a cohort approach to show any significant difference between their subsequent rates of serious neurologic illnesses.

11. NCES, pp. 141, 143.

12. NCES, p. 143.

13. NCES, p. 145.

14. D. Miller, J. Wadsworth, and E. Ross, "Severe Neurological Illness: Further Analyses of the British National Childhood Encephalopathy Study," (Fifth International Symposium on Pertussis) 13 Tokai J. Exp. Clin. Med. 145-55, 146 (Supp. 1988). P. Doc. 1858.

15. D. Miller, N. Madge, J. Diamond, J. Wadsworth, and E. Ross, "Pertussis immunization and serious acute neurological illnesses in children," 307 Brit. Med. J. 6913: 1171-76, 1175 (1993). P. Doc. 2492.