In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS
No. 07-138V
July 30, 2010
To be Published

JENNIFER B. JOHNSON, as Mother and Legal Representative of the Estate of ALEXANDER L. JOHNSON,	*	
Petitioner,	*	
v.	*	DTaP; brief seizure, cardiac arrest, pulmonary arrest; death; case child under NCES
SECRETARY OF THE DEPARTMENT OF HEALTH AND HUMAN SERVICES,	*	
Respondent.	*	

David L. Terzian, Richmond, VA, for petitioner.
Michael P. Milmoe, Washington, DC, for respondent.

MILLMAN, Special Master

DECISION[1]

Petitioner filed a petition on March 2, 2007 under the National Childhood Vaccine Injury Act, 42 U.S.C. § 300aa-10 et seq., alleging that her son Alexander Johnson (hereinafter

[1] Vaccine Rule 18(b) states that all decisions of the special masters will be made available to the public unless they contain trade secrets or commercial or financial information that is privileged and confidential, or medical or similar information whose disclosure would constitute a clearly unwarranted invasion of privacy. When such (a decision or designated substantive order) is filed, petitioner has 14 days to identify and move to delete such information prior to the document's disclosure. If the special master, upon review, agrees that the identified material fits within the banned categories listed above, the special master shall delete such material from public access.

"Alexander") died on May 11, 2005 as a result of seizure and encephalopathy which his two-month vaccinations on April 25, 2005 caused in fact. Those vaccines were DTaP, HiB and Hepatitis B (combined as Comvax), inactivated polio, and Prevnar. The disagreement between the parties concerns whether Alexander had a primary epileptic seizure, leading to cardiac arrest, pulmonary arrest, and death (petitioner's view) or Alexander had a electrical conduction difficulty in his heart, cutting off oxygen to his brain, leading to cardiac arrest, pulmonary arrest, and death (respondent's view).

Because the medical records reflect only that Alexander had a low-grade fever for two days after vaccination but the parents assert Alexander had additional symptoms between his vaccinations and hospitalization, the undersigned held a fact hearing on August 5, 2008 to hear the testimony of Alexander's parents. Based on the parents' credibility, the undersigned accepts that Alexander seemed a little bit subdued and ate a little bit less during the four days between his vaccinations and his April 29th seizure. His low-grade fever for two days is in the medical records and is not in dispute.

Subsequent to the factual hearing, the undersigned held a hearing on September 22, 2009 to hear each side's expert witness. Dr. Yuval Shafrir testified for petitioner. Dr. Max Wiznitzer testified for respondent.

FACTS

Alexander was born on February 17, 2005, five weeks premature due to induction for intrauterine growth retardation and two first trimester spontaneous abortions. Med. recs. at Ex. 5, p. 19.

On April 25, 2005, at the age of two months, he received DTaP, Comvax (consisting of haemophilus B influenza and hepatitis B), inactivated polio, and Prevnar vaccines.

On April 26, 2005, Dr. Thomas Lacy's office called Alexander's mother with a scheduled appointment for Alexander to receive a CT scan of his head on April 27, 2005. She was instructed not to feed him four hours before the CT scan, and she understood to give Alexander Pedialyte. Med. recs. at Ex. 7, p. 5.

On April 29, 2005, at 2:40 p.m., Alexander was brought by ambulance to the Florida Hospital East. His father said Alexander had no history of symptoms. Med. recs. at Ex. 10, p. 3.

From April 29, 2005 until May 11, 2005 when he died, Alexander was at Florida Hospital South. Alexander's father said that Alexander had had a seizure. Alexander had a negative history except for being premature. The parents had some concern about his head growth and a CT scan had been done the prior week which was normal. Med. recs. at Ex. 11, p. 15. Dr. Ben Guedes diagnosed Alexander with anoxic encephalopathy with overwhelming brain damage and cardiorespiratory arrest. ("Anoxic" means lack of oxygen.) Alexander's mother denied that Alexander had sweating, tremors, tachypnea, gagging, choking, vomiting, diarrhea, constipation, floppiness, or stiffness. About seven days earlier, shortly after Alexander's father fed him, Alexander had stretching and jerking movements of his arms and stopped breathing. The parents called the EMS which found him asystolic. He was resuscitated in the emergency room and transferred to the hospital. Med. recs. at Ex. 11, pp. 9, 10. Dr. Guedes did not think Alexander was recoverable since he already showed evidence of severe brain damage or brain death. Med. recs. at Ex. 11, p. 16.

On April 30, 2005, Dr. Lacy wrote that, on April 29, 2005, Alexander possibly had a seizure at home. Dr. Lacy saw Alexander at one point in the emergency room. Alexander's parents indicated to him that Alexander was totally normal prior to the event. He had his two-month shots on April 25, 2005, and had a low-grade temperature for two days. He had no irritability, fussiness, or abnormal reactions. The CT scan on Wednesday showed benign extra axial fluid. Med. recs. at Ex. 7, p. 5.

Alexander remained on a respirator the entire time he was in the hospital with pupils nonreactive. In the opinion of the attending physician and attending neurologist, he had an end-stage condition which was irreversible and for which no probable treatment would be effective nor would he survive. The family requested that artificial ventilation be removed. On May 11, 2005, Alexander died. Med. recs. at Ex. 11, p. 9.

On May 19, 2005, Dr. Jan C. Garavaglia performed an autopsy, writing that the cause of death was undetermined. Alexander had diffuse anasarca (generalized edema). Dr. Garavaglia suspected either heart arrhythmia or primary brain seizure as the cause. Med. recs. at Ex. 14, pp. 10, 11. Alexander's brain was consistent with a soft "respirator" brain from anoxic encephalopathy with no focal abnormalities evident. Med. recs. at Ex. 11, p. 16.

TESTIMONY

Alexander's mother testified first. Tr. at 4. After Alexander's two-month vaccinations, he was hysterical and it took him 30 minutes to calm down. Tr. at 13. He had two vaccinations in each thigh. Tr. at 14. She lives 20 minutes from the pediatrician. Tr. at 15.

At home, in a couple of hours, Alexander went from being fussy to being hysterical. Tr. at 18. His temperature was 99.6 degrees. He screamed himself out and fell asleep on her chest.

Id. He had screamed for a couple of hours. Id. She did not call Dr. Lacy to report these events. Tr. at 19.

Alexander did not want to eat. Tr. at 19-20. His vaccine sites felt warm. Tr. at 21. Alexander woke up in the middle of the night and she fed him a quarter of his bottle. Tr. at 22. Alexander normally ate every couple of hours at that point. Tr. at 25. The night after the vaccinations, Alexander woke up multiple times and ate a little. Tr. at 26. She changed his diaper. Tr. at 26-27. He was more lethargic. Tr. at 27. There was nothing specific about the way Alexander was looking at her that was unusual or different. Tr. at 28.

On April 26, 2005, Alexander was a little bit more lethargic and eating a little more but not as he did normally. Id. He seemed a little bit more subdued during the day. Id. She thought he did not feel good because of the vaccinations. Tr. at 29.

One of Dr. Lacy's nurses called to give Alexander's mother instructions for the location he needed to be on April 27th, and not to feed him. He was to have a CT scan because his head seemed big and they wanted to rule out fluid on the brain (hydrocephalus). Tr. at 29. Alexander's mother did not tell the nurse that Alexander was not behaving normally. Tr. at 30. She figured Alexander was going to get better. Id.

Between the evening of April 26th and the morning of April 27th, Alexander's mother tried to give him Pedialyte, which he did not want. Id. He took a couple of sips and looked at her. Tr. at 31. She and her husband took Alexander to the hospital for the CT scan and the blood tests. Id. Alexander was very quiet during the CT scan. Tr. at 32. He also had x-rays which made him cry because the technicians were holding his legs down. Id. When Alexander came back from the blood tests, his arms were bruised. Tr. at 33.

She and her husband took Alexander home and tried to feed him. Tr. at 34. He ate a little. Tr. at 35. Alexander weighed only a little over eight pounds and she figured maybe he did not feel good. Id. He slept a lot but babies do at that age. Tr. at 36. She changed his diapers and they were a little wet. Tr. at 38. They were drier than usual. Id. He still had some bowel movements. Tr. at 39.

During the night of April 27th to 28th, Alexander woke up every couple of hours and he would eat some of what his mother gave him. Tr. at 40. On April 28th, he was eating a little bit more. Tr. at 41. On April 29th, he seemed to be doing about the same. Id. She spoke with Dr. Lacy on April 28th when he called her to say there was just minimal fluid on the brain scan. Id. Also, Dr. Lacy told her Alexander's legs were fine and his blood work was fine. Id. She told him that Alexander had a really rough night on Monday, but Alexander was doing better. Dr. Lacy said he was glad to hear it. Id. Alexander was still yellow from jaundice. Tr. at 44.

On April 29th, she left the house to get a haircut. Alexander was looking up at his mobile and getting ready to go back to sleep. This was about 11:30 a.m. Tr. at 46. On her way back from the beauty parlor, Alexander's mother received a frantic call from her husband that he thought Alexander had had a seizure and the EMTs were at the house, working on him. Tr. at 47. She telephoned Dr. Lacy and told him Alexander was on his way to the emergency room at Florida Hospital East and he just had his vaccinations. Tr. at 47-48. Dr. Lacy said he would meet her at the emergency room, which he did. Tr. at 48. She called her best friend Dawn and told her to research vaccines. Id.

Alexander was on a ventilator at the emergency room. Id. Alexander's mother told every doctor that Alexander had just had his vaccines a few days before. Tr. at 48-49. She states

that the people to whom she spoke said it could not possibly be related to the vaccines Tr. at 49. She does not understand how they could know that. Id. She had to talk to the police officers because they wanted to know from her and her husband what happened. Id. She spoke with Dr. Lacy and mentioned the vaccines, but he said they were on Monday and this was Friday. Id.

Alexander was transported to Florida Hospital South because they have a pediatric intensive care unit. Tr. at 50. The doctors there were very quick to tell her that the vaccines were not the cause. She mentioned the vaccines to every single doctor there. Tr. at 51. The next day, she met two pediatric neurologists, Dr. Barr and Dr. Davis, and had extensive conversations with them, again mentioning the vaccines. Tr. at 51-52. They told her the cause was metabolic. Tr. at 52. The EEGs showed Alexander was having seizure activity. Id. Dr. McReynolds from the Neumorris Clinic who heads the genetic and metabolic division did a consult and determined that Alexander's metabolic changes were secondary to his event on April 29th. Tr. at 53. She spoke with the medical examiner who said that Alexander was normal anatomically and chromosomally. Id. Everyone concluded there was no discernable cause for Alexander's death. Id.

Alexander's mother disagrees with Dr. Lacy's medical note that she told him everything was fine when she spoke to him on April 28th. Tr. at 55. She says she told him specifically that they had had a horrible night on Monday and Alexander was doing better and had a low-grade fever. Tr. at 56. She did not tell him Alexander was totally normal. Id.

Alexander's mother said that all the doctors told her that Alexander's event was too far removed from the vaccinations to be related to them. Tr. at 60. The pediatric neurologists were sure Alexander had a metabolic problem. Tr. at 61. The hospital tests on April 29th showed

some abnormal levels. Id. In the testing Dr. McReynolds did of Alexander, he found nothing metabolically wrong with him and ascribed the test results showing metabolic abnormality to the April 29th event. Id.

Alexander's father testified next. Tr. at 84. Alexander was a mild-mannered baby. Tr. at 91. When he cried, he whimpered. Tr. at 92. He cried a lot less than the other babies in the ICU when he was born. Id. When Alexander was vaccinated, he was angry and screaming. Tr. at 93. That did not last more than a few minutes. Id. At home, he really started crying and screaming red-faced. Tr. at 94. He did that periodically for two hours. Id. He eventually calmed down and his mother gave him Tylenol. Tr. at 94-95. His appetite seemed suppressed. Tr. at 96. Alexander's father did not notice anything different about Alexander's diapers the first night after the vaccinations. Tr. at 97. Alexander never resumed his normal eating and seemed more subdued. Tr. at 98.

On April 29th, Alexander was in his crib and his father decided to feed him. Alexander drank maybe three-quarters of a bottle. His father burped him and tried to feed him the rest of the bottle. Tr. at 100. Then Alexander punched the air a couple of times and went completely limp. Id. Within a minute, Alexander turned white. Tr. at 101. Alexander's father called 911 and reported Alexander had had a seizure. Id. The event occurred when Alexander's father had Alexander down on his knees. Tr. at 103. Alexander had stiffened and punched very hard twice and fell backwards completely limp. Id.

Alexander's father does not remember telling any of the doctors about Alexander's eating. Tr. at 115. When he spoke to Dr. Lacy, he told him that Alexander had screamed the night of the vaccinations as well as run a low-grade fever. Tr. at 116. He and his wife did not

know that screaming was anything to worry about. Tr. at 117. Alexander was extremely fussy. Tr. at 118-19. The doctors thought Alexander's event was outside the time limit for a vaccine reaction. Tr. at 129.

Dr. Yuval Shafrir testified for petitioner. Tr. at 153. He is board-certified in pediatrics and in neurology with a specialty in pediatric neurology. Tr. at 154. Dr. Shafrir attributes Alexander's death to a seizure that pertussis vaccine encephalopathy caused. Tr. at 158. He referred to the National Childhood Encephalopathy Study (NCES) done in England which analyzed severe acute encephalopathy within seven days of vaccination with whole-cell DPT. Tr. at 159. Even though Alexander received acellular, not whole-cell, DPT, a recent article filed as Exhibit 40 shows that severe reactions to DTaP, although significantly less in number compared to whole-cell DPT reactions, still occur, including encephalopathy. Tr. at 160.

Dr. Shafrir testified that Alexander had encephalopathy and seizures. Id. He stated that a seizure caused his death. Tr. at 160-61. He testified that Alexander had a prolonged coma because he had a seizure, lost consciousness, stopped breathing, and had cardiac arrest. "And from that moment, he never woke up until his death. And he was in coma all this period." Tr. at 161.

Dr. Shafrir also testified that Alexander had an encephalopathy before he had a seizure. Tr. at 162. He explained:

> Before the seizure he had some irritability and decreased appetite, low-grade fever. This is not considered encephalopathy. But in retrospect, as we usually have patients who [are] admitted with acute encephalopathy, seizures, meningitis, we always have the

> prodromal[2] symptoms that presented before the patient became really sick. So by themselves, those symptoms do not constitute encephalopathy. But looking at the entire case, I can say that they were the prodromal signs of encephalopathy.

Id.

Dr. Shafrir testified that Alexander's seizure led to his cardiopulmonary arrest. Tr. at 163. Regarding respondent's position that Alexander's cardiopulmonary arrest preceded his seizure, Dr. Shafrir responded:

> It's a strange statement, that's the best I can say. I mean, why a child would suddenly have cardiac arrest? It's not a common occurrence, it just happens.
> THE COURT: What just happens?
> THE WITNESS: Suddenly a child who is eating suddenly have [sic] cardiac arrest. Those things don't happen like this. ... Cardio-pulmonary arrest should have a cause. And it's, those things don't happen out of the blue in a healthy child. So a child who was just healthy a minute before the cardiac arrest, and irritable, miserable, eating less, but overall healthy, they will not go to a cardiac arrest without a specific reason. So the reason can be a cardiac disease, the reason can be a metabolic disorder, the reason can be a seizure. Here we have clearly a description of a seizure, and the description of the seizure is repeated throughout the entire medical records. And the seizure we know, with ample medical literature supporting it, can cause cardiac arrest.

Tr. at 163-65.

Dr. Shafrir's basis for concluding Alexander had a seizure is Alexander's father's description of Alexander jerking and making boxing movements with his arms, stiffening for a few seconds, and then turning limp and being unresponsive. The paramedics found Alexander in cardiorespiratory arrest. Tr. at 165. Dr. Shafrir considers the seizure to be part of Alexander's

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[2] "Prodromal" means "premonitory; indicating the onset of a disease or morbid state." Dorland's Illustrated Medical Dictionary, 30th ed. (2003) at 1513.

encephalopathy. Id. He stated someone does not need a high fever in order to have a seizure and that Alexander's low-grade fever was consistent. Someone can have encephalopathy as a result of infection or other brain condition. Tr. at 166. This is encephalopathy under the NCES. Tr. at 168. Alexander's seizure was followed by a prolonged coma, making it encephalopathy. Id. (Petitioner's counsel stated that petitioner was not alleging a Table encephalopathy because Alexander's seizure occurred four days after vaccination. Tr. at 170.)

Dr. Shafrir testified that Alexander's irritability, decreased appetite, and low-grade fever between the time he received DTaP and the time he seized are linked to his seizure. Id. Alexander would have been included in the NCES because this occurred within seven days. Tr. at 172. The prodromal symptoms are highly supportive of Dr. Shafrir's opinion because they follow naturally one upon the other. Id.

Alexander was treated with anti-seizure medication after he was admitted to the hospital. Tr. at 173. Unfortunately, Alexander was completely unresponsive in the hospital with fixed, dilated pupils. Id. In between Alexander's first seizure and his subsequent seizures, he had cardiopulmonary arrest, coma, and significant brain damage. Tr. at 175.

Dr. Shafrir read from the NCES article describing how the authors included children with encephalitis or encephalopathy, unexplained coma, convulsion lasting more than 30 minutes and/or followed by persistent neurological complications. Tr. at 193. Seizure is one expression of encephalopathy, but encephalopathy is a wider term than seizure. Tr. at 196. The actual mechanism of pertussis encephalopathy is unknown, but it is thought to be an immune response. Tr. at 197. Pertussis toxin is a very strong immune modulator. Id.

Alexander was two months old and his immune system did not have a chance to express itself. Tr. at 201. He was born five weeks premature. Id. He had intrauterine growth retardation, making him more susceptible, fragile, and sensitive. Tr. at 201-02. His immune system was less mature and he had less time for the placental transfer of maternal antibodies. Tr. at 202. This made him more susceptible to infections. Id.

Dr. Max Wiznitzer testified for respondent. Tr. at 209. He is a pediatric neurologist, board-certified in pediatrics, neurology with special competence in children, and neuro-developmental disabilities. Tr. at 210, 212. Dr. Wiznitzer's opinion is that, in the three to four days after the immunizations on April 25, up to the day he had cardiorespiratory arrest on April 29th, there is no evidence in the medical records that Alexander had an encephalopathy. Tr. at 222. Moreover, there is no evidence of an acute encephalopathy. Id.

The medical records do not describe any behaviors or events preceding the cardio-respiratory arrest on April 29th that are consistent with an acute encephalopathy, i.e., no significant change in mental status, no significant decrease in level of responsiveness, and no stupor, significant lethargy, or coma. Tr. at 223.

Dr. Wiznitzer read the transcript of Alexander's parents' testimony at the earlier hearing. Alexander's father described minor changes: a little decrease in eating, a little bit more subdued. Id. These are all minor reactions that are well-known minor reactions to vaccines. There is no evidence that Alexander had a significant impairment in eating. Id. At the doctor's office on April 25th, Alexander weighed eight pounds, six ounces. When he was admitted to the hospital on April 29th, he weighted about eight pounds, 10 ounces. There was no significant loss of weight documented. Tr. at 224.

The records do not reflect any dehydration. If Alexander's eating were significantly impaired, he would have been dehydrated and blood tests done two days after his immunizations would not have shown normal values, but his BUN and creatinine were normal. Id. Alexander was continuing to eat on April 29th, the day he had cardiorespiratory arrest. Tr. at 226. If there were a significant change in mental status, he would not be eating well. Id. Alexander's father testified Alexander was even making eye contact. Id.

Dr. Wiznitzer testified that Alexander had a minor reaction to his vaccinations with a low-grade fever, less feeding, and being more subdued. Tr. at 232. Alexander's pathology at autopsy showed the consequences of an anoxic encephalopathy, the lack of oxygen to the brain. Tr. at 239. After Alexander was admitted to the hospital, the CT scan of his brain suggests early features of anoxic encephalopathy. Id. The cerebral hemispheres looked different than the cerebellum, indicating the beginning of acute swelling. Tr. at 239-40. No encephalopathy was present prior to his cardiorespiratory arrest. Tr. at 240.

Irritability after vaccination is unsurprising and does not mean there is an encephalopathy present. Id. After Alexander received pain medication, he was able to calm down. Id. Low-grade fever was present for two days. Tr. at 241. When studies were done on April 27th of Alexander's leg, he had to be restrained and held. This is not what persons with a significant encephalopathy are like. Id. They do not fight. Id.

Dr. Wiznitzer believes that Alexander had a seizure before his cardiopulmonary arrest due to a primary cardiac event that led to poor perfusion (lack of blood flow). Tr. at 242, 244-45. Alexander's father's description of the seizure was of an event lasting one to two seconds. He said there was body stiffening and then a punching of the arms. Tr. at 242. This is classic

behavior in individuals who have a seizure due to lack of oxygen to the brain. Tr. at 242-43. If someone has a drop in brain perfusion, the body will briefly stiffen (atonic posturing) or the person will have rapid motor movements (myoclonic jerks). Tr. at 243. Alexander's movements clearly represent the paroxysmal activity associated with a lack of perfusion to the brain. Id. The coroner listed two possible reasons for the lack of blood flow to the brain: a seizure and an arrhythmia (heart rhythm disturbance). Tr. at 244. Dr. Wiznitzer thinks, because of the brief duration of the paroxysm, that it is more likely that Alexander had a primary cardiac event that led to poor perfusion or blood flow in Alexander's body. Tr. at 244-45. He agrees that a seizure is a rare possibility, but he would expect the seizure to show features of a seizure before the cardiorespiratory arrest. A seizure would go on for a period of time, including stopping, staring, and posturing. Tr. at 245.

Arrhythmia is a disturbance of the heartbeat. Tr. at 246. The cause in a child this age would be structural in the heart, some sort of abnormality of the conduction pathways that conduct electrical signal throughout the heart. Id.

Dr. Wiznitzer testified that Alexander did receive maternal antibodies even though he was premature; he just did not receive the full complement. Maternal antibodies cross the placenta throughout the pregnancy. Tr. at 247. He regards Alexander's receipt of DTaP and his cardiopulmonary arrest as coincidental. Tr. at 248.

The one- or two-second episode Alexander experienced was clinically a seizure. Tr. at 249. But it was not an epileptic seizure, i.e., connoting abnormal discharges in the brain seen in epilepsy. There are other causes for seizures such as dangerously low sugar levels and fainting spells. Id. Alexander had an anoxic injury to his brain and his EEG abnormalities after that

were a result of that brain insult. Tr. at 251. Alexander was also having clinical events of posturing, body stiffening, and quick little jerks. There were paroxysmal events, all a reaction to the anoxic insult to his brain and not because of a preexisting seizure disorder. Id. Initially, Alexander's brain went without oxygen for at least 10 minutes because that is how long it took for the paramedics to get to his house. Tr. at 252. His oxygen deprivation was even longer because it took a while after the paramedics arrived before they could get a heart rate. Id. The call went to the paramedics at 2:20 p.m. and they did not establish a heart rate until 2:54 p.m., which is 34 minutes. Id.

Dr. Wiznitzer testified that Alexander would not have been included in the NCES. Tr. at 255. The authors were looking for five categories of information: (1) acute or subacute encephalitis/encephalopathy; (2) unexplained loss of consciousness; (3) convulsions with a total duration of more than 30 minutes or followed by coma lasting two hours or more or followed by paralysis or other neurologic signs not previously reported (lasting 24 or more hours); (4) infantile spasms; and (5) Reye's syndrome not previously present. Tr. at 256. They did not want to be notified if the cause was confirmed as toxic, bacterial, metabolic, neoplastic, or traumatic. Tr. at 257. That means the NCES authors would not have wanted to be notified about Alexander because he had a metabolic cause for his encephalopathy. Id. It was metabolic because he had a hypoxic-ischemic encephalopathy. Id. Lack of oxygen is a metabolic cause. Id. "Ischemic" means poor blood flow. Tr. at 258. "Hypoxic" means lack or decrease of oxygen. Id. The NCES did not list any cases of anoxic encephalopathy. Id. Table IX of Ex. 19, p. 1598, lists the cases and there is no listing of an anoxic encephalopathy. Id. Stephenson's article, which is Exhibit C, page 5 (the article's page 160), lists the encephalopathies included in the NCES

within seven days of DPT vaccination and the diagnoses the practitioners made. None of them is an anoxic encephalopathy. Tr. at 259. Anoxic encephalopathy was not listed because it is a known metabolic cause for brain damage. Id. There is no listing of a hypoxic-ischemic encephalopathy because that is a known metabolic insult to the brain. Tr. at 262.

Dr. Wiznitzer testified that Alexander does not fit the entrance criteria for the NCES because he did not have a reportable injury. Id. The criteria included unexplained coma, but Alexander's coma was not unexplained. It was related to an anoxic encephalopathy. Id. According to the NCES's inclusion criteria, Alexander would not have been included because his encephalopathy was anoxic, due to a known cause. An anoxic encephalopathy is metabolic in nature. Tr. at 266-67.

Secondly, the NCES dealt only with DTP, not with DTaP (the vaccine Alexander received). Tr. at 263. DPT contains a few thousand antigenic components. DTaP is a tailored immunization containing between two and four components and detoxified pertussis toxin. Id. In DTaP, the pertussis toxin has been processed to rid it of its functional ability while maintaining its ability to provoke an immune response. Id. The percent of reaction is lower for acellular vaccine compared to the whole-cell vaccine. Tr. at 265. The rate of seizures after DTaP is only a third of seizures occurring after DPT. Tr. at 267. If one were to use the NCES in the context of seizures, one would have to recalculate the numbers and decrease them by a third. Id.

Regular pertussis toxin is a strong immunomodulator. Tr. at 274.75. But the detoxified pertussis is not. Tr. at 276. What is left in detoxified pertussis is the physical toxin as the

antigen. Tr. at 281, 282. Because it is a foreign protein, the body recognizes it and forms an antibody. Tr. at 283.

Dr. Wiznitzer testified that if Alexander had had an epileptic seizure, it occurred without fever, but there is no relationship between DTaP and an isolated seizure. Tr. at 289.

Alexander's autopsy did not reveal any abnormality in his heart. Tr. at 293. There was no detailed examination of the conduction pathway. Tr. at 294. More likely than not, Alexander had a cardiac event and most likely that occurred because of an abnormality in the conduction system leading to a lethal arrhythmia. Tr. at 295. Dr. Wiznitzer believes Alexander had a seizure before the cardiac arrest but it did not cause the cardiac arrest. Tr. at 296. The coroner basically stated that heart arrhythmia or primary brain seizure was the suspected cause. Id.

A significantly impaired consciousness would mean a child was unresponsive, not feeding. Tr. at 305. Fever is not a symptom of encephalopathy. Tr. at 306. If DTaP provokes a fever, the fever can provoke a seizure. Tr. at 309. But that did not happen in this case. Tr. at 312. Alexander had a cardiac event that led to poor perfusion, initially manifested by a one- to two-second seizure. Because the poor perfusion continued for tens of minutes, it resulted in anoxic encephalopathy. Tr. at 313. This caused his brain damage. Tr. at 314. Even if he had not had the seizure, he would have had brain damage from the cardiac event. Id. The anoxic encephalopathy was clearly caused by inadequate brain blood flow. Tr. at 315. Dr. Wiznitzer does not know why Alexander's heart was not pumping. Tr. at 315-16.

Dr. Shafrir testified on rebuttal. Tr. at 320. He stated that Alexander was eating poorly according to the parents' testimony and when he got to the hospital, he was given fluid. Tr. at 321. A normal CT scan does not mean there is no encephalopathy. Tr. at 323. He stated that

children do not wake up, eat, and then have cardiac arrest. Id. Alexander had been five weeks in the neonatal intensive care unit, monitored continuously, and there was no abnormality in his conduction system. Id. Alexander did not turn blue. He ate, seized, became limp, and was in cardiac arrest. Tr. at 325. He was not in respiratory arrest but in cardiac arrest. Id. Seizure can cause cardiac arrest in children. Id. (Petitioner's counsel again stated that the onset of Alexander's encephalopathy was four days after his DTaP vaccination. The seizure was the first sign of Alexander's encephalopathy. Tr. at 337, 353, 354-55.) However, Dr. Shafrir stated that Alexander had prodromal symptoms shortly after the vaccine was given, staying in the pediatrician's office for 30 minutes because of his extreme screaming after vaccination. Tr. at 338.

Dr. Wiznitzer stated that just because Alexander was monitored for five weeks after he was born without any cardiac abnormalities appearing does not mean nothing was wrong with his cardiac function. Rhythm disturbances show up whenever they show up. Id. The effect on the brain is metabolic because of the lack of blood flow to the brain. Tr. at 347. Commenting on petitioner's allegation that the seizure was the first sign of Alexander's encephalopathy, Dr. Wiznitzer stated that an isolated seizure is not the sole manifestation of an encephalopathy. Tr. at 355. Seizures can cause cardiac arrest. Tr. at 355-56. But the event that lasted one to two seconds easily describes a seizure provoked by poor brain perfusion or blood flow. Tr. at 356. Prior to that event, there was nothing to suggest that Alexander was experiencing an epileptic seizure: no staring, confusion, shaking, or lip smacking. One would typically expect to see that. Tr. at 357. The medical references always describe other clinical phenomena consistent with a seizure before the actual asystolic event. Id. Alexander's pulmonary arrest was due to the brain

insult. Tr. at 358. After the heart rhythm disturbance, there was poor blood flow to the brain. The brain centers that control breathing stopped and Alexander stopped breathing. Tr. at 359.

Dr. Shafrir agreed with Dr. Wiznitzer that the cardiac arrest preceded the pulmonary arrest. Tr. at 360. The only difference between the two sides is whether the seizure or the cardiac arrest came first. Petitioner alleges that the seizure came first, followed by the cardiac arrest and then the pulmonary arrest. Respondent says the cardiac arrest came first, followed by the seizure, and then the pulmonary arrest. Tr. at 361.

Dr. Shafrir agreed that anoxic encephalopathy is metabolic. Tr. at 363. He stated no one in the NCES used the term "metabolic encephalopathy" as an exclusion criterion for a patient who had a seizure followed by hypoxic-ischemic encephalopathy. Tr. at 365. One cannot tell from a two-second seizure whether it was generated from the brain or from a heart not pumping enough blood. Tr. at 369.

Medical Literature

Petitioner filed as Exhibit 18 the NCES: "The National Childhood Encephalopathy Study. A Report on 1000 Cases of Serious Neurological Disorders in Infants and Young Children from the NCES Research Team," part of "Whooping Cough. Reports from the Committee on Safety of Medicines and the Joint Committee on Vaccination and Immunisation," Department of Health and Social Security (London: Her Majesty's Stationery Office, 1981), in particular pp. 79-184. The authors include: R. Alderslade, M.H. Bellman, D.L. Miller, N.S.B. Rawson, and E.M. Ross. Id. at 79. The authors explain that the NCES was set up in 1976 because of widespread concern over the safety of pertussis immunization. Id. at 80. They assumed that children with serious neurological disorders, particularly those severe enough to

result in lasting damage, would be admitted to the hospital and would be between two and 36 months of age. The authors attempted to include all cases in England, Scotland, and Wales. Id. at 101.

They state, "The Study was concerned primarily with cases of acute neurological illnesses which could result in permanent brain damage or death." Id. There were three categories of cases: (1) children who were normal before the vaccination and normal afterward at 15 days (category IA); (2) children who were normal before the vaccination and abnormal afterward at 15 days (category IB); and (3) children who were abnormal before the vaccination and abnormal afterward at 15 days (category II). Id. at 107-08. Those who were categorized as having continuing neurologic abnormality up to 15 days included any child who died in the hospital. Id. at 108. Most of the 1,000 children were under 18 months of age. Id. at 109. Excess risk was present for seven days although the greatest risk was within 72 hours of DTP vaccination. Id. at 142, 148. A causal association between pertussis vaccination and the development of serious neurological disorders "is widely regarded as being biologically plausible. Several mechanisms could be operating in the case of pertussis vaccine. These include a direct neuro-toxic effect, an immediate immune reaction of the humoral type and a delayed cellular hypersensitivity reaction. It has also been postulated that pertussis vaccine may activate a previously latent neurotropic virus infection [referring to an article by Ross and Bellman]." Id. at 142.

Even in cases where there existed a possible alternate explanation of the illness, the authors included the case because the immunization may have "acted as a 'trigger' in children who would not otherwise have developed a serious neurological illness...." Id. at 143. The

authors state, "All serious neurological conditions which have been advanced as possible complications of pertussis immunization, including prolonged febrile convulsions or those complicated by coma or neurological damage, were included." Id. at 146.

In the NCES guidelines for notification, the authors requested notification of any child with, inter alia: (1) unexplained loss of consciousness; (2) convulsions (a) with a total duration of more than 30 minutes or (b) followed by coma lasting two hours or more or (c) followed by paralysis, or other neurological signs not previously present lasting 24 hours or more. Id. at 157. The participants were not to notify the NCES if these were neurological disorders in which the cause was confirmed as toxic, bacterial, metabolic, neoplastic, or traumatic, inter alia. Id. The medical personnel were instructed that, if in doubt, they were to notify the NCES of the child. Id.

Petitioner filed as Exhibit 40 an article entitled "Comparison of Adverse Effects Following Immunization with Vaccine Containing Whole-Cell vs. Acellular Pertussis Components" by A. Zielinski and M. Rosinska, 62 Przegl Epidemiol 589-96 (2008). The authors studied the incidence of adverse effects following whole-cell DTP vaccination and acellular DTP vaccination, and found that children under the age of two years had statistically significant differences in the incidence of systemic adverse effects in that there were twice as many systemic adverse effects after whole-cell vaccination than after acellular vaccination. Id. at 593. The authors state that this result of a higher incidence of systemic adverse effects after whole-cell pertussis than acellular pertussis confirms general knowledge. Id. at 594.

DISCUSSION

To satisfy her burden of proving causation in fact, petitioner must prove by preponderant evidence "(1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of a proximate temporal relationship between vaccination and injury." Althen v. Secretary of HHS, 418 F.3d 1274, 1278 (Fed. Cir. 2005). In Althen, the Federal Circuit quoted its opinion in Grant v. Secretary of HHS, 956 F.2d 1144, 1148 (Fed. Cir. 1992):

> A persuasive medical theory is demonstrated by "proof of a logical sequence of cause and effect showing that the vaccination was the reason for the injury[,]" the logical sequence being supported by "reputable medical or scientific explanation[,]" *i.e.*, "evidence in the form of scientific studies or expert medical testimony[.]"

In Capizzano v. Secretary of HHS, 440 F.3d 1317, 1325 (Fed. Cir. 2006), the Federal Circuit said "we conclude that requiring either epidemiologic studies, rechallenge, the presence of pathological markers or genetic disposition, or general acceptance in the scientific or medical communities to establish a logical sequence of cause and effect is contrary to what we said in Althen . . . ." Such an approach is inconsistent with the use of circumstantial evidence. Id. The Federal Circuit stated in Althen, 418 F.3d at 1280, that "the purpose of the Vaccine Act's preponderance standard is to allow the finding of causation in a field bereft of complete and direct proof of how vaccines affect the human body."

Close calls are to be resolved in favor of petitioners. Capizzano, 1440 F.3d at 1327; Althen, 418 F.3d at 1280. *See generally*, Knudsen v. Secretary of HHS, 35 F.3d 543, 551 (Fed. Cir. 1994).

Without more, "evidence showing an absence of other causes does not meet petitioners' affirmative duty to show actual or legal causation." Grant, 956 F.2d at 1149. Mere temporal association is not sufficient to prove causation in fact. Id. at 1148.

Petitioner must show not only that but for the vaccine, Alexander would not have had the injury and death, but also that the vaccine was a substantial factor in bringing about his injury and death. Shyface v. Secretary of HHS, 165 F.3d 1344, 1352 (Fed. Cir. 1999).

In essence, the special master is looking for a medical explanation of a logical sequence of cause and effect (Althen, 418 F.3d at 1278; Grant, 956 F.2d at 1148), and medical probability rather than certainty (Knudsen, 35 F.3d at 548-49). To the undersigned, medical probability means biologic credibility or plausibility rather than exact biologic mechanism. As the Federal Circuit stated in Knudsen:

> 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. The Vaccine Act established a federal "compensation program" under which awards are to be "made to vaccine-injured persons quickly, easily, and with certainty and generosity." House Report 99-908, *supra*, at 3, 1986 U.S.C.C.A.N. at 6344.
>
> The Court of Federal Claims is therefore not to be seen as a vehicle for ascertaining precisely how and why DTP and other vaccines sometimes destroy the health and lives of certain children while safely immunizing most others.

35 F.3d at 549.

As the Federal Circuit stated in Knudsen, 35 F.3d at 548, "Causation in fact under the Vaccine Act is thus based on the circumstances of the particular case, having no hard and fast *per se* scientific or medical rules." The undersigned's task is to determine medical probability

based on the evidence before the undersigned in this particular case. Althen, 418 F.3d at1281 ("judging the merits of individual claims on a case-by-case basis").

Dr. Shafrir, petitioner's expert, testified that Alexander would have been a case child in the NCES because he had prolonged coma within seven days of vaccination. Moreover, he stated Alexander's first seizure was evidence of encephalopathy, leading to coma, cardiac arrest, respiratory arrest, and death. The authors of the NCES included in their study children who were hospitalized with acute encephalopathy, who had an unexplained loss of consciousness, or who had a seizure lasting more than 30 minutes or a seizure followed by a coma lasting two hours or more within seven days after receiving whole-cell DPT vaccine.

A great deal of discussion arose between Dr. Shafrir and Dr. Wiznitzer, respondent's expert, over whether Alexander would have become a case child in the NCES because his encephalopathy was metabolic, i.e., caused by a lack of perfusion or blood flow to the brain. Both experts agreed that an anoxic encephalopathy, i.e., an encephalopathy caused by a lack of oxygen, is metabolic. Presumably, this is basic science and, had a medical professional in England, Scotland, or Wales in the 1970s been faced with a child whose encephalopathy was due to a lack of blood perfusion to the brain, starving the brain of oxygen, he or she would have refrained from notifying the NCES because a failure to breathe is viewed as metabolic.

However, the diagnosis of encephalopathy is not essential to Alexander's being a case child in the NCES because the NCES authors also sought reports of those children who had an unexplained loss of consciousness. Dr. Wiznitzer denies that Alexander's loss of consciousness is unexplained because he attributes the cause to a failure of electric conduction in Alexander's heart. But the coroner who performed the autopsy on Alexander wrote the cause of Alexander's

death was undetermined, further writing that Alexander died from either heart arrhythmia or primary brain seizure. The former--heart arrhythmia--is respondent's position. The latter--primary brain seizure--is petitioner's position. Although each party in this litigation has an explanation for Alexander's death, the coroner did not. The NCES was not conducting its investigation in the courthouse. It was reliant on physicians' opinions of the diagnoses of the children entering hospitals with acute neurological injury. Because the coroner could not determine the cause of Alexander's death, Alexander's loss of consciousness was unexplained. His loss of consciousness, being prolonged until the respirator was removed, is the reason for his diagnosis in the hospital of anoxic encephalopathy (lack of oxygen caused irreversible brain damage). "Anoxic encephalopathy" is a diagnosis, but not an explanation. Neither the treating doctors nor the coroner had an explanation for his loss of consciousness. Therefore, Alexander would have been a case child in the NCES because he fit within the NCES category of unexplained loss of consciousness.

Alexander also satisfied a second criterion that would have made him a case child in the NCES. The NCES authors sought children who had convulsions followed by coma lasting two hours or more. Alexander had a seizure (convulsion) followed by a non-responsive state in which he could not breathe on his own (he was noted to have "respirator brain") and was completely nonreactive with his pupils fixed. He remained in that condition for 15 days when he died after his parents agreed to remove the respirator from him. Alexander would have been a case child in the NCES also under the provision asking for reports of children who had convulsion followed by coma lasting two hours or more.

Thus, had Alexander been in England, Scotland, or Wales in the 1970s with an unexplained loss of consciousness which led to his death whose cause was undetermined according to the coroner, and with a convulsion followed by coma lasting more than two hours, he would have been a case child in the NCES. Both events qualified him for reporting to the NCES as a case child.

The Federal Circuit's 1994 Knudsen decision states that "causation may be found in vaccine cases based on epidemiological evidence and the clinical picture regarding the particular child." 35 F.3d at 549. The NCES is an epidemiologic study and Alexander's clinical picture (unexplained loss of consciousness, convulsion followed by coma lasting more than two hours) would have made him a case child in the NCES. Under the Federal Circuit's holding in Knudsen, petitioner has proven causation in fact.

The fact that the NCES dealt with whole-cell DTP and not acellular DTP does not mean that there are no adverse reactions to DTaP. There are just fewer reactions to DTaP than to whole-cell DTP. This is explicit in the Polish article filed as Exhibit 40 in which the authors studied the rate of systemic adverse reactions to whole-cell DTP compared with acellular DTP and found that systemic adverse reactions occurred after receipt of either vaccine, but twice as often with receipt of whole-cell DTP. The undersigned extensively discussed evidence showing that acellular DTP also causes adverse reactions, but to a lesser extent than whole-cell DTP, in Romero v. Sec'y of HHS, No. 07-671V, 2010 WL 2766761 (Fed. Cir. Spec. Mstr. 2010), concerning a six-month-old's seizure disorder following receipt of DTaP. In Romero, respondent filed as an exhibit an issue of the Morbidity and Mortality Weekly Report (MMWR), which the Department of Health and Human Services publishes, warning that afebrile seizures

after either DTP or DTaP vaccination may contraindicate future DTaP vaccinations. 2010 WL 2766761, at *7,*15. Respondent in Romero also filed an article discussing risks of DTaP, clarifying that adverse reactions to it are fewer than to whole-cell DTP, and another article describing the rate of occurrence of afebrile seizures following DTaP. 2010 WL 276676, at *6, *7, *15. In the instant action, petitioner's Exhibit 40, the Polish article, is consistent in describing the same phenomenon that acellular DTP, although safer than whole-cell DTP, can result in systemic adverse reactions.

The NCES itself states that DTP vaccination causing acute neurological injuries within seven days of vaccination is biologically plausible (the first Althen prong), giving a variety of mechanisms explaining how the vaccine may cause the acute neurological injuries: a direct neuro-toxic effect, an immediate immune reaction of the humoral type, and a delayed cellular hypersensitivity reaction. Evidence in the form of scientific studies is one way in which to prove biologic plausibility, as the Federal Circuit stated in Grant. 956 F.2d at 1148.

Dr. Shafrir testified that there was a logical sequence of cause and effect in DTaP's causing Alexander's injury and death in that the prodromal symptoms of having a low-grade fever, being more subdued, and eating a bit less followed naturally one upon the other from the vaccination on April 25, 2005 until the climactic events of seizure, cardiac arrest, and pulmonary arrest four days later (the second Althen prong).

The NCES established a higher incidence of acute neurological injury following DTP vaccination (and, here, through Dr. Shafrir's testimony, DTaP vaccination) within seven days of vaccination. Onset of Alexander's seizure, cardiac arrest, and pulmonary arrest was four days after vaccination, a medically appropriate time frame for causation (the third Althen prong).

Petitioner has proven causation in fact.

CONCLUSION

Petitioner is entitled to $250,000.00, the award for a vaccine-related death under § 300aa-15(a)(2) of the Vaccine Act. A check shall be made payable to petitioner in the amount of $250,000.00. In the absence of a motion for review filed pursuant to RCFC, Appendix B, the clerk of the court is directed to enter judgment herewith.[3]

IT IS SO ORDERED.

July 30, 2010
DATE

s/ Laura D. Millman
Laura D. Millman
Special Master

[3] Pursuant to Vaccine Rule 11(a), entry of judgment can be expedited by each party's filing a notice renouncing the right to seek review.