In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS
No. 07-671V
June 22, 2010
To be Published

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TERAH ROMERO and NICHOLAS ROMERO, SR., as Next Friends of NICHOLAS ROMERO, JR.,	*	
Petitioners,	*	
v.	*	DPaT; one day to seizure; applicability of Andreu and Moberly; case child in epidemiologic studies
SECRETARY OF THE DEPARTMENT OF HEALTH AND HUMAN SERVICES,	*	
Respondent.	*	
* *		

Brian R. Arnold, Dallas, TX, for petitioners.
Lisa A. Watts, Washington, DC, for respondent.

MILLMAN, Special Master

RULING ON ENTITLEMENT[1]

Petitioners filed a petition on September 17, 2007, under the National Childhood Vaccine Injury Act, 42 U.S.C. §300aa-10 et seq., alleging that their son Nicholas Romero, Jr.

[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 clearly be an 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.

(hereinafter, "Nicholas"), received acellular DPT (DPaT), hepatitis B, haemophilus B influenza, Prevnar, and inactivated polio vaccines on September 20, 2004, when he was six months old, and had encephalopathy and a seizure disorder whose onset was the next day. They also assert that Nicholas had a Table injury, without specifying which Table injury. Petition at 3.

Two recent Federal Circuit cases have particular significance for the instant action since both also concern infants who had seizures within a day or two of vaccination. In the two Federal Circuit cases, the vaccine was DPT. In the instant action, the vaccine is DPaT. These cases are Andreu v. Sec'y of HHS, 569 F.3d 1367 (Fed. Cir. 2009), and Moberly v. Sec'y of HHS, 592 F.3d 1315 (Fed. Cir. 2010). In Andreu, petitioners prevailed. In Moberly, petitioner did not prevail. The Federal Circuit distinguished between the two cases with similar facts on two grounds: (1) in Andreu, respondent's expert agreed with the medical theory petitioners' expert provided to link the vaccine to the seizures whereas in Moberly, respondent's expert disagreed with petitioner's expert's medical theory, and (2) in Andreu, the vaccinee's doctors opined that the vaccine caused Enrique Andreu's seizures, whether or not they were febrile or afebrile, whereas in Moberly, the vaccinee's doctors were silent or doubtful as to causation.

As in Andreu, in the instant action, Nicholas had a temperature when he was brought to the emergency room (100.4° F), but his temperature was normal when the emergency medical technicians measured it earlier at Nicholas's home. Some medical records described each child in both cases as having a febrile seizure while others stated it was afebrile. In Andreu, the Federal Circuit stated whether or not the seizure was febrile or afebrile made no difference in its consideration that petitioners had made a prima facie case of causation in fact, recognizing there was considerable dispute over the matter. 569 F.3d at 1378. In the instant action, there is also

disagreement over whether Nicholas's initial seizure was febrile or afebrile. Petitioners' expert Dr. Toler's opinion is premised on Nicholas's initial seizure being febrile. Respondent's expert Dr. Herskowitz's opinion is premised on Nicholas's initial seizure being afebrile.

As in Andreu, Nicholas's first seizure occurred one day after his vaccinations. 569 F.3d 1367. (In Moberly, the vaccinee's first seizure occurred two days after vaccination. These seizures were brief, unlike Nicholas's first seizure which lasted 20-30 minutes. 592 F.3d 1315.)

As in Andreu, where Enrique had a cold and ear infection just prior to his vaccination, Nicholas had a chronic cough when he received his vaccinations. 569 F.3d at 1367.

In Andreu, the Federal Circuit was impressed with "the striking temporal connection between the vaccine and Enrique's initial seizure." 569 F.3d at 1282. However, unlike in Andreu, Nicholas's treating doctors were silent as to the cause of his seizures, and respondent's expert in the instant action did not agree with petitioners' expert's theory of causation. Thus, neither of the two elements in Andreu that the Federal Circuit emphasized in Moberly is present in the instant case that would dictate entitlement: (1) the experts disagree on theory, and (2) no treating doctor opined there was causation. If petitioners are to prevail in the instant action, it must be on a different basis than the Federal Circuit's in Andreu.

A hearing was held in this case on January 26, 2009. Testifying for petitioners were Eva M. Granados (Nicholas's grandmother), Dr. Kathy Toler, and Terah Romero (Nicholas's mother). Testifying for respondent was Dr. Joel Herskowitz.

On August 10, 2009, petitioners filed their post-hearing memorandum. Petitioners only mention causation-in-fact seizures (although they also include allergic reaction and anaphylaxis but their expert Dr. Toler never expressed an opinion about these illnesses). Petitioners insist

there is a Table injury here because the onset of Nicholas's seizures occurred within Table time (three days). Seizures have not been a Table injury since March 10, 1995 when, by regulation, respondent removed "residual seizure disorder" from the Vaccine Injury Table, which petitioners recognize at p. 15 of their memorandum. Petitioners admit that Nicholas did not have a Table encephalopathy.

On September 17, 2009, respondent filed her post-hearing memorandum.

FACTS

Nicholas was born on March 18, 2004.

On Monday, September 20, 2004, when he was six months old, Nicholas received hepatitis B, DPaT, HiB, Prevnar, and IPV vaccines. Nicholas had an ingrown toenail and a chronic cough for which he was prescribed Keflex. Med. recs. at Ex. 4, p. 7.

On September 21, 2004, the San Antonio Fire Department EMS responded to Nicholas's grandmother's call at 8:46 a.m. because Nicholas was having a seizure lasting 20 minutes. Ex. 14, p. 1. Nicholas's temperature was 98.5° F. The EMS took a history that Nicholas received his shots the day before. He was a little irritable and possibly postictal[2] following the seizure that his grandmother stated lasted at least 20 minutes prior to her calling the EMS. She described it as full body shaking with an unusual stare. Ex. 14, p. 2. About five minutes from the hospital emergency department, Nicholas became very consolable and responsive to his environment. Id.

[2] Postictal means "occurring after a seizure or sudden attack." Dorland's Illustrated Medical Dictionary, 30th ed. (2003) at 1494.

Nicholas was taken to Christus Santa Rosa Emergency Department. He had shaking in his upper and lower extremities which lasted 20-30 minutes. Med. recs. at Ex. 15, p. 2. He was alert and crying, but consolable. Med. recs. at Ex. 15, p. 3. His temperature was 100.4° F rectally. The diagnosis was afebrile seizure. Nicholas was happy, playful and smiling. Id. The notes continue that Nicholas was alert and afebrile, and that his grandmother reported he did not have any fever at home. The chief complaint was "questionable febrile seizure" and the notation that Nicholas had been vaccinated the day before. Nicholas was well-hydrated. Med. recs. at Ex. 15, p. 4. A brain CT scan done on September 21, 2004 by Dr. Jorge A. Velez notes clinical history: febrile seizure. The CT scan was unremarkable. Med. recs. at Ex. 15, p. 11.

On Thursday, September 23, 2004, Nicholas saw Dr. Alicia V. Valdez. Med. recs. at Ex. 4, p. 12. He had had a seizure Tuesday night (September 21, 2004). Nicholas was asleep with his grandmother. He was shaking and then limp. His eyes rolled back and he foamed at the mouth. It took the EMT 30 minutes to arrive and the seizure did not stop until they arrived. Nicholas's temperature at the emergency department was 100.4° F rectally. All tests were negative and he had not had an episode since then. Id.

On Monday, October 4, 2004, Nicholas saw Dr. Valdez again. His mother complained of a second seizure on Saturday, October 2, 2004. His temperature was 101.5° F rectally at the time of the seizure. The seizure lasted about 15 minutes. When the EMS arrived, his temperature was 99° F. He remained sleeping for about 10 minutes after the seizure. He did not have a seizure at the hospital, where he was started on Phenobarbital. The seizures were probably febrile in nature. Med. recs. at Ex. 4, p. 10.

On October 20, 2004, Nicholas saw Dr. Wilfred Castro-Reyes, a neurologist. In September 2004, he received vaccinations and went to sleep. The next night, he had a grand tonic clonic seizure for about one-half hour. The EMS gave him oxygen and the seizure was self-limiting. He had a temperature of 101° F but at the emergency room, he had no fever. Med. recs. at Ex. 7, p. 11.

On October 11, 2004, Nicholas went to the South Alamo Medical Group. He had been seen three weeks before at the emergency department for seizures after his vaccinations. He did not have temperature at the time. His paternal cousin has seizures. Med. recs. at Ex. 5, p. 18.

On January 31, 2005, Nicholas had a brain MRI which was normal. Med. recs. at Ex. 7, p. 15.

On March 14, 2005, Nicholas had an EEG which was normal. Med. recs. at Ex. 7, p. 21.

From April 7-8, 2005, Nicholas had a 24-hour video EEG. It was abnormal due to paroxysmal activity consistent with absence type of epilepsy. He had 10 push-bottom events: brief stare with slight eye blinking; diffuse bursts of high amplitude spike and slow wave complexes lasting between three and six seconds without convulsive activity or postictal state, and with return to background activity; there were other two- to four-second bursts of diffuse regular and rhythmic high amplitude 2.5-3 hertz spike and slow wave complexes. Med. recs. at Ex. 7, p. 22.

On July 8, 2005, Dr. Jorge A. Saravia, a neurologist, noted that Nicholas had a total of 25-30 seizures and was diagnosed with epilepsy at six months of age. Med. recs. at Ex. 5, p. 3. He had spells related to elevated fever and others that were not. Id.

On September 22, 2006, Nicholas saw Dr. Rebecca L. Huston. On the day after he received his third set of vaccinations, he developed a seizure. Nicholas's mother reported that fever was not noted with the seizure. Med. recs. at Ex. 5, p. 1.

Other Submitted Material

Petitioners filed the affidavit of Terah Romero (Nicholas's mother), dated November 20, 2007. Ex. 16. The evening after Nicholas's vaccinations, everything seemed normal. Ex. 16, p. 1. Nicholas played and did not seem to be in pain or have a sore leg. Ex. 16, p. 2. He did not feel feverish to her when he awoke in the night for a feeding. He went right back to sleep after a burping. Id. The hospital staff told her it was not unusual for children to get febrile seizures after vaccination and "although Nicholas did not have a fever right that minute, that he may have 'spiked' one while sleeping." Ex. 16, p. 3.

Petitioners filed the affidavit of Nicholas D. Romero, Sr. (Nicholas's father), dated November 20, 2007. Ex. 17. The doctors told him and his wife that Nicholas may have spiked a fever and that is what may have caused the seizure. Ex. 17, p. 2. The doctors and staff also told them Nicholas may have had a vaccine reaction. Id.

Petitioners filed the affidavit of Eva M. Granados (Nicholas's grandmother), dated November 20, 2007. Ex. 18. She states she was with Nicholas the morning he had his first seizure after his immunizations. Ex. 18, p. 1. Nicholas was lying with her when she felt a jerk. She looked at him and saw he was not breathing and was foaming from the mouth. Before the ambulance arrived, the jerking stopped but he was not responsive to her voice. Id. The EMTs asked her if Nicholas had been sick and she said no. Ex. 18, p. 2.

Petitioner filed a supplemental affidavit from Eva M. Granados (Nicholas's grandmother). Ex. 25. She states that she checked on Nicholas when he was lying in his crib on September 20, 2004 and he seemed warm to the touch. Id. at 2. She put him in bed with her and he was warm to the touch but she did not take his temperature since he had been given Tylenol before he went to bed. Ten minutes later, she felt Nicholas jerk. Id.

Petitioners filed the expert report of Dr. Kathy A. Toler, a neurologist, dated February 20, 2008. Ex. 19. Her opinion is that Nicholas's vaccinations caused an intractable seizure disorder. There is no evidence of any other risk factor or cause to explain his seizures. Ex. 19, p. 2.

Petitioners filed the supplemental expert report of Dr. Toler on May 23, 2008. Ex. 20. Nicholas had an elevated white count at his September 21, 2004 hospital visit and a left shift with neutrophils being elevated. Relying on a medical article depicting a febrile seizure with a fever as low as 100.4° F, Dr. Toler thinks that Nicholas had a febrile seizure on arrival to the emergency room where his temperature was measured at 100.4° F. Ex. 20, p. 1. Moreover and more importantly to Dr. Toler, Nicholas had an inflammatory state. His white blood cell count was elevated at 10.1 (normal being between 6.0 and 17.0) with a left shift with neutrophils being elevated to 10.8 (normal being between 1.0 to 8.5). She states:

> Although the precise mechanism of febrile seizures is unknown, one theory is that during an inflammatory state pro-inflammatory cytokines, such as interleukin-1B are elevated in the [cerebrospinal fluid] of patients with febrile seizures and may have a neurotoxoic effect on neurons and lead to the development of seizures....

Ex. 20, p. 2.

A second issue is the length of Nicholas's first seizure and the subsequent development of epilepsy. Id. Nicholas's first seizure was prolonged: 20 to 30 minutes. This satisfies the

definition of a complex febrile seizure which requires a duration longer than 15 minutes, focal or lateralized seizures, and more than one episode in a 24-hour period or status epilepticus. Id. The important point is that prolonged seizures can injure the hippocampus and lead to future development of epilepsy. Lastly, the temporal relationship between the vaccination and the initial seizure is clear. Medical literature supports convulsion as the most common central nervous system sequela of DPaT vaccine, most of which occurs in the first 24 hours as in Nicholas's case. Id. Dr. Toler concludes that Nicholas's presentation one day after vaccination of inflammation not related to a central nervous system infection led to a complicated initial febrile convulsion. Id.

Dr. Toler presented numerous articles in support of her opinion, filed as Exhibit 21. Among those articles is "Pertussis immunization and serious acute neurological illness in children" by D.L. Miller, et al., 282 BMJ 1595-99 (1981). These are the same authors of the National Childhood Encephalopathy Study (NCES) which the Federal Circuit described in Andreu and Moberly, agreeing that Enrique Andreu and Molly Moberly would not have been case children in the NCES because their seizures were too brief. The Federal Circuit in Andreu commented that the NCES was relevant generally for the proposition that DPT can cause acute neurological illness (encephalopathy or a seizure of at least 30 minutes). 569 F.3d at 1380-81 and n.8. The NCES studied whole-cell DPT whereas, in the instant action, Nicholas received DPaT.

In Moberly, petitioner's expert described the exception to the NCES requirement that a case child have a seizure lasting more than 30 minutes within seven days of vaccination if the child had a number of seizures within a month of vaccination. The duration of brief seizures

could be added together to make the required 30 minutes if they were considered part of a single pathological process and the first seizure occurred within seven days of vaccination. 592 F.3d at 1319.

In the instant action, the 1981 Miller article filed as part of petitioners' Exhibit 21 summarizes the findings of the NCES. The authors state, at 1596:

> We aimed to collect as many cases as quickly as possible by identifying all children in England, Scotland, and Wales with specified serious acute neurological illnesses, including those possibly caused by pertussis immunisation. These included encephalitis or encephalopathy, unexplained coma, convulsions lasting more than 30 minutes or followed by persistent neurological complications, infantile spasms and Reye's syndrome. Any such illnesses severe enough to be associated with the risk of subsequent permanent brain damage were thought likely to lead to admission to hospital.

The children's occurrence of illness was from July 1, 1976 to June 20, 1979. Id. A total of 1,182 children were included in the NCES. Id. The authors found that vaccinees who were apparently previously normal had higher incidences and thus higher relative risks of neurological disorders within seven days of DPT vaccination. Id. at 1597. Twelve children were in the category of normal-abnormal (category 1B), two of whom had prolonged convulsions. Id. In Table IX, the authors discuss, inter alia, the outcome a year later of these two children with prolonged convulsions: (1) minor delay in speech/social development, and (2) major delay in global development. The authors do not discuss whether these children had febrile or afebrile convulsions. Id. The authors state, at 1598:

> A close time relation was found between the onset of illness and preceding immunisation with diphtheria, tetanus, and pertussis vaccine. The mechanism for pertussis-vaccine-associated neurological disease remains obscure: it may be either caused by a

> direct neurotoxic effect or be mediated indirectly by immune mechanisms.

Another article in petitioners' Exhibit 21 is "Nature and Rates of Adverse Reactions Associated with DTP and DT Immunizations in Infants and Children" by C.L. Cody, et al., 68 Ped 650-60 (1981). The authors studied reactions to DPT within 48 hours of vaccination. In this epidemiological study, the authors do discuss whether the children's convulsions were febrile or afebrile. Nine children had convulsions, of which two children had afebrile convulsions. Id. at 653, 654 (Table 3). No seizure in the group of nine children lasted more than five minutes. Id. at 654. The authors state, "Convulsions appear to be the most common serious reaction observed following pertussis immunization." Id. at 655. None of the study participants had permanent sequelae. Id. at 657. The authors recommend that children who previously had convulsions after DPT forego future DPT vaccinations and receive DT vaccine instead. Id.

Respondent filed the expert report of Dr. Joel Herskowitz, a neurologist, as Exhibit A. He states Nicholas did not manifest the symptoms of a Table encephalopathy or encephalitis since Nicholas did not have a significantly decreased level of consciousness for 24 or more hours. Id. at 2-3. He also states that Nicholas had an afebrile seizure although he did have a temperature elevation of 100.4° F at 9:49 a.m. at the hospital. Id. at 3. He states that the medical literature does not support that DPT or DPaT causes afebrile seizures. Id. at 5.

Respondent filed literature with her pre-hearing submission at Tabs C through F. Tab D is an article entitled "Acellular Pertussis Vaccines" by M.D. Decker and K.M. Edwards, 47 Ped Clinics of N America 2:309-35 (2000). The authors state, under the subheading "Contraindications and Precautions" for healthy infants and children after acellular DPT vaccination: "The following events are considered precautions: ... convulsions occurring within 3

days, **with or without fever**. Many pediatricians treat these precautions as though they were contraindications...[emphasis added]." Id. at 315. The authors note that children who received acellular pertussis vaccine had an increase in reaction rates with each booster dose, although at a lower rate than those children who received whole-cell DPT vaccine. Id. at 317. (Nicholas had his initial seizure after his third acellular DPT vaccination.) Per 100,000 vaccinations, there were 0.5 seizures among recipients of acellular DPT compared to 1.7 seizures among recipients of whole-cell DPT vaccine. (In other words, for every 200,000 vaccinations, one recipient of acellular DPT had a seizure and over three recipients of whole-cell DPT had seizures.) Id. at 321. The authors state that acellular DPT reduces uncommon adverse events such as seizures by two-thirds compared to whole-cell DPT. Id. at 330.

Respondent's Tab E is the MMWR (Morbidity and Mortality Weekly Report) issued by the Centers for Disease Control (CDC)[3] entitled "Pertussis Vaccination: Use of Acellular Pertussis Vaccines Among Infants and Young Children. Recommendations of the Advisory Committee on Immunization Practices (ACIP)," by D. Guris, et al., 46 MMWR No. RR-7:1-25 (Mar. 28, 1997). Under "Precautions," the CDC states, at 21, 22:

> If any of the following events occurs within the specified period after administration of either whole-cell DTP or DTaP, vaccine providers and parents should evaluate the risks and benefits of administering subsequent doses of a pertussis-containing vaccine:

[3] "The MMWR series of publications is published by the Epidemiology Program Office, Centers for Disease Control and Prevention (CDC), Public Health Service, U.S. Department of Health and Human Services, Atlanta, GA 30333." First (unnumbered) page after title page. The material in this report was prepared for publication by Walter A. Orenstein, M.D., Director of the National Immunization Program together with Stephen C. Hadler, M.D., Director of the National Immunization Program's Epidemiology and Surveillance Division. Id. Dr. Hadler was one of five CDC staff members from the Division of Epidemiology and Surveillance of the National Immunization Program who prepared this report. Id. at iv.

> ...convulsions **with or without fever**, occurring within 3 days. [emphasis added].

Respondent's Tab F is an article entitled "Critical Review and Invited Commentary. Pertussis vaccination and epilepsy–an erratic history, new research and the mismatch between science and social policy" by S. Shorvon and A. Berg, 49 Epilepsia 2:219-25 (2008). The authors conclude that the risk of pertussis vaccine-induced encephalopathy and/or epilepsy, if it exists, is very low. These include risk of a febrile seizure of 1 per 19,496 DPT vaccinations and risk of an afebrile seizure of 1 per 76,133 DPaT vaccinations. Id. at 219, 223.

TESTIMONY

Eva M. Granados, Nicholas's maternal grandmother, testified first for petitioners. Tr. at 3. Nicholas's mother gave Nicholas Tylenol the night of his vaccination. Tr. at 6. Ms. Granados was on the living room sofa bed during the night. When her daughter left for work the next morning, Ms. Granados went to Nicholas's crib to see how he was doing. She touched his face and it seemed warm. Tr. at 7. A little while later, she came and got Nicholas out of the crib and put him next to her while she watched television. She felt jerking and heard Nicholas choking. Nicholas was shaking and his eyes rolled back. She screamed. Foam was coming from his mouth. Tr. at 8. She called 911. Tr. at 9. The fire department and ambulance arrived and they gave Nicholas oxygen. A person asked her if Nicholas had been sick and she said no. Tr. at 10. She rode in the ambulance with Nicholas. Tr. at 12. She did not take Nicholas's temperature at any time. Tr. at 14.

Dr. Kathy Toler, an adult neurologist, testified next for petitioners. Tr. at 36. Nicholas had an elevated white count in the Emergency Department, which means he had some kind of inflammatory state. Tr. at 48. That could mean the presence of an autoimmune or bacterial

response. Tr. at 50. Dr. Toler said that Nicholas's temperature of 100.4° would be considered elevated. Tr. at 51. Nicholas's temperature could have been higher had he not been given Tylenol the night before, although since it was 11 hours since he had received it, the Tylenol would have worn off by the time he had his seizure. Tr. at 52, 53.

Dr. Toler said that prolonged seizures damage neurons. Tr. at 53. The area of the seizure becomes more susceptible for another seizure. She called this the "kindling theory." Id. Nicholas's first seizure lasted over 15 minutes and was therefore "prolonged," meaning it predisposed him to further seizures. Tr. at 56. There was no other cause for Nicholas to have a seizure: meningitis, virus, bacterial infection. Tr. at 58.

Dr. Toler's opinion is that Nicholas's vaccination caused his seizure disorder. Tr. at 61. Her basis is that there was no other cause for his seizures. It was temporally related. Even though the adverse reaction incidence to acellular pertussis vaccine is substantially less than with whole-cell, these reactions still occur. Tr. at 62. What is elicited in febrile seizures is an immune response. Id. The body reacts to the protein antigen inappropriately and, if the seizure is prolonged as it was in Nicholas's case, this leads to the development of epilepsy which he has. Id. There is no other reasonable explanation for his epilepsy than the vaccination and Nicholas had a fever on arrival to the ER. Id. Although his fever was not high, it was at a level used in studies as indicative of febrile seizure. Tr. at 62-63. Nicholas's seizures progressed to status epilepticus. Tr. at 63.

On cross-examination, Dr. Toler admitted that she does not have any patients younger than 12 in her private practice and she is not board-certified in child neurology. Tr. at 64, 65. She agreed that the cause of seizures in children is frequently unknown. Tr. at 66-67. She

admitted that Nicholas's temperature when the emergency personnel took it on arrival to his home at 8:43 a.m. was 98.5°. Tr. at 67, 72. That temperature would not meet the cutoff for the definition of febrile seizure. Tr. at 75-76. When Nicholas's temperature was recorded as 100.4° in the ER, it was at 9:49 a.m. On three subsequent times, his temperature was essentially normal. Tr. at 69. Dr. Toler agreed that an elevated white blood count is a nonspecific finding. Tr. at 76.

Dr. Toler proposed a possible mechanism of febrile seizures that during an inflammatory state, proinflammatory cytokines, such as interleukin-1B, are elevated in cerebrospinal fluid and may have a neurotoxic effect on neurons leading to seizures. Tr. at 79. However, that mechanism would not apply if Nicholas's first seizure was afebrile. Tr. at 80. If Nicholas's first seizure were afebrile, Dr. Toler said she would still think that the acellular DPT caused it, but the medical literature does not support any connection between afebrile seizures and epilepsy. Id. She would have no basis for her opinion of causation if the first seizure were afebrile. Tr. at 80-81. The medical literature would not support her. Tr. at 81.

None of Nicholas's doctors ascribed his seizures to his vaccinations. However, they did refer to his seizures as febrile. Tr. at 82. Nicholas continued to received his childhood vaccinations, including acellular DPT. Id.

Terah Romero, Nicholas's mother, testified next for petitioners. Tr. at 88. Nicholas had been taking Balamine DM because of allergies causing congestion. Tr. at 89. He was not congested on the day he received his vaccinations and she does not recall giving him Balamine DM on that day. Id. On the night of the vaccinations, Nicholas woke up at his usual interval of every four hours to feed. Tr. at 91. She did not notice anything unusual about him. Tr. at 92.

The ER gave Nicholas Tylenol because his temperature was over 100.3° on September 21, 2004. Tr. at 97. The doctor at the ER suggested to Mrs. Romero that Nicholas could have had fever overnight which caused the seizure. Tr. at 102. They lived 20 minutes from the hospital. Tr. at 103. Now, when Nicholas gets a temperature of 99.7°, he has a seizure. Tr. at 104.

Dr. Joel Herskowitz, a pediatric neurologist, testified for respondent. Tr. at 112. He has been a pediatric neurologist for 30 years. Tr. at 113. His opinion is that Nicholas's first seizure on September 21, 2004 was not related to his DPaT vaccination the day before. Tr. at 115. His basis is that the medical literature does not support the idea that acellular pertussis vaccine causes afebrile seizure disorders. Tr. at 116. He thinks that Nicholas's first seizure was afebrile. Id.

When Nicholas received his vaccinations on September 20, 2004, the pediatrician noted that he had an upper respiratory infection. Tr. at 117. He was prescribed Balamine DM and Tylenol as needed. Id. Nicholas had swollen toes and chronic congestion. Tr. at 119. Nicholas was prescribed Zerotech, which is some sort of antihistamine, for his chronic congestion, and Keflex, an antibiotic, used for bacterial illnesses. Id. Dr. Herkowitz thinks that Nicholas's elevated white blood cell count on September 21, 2004 was due to the inflammation of his toes. Tr. at 120. Nicholas saw the doctor on August 10, 2004, over a month before his vaccinations, with gastroenteritis and a slightly ingrown toenail on the left big toe. Tr. at 125. Nicholas's swollen toes continued to the October 27, 2004 visit. Tr. at 126. Nicholas had significant inflammation because he had weeks, if not months, of an inflammatory process that required at least two courses of antibiotics. Tr. at 128.

Dr. Herskowitz said that Nicholas did not seem to have had a seizure with fever. Tr. at 129. Nicholas had two very good reasons to have an inflammatory response and a bit of a fever (although Dr. Herskowitz is not convinced he had a fever): his history of chronic congestion and a "hot" toe. Tr. at 130. A 20-minute seizure without kicking off the blankets is enough to make someone a little bit warm. Id. Dr. Herskowitz thinks that healthy babies tend to feel warm. Id. He did not know what to make of Nicholas's temperature in light of the 98.5° measurement of the emergency medical technicians. Tr. at 131.

This case does not concern a Table encephalopathy because Nicholas did not have a significantly decreased level of consciousness. Tr. at 116, 131. At the hospital, he was repeatedly described during his seven-hour visit as awake, alert, smiling, playful, and happy. Tr. at 131-32. (Petitioners' counsel stated that petitioners are no longer alleging a Table encephalopathy or a causation in fact encephalopathy. Tr. at 138.)

Dr. Herskowitz does not have a specific cause for Nicholas's seizure although Nicholas had two types of inflammatory processes going on and was not well. Tr. at 132. He had congestion and a chronically inflamed toe. Tr. at 133. He was prescribed an antihistamine and an antibiotic. Id. There are cases of children with seizure where the cause is unknown. Id

Dr. Toler testified again and agreed that Nicholas did not have encephalopathy. Tr. at 148. She also stated that if Nicholas's big toe inflammation had anything to do with his seizure, she would have expected him to be sicker, i.e., encephalopathic. Id. She agrees that the toe inflammation could be the cause of the elevation of Nicholas's white blood count. Tr. at 149. All Nicholas had to have in order to prove causation from the vaccinations is the fever. Tr. at 151.

DISCUSSION

This is a causation in fact case. To satisfy their burden of proving causation in fact, petitioners must offer "(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. Sec'y of HHS, 418 F.3d 1274, 1278 (Fed. Cir. 2005). In Althen, the Federal Circuit quoted its opinion in Grant v. Sec'y 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. Sec'y of HHS, 440 F.3d 1274, 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...."

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

Petitioners must show not only that but for DPaT vaccine, Nicholas would not have had seizures, but also that the vaccine was a substantial factor in bringing about his seizures. Shyface v. Sec'y of HHS, 165 F.3d 1344, 1352 (Fed. Cir. 1999) (a baby developed a high fever after receiving DPT vaccine; he was also harboring E. coli infection which can cause fever;

testimony showed that both the vaccine and the infection were substantial factors in causing his high fever that led to his death; petitioners prevailed because the vaccine was a substantial factor). Petitioners are no longer pleading a Table encephalopathy or a causation-in-fact encephalopathy.

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. Sec'y of HHS, 35 F.3d 543, 551 (Fed. Cir. 1994).

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 an 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.

Prior to the Federal Circuit's decision in Andreu, petitioners in the Vaccine Program prevailed rarely when they alleged that DPT vaccine caused an afebrile seizure: see, e.g., Almeida v. Sec'y of HHS, No. 96-412V, 1999 WL 1277566 (Fed. Cl. Spec. Mstr. 1999).

Petitioner in Almeida actually alleged that DPT significantly aggravated Lorena Almeida's pre-existing neurological condition. Id. at *1. Dr. Marcel Kinsbourne testified for petitioner. Dr. Joel Herskowitz (the same expert as in the instant action and in Andreu) testified for respondent. On the evening of six-month-old Lorena's third DPT vaccination, she had an afebrile tonic-clonic seizure lasting 45 minutes. Id. A treating pathologist diagnosed Lorena with a generalized seizure disorder of unknown etiology precipitated by vaccinations. Id. Doctors instructed that she no longer receive pertussis in her vaccinations. Id. Lorena had had a brief seizure prior to her third DPT vaccination. Id. at *2. Former Special Master E. LaVon French held that there was no question that Lorena's condition after her third DPT vaccination was significantly worse than her condition prior to this vaccination. The only question remaining was what caused the significant worsening. Id. at *6.

Dr. Herskowitz acknowledged that Lorena would have been a case child in the National Childhood Encephalopathic Study (NCES) because of the length of her post-vaccinal seizure. The NCES "was a major epidemiological study of the incidence of neurological injury following the administration of the DPT vaccine." Id. at *7. He did not believe, however, that her subsequent neurologic devastation was due to this seizure, but rather to the underlying neurological condition which manifested in a brief seizure before this vaccination. Id.

Subsequently, respondent filed a report in Almeida from another pediatric neurologist, Dr. Robert J. Baumann (who was also respondent's expert in Moberly). He stated that if Lorena's seizure post-vaccination caused her subsequent brain injury, the seizure should have been accompanied by encephalopathy. Moreover, he wrote that seizures do not damage the brain; neurologic disease of which seizures are only markers damage the brain. Dr. Baumann

wrote that since a pertussis-related injury looks no different than an injury from other causes, no one can identify a pertussis-related injury or rely on an epidemiologic study such as the NCES for proof that an individual child had a vaccine injury. Id. at *8. As Special Master French realized, to accept Dr. Baumann's view would mean that no petitioner could ever prove a causation-in-fact seizure disorder or significant aggravation of a pre-existing seizure disorder unless the seizures were accompanied by an on-Table encephalopathy. Id. at *9.

Special Master French found Dr. Kinsbourne's opinion superior to, and more persuasive and rational than, respondent's experts's opinions. Id. at *9. She found that the third DPT vaccination not only triggered the 45-minute seizure but also caused Lorena to have further brain damage through an intractable seizure disorder. Id. She also found that the third DPT vaccination significantly aggravated Lorena's underlying seizure disorder. Id. Special Master French cited the Federal Circuit's 1994 Knudsen decision stating that "causation may be found in vaccine cases based on epidemiological evidence and the clinical picture regarding the particular child." Id. at *15 (citing 35 F.3d at 549). Lorena would have been a case child in the NCES because one of the criteria for being included in the study was a vaccinee's having a seizure of at least 30 minutes within seven days of vaccination. Id. and n.13. Lorena's seizure lasted 45 minutes.

Special Master French rejected respondent's contention that DPT may cause only febrile seizures by stating that "the NCES *did not distinguish* between febrile and afebrile seizures in its analysis of relative risk [emphasis in original]." Id. at *16. Special Master French noted that "standard protocol has been to withhold the pertussis component of the DPT vaccine if infants or children were known to have had a prior history of seizure activity. Such cautionary procedures

have existed for many years for the reason that doctors believe that the vaccine poses a risk of causing or triggering further seizures." Id. at *17.

The Federal Circuit cited Almeida favorably four times in Andreu: 569 F.3d at 1377, 1378, and 1382 (twice). The Federal Circuit also cited Liable v. Sec'y of HHS, No. 98-120V, 2000 WL 1517672 (Fed. Cl. Spec. Mstr. 2000), favorably six times in Andreu: 569 F.3d at 1374, 1375 n.1, 1376, 1378 n.6, 1380, and 1382.

Liable concerned six-month-old Sierra Liable's 30-60 minute seizure five hours after she received her third DPT. Id. at *1. She developed a severe seizure disorder. Id. Special Master George Hastings ruled for petitioners. Id. at *2. The basis of Special Master Hastings's decision is that Sierra had a serious acute neurologic illness within seven days after receiving DPT and, under the NCES, this is consistent with a causal relationship. Id. at *12. The NCES calculated the relative risk of children experiencing a severe acute neurologic illness within seven days of DPT vaccination as 3.3 times the risk of non-vaccinated children of similar age experiencing a severe acute neurologic illness. A relative risk greater than 2 supports causality. Id. at *15.

Special Master Hastings stated that since Sierra had a seizure lasting more than 30 minutes on the day of vaccination, she qualified as a case child under the NCES as having suffered a serious acute neurologic illness within seven days of vaccination. Id. and n.12. Special Master Hastings commented that the records indicate that Sierra's first seizure was afebrile. Id. at *19. The experts in the case however did not focus on the issue of whether her initial seizure or subsequent seizures were febrile or afebrile. Id. However, Special Master Hastings concluded that Sierra's first seizure was febrile even though the records quote the parents as stating there was no fever preceding the event because other records stated she did

have a fever when seizing. Id. When she reached the hospital, the temperature taken was 100.4° F (the same temperature Nicholas had at the hospital in the instant action). Id. When Sierra had her second seizure a month later, she had a very high fever. Id. Special Master Hastings concluded that Sierra's first and second seizures were both febrile, just somewhat febrile at first and very high secondly. Id. at *20. Special Master Hastings continued:

> Finally, I add that I do not mean to indicate that I am persuaded that if Sierra's initial seizure or all of her seizures had been *strictly afebrile*, her neurologic disorder would therefore be excludable from the vaccine-caused category. To the contrary, it would seem logical that since any seizure of greater than 30 minutes in duration would fit within the NCES criteria, even in the case of a totally afebrile seizure, the causation theory should be applied [emphasis in original].

Id.

In Andreu, Enrique Andreu had a brief seizure one day after he received his first DPT vaccination. He would not have been a case child under the NCES. The Federal Circuit could not determine if that seizure were febrile or afebrile. 569 F.3d at 1370, 1372, 1378, 1380 n.8. The Federal Circuit was struck with the close temporal connection between the DPT vaccination and Enrique's first seizure. Id. at 1382. Based on petitioners' expert's theory as related to Enrique's case, the fact that respondent's expert agreed with the theory but not on its applicability to Enrique's case, and the supportive opinions of Enrique's treating doctors, the Federal Circuit ruled in petitioners' favor.

Following the Federal Circuit's decision in Andreu is its decision in Moberly. Molly Moberly had a brief seizure two days after her second DPT. She would not have been a case child under the NCES. The Federal Circuit never discussed whether that first seizure was febrile or afebrile. 592 F.3d at 1318, 1324. The Federal Circuit affirmed the dismissal of the case,

distinguishing Moberly from Andreu (both concerning children with brief seizures within a day or two of DPT vaccination) by stating that, in Andreu, respondent's expert agreed with petitioner's expert's theory of medical causation in general whereas in Moberly, he did not, and, in Andreu, Enrique's treating physicians opined that DPT caused his seizures whereas, in Moberly, they did not and one expressed scepticism of causality. Id. at 1324-25.

The undersigned does not know in the instant action if Nicholas's first seizure, coming within one day of his DPaT vaccination, was febrile or afebrile. His grandmother testified his face was warm, but no one measured his temperature until the emergency medical technicians came and found it normal. Yet, when he arrived at the hospital, it was elevated at 100.4° F, the same temperature as the child in Liable and one point higher than the child in Andreu. Just as the Federal Circuit expressed in Andreu and Special Master Hastings expressed in Liable, it is difficult to know if Nicholas's first seizure was febrile or afebrile. But here, unlike in Andreu, but the same as in Liable, Nicholas would have been a case child in the NCES. (Petitioners in the instant action filed as part of Exhibit 21 an article by the NCES authors summarizing the NCES rather than the NCES itself. This is a distinction without a difference.)

The NCES authors included as case children those who had an acute encephalopathy or a seizure lasting more than 30 minutes during the critical first seven days after DPT vaccination. Nicholas's first seizure was noted as 20 minutes in the first two records discussing it, but another record noted it as lasting 30 minutes. Even if the 20 minutes is accepted as the actual length of duration, 11 days later, still within one month of vaccination,[4] Nicholas had another seizure

[4] The NCES had an exception to the requirement of having a seizure lasting more than 30 minutes within seven days of a DPT vaccination if the child had a seizure within one month of vaccination preceded by a seizure or seizures within the one-week period, and the total added

lasting between 10-15 minutes. Adding the duration of the second seizure to that of the first yields a total of more than 30 minutes, sufficient to designate Nicholas as a case child.

As Special Master French noted in Almeida, in which Lorena also would have been a case child, being a case child is sufficient to prove causation by itself, quoting the Federal Circuit in Knudsen:

> [C]ausation can be found in vaccine cases based on epidemiological evidence and the clinical picture regarding the particular child without detailed medical and scientific exposition on the biological mechanisms.

35 F.3d at 549.

Moreover, in Liable, when Special Master Hastings concluded that whether Sierra had a febrile or afebrile seizure was indeterminable, he stated that even if he had held that the seizure was afebrile, he would still rule for petitioners because Sierra would have been a case child in the NCES because her first seizure lasted 45 minutes. 2000 WL 1517672, at *20 n.21.

In addition, petitioners in the instant action also filed another epidemiological study (the Cody study) in which Nicholas would also have been a case child. The Cody study did not involve the vast populations that the NCES did, although it does deal with DPT, and it did not have a minimum time of a 30-minute seizure for inclusion as the NCES did. Of the nine case children who had seizures after DPT, two of them had afebrile seizures. Cody and his co-authors did not weed out the two children with afebrile seizures from their study but included them in their conclusions. Nicholas satisfies the proof of causation that the Federal Circuit discussed in

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up to 30 minutes and the seizures were pathologically related. The Federal Circuit described this exception in Moberly. 592 F.3d at 1320.

Knudsen not only because he would have been a case child in the NCES, but also because he would have been a case child in the Cody study.

Special Master French mentioned an issue in Almeida which also arises in this case. She stated that the common pediatric practice is not to continue to immunize a child with pertussis vaccine who had had prior seizures following DPT vaccination. 1999 WL 127566, at *17. In the instant action, respondent (the Secretary of the Department of Health and Human Services) filed the Morbidity and Monthly Weekly Report (MMWR) (Tab E) that HHS prints and distributes through the Centers for Disease Control, which explicitly cautions parents and pediatricians to consider seriously whether to vaccinate a child with DPaT in future who has previously had either febrile or afebrile seizures within three days of a prior DPT or DPaT vaccination.

The Federal Rules of Evidence do not apply in the Vaccine Program, but the undersigned does not consider that liberality a prohibition against considering respondent's warning in a public health context to be an admission against interest in litigation. Rule 8(b)(1) of the Vaccine Rules states:

> In receiving evidence, the special master will not be bound by common law or statutory rules of evidence but must consider all relevant and reliable evidence governed by principles of fundamental fairness to both parties.

Rule 8(b)(1) frees the undersigned to include evidence that the Federal Rules of Evidence would exclude. That is why there are so few objections at trial, e.g., to hearsay. Once evidence has been admitted in a vaccine case, as respondent's MMWR exhibit has been (anything filed in this Program is evidence when filed), the undersigned does not consider Rule 8(b)(1) a bar from considering whether indeed respondent has made an admission against interest in this case by

warning parents and pediatricians that afebrile seizures after DPT or DPaT vaccination may contraindicate future DPaT vaccination.

"[A]ll admissions may furnish, as against the [party], the same discrediting inference as that which may be made against a witness in consequence of a prior self-contradiction...." 4 Wigmore on Evidence §1048 (Chadbourn rev. 1972) at 7. At the very least, HHS's public health stance makes its litigative defense that DPaT vaccine does not cause afebrile seizures less credible. If HHS truly believes there is no causal relation between DPaT vaccine and afebrile seizures, it would advise pediatricians and parents that the occurrence of seizures within three days of receiving DPT or DPaT vaccine to weigh the risks and benefits of future DPaT vaccination only if the seizures were febrile, not if they were either febrile or afebrile.

In addition, respondent filed as Tab D an article concerning, inter alia, contraindications to receiving future DPaT vaccinations when the child experienced either febrile or afebrile seizures. Both this article and the MMWR support the opinion that children who receive the acellular form of DPT also experience adverse reactions in the form of seizures. Therefore, although the NCES and the Cody article describe epidemiological results following DPT vaccination, respondent's Tabs D and E confirm that adverse reactions such as afebrile seizures also occur after DPaT vaccinations. Hence, the warning about future DPaT vaccinations.

Respondent's Tab F gives the rate of occurrence of afebrile seizures following DPaT vaccination (citing an article describing reactions to DPaT), which is a smaller rate than that of febrile seizures following DPT vaccination (citing Cody, the same article petitioners filed herein). Respondent, by filing the articles in Tabs D, E, and F, confirms that DPaT vaccine is

considered related to afebrile seizures in the medical literature, a position respondent's expert explicitly denied at the hearing.

Petitioners have proven by preponderant evidence that DPaT can cause a prolonged seizure, either febrile or afebrile, and did so in this case. This satisfies the first two prongs of Althen.

Petitioners have also proven by preponderant evidence that the time interval of one day between Nicholas's DPaT vaccination and his seizure onset was medically appropriate to show causation. Indeed, the Federal Circuit in Andreu called a similar time period between DPT vaccination and Enrique's first seizure a "striking temporal connection." 569 F.3d at 1382. This sastisfies the third Althen prong.

Petitioners have proven causation in fact.

CONCLUSION

Petitioners are entitled to reasonable compensation. The undersigned hopes the parties may reach an amicable settlement. A telephonic status conference will be set soon to discuss how the parties will proceed in resolving damages.

IT IS SO ORDERED.

June 22, 2010
DATE

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