OFFICE OF SPECIAL MASTERS
No. 94-0136V
(Filed: June 5, 1998)

* *		
TIMOTHY McCOLLUM and LEE ANN McCOLLUM as Parents and Natural Guardians of GRANT F. McCOLLUM,	*	
Petitioners,	*	**TO BE PUBLISHED**
v.	*	
SECRETARY OF HEALTH AND HUMAN SERVICES,	*	
Respondent.	*	
* *		

Joel D. Hanig, Poughkeepsie, NY, for petitioners.

Althea W. Davis, Washington, DC, for respondent.

DECISION AND ORDER

MILLMAN, Special Master

On March 7, 1994, Timothy and Lee Ann McCollum, on behalf of their son, Grant F. McCollum (hereinafter "Grant"), filed a petition for compensation under the National Childhood Vaccine Injury Act of 1986[(1)] (hereinafter the "Vaccine Act" or the "Act"). Petitioners have satisfied the requirements for a prima facie case pursuant to 42 U.S.C. § 300aa-11(c) by showing that: (1) they have not previously collected an award or settlement of a civil action for damages arising from the vaccine injury; (2) DPT vaccine was administered to Grant in the United States; and (3) they have incurred $1,000.00 in unreimbursable medical expenses prior to filing the petition.

Petitioners allege that Grant suffered an on-Table residual seizure disorder (hereinafter "RSD") as a

result of his DPT. 42 U.S.C. §§300aa-11(c)(1)(C)(I); 14(a)(I)(D). The court previously held in an Order that petitioners have clearly demonstrated a prima facie case of either on-Table RSD or on-Table significant aggravation.[(2)] Respondent defends by stating that known factors unrelated, agenesis of the corpus callosum and other brain anomalies, are the cause in fact of Grant's seizure disorder. 42 U.S.C. §300aa-13(a)(1)(B) and (2). The court held a hearing in this case on March 25, 1998. Testifying for petitioners were Lee Ann McCollum, Dr. Robin J. Mitnick, and Dr. Bruce Roseman. Testifying for respondent were Dr. Gilbert Vezina and Dr. Robert J. Baumann.

FACTS

Grant was born on April 21, 1992. Med. recs. at Ex. 1 (unpaginated). His birth was complicated by fetal tachycardia. Med. recs. at Ex. 4, p. 7. He had a weak respiratory effort at birth and was given full-flow oxygen for about one minute. Id. His APGARs showed zero for tone at one minute and five minutes. Med. recs. at Ex. 4, p. 4.

Dr. David Goldfarb saw Grant on July 21, 1992 for a well baby check-up, during which time he administered DPT, polio, and hemophilus B influenza vaccines. Med. recs. at Ex. 4, p. 35; Ex. 5, p. 3. Following the vaccinations, Grant had a temperature of 103 degrees. Med. recs. at Ex. 4, p. 35.

On July 22, 1992, Grant was taken to Julia L. Butterfield Hospital Emergency Room due to an apneic episode. Med. recs. at Ex. 4, p. 66. The medical records reveal that he was laughing when his mouth turned blue, his eyes rolled back, and he went limp for about three minutes. Id. He had a temperature of 101 degrees that morning. Med. recs. at Ex. 4, p. 35. However, upon admittance to the hospital, he had a temperature of 99 degrees and he had been eating well. Id.

Grant was then transferred to Vassar Brothers Hospital where he was diagnosed with a seizure disorder. Med. recs. at Ex. 4, pp. 31, 33-34. A history taken reflects that Grant was well until 6:00 p.m. on July 22, 1992 when he seized briefly. Med. recs. at Ex. 4, p. 33. His eyes rolled upward, his extremities became rigid, he twitched, and he arched his back. Id. He had several more seizures from which he recovered promptly. Id. These seizures lasted for approximately fifteen seconds. Id. The medical record further reflects that his temperature was 99.5 degrees and he was alert and in no distress. Med. recs. at Ex. 4, p. 33. His anterior fontanelle was not open, his ears, nose, and throat were normal, his neck was supple, and he was neurologically within normal limits. Id. A brain CT scan showed that Grant had agenesis[(3)] of the corpus callosum[(4)] (hereinafter "ACC"). Id. The hospital prescribed Phenobarbital for his seizures. Med. recs. at Ex. 4, p. 34. He was discharged on July 23, 1992. Id. An EEG performed on August 4, 1992 was abnormal, suggesting encephalopathy. Med. recs. at Part II, p. 185.

From August 22, 1992 to September 9, 1992, Grant was hospitalized at St. Agnes Hospital under the care of Dr. Bruce Roseman, a pediatric neurologist. Med. recs. at Ex. 9, p. 3. An EEG performed on September 2, 1992 was abnormal, with bilateral cerebral dysfunction and occasional potential epileptogenic discharges. Med. recs. at Ex. 9, p. 26.

A vaccine adverse reaction report (VAERS) dated October 18, 1992 stated that Grant had a prolonged seizure disorder (infantile spasms) whose onset was approximately thirty-six hours post-vaccination. Med. recs. at Ex. 5, p. 4. He required a two-week hospitalization and ACTH therapy. Id.

On December 21, 1992, Grant's head circumference was measured at 42.25 centimeters, which put him in the second percentile. Med. recs. at Ex. 5, p. 27.

An EEG performed on June 7, 1994 was abnormal, showing multifocal epileptiform activity, which predominantly affected the left anterior area with an independent focus in the right central parietal

region. Med. recs. at Ex. 37, p. 19. Grant had a PET scan at Children's Hospital of Michigan on June 7, 1994. Med. recs. at Ex. 37, p. 19. Dr. Harry T. Chugani, Director of the Positron Emission Tomography Center, concluded that Grant had an abnormal cerebral glucose metabolism which was typical in ACC. Med. recs. at Ex. 37, p. 17. In addition, he further noted that Grant had hypometabolism in the right temporal cortex and slightly in the left temporal cortex. Id. Dr. Chugani stated that hypometabolism in the cortex seen in ACC and epilepsy most likely represented microdysgenesis. Med. recs. at Ex. 37, pp. 17-18. The overall pattern of glucose metabolism was almost normal in Grant's brain. Med. recs. at Ex. 37, p. 18.

An MRI performed by Dr. Andre Khouri on January 21, 1995 showed ACC with suggestive changes of pachygyri. Med. recs. at Ex. C (unpaginated). On September 25, 1995, Dr. Nikhil Amin, a pediatric pulmonologist, diagnosed Grant with thymic enlargement which may have contributed to respiratory symptoms due to compression of the airway. Med. recs. at Ex. 45, pp. 6-7. He removed part of the thymus during biopsy. Id.

On May 24, 1996, Dr. Robert F. Ward wrote to Dr. Amin about Grant's recurrent pneumonia. Med. recs. at Ex. 45, p. 10. Grant had recurrent nasal drainage which may trigger problems with seizures as well as pneumonia. Id. On November 18, 1996, Dr. Amin wrote Dr. Ann Nunez, stating that Grant was "in a vicious cycle of seizures causing aspiration causing fever which might be contributing to increased seizure activity." Med. recs. at Ex. 45, pp. 15-16.

In June 1997, Dr. Chugani wrote Dr. Roseman to recommend brain resection on the right. Med. recs. at Ex. 40, p. 17. He further noted that Grant had bitemporal abnormalities consistent with his clinical phenotype of speech and language disturbances. Id. An MRI done on July 24, 1996 showed partial ACC. Med. recs. at Ex. 37, p. 69. On November 18, 1997, Dr. Alexa I. Canady performed a right frontoparietal craniotomy, placing three grids over Grant's temporal, parietal, and frontal regions. Med. recs. at Ex. 40, p. 5. The brain looked normal on the surface. Id. On November 25, 1997, Dr. Canady reopened Grant's cranium, removed the subdural grids, and performed an extensive right temporal lobectomy. Med. recs. at Ex. 40, p. 3.

A surgical pathology report dated December 10, 1997 from Dr. William J. Kupsky, a neuropathologist, questioned whether Grant had metabolic or storage disease because the nature of intracellular inclusions was not clear. Med. recs. at Ex. 41 (unpaginated). There were four specimens of tissue. Id. On microscopic analysis, polymorphonuclear leukocytes were evident, and the cortical cytoarchitecture appeared normal. Id. The white matter appeared well-myelinated. Id.

An addendum report to the surgical pathology report, dated January 12, 1998, from Dr. Kupsky, states that on ultrastructural examination, the structures appear moderately well preserved. Med. recs. at Ex. 51, p. 3. No definite storage material was noted in cytoplasm of neurons or glial cells. Id.

TESTIMONY

Lee Ann McCollum testified first for petitioner. Grant weighed almost twelve pounds at birth and his face was big. Tr. at 10. When Grant was a baby, he smiled, cooed, interacted with others, and clasped his hands to the bottle. Id. He had three normal well-baby visits. Id. On July 21, 1992, he received his first DPT vaccination in his right thigh. Tr. at 10-11. Approximately fifteen minutes after the shot, Grant's eyes moved to the right. Tr. at 11. He looked blank. Id. Mrs. McCollum called him and, within seconds, he smiled and looked at her. Id. Later that day, Grant's eyes moved again. Tr. at 12. Mrs. McCollum picked him up and he looked at her and smiled. Id. Grant had a temperature of 102 degrees the evening of his vaccination. Tr. at 21-22. The next day, Mrs. McCollum gave him Tylenol and his temperature decreased. Tr. at 22.

On the evening of July 22, 1992, Grant became rigid, stopped breathing, and his lips turned blue. Tr. at 12-13. A neighbor turned him over to resuscitate him. Tr. at 13. Grant was then taken to Butterfield Hospital. Id. He remained at the hospital for two to three hours during which time he had nine to ten seizures. Id. He was then transferred to Vassar Brothers Hospital and later to St. Agnes Hospital. Tr. at 13-14. When Grant was put on ACTH, his face ballooned in size. Tr. at 14-15. He lost the swelling within six months of going off ACTH. Tr. at 16.

In 1997, Grant had brain resection surgery at Children's Hospital of Michigan. Id. He was seizure-free for sixty-four days after the surgery. Id. However, he had two post-surgery seizures in January 1998.(5) Tr. at 17. Currently, Grant is able to say a few words. Tr. at 18. He is a clumsy walker. Id. Although his gross motor skills are improving, his fine motor skills are poor. Id. He attends a regular elementary school where he is enrolled in a special program for children with disabilities. Id. He receives occupational therapy, physical therapy, and speech therapy.(6) Id. He uses thirty different signs to indicate when he wants to drink, eat, etc. Tr. at 19. He has slight to severe mental retardation. Id. Grant has just started horseback riding lessons. Id. Although he is six years old chronologically, he is two years old developmentally. Tr. at 20.

Dr. Gilbert Vezina, a pediatric neuroradiologist who is board-certified in diagnostic radiology, testified for respondent.(7) Tr. at 28-29. He is Director of Pediatric Neuroradiology at Children's Hospital, Washington, DC. Tr. at 28. He reads MRIs as a regular course of his profession. Tr. at 29-30. Dr. Vezina admitted he is not board-certified in neuroradiology; however, he will be taking the test for board certification. Tr. at 95.

Dr. Vezina testified that all the cases of ACC which he has reviewed have not been merely incidental, but have included macrocrania, craniofacial abnormalities, or seizures. Tr. at 34-35. Based on Grant's MRIs as well as the medical records and reports, Dr. Vezina opined that Grant has ACC and cortical dysplasia involving the parietal and temporal right insula.(8) Tr. at 37-39. Grant's corpus callosum abnormalities were formed between the eighth and sixteenth week of gestation. Tr. at 81. In Dr. Vezina's opinion, the cortical dysplasia of the right parietal area is more likely than not microdysgenesis. Tr. at 78. However, Grant does not have macrocrania or hydrocephalus.(9) Tr. at 47-48.

Dr. Vezina stated that in a normal brain there is symmetry between the left and right side, with a sharp demarcation between the white and gray matter. Tr. at 51-53, 55. When a brain has microdysgenesis, however, there is abnormality in the shape of the cortex because the brain cells fail to migrate, resulting in a blurred junction between the gray and white matter.(10) Tr. at 55. In the Sylvan region of Grant's brain, there are more white matter tracts on the left than on the right, causing asymmetry. Tr. at 53. Based on this, Dr. Vezina believes that Grant has microdysgenesis. Tr. at 54.

Dr. Vezina stated that Grant's pathology report does not diagnose it. Tr. at 56. However, since Grant did not have a post-resection MRI, it is difficult to determine exactly what parts of his brain were removed. Tr. at 57. Moreover, microdysgenesis is difficult to diagnose for numerous reasons. First, the removal of the pieces of brain itself may deform it. Id. Secondly, the pathologists in the instant case did not look at all the tissue. Tr. at 58. Dr. Vezina further noted that microdysgenesis is truly a microscopic diagnosis which is not detectable by conventional MRI imaging. Tr. at 55.

Dr. Vezina testified that Grant's cortex appeared thicker than normal due to the blurring of the demarcation between the grey and white matter. Tr. at 63. Although Grant may have pachygyria, Dr. Vezina believes that he more likely has a dysplastic cortex. Tr. at 64-65. He has only one azygous (unpaired) cerebral artery rather than the normal two. Tr. at 67. However, a normal individual can have

only one azygous cerebral artery. Tr. at 75. While Grant has a cortical abnormality, Dr. Vezina is not convinced that he has holoprosencephaly although that was his initial opinion.(11) Tr. at 67-69. Grant also has maldevelopment of the midline structures. Tr. at 75.

Dr. Vezina further testified that Grant's eyes are a little closer together than normal. Tr. at 71. However, he could not conclude whether the distance between Grant's eyes was normal or due to hypotelorism. Id. Although Grant's orbits in his eyes may be hypoteloric, he has no other eye abnormalities. Tr. at 110-12. His pituitary gland is hypoplastic, but it is difficult to attach clinical significance to this since Grant is not growth retarded. Tr. at 115. Dr. Vezina stated that Grant's hippocampal structure is not evident which may be due to dysgenesis. Tr. at 120-21. His cortical cytoarchitecture appears normal. Tr. at 121. One cannot detect gyrational defects on gross examination since it appears microscopically if at all. Tr. at 126. Grant's right posterior ventricle is larger than his left which indicates that the right side of his brain is underdeveloped. Tr. at 128.

Dr. Vezina stated that ACC itself is quite rare. Tr. at 77. Most patients with microdysgenesis do not have ACC. Tr. at 76. However, fifty percent of individuals with ACC have a seizure disorder and many have migrational disorders. Id. Dr. Vezina believes that Grant has complete, rather than partial, ACC. Tr. at 127-28. Dr. Vezina identified the structure seen on Image 8 of Grant's MRI as the midline commissure.(12) Tr. at 79. The commissure is made up of white matter structures that interconnect the fornix.(13) Tr. at 79-80.

Dr. Vezina testified that PET scanning is a method by which metabolic activity in cells can be assessed. Tr. at 138. He stated that Grant's June 7, 1994 PET scan showed a normal cerebral glucose metabolism for a patient with ACC. Tr. at 86. This PET scan also reflected that Grant had hypometabolism in the right and left temporal cortex. Id. According to Dr. Harry Chugani, areas of hypometabolism in children with ACC is caused by microdysgenesis. Tr. at 138-39. Microdysgenetic tissue is hypometabolic. Tr. at 144. Dr. Vezina could not say if Grant's hypometabolism occurred pre- or post-DPT; no one knows if DPT causes hypometabolism. Tr. at 139, 146. Grant's hypometabolism was probably of congenital origin. Tr. at 141-42.

Dr. Vezina testified that Grant's January 21, 1995 MRI reflects that the right temporal part of his brain was the source of epileptic discharge and microdysgenesis. Tr. at 86. The MRI shows marked thickening of the cortex in the right parietal region and frontal lobes, suggestive of pachygyri. Tr. at 92. He further noted that Grant's July 23, 1996 PET scan is consistent with the June 7, 1994 PET scan, similarly finding that the right temporal area of the brain is hypometabolic. Tr. at 88.

Dr. Vezina stated that Grant was not microcephalic at birth, one month, or three months. Tr. at 100-01. He stated that Grant's head circumference probably decreased after eight months because he was in the fifth percentile which is borderline microcephalic. Tr. at 102.

Dr. Robert Baumann, who is board-certified in pediatrics and in neurology with special competence in child neurology, testified next for respondent. Tr. at 153-54. Dr. Baumann opined that Grant's brain was abnormal from in utero. Tr. at 157. In his opinion, Grant's seizures and mental retardation were caused by the congenital chronic encephalopathy with which he was born. Tr. at 157-58. His striking hypotonia at birth evidences that he was abnormal from birth. Tr. at 158. Grant had zero APGARs for tone at both one and five minutes of life.(14) Tr. at 158. While the maximum score is two for tonicity, a score of zero is uncommon. Tr. at 158-59. According to Dr. Baumann, Grant has microdysgenesis which presented itself before he was born and resulted in his seizures. Tr. at 189-90. He concluded that Grant's seizures came from an abnormal area of his cortex because his seizures have ended since his resection. Tr. at 164-65. Grant has hypometabolism in the left temporal lobe. Tr. at 224. His hypometabolism and

seizures indicate that he has microdysgenesis. Tr. at 239. Dr. Baumann stated that Grant would have had seizures even without receiving DPT. Tr. at 172. He further noted that DPT did not significantly aggravate Grant's seizure disorder or prior condition. Id.

Dr. Baumann testified that Grant's brain is anomalous according to his MRI. Tr. at 159. He thinks Grant has anomalies throughout his brain rather than just on the right side. Tr. at 224-25. ACC is closely associated with other anomalies. Tr. at 159-60. Since ACC is exceedingly uncommon by itself, one looks for other abnormalities when one finds ACC. Tr. at 191-92. These other abnormalities, not ACC, are what cause seizures. Tr. at 194-95. Even if Grant's ACC were partial, rather than complete, he could have other abnormalities in his brain. Tr. at 161-62.

Dr. Baumann noted that Grant is microcephalic. Tr. at 176. His head circumference at birth was in the 98th percentile. Tr. at 212. His brain grew from birth to three months. Id. At twelve months, he was microcephalic. Tr. at 214. He had an abnormal pattern of head growth. Tr. at 219. From the fourth to the eighth months, he had flat-line growth. Tr. at 218. However, Grant's length and weight continued to be normal. Tr. at 229-30.

Grant's brain does not show storage disease. Tr. at 186-87. The pathological report after his resection raises the issue of cortical anomaly in his hippocampus. Tr. at 187-88. Dr. Baumann testified that the results of Grant's pathological report of his resection would have been different if a large section had been taken. Tr. at 232, 236. The pathologists did not see microdysgenesis in the section they took because they cut only a representative section for examination. Tr. at 237. In addition, it is uncommon to detect microdysgenesis. Id.

Cortical dysplasia or dysgenesis also causes seizures.[(15)] Tr. at 162. Dr. Baumann testified that Grant would have seized at three months without DPT. Tr. at 241. Although Grant's 103 degree fever may have made a seizure more likely, the fever did not alter the underlying course of events. Tr. at 163. Although DPT was coincidental to his seizure, fever could worsen the seizures. Tr. at 241-42. When asked if a child would be in better condition if his seizure onset were delayed, Dr. Baumann responded that most seizures do not injure the brain. Tr. at 244. However, patients who have onset of infantile myoclonic seizures at a young age have a worse prognosis than patients whose onset occurs at an older age. Tr. at 244-45. This is because early onset reflects a worse encephalopathy, meaning that the underlying abnormality is more severe. Id.

Dr. Robin J. Mitnick, a board-certified neuroradiologist, testified for petitioners. Tr. at 250. She has a certificate with an added qualification in neuroradiology. Tr. at 250-51. Dr. Mitnick is Associate Professor of Clinical Radiology at Albert Einstein School of Medicine. Tr. at 251. One-fifth to one-third of her practice is pediatric radiology. Tr. at 252.

Dr. Mitnick stated that Grant has a small amount of pituitary tissue; however, the significance of that is unclear. Tr. at 256. Dr. Mitnick noted that ninety percent of Grant's corpus callosum is missing. Tr. at 294. She did not see much of a difference between the left and right sides of Grant's insula. Tr. at 257. She felt that Grant's head was slightly rotated when the MRIs were performed. Tr. at 257-58. This is what Dr. Vezina interpreted to be asymmetry. Grant has an azygous cerebral artery which is an uncommon finding. Tr. at 258. She has found this condition in 3 out of 400 angiograms that she has seen. Id.

Dr. Mitnick did not see any abnormal signal in Grant's white matter. Tr. at 268. There was some signal in the right parietal region; however, this section is the last to myelinate; thus, increased signal can be present into adulthood. Id. There was no evidence of hypotelorism. Id. Grant's overall cranium may be

small compared to his face. Tr. at 269.

Dr. Mitnick did not see cortical dysplasia on Grant's MRI. Tr. at 270. If cortical dysplasia were present, she would have seen abnormal thickening of the brain. Tr. at 273. Dr. Mitnick found neither abnormality in the formation of Grant's cortex nor blurring of the demarcation between his white and grey matter. Tr. at 274-75. In her opinion, Grant's ACC is isolated. Tr. at 280. She saw another case of isolated ACC more than a year ago. Id.

Hypometabolism can indicate numerous conditions other than microdysgenesis, such as a tumor, scarring, or head trauma. Tr. at 285-87. Any insult to the brain can cause hypometabolism. Tr. at 287. It does not relate specifically to DPT. Tr. at 287. Some people with ACC develop seizures. Tr. at 288-89.

One does not do epileptic surgery on patients who have only ACC. Tr. at 294. Abnormalities in electrical impulse on Grant's PET scan led to his resection. Tr. at 298. She did not find evidence of pachygyri in Grant's brain or evidence of injury to his brain. Tr. at 301-02. One may or may not see evidence of epilepsy on MRI. Tr. at 302.

Dr. Bruce Roseman, Grant's pediatric neurologist, who is board-certified in pediatrics and in neurology with special competence in child neurology, testified next for petitioners. Tr. at 308. He is Chief of Pediatric Neurology at New York Medical College. Id. He has written an article on the association between ACC and kidney anomalies. Tr. At 308-09. He has treated children with ACC for the past twenty years. Tr. at 309-310.

Dr. Roseman testified that incidental ACC is rare. Tr. at 310. In cases of isolated ACC, approximately forty-five percent of people with ACC have seizures. Tr. at 354. He saw Grant when he was three and one-half months old. Id. For his first three months, Grant developed normally. Id. His head circumference was in the 75th percentile at birth. Tr. at 314. However, after his DPT, he was no longer normal. Tr. at 314-15. He stopped developing at three months and no longer rolling over or interacting. Tr. at 314-15. In Dr. Roseman's opinion, DPT caused Grant's seizures. Tr. at 313. DPT is an insult which can cause brain damage and seizure. Tr. at 336. According to Dr. Roseman, Grant would not have had psychomotor retardation or seizures if he had not received DPT. Tr. at 353-54. Dr. Roseman stated that Grant had myoclonic infantile epilepsy. Tr. at 315-16. The onset of the condition varies. Tr. at 316. The earlier one seizes, the worse one is. Tr. at 316.

Although Grant is currently six years old, he functions at a two-year-old level. Tr. at 330. He is mentally retarded. Id. He can scribble and is starting to use a spoon, but he is a clumsy walker. Tr. at 332. His head circumference has grown slowly. Tr. at 333. Grant is still seizing. Tr. at 317. Right before his surgery, he would drop to the floor with akinetic seizures. Tr. at 328. In Dr. Roseman's opinion, Grant's current condition is a sequela of his vaccine injury. Id.

Grant had multifocal areas on PET scan and EEG. Tr. at 318. He has had no growth or thyroid problems despite the size of his pituitary gland. Tr. at 320. It did not surprise Dr. Roseman that Grant's midline defects occurred together; however, they did not cause his seizures. Tr. at 320. Grant did not have microdysgenesis on his pathology report after his resection. Tr. at 325-35. Dr. Harry Chugani saw sections of Grant's brain and told Dr. Roseman that Grant had a normal brain. Tr. at 344-45. Prior to talking to Dr. Chugani, Dr. Roseman thought Grant had pachygyri. Tr. at 355. However, his opinion changed once Dr. Chugani examined Grant's brain sections and determined that his brain was normal. Id. Dr. Roseman thinks that Grant has complete, not partial, ACC. Tr. at 340. PET scans were used to look for areas of focality in Grant's brain so that a resection could be performed. Tr. at 342. Children with severe congenital anomalies have problems right from birth. Tr. at 352.

OTHER EVIDENTIARY MATERIAL

Respondent submitted an excerpt from Kenneth Swaiman's Pediatric Neurology - Principles and Practice, which states that, "[a]bsence of the corpus callosum alone may be accompanied by very mild or subtle clinical manifestations . . . Normal intelligence is not unusual . . . It has also been associated with approximately 25 different syndromes...."(16)

Respondent next submitted an excerpt from Harvey B. Sarnat's Cerebral Dysgenesis - Embryology and Clinical Expression, which states that "[c]omplete or partial absence of the corpus callosum is a common cerebral malformation and often has only subtle clinical expression."(17) "Small focal cortical dysplasias probably explain the seizure disorders in some children with callosal agenesis."(18) Furthermore, "[m]ental retardation is common but not universal . . . Learning disabilities, mental retardation, seizures, and other neurological manifestations are present in more severe cases. Some of these features probably are more related to additional focal cortical dysplasias than to the callosal agenesis itself."(19)

Respondent also submitted an article on Aicardi's syndrome (AS) which notes that, "[m]ental retardation, seizure disorder, and electrographic abnormalities in AS may be related to these cortical developmental abnormalities rather than to the callosal defect per se; for example, epilepsy may be absent in patients with isolated callosal agenesis while cortical migration defects seen by MRI are often associated with seizure disorders."(20)

Another article respondent submitted states that, "it is suspected that poor seizure control leads to progressive brain damage."(21) "All patients [with diffuse cortical dysplasia] presented in the first few months of life with hypotonia . . . Four of the five had severe microcephaly . . . Only one had a frank seizure disorder, although three had infantile spasms."(22) The authors further noted that "[t]he cerebral cortex in all of these patients showed normal to increased cortical thickness and an irregular, bumpy gyral pattern with shallow sulci. All had diminished underlying cerebral hemispheric white matter."(23)

Dr. Vezina co-authored an article that respondent submitted. This article discusses twelve pediatric patients with bilateral perisylvian syndrome (PCBPS).(24) The authors noted that epilepsy is not a constant feature in children and varies in type and severity.(25) The lesions in PCBPS are caused by a cerebrovascular accident but may also result from destructive viral encephalitis.(26) On MRI, the patients had bilateral abnormally thickened parietal parasylvian cortexes consistent with bilateral parietal polymicrogyria.(27)

Finally, respondent submitted an article co-authored by Dr. Chugani.(28) The authors state that, "[a]lthough it is sometimes an asymptomatic and incidental finding, ACC is frequently (in about 42% of patients) associated with epilepsy."(29) The authors also found a correlation between cortical hypometabolism on PET scan and the presence of seizures in ACC patients.(30)

DISCUSSION

Since petitioners have made a prima facie case of on-Table RSD, respondent has the burden of proving by a causation-in-fact analysis that a known factor unrelated caused Grant's seizures and current condition, rebutting the statutory presumption that DPT is the cause.

To satisfy its burden of proving causation in fact, respondent must offer "proof of a logical sequence of cause and effect showing that [the factor unrelated] was the reason for the injury. A reputable medical or scientific explanation must support this logical sequence of cause and effect." See Grant v. Secretary, HHS, 956 F.2d 1144, 1148 (Fed. Cir. 1992); Agarwsal v. Secretary, HHS, 33 Fed. Cl. 482, 487 (1995); see also Knudsen v. Secretary, HHS, 35 F.3d 543, 548 (Fed. Cir. 1994); *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 509 U.S. 579 (1993).

It is undisputed that Grant has ACC; however, petitioners believe it is partial while respondent believes it is complete. Respondent's defense rests on the thesis that Grant has ACC accompanied by cortical dysplasia or microdysgenesis. Respondent posits that Grant must have these anomalies because he has a seizure disorder and he is mentally retarded. However, no doctor has found cortical dysplasia or identified microdysgenesis through pathological analysis of Grant's resected brain tissue. Nevertheless, respondent asserts that, even though Grant's seizure onset was on-Table, it was merely coincidental because he would have seized anyway due to his congenital anomalies.

Petitioners assert that Grant's ACC is clinically insignificant and that respondent has failed to show that any other defect caused his injury, although Dr. Mitnick admitted that Grant would not have had brain resection for isolated ACC. Dr. Mitnick testified, contrary to Dr. Vezina, that Grant's MRIs fail to show blurred demarcation between the white and gray matter of his brain or any abnormality other than the ACC.[(31)]

The neuroradiologic testimony was of little help to the undersigned because it was diametrically opposed. Whatever Dr. Vezina said, Dr. Mitnick countered. The experts themselves testified that neuroradiologists frequently disagree with each other.

In light of the complexity of the neuroradiologists' testimony, and the impossibility of the special master's knowing who, if either, is more accurate, the court holds that their testimony is in equipoise which means respondent has not met its burden through Dr. Vezina's testimony.

The court now turns to the testimony of the pediatric neurologists to determine whether or not respondent has met its burden with the testimony of Dr. Baumann. Dr. Roseman is an unusual witness because he is Grant's treating pediatric neurologist, involved since Grant was three and one-half months old. Dr. Roseman is firmly convinced that DPT vaccine caused Grant's seizure disorder.

Dr. Roseman previously entertained the possibility that Grant had other cortical anomalies, i.e., pachygyri, besides ACC; however, once Dr. Chugani saw sections of Grant's brain and found them to be normal, Dr. Roseman changed his opinion. Dr. Roseman could ascribe no preexisting reason for Grant's condition. Significantly, he testified that the earlier a child has infantile myoclonic epilepsy, the worse his condition will be. This is contrary to Dr. Baumann's testimony that seizures do not injure the brain. It would be strange indeed to have a vaccine Table injury for which there could not be any damage, i.e., RSD.

It is inconsistent for Dr. Baumann to concede that the DPT-caused fever made onset of Grant's seizures more likely while also opining that the onset was coincidental and would have occurred without DPT vaccine. In addition, the medical articles that respondent submitted uniformly indicate that the cause of seizures in those with ACC are the brain anomalies which accompany ACC. In the case of isolated ACC, this clinical presentation is not found.

Respondent has the burden of proving that a known factor unrelated caused Grant's seizures. However, the evidence respondent has produced does not actually show what Grant has, i.e., cortical dysplasia,

microdysgenesis, or something else. MRIs, EEGs, and PET scans, and resection on both gross and microscopic examination, have failed to reflect cortical dysplasia and microdysgenesis. To fill this gap, respondent posits that Grant must have something other than ACC because he has seizures and developmental delay. This, however, is not a legally tenable argument.

The instant case is akin to two recent cases, Spence v. Secretary, HHS, No. 95-57V, 1998 WL 211909 (Fed. Cl. Spec. Mstr. April 13, 1998), and Connor v. Secretary, HHS, No. 90-3327V (to be published), decided by the undersigned. In those cases, respondent presented a known factor unrelated defense premised on the theory that since the vaccinee has certain symptoms (seizures), the vaccinee must have a preexisting condition that caused it.

In Spence, the vaccinee, Sarah Spence, has trisomy 5p. Although no one knew what her genetic aberration would cause, she did have an on-Table seizure disorder. Respondent asserted that the pre-existing trisomy 5p must be the cause of her seizures because she had seizures. This court held that such reasoning, while possibly tenable medically, is legally insufficient to defeat the statutory presumption of causation.

In Connor, the vaccinee, Charles Connor, has an undefined metabolic disorder. Under the statute, respondent need not identify what metabolic disorder petitioner has to prove a known factor unrelated. But, respondent must prove what petitioner's metabolic disorder would cause in fact in order to defeat the statutory presumption that MMR caused the seizure disorder. In Connor, respondent similarly focused on the vaccinee's symptoms and posited that the undefined metabolic disorder must have caused them because he had them. Again, this was legally insufficient to defeat the statutory presumption. To say in the instant case that Grant must have cortical dysplasia or microdysgenesis because he has a seizure disorder and psychomotor retardation is again to proceed backwards from the injury to the cause as respondent attempted to do in Spence and Connor.

In the instant case, the degree of Grant's brain anomalies is hotly disputed. Dr. Roseman and Dr. Chugani believe that Grant has a normal brain besides the ACC and his hypoplastic pituitary and azygous cerebral artery. According to Dr. Roseman, forty-five percent of individuals with ACC will have seizures; however, the date of onset is unknown. However, this statistic does not make it more likely than not that Grant would seize. Although no one knows when Grant would have seized absent DPT, it is clear when he did seize with DPT.

Dr. Mitnick admitted that epileptic patients with incidental ACC do not undergo resection, as Grant did. But no one in this hearing could provide proof of the microdysgenesis or cortical dysplasia that respondent tried to indicate cirumstantially was there. The court cannot leap over the presumption to find these defects in the absence of direct proof.

This situation can be likened to a causation-in-fact case in which petitioners attempt to prove that DPT caused a seizure disorder merely by stating that since a seizure disorder exists, DPT caused it. Respondent has repeatedly and rightly objected to the legal sufficiency of such evidentiary attempts. Respondent should similarly recognize the inadequacy of its own evidence in cases in which the preexisting illness' effects are unknown (Spence) or the illness itself is undeterminable (Connor and the instant action).

There is not much point in discussing significant aggravation because it is unclear from the evidence what exactly DPT would have aggravated in Grant. Even if, arguendo, Grant's ACC would have caused him to seize, the fever from the DPT prompted the onset. However, this is merely dictum. Petitioners have satisfied their burden of proving an on-Table RSD. Respondent has not satisfied its burden of

proving that a known factor unrelated caused Grant's seizure disorder and mental retardation.

CONCLUSION

Petitioners are entitled to a program award. The court hopes that the parties will be able to settle the damages portion of this case and will schedule a status conference in aid of determining damages or encouraging settlement.

IT IS SO ORDERED.

DATE: _____ _____

Laura D. Millman

Special Master

1. The National Vaccine Injury Compensation Program comprises Part 2 of the National Childhood Vaccine Injury Act of 1986, 42 U.S.C.A. §300aa-1 et seq. (West 1991), as amended by Title II of the Health Information, Health Promotion, and Vaccine Injury Compensation Amendments of November 26, 1991 (105 Stat. 1102). For convenience, further references will be to the relevant subsection of 42 U.S.C.A. § 300aa.

2. See Order dated February 26, 1998

3. "Agenesis" is "absence of an organ; frequently used to designate such absence resulting from failure of appearance of the primordium of an organ in embryonic development...." Dorland's Illustrated Medical Dictionary, 37 (27th ed. 1988).

4. "Corpus callosum" is "an arched mass of white matter, found in the depths of the longitudinal fissure, comprised of transverse fibers connecting the cerebral hemispheres and consisting, from the anterior to the posterior, of rostrum, genu, trunk, and splenium...." Id. at 384.

5. Grant experienced a tonic seizure on January 1, 1998 which lasted for fifteen minutes. Tr. at 17. He received Valium for this seizure. Id. On January 20, 1998, Grant had a partial seizure which lasted five

to ten minutes. Id. After this seizure, he was put on 1500 mg. of Vigabatran and 50 mg. of Dilantin. Id.

6. He receives these therapies a total of five times per week. Tr. at 18. Three times per week, he receives therapy separately while two times per week, he receives therapy in a group. Id.

7. Since petitioners had a prima facie case of on-Table RSD or, in the alternative, of on-Table significant aggravation, the burden of proving a known factor unrelated caused Grant's condition passed to respondent and, therefore, respondent's experts testified first.

8. Insula is the portion of the brain along the lateral surface which is bordered by the frontal, temporal, and parietal lobes. Tr. at 38-39. The insula is located in front of the ear and is also referred to as the "Sylvan region" because the Sylvan fissure is there. Id.

9. Macrocrania is a cranium that is too large, meaning that there is either too much brain tissue or hydrocephalus. Tr. at 46. Hydrocephalus is an accumulation of cerebrospinal fluid within the skull. Tr. at 46-47.

10. Microdysgenesis occurs when the cells are directed to migrate incorrectly within the brain tissue as the fetus develops. Tr. at 141. Neuronal migration starts at the eighth week and goes to the twenty-fifth or twenty-sixth week. Id.

11. Dr. Vezina testified that many patients with holoprosencephaly do have abnormalities of the corpus callosum; however, it is rare for these patients to have complete agenesis of the structure. Tr. at 74-75.

12. As discussed infra, Dr. Mitnick testified that Grant has partial ACC rather than complete ACC. Tr. at 255-56.

13. The fornix are structures that extend near the midline on either side of the brain. Tr. at 80.

14. Having an AGPAR score of zero for tone can be caused by asphyxiation, meconium aspiration, difficulty in making the transition from the uterus, and the mother's sedation. Tr. at 199. Babies whose brains are abnormal have trouble making the transition from the uterus. Tr. at 200.

15. Cortical dysgenesis is a larger category which encompasses cortical dysplasia. Tr. at 163.

16. Swaiman, K.F., Pediatric Neurology - Principles and Practice, 2d ed., ch. 26, "Congenital Structural Defects," by Stephen Ashwal 421, 441-42 (R. Ex. F).

17. Sarnat, Harvey B., Cerebral Dysgenesis, Embryology, and Clinical Expression, 215 (1992)(R. Ex. G).

18. Id. at 222.

19. Id. at 225.

20. Smith, C.D., et al., "Magnetic Resonance Imaging of the Brain in Aicardi's Syndrome," 6 J. Neuroimaging 214, 219 (1996)(R. Ex. H). Dr. Baumann is the last author on this paper.

21. Barkovich, A.J. & Kjos, B.O., "Nonlissencephalic Cortical Dysplasias: Correlation of Imaging Findings with Clinical Deficits," 13 Amer. J. Neuroradiology 95, 102 (1992)(R. Ex. I).

22. Barkovich, A.J. & Kjos, B.O., "Nonlissencephalic Cortical Dysplasias: Correlation of Imaging Findings with Clinical Deficits," 13 Amer. J. Neuroradiology 95, 96 (1992)(R. Ex. I).

23. Id. at 97-98.

24. Gropman, A.L., et al.,"Pediatric Congenital Bilateral Perisylvian Syndrome (PCBPS): Clinical and MRI Features in 12 Patients."(unpaginated)(R. Ex. J). This source was submitted to the court in manuscript form and was submitted for publication to Neurology in 1997.

25. Id.

26. Id.

27. Id.

28. Khanna, S., et al.,"Corpus Callosum Agenesis and Epilepsy: PET Findings," 10 Ped. Neur. 221, 227 (1994)(P. Ex. L).

29. Id. at 224.

30. Id. at 226.

31. Grant does, however, have hypometabolism in his brain as well as a small pituitary gland without apparent effect.