In the United States Court of Federal Claims

No. 06-287V
March 19, 2007
To be Published

WILLIAM STEWART and LEONOR SOTELO, on Behalf of WILLIAM STEWART- SOTELO, a Minor,	*	
Petitioners,	*	
v.	*	Entitlement; acute cerebellar ataxia caused by hepatitis A vaccine
SECRETARY OF THE DEPARTMENT OF HEALTH AND HUMAN SERVICES,	*	
Respondent.	*	

Richard Gage, Cheyenne, WY, for petitioners.
Robin L. Brodrick, Washington, DC, for respondent.

MILLMAN, Special Master

RULING ON ENTITLEMENT[1]

[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 ruling is filed, petitioners have 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.

Petitioners filed a petition on April 10, 2006 under the National Childhood Vaccine Injury Act, 42 U.S.C. §300aa-10 et seq., alleging that their son William Stewart-Sotelo (hereinafter "Will") experienced cerebellar ataxia after receiving hepatitis A vaccine.

A hearing was held on December 1, 2006. Testifying for petitioners were William Stewart (Will's father) and Dr. Donald H. Marks. Testifying for respondent was Dr. John T. MacDonald.

FACTS

Will was born on March 26, 2000. Med. recs. at Ex. 1, p. 1.

On September 8, 2000, Will saw his pediatrician with an upper respiratory infection and a possible ear infection. Med. recs. at Ex. 4, p. 38.

On November 6, 2000, Will saw Dr. Rebecca Mouser for an upper respiratory infection, diarrhea, and otitis media. Med. recs. at Ex. 4, p. 35. Dr. Mouser diagnosed acute gastroenteritis. Med. recs. at Ex. 4, p. 36.

On January 8, 2001, Will saw Dr. Mitchell for ear pain. He had had fever. His father had had a cold. Will was very fussy. Med. recs. at Ex. 4, p. 33. Will's right tympanic membrane was erythematous and purulent. Dr. Mitchell diagnosed right otitis media and upper respiratory infection. Med. recs. at Ex. 4, p. 34.

On January 28, 2001, Will's mother called the pediatrician because of suspected right otitis media. Med. recs. at Ex. 33, p. 169. His right tympanic membrane was bulging and erythematous. Med. recs. at Ex. 4, p. 27.

On February 1, 2001, Will's mother phoned the pediatrician that Will's ear infection was not improved. Med. recs. at Ex. 4, p. 30. He had been on Amoxicillin for five days. Med. recs. at Ex. 4, p. 31.

On February 9, 2001, Will went to his pediatrician to have his ears checked. He had congestion and a cough. Med. recs. at Ex. 4, p. 29. His right tympanic membrane was red and bulging. The doctor placed him on antibiotics and asked Will's mother to wait 20 minutes for a possible reaction to the antibiotic. *Id.*

On February 15, 2001, Will returned to his pediatrician to have his ears rechecked. Med. recs. at Ex. 4, p. 28.

On February 20, 2001, Will saw his pediatrician to check his ears. He was teething. Med. recs. at Ex. 4, p. 25.

On March 6, 2001, Will had audiologic tests because of recurrent otitis media. He had recently completed antibiotic treatment. Med. recs. at Ex. 33, p. 202. Dr. Kent P. Jones wrote that Will had his first ear infection in January and was treated with Amoxicillin. Med. recs. at Ex. 33, p. 207. He continued to be fussy and still had dull tympanic membranes. On February 1, 2001, he was put on Cefzil. He was all right for a few days, but started getting very fussy. The eardrum was bulging. He was put on Rocephin and Zithromax. Again the symptoms calmed down, but on recheck, there was otitis media about two weeks previously. He was put on Augmentin. He was acting normally for about a week. The drawn out episode of otitis media seemed to have cleared. *Id.*

On March 19, 2001, Will saw his pediatrician because of an ear infection. Med. recs. at Ex. 4, p. 23. The diagnosis was teething. Med. recs. at Ex. 4, p. 24.

On May 11, 2001, Will's mother called the pediatrician because of green drainage in the left eye. Med. recs. at Ex. 33, p. 163.

On May 23, 2001, Will saw Dr. Alan White because of yellow eye drainage. Med. recs. at Ex. 4, p. 19. He had had this for two weeks and associated congestion. Dr. White diagnosed conjunctivitis. Med. recs. at Ex. 4, p. 20.

On June 2, 2001, Will saw his pediatrician Dr. Bryant because of an ear infection. Med. recs. at Ex. 4, p. 17.

On July 3, 2001, Will saw his pediatrician because of fever. Med. recs. at Ex. 4, p. 16.

On July 5, 2001, Will saw his pediatrician for irritability and fever. He was diagnosed with otitis media and upper respiratory infection. Med. recs. at Ex. 33, p. 148.

On July 17, 2001, Will saw the triage nurse and Dr. Lingle because he was pulling at his ear and fussy. Med. recs. at Ex. 4, p. 12. He was teething. Med. recs. at Ex. 4, p. 13.

On September 12, 2001, Will saw the triage nurse because he was pulling on his ears. He had been fussy for two days. Med. recs. at Ex. 4, p. 9. The diagnosis was probable teething. Med. recs. at Ex. 4, p. 10.

On January 22, 2002, Will saw Dr. Maken because of decreased appetite, fever, vomiting, and loose stools. Dr. Maken diagnosed an upper respiratory infection. Med. recs. at Ex. 4, p. 8.

On January 23, 2002, Will saw the triage nurse for a check-up of his ear and fever. Med. recs. at Ex. 4, p. 7.

On February 15, 2002, Will saw Dr. Elizabeth Knapp, complaining of diarrhea and vomiting. Med. recs. at Ex. 4, p. 6.

On March 3, 2002, Will's mother phoned the pediatrician because Will had yellow eye drainage and matting. He was afebrile. Med. recs. at Ex. 33, p. 144.

On March 26, 2002, Will saw Dr. William F. Getman for his 24-month well-baby check-up. Med. recs. at Ex. 5, p. 6. He received hepatitis A vaccine. *Id.* Dr. Getman gave Will a physical examination which was within normal. His ears were normal. His chest was clear to auscultation (CTA). The pupils of his eyes were equal and reactive to light (PEARL). *Id.* Dr. Getman concluded that Will was a well child and recommended that he return in one year at the age of three. *Id.*

On Friday, March 29, 2002, at 11:10 a.m., a triage nurse saw Will. Med. recs. at Ex. 33, p. 140. His general appearance was normal. *Id.* At 10:54 at an unknown date, there was a phone call about a possible otitis media. *Id.*

On Sunday, March 31, 2002, Will saw one of his pediatricians. He had mild upper respiratory symptoms but no fever. He was unsteady, falling a lot in the past two days (putting onset on Friday, March 29th.) Med. recs. at Ex. 33, p. 141. His right and left tympanic membranes were retracted. The doctor diagnosed an upper respiratory infection. *Id.* Will ran well but often staggered with walking. *Id.*

On April 1, 2002, Will saw Dr. Coldwater, one of his pediatricians. He was unbalanced, had a runny nose, his right ear had fluid, his throat and lungs were clear, but he was very ataxic and had tremors. When sitting, he started to rotate. Med. recs. at Ex. 33, p. 139. Will's tremor and imbalance started on March 28, 2002. *Id.* Dr. Coldwater's impression was sudden onset ataxia/tremor and he recommended that Will see Dr. Kane. *Id.*

On April 1, 2002, Will was brought to Seton Emergency Department (ED). The history Will's parents gave was that he had a five- to six-day history of abnormal walking and was unsteady. That morning, he awoke and was tremulous. He attempted to grasp a glass and was shaking so badly, he could not hold it. He had viral upper respiratory symptoms for about a week, but no fever. Med. recs. at Ex. 7, p. 1. A review of Will's ear, nose, and throat showed he had nasal congestion. *Id.* Will had staggering ataxia and fell left and right. He also had bilateral intentional tremor. Med. recs. at Ex. 7, p. 2. The ED Record states that he had an unsteady gait and trembling since Tuesday. Med. recs. at Ex. 7, p. 4. (Tuesday was March 26, 2002.)

On April 1, 2002, at Children's Hospital, Will saw Dr. Jeffrey Kane, a pediatric neurologist. Med. recs. at Ex. 8, p. 1. The history Will's parents gave was that Will had been completely healthy. He received hepatitis A vaccine the prior Tuesday. That night, he stumbled several times, but his parents thought nothing further about it. He had a concurrent upper respiratory infection with green nasal discharge, but no fever. On Friday (March 29, 2002), he developed some unsteadiness and increased falling again. This progressed over the weekend and the parents brought him to their pediatrician on Sunday, March 31, 2002, for evaluation. The morning of April 1st, he woke and was significantly more impaired than on prior days. He stumbled after every few steps. He had tremors in his hand whenever he reached for an object. This improved significantly over the prior two to three hours, but still persisted. Dr. Kane spoke with Dr. Coldwater, who was covering for Dr. Getman that morning, and on the basis of this history, they decided to have an MRI done of Will's brain to rule out a tumor. *Id.*

Will had not had any sick contacts. Dr. Kane's impression was progressive ataxia over the prior four days (which would put onset on Friday, March 29th). He thought Will had postinfectious cerebellitis. *Id.*

On April 4, 2002, Will had an MRI of his brain done, which was normal except for some opacification of the paranasal sinuses and right mastoids. Med. recs. at Ex. 9, p. 20.

On April 8, 2002, Dr. Kane wrote a letter to Dr. Getman, having seen Will that day. Med. recs. at Ex. 10, p. 1. His parents said Will was getting a little worse. Will became unsteady on his feet and occasionally had tremors when reaching for objects. These symptoms waxed and waned. *Id.* Given Will's normal head MRI, Dr. Kane thought that he had acute cerebellar ataxia on a postinfectious basis. Med. recs. at Ex. 10, p. 2.

On April 13, 2002, at 9:00 p.m., Will's mother phoned the pediatrician. Will had been ill for two weeks and was seen several times. Dr. Coldwater saw him on April 1st and sent him to the ED. Med. recs. at Ex. 33, p. 135. He was diagnosed with ataxia and a virus. The mother stated Will's symptoms began when he received hepatitis A vaccine on March 26th. That day, his symptoms were worse and he was unable to walk unassisted. He had an increased loss of balance. *Id.* She was to go to the ED then. *Id.*

On April 13, 2002, Will came back to the Seton ED because of ataxia. He could not walk unassisted. Med. recs. at Ex. 11, p. 1. Will had a temperature of 101.9°. Med. recs. at Ex. 11, p. 5.

On April 18, 2002, Dr. Kane wrote a letter to Dr. Getman, after having seen Will that day. His ataxia was not better and was somewhat worse. He had difficulty walking independently and could do so for only a few steps. Med. recs. at Ex. 12, p. 1. He had an intercurrent illness the

prior weekend resulting in high fevers. During that illness, his ataxia worsened. On physical examination, Will had marked truncal ataxia. Dr. Kane still thought Will had acute cerebellar ataxia on a postinfectious basis, but the fact that this had been going on for nearly one month meant Dr. Kane should look at more severe causes for the ataxia than a cold. *Id.*

On May 2, 2002, Dr. Kane wrote a letter to Dr. Getman, having seen Will that day. Will had made some significant improvement since his last visit. He went to daycare for a full week and could ambulate well if he held onto walls or furniture. But, he developed an intercurrent viral infection which he caught from his father, and Will's ataxia immediately worsened to its worst level. Med. recs. at Ex. 13, p. 1. Dr. Kane continued to believe that Will had a prolonged acute cerebellar ataxia with a postinfectious cause. Med. recs. at Ex. 13, p. 2.

On May 21, 2002, Dr. Kane wrote a letter to Dr. Getman, having seen Will that day. Will had deteriorated further in functioning over the prior month. He was completely non-ambulatory. He could sit unassisted, but was unsteady. His fine motor skills decreased. He had regression of his speech. Med. recs. at Ex. 14, p. 1. Dr. Kane's impression was that Will had acute cerebellar ataxia. However, it appeared to be much more severe than the run-of-the-mill ataxia cases he saw after varicella infections. Dr. Kane was concerned, as were Will's parents, that its onset was right after Will's hepatitis A vaccination. Will's mother believed she saw symptoms the night the vaccination was given, but the symptoms were markedly evident within four to five days of the vaccination. Med. recs. at Ex. 14, p. 2. Dr. Kane continued:

> I have filed a report with the Vaccine Reporting Center of the CDC. I have done literature searches. I have found reports of similar symptoms after hepatitis B vaccine (a single case report, the severity of which I cannot tell) and a single report of cerebellar ataxia after a hepatitis A infection. I have abstracts only of these

> reports. I have also discussed the case with a friend of mine who is an expert in neuroimmunology at the University of Texas Southwestern Medical Center. He in turn has contacted other colleagues who agree that this is the most likely diagnosis and believe that there is a possible association with the vaccine. However, this is clearly a rare situation without any available recommendations for further workup or management.

Id.

Dr. Kane recommended repeating Will's MRI to look for any demyelinating encephalomyelitis which would be a more typical post-vaccine reaction as well as to look for any occult tumors that the first MRI might have missed. *Id.* While Will was sedated, he would perform a lumbar puncture to look for evidence of subtle infection but more especially for markers of autoimmune disease. *Id.* Assuming Will had an autoimmune disease, the options for treatment included immunoglobulin. He favored immunoglobulin over plasmapharesis in Will's age group because of the difficulty of access and fluid volume shifts during plasmapharesis. Med. recs. at Ex. 14, pp. 2-3. If Will had demyelination, he would favor steroids. Med. recs. at Ex. 14, p. 3.

On May 22, 2002, Will had another MRI of his brain which was unremarkable. His pneumatized paranasal sinuses and mastoid cavities were clear. Med. recs. at Ex. 15, p. 1.

From May 28 to 30, 2002, Will was admitted to Children's Hospital of Austin where he received two days of IVIG (intravenous immunoglobulin) for a presumptive post-vaccination reaction. Med. recs. at Ex. 16, p. 4. On May 28, 2002, Dr. Kane wrote a history and physical report. Med. recs. at Ex. 16, p. 13. Will was in his usual state of complete good health until the end of March when he received hepatitis A vaccination. Within hours of receiving the vaccine, he was unsteady on his feet. This resolved temporarily. Within three days, he was completely

ataxic and stumbling and falling. He remained ambulatory. Dr. Kane saw him in the ER and diagnosed him with acute cerebellar ataxia. Over the next two months, his symptoms got worse. He had worsened symptoms when he had intercurrent minor febrile illnesses. He became completely ataxic to where he could not walk for nearly a month and now had trouble even sitting erect. His speech regressed. Testing had found the presence of oligoclonal bands in his spinal fluid in spite of a normal white count and a normal IgG synthetic rate. Will had a presumptive diagnosis of vaccination-induced autoimmune ataxia. The federal agency in charge of vaccine side effects had been notified as had the drug vaccine manufacturer. He could find no real precedent for this in the medical literature. But, as Will continued to deteriorate, Dr. Kane felt it necessary to attempt some therapeutic intervention. Will was admitted for treatment with IVIG. *Id.* Dr. Kane was going to consult Dr. Hauger, an infectious disease specialist, for any insight she might have into the immune or vaccine-related complication. Med. recs. at Ex. 16, p. 14; Ex. 33, p. 93 (positive oligoclonal bands).

On May 28, 2002, Dr. Kane wrote in the progress notes that Will had two months of progressive ataxia following hepatitis A vaccination. He had a full work-up including two MRIs of his brain, a lumbar puncture, a metabolic screen of organic acids, amino acids, and lactate, and a CT of his body to rule out a neuroblastoma. All were negative. Med. recs. at Ex. 16, p. 15. The only positive finding was cerebrospinal fluid oligoclonal bands, suggesting a positive autoimmune reaction consistent with but not diagnostic of a vaccine reaction. *Id.* Dr. Kane's impression was progressive ataxia, presumed post-vaccination autoimmune process. *Id.*

On May 29, 2002, Dr. Hauger wrote that Dr. Kane asked her to see Will because of progressive ataxia, possibly secondary to an immune response to hepatitis A vaccine. Med. recs.

at Ex. 16, p. 16. Will's mother stated that Will received hepatitis A vaccine on March 26, 2002 and, within three hours, she noted he had poor balance and falling. *Id.* His symptoms progressed to clear tremors and ataxia. He was seen in the ER at the end of March 2002 and diagnosed with acute cerebellar ataxia. His MRI was normal. He had no focal infections. The symptoms persisted and worsened with intercurrent illnesses. Med. recs. at Ex. 16, p. 17. Dr. Hauger's assessment was possible post-vaccination immune-mediated encephalitis. She wrote that central nervous system findings from association with hepatitis A natural infection are extraordinarily rare. but have been reported. Most commonly, there are Guillain-Barré syndrome and reports of cerebellar ataxia. Vaccination may promote an immune response which could be more targeted in the central nervous system. Dr. Hauger concluded that the presence of oligoclonal bands supported such a cause in Will's case. Med. recs. at Ex. 16, p. 18. Dr. Hauger stated she would call the manufacturer to check about other reports. She also gave Dr. Kane a VAERS form. She agreed with the dosage of IVIG for Will. If IVIG were helpful, she suggested a trial of three infusions of IVIG. *Id.*

On May 31, 2002, Dr. Kane wrote a report that Will had acute progressive ataxia over two months whose symptoms began on the day of a hepatitis A vaccination. Extensive evaluation for other causes had been negative. Will had been admitted to Children's Hospital of Austin for a two-day course of IVIG as the treatment for a presumptive post-vaccination reaction. Med. recs. at Ex. 16, p. 4. Will received CT scans of his neck, chest, abdomen, and pelvis to rule out a neuroblastoma as a potential cause for an autoimmune ataxia. The scans were completely negative. *Id.*

On June 7, 2002, Dr. Kane saw Will again and noted his improvement in a letter to Dr. Getman. Med. recs. at Ex. 17, p. 1. He states, "William is a 2-year-old boy with a presumed autoimmune ataxia following hepatitis A vaccination." *Id.* at p. 2.

On June 21, 2002, Dr. Kane wrote a letter to Dr. Getman. Med. recs. at Ex. 18, p. 1. He recounted Will's progress and stated further:

> I am persuaded at this point that William's symptoms are most likely a reaction to the Hepatitis A vaccine and we [Dr. Kane and Will's parents] discussed this at some length.

Id.

On July 19, 2002, Dr. Kane saw Will and noted his progress in a letter to Dr. Getman. He stated, "I still think that an autoimmune response to the Hepatitis A vaccine is the most likely cause for the severe ataxic syndrome." Med. recs. at Ex. 19, p. 1.

From July 22 to 24, 2002, Will was admitted to Children's Hospital of Austin for a second round of IVIG therapy. Med. recs. at Ex. 20, p. 3. Dr. Kane wrote the discharge summary, stating:

> The patient is a 2-year-old boy with ataxia for six months. This began immediately following a hepatitis A vaccine and is presumptively diagnosed as a post vaccine, autoimmune cerebellar ataxia.

Id.

On July 22, 2002, Dr. Hauger wrote a record stating that Will had encephalopathy possibly secondary to hepatitis A vaccine and that she first saw Will during his May 2002 admission. She recommended a cerebrospinal fluid hepatitis A polymerase chain reaction (PCR) test be run, the results of which were pending. The enterovirus detection by PCR was negative.

Dr. Hauger recommended Will receive three IVIG infusions and Will had already received one. Med. recs. at Ex. 20, p. 13.

On August 16, 2002, Dr. Kane wrote Dr. Getman that Will had done well on his last dose of IVIG, but after an intercurrent viral infection, he had steadily worsened in function. Med. recs. at Ex. 21, p. 1. Urine catecholamines tested at his last hospitalization proved negative, ruling out a neuroblastoma as a cause for Will's autoimmune ataxia. *Id.* Dr. Kane's impression was that Will had autoimmune ataxia that began on the day of his hepatitis A vaccination. *Id.* at p. 2.

On August 21, 2002, Will fell from his bed, fracturing his right forearm. Med. recs. at Ex. 22, p. 4. Will had surgery to resolve the fracture on August 23, 2002. *Id.* at p. 12.

On December 18, 2002, Dr. Kane wrote a letter to Dr. Getman after seeing Will and his mother that day for the first time in almost four months. Med. recs. at 23, p. 1. Will had improved although he continued to fall frequently and sometimes wore a helmet at home. He continued to have exacerbations of his symptoms. Dr. Kane stated he continued to think that an autoimmune process was the most likely explanation. *Id.* He also stated:

> There is a very good chance that this was induced by the hepatitis A vaccine that he received on the day of the onset of his symptoms. ... Given the devastating reaction that William has had to the hepatitis A vaccine, I do not think that I can reassure them [Will's parents] that future vaccines would not pose an increase[d] risk for William as compared to other children.

Id. at 2.

On December 18, 2002, Dr. Kane wrote a "To Whom It May Concern" letter, saying:

> William is a patient in my neurologic clinic. He has had a ... severe neurologic reaction to the hepatitis A vaccine. I think

> decisions about his future vaccinations should be left up to the judgment of his parents because William has demonstrated an increased risk of reactions. Further immunizations, I believe, pose a significant risk to William's health that could be catastrophic and irreversible. Therefore, I think that it is medically justified to withhold further vaccinations from William at the discretion of his parents.

Med. recs. at Ex. 24, p. 1.

On March 3, 2003, the Austin Independent School District completed a Full and Individual Initial Evaluation of Special Education Eligibility for Will. Med. recs. at Ex. 33, p. 14. Stephen C. Lansdowne, Ph.D., a licensed specialist in school psychology, wrote that "William had a severe neurologic reaction to the hepatitis A vaccine given on his second birthday that affected his motor and speech functioning. ... The eventual diagnosis was Post Viral Cerebellar Ataxia." *Id.*

A note dated the week of March 31, 2002 by Ina Glenn (the daycare provider) states that William had had a very good week. He enjoyed all the fine and gross motor activities. Med. recs. at Ex. 33, p. 23. Will would have a special chair for balance. *Id.* at 25. (The year for this note probably should be 2003, not 2002, because there is a responsive note dated April 27, 2003 from Will's father to Ms. Glenn's note for the week of April 21st recommending that Will have hightop shoes to provide him with more stability. *Id.* at 29, 30, 31. March 31, 2003 was a Monday.)

On July 18, 2003, Dr. Kane wrote a letter to Dr. Getman after seeing Will three days earlier. Will's progress was slow since he last saw him in December. He had speech delay. A cold or fever would cause significant worsening of his ataxia, but a wasp sting dramatically

improved his symptoms. Med. recs. at Ex. 25, p. 1. Dr. Kane stated that Will's ataxia "most likely represents an autoimmune side effect to his hepatitis A vaccine." *Id.* at 2.

On December 24, 2003 and February 3, 2004, revised February 16, 2004, Nancy L. Nussbaum, Ph.D., a licensed psychologist, did a neuropsychological summary. Med. recs. at Ex. 33, p. 1. After Will's hepatitis A vaccination on March 26, 2002, his parents noted increased clumsiness, such as bumping into walls and furniture that evening. *Id.* at 2. In the days following his vaccination, his daycare noted more frequent falling. *Id.* Will's pediatrician saw him on April 1, 2002, noting sudden onset ataxia/tremor, and Will was referred to Dr. Kane, a pediatric neurologist. *Id.* Dr. Kane diagnosed Will with a presumed autoimmune ataxia following hepatitis A vaccination. *Id.*

On March 2, 2006, Dr. Getman wrote a letter, stating he saw Will for a routine check-up in March 2002, during which time Will received hepatitis A vaccine. In the days following administration of the vaccine, Will developed cerebellar ataxia. Med. recs. at Ex. 31, p. 1. Dr. Getman understood that cerebellar ataxia can have many causes, including viral infections, and he was not sure what caused Will's cerebellar ataxia. *Id.* Dr. Getman deferred to Dr. Kane's judgment in determining the cause of Will's cerebellar ataxia. *Id.*

On March 5, 2006, Dr. Kane dictated a "To Whom It May Concern" letter. Med. recs. at Ex. 33, p. 1. Will was extensively evaluated for the potential causes of his ataxia. The only abnormality of his testing was abnormal antibody production in his spinal fluid. Given his sudden presentation of symptoms and this finding (oligoclonal bands), Dr. Kane diagnosed Will with autoimmune cerebellar ataxia. Because the onset occurred immediately after vaccination against hepatitis A, Dr. Kane felt it more likely than not that the vaccine triggered Will's

autoimmune ataxia. Dr. Kane has never changed his opinion about Will's diagnosis. "I still believe that an autoimmune process triggered by his hepatitis A vaccine is the most likely explanation for his symptoms." *Id.*

On December 27, 2006, Dr. Kane wrote to Dr. Mouser after having seen Will for the first time in several years. P. Ex. 51. Will's parents reported that Will's symptoms continued to worsen temporarily with any intercurrent illness. *Id.* at 1. Dr. Kane opined once more that the hepatitis A vaccine triggered an autoimmune disease in Will. *Id.* at 2. He stated that Will had a very severe postinfectious ataxia and the most likely cause was autoimmune because of the presence of oligoclonal bands in his spinal fluid, his transient improvement on intravenous immunoglobulin (IVIG), his worsening with intercurrent infections, and his clinical pattern. *Id.* Dr. Kane concluded that since Will's symptoms began several days after his hepatitis A vaccination, Will had an unusual immune response to the vaccine which was the most likely cause of his cerebellar ataxia. *Id.*

Other Submitted Material

Respondent filed Ex. C, "Acute Cerebellar Ataxia After Subclinical Hepatitis A Infection," by D. Tuthill, et al., 15 *Ped Infectious Dis J* 6:546-57 (1996). This case report describes a five-year-old girl with slurred speech and inability to bear weight or feed herself. Her eldest sister had clinical hepatitis A infection three weeks earlier. *Id.* at 546. Liver function tests were abnormal and an ELISA (enzyme-linked immunosorbent assay) test for hepatitis A IgM antibody was positive. *Id.* The authors state that the first cerebellar ataxia case was described in 1907 and, until the mid-1950's, there were only three recorded cases in the British journals. Since then, many cases with a wide ranging etiology have been reported. Causes of cerebellar

ataxia have included: chickenpox, echovirus, *Legionella*, *Mycoplasma*, mumps, malaria, typhoid, polio, and hyponatremia. Other causes have been drugs, including phenytoin, isoniazid, and alcohol. Neuroblastoma can mimic cerebellar ataxia initially. The pathogenesis of cerebellar ataxia was as yet unknown, but "there is some evidence for an immunologic mechanism." *Id.* The authors assumed that the little girl had a subclinical episode of hepatitis A viral infection. Although subclinical hepatitis A viral infection had not previously been part of the list of associated causes of cerebellar ataxia, the authors thought it "should be added to the list of documented causes." *Id.* at 547.

Respondent filed Ex. D, "Course and Outcome of Acute Cerebellar Ataxia," by A.M. Connolly, et al., 35 *Ann Neurol* 673-79 (1994). This was a study of 73 consecutive children with acute cerebellar ataxia (ACA) over a 23-year period whom St. Louis Hospital evaluated. Causation of these children's ACA was as follows: 26% had chicken pox, 52% had other illnesses presumed to be viral, and three percent had ataxia related to vaccines. *Id.* at 673. Epstein-Barr virus and vaccination-related ACA were found in older children. *Id.* at 674. The two children who developed ataxia after immunization had received either smallpox vaccine or measles vaccine. *Id.* The latency period for those children in whom viruses caused the ACA was one day to 21 days. *Id.* The latency for the two children who had received either smallpox or measles vaccine was 8 and 14 days. *Id.* Among 36 patients with presumed viral illnesses other than varicella, 5 had gastrointestinal and 31 had upper respiratory symptoms. *Id.* In 24 children who had viral cultures performed, Epstein-Barr virus (EBV) was the only specific agent found in two of them. *Id.* The latency period was longer after EBV (14-21 days) than for those with other known or presumed viral illnesses or immunizations. *Id.* Ataxia was worse in patients whose

ACA was related to varicella, EBV and vaccination as 57% of these children were unable to walk. *Id.* at 675. Only 31% of children with an unspecified viral illness and 21% of children without a prodrome had such a severe gait abnormality. *Id.* The authors documented mild speech and language difficulties in several of their patients. *Id.* at 679.

Respondent filed Ex. E, "Acute Cerebellar Ataxia in Childhood," by M.M. Ryan, et al., 18 *J Child Neurology* 309-16 (2003). The authors state that possible causes include immunization. *Id.* at 309.

Respondent filed Ex. G, "Post-Infectious Cerebellar Ataxia in Children," by M. Nussinovitch, et al., 42 *Clin Pediatrics* 7:581-84 (2003). The authors state that acute cerebellar ataxia (ACA) "can occur at any age but is most prevalent during the second year of life." *Id.* at 581. The authors state that the most common cause of ACA is a specific or nonspecific infectious illness, listing viral infections: varicella, mumps, enteroviruses, Epstein-Barr virus, typhoid fever, parvovirus B19, hepatitis A, mycoplasma, malaria, legionella, and meningococcal meningitis. *Id.* They also state that "ACA may also occur after vaccination," listing two references, anecdotal reports of acute cerebellar ataxia following varicella (chickenpox) vaccination and following hepatitis B vaccination. *Id.* at 583.

Petitioners filed a videotape of Will's two-year birthday party the evening of his hepatitis A vaccination to prove that Will's onset of cerebellar ataxia was not that evening. The party videotape lasts one hour. Will is playing with his older brother and father a variety of games (children's softball, basketball, etc.) as well as eating birthday cake. He does not stumble in the videotape. For an hour, Will is jumping up and down from a sofa, swinging a baseball bat and

trying to hit a ball thrown at him, bounding around a low basketball hoop, trying to make baskets, and running around spraying a plastic stream of colored substance. His activity is endless. He not only walks, he runs, hits, jumps, swings, and bounds. The last four minutes of the tape taken three months later in May 2002 show a very different little boy who can barely walk.

After the hearing on December 1, 2006, the medical experts were to watch the videotape and prepare reports for the parties to file concerning whether they thought the videotape showed onset of cerebellar ataxia on the evening of the vaccination, March 26, 2002.

Respondent filed Ex. I, Dr. MacDonald's report, dated Jan. 8, 2007, giving his interpretation of the videotape. He noted only subtle signs of unsteadiness with a somewhat wide-based gait, a slip and fall on one occasion, and some corrective maneuvers when Will quickly shifted weight and turned quickly. Dr. MacDonald noted that Will tended to sit on his legs in the W position, which he stated was a sign of low muscle tone. Dr. MacDonald said that low tone is associated with ataxia. He stated, "These may represent the early signs of ataxia, but are subtle and not diagnostic of a typical ataxic gait, as seen on the later video taken in June, where he is clearly ataxic." *Id.* Dr. MacDonald did not think the video added much to the issue of when Will's ataxia began. He expected that, at the beginning, Will's symptoms would be subtle and intermittent. Dr. MacDonald concluded that his opinion did not change substantially.

Petitioners filed Ex. 50, a letter from Dr. Jeffrey S. Kane, dated February 12, 2007, in lieu of a report from Dr. Marks, analyzing the videotape. Dr. Kane is Will's treating pediatric neurologist. He states that the videotape does not show any evidence of ataxia either in Will's gait or limbs on March 26, 2002. Dr. Kane says that the videotape is persuasive that the onset of Will's cerebellar ataxia occurred some time after March 26, 2002. He recognizes that his own

records add to the confusion about onset, but, in reviewing the tape, he believes that the tape is more reliable as to exact timing of onset than his later medical records. Ex. 50.

Petitioners initially sued civilly Merck & Co., Inc. (the manufacturer of the vaccine), and medical providers, a suit which was dismissed on March 20, 2006. Med. recs. at Ex. 28, p. 1. While the civil suit was pending, petitioners took the deposition testimony of Linda Hostelley, a corporative representative of Merck. Med. recs. at Ex. 29, p. 3. Her responsibilities included directing the adverse experience reporting compliance globally for all of Merck's investigational and marketed products. *Id.* at p. 4. VAQTA is the inactivated hepatitis A vaccine, first marketed in the United States in 1996. *Id.* Will's cerebellar ataxia was reported to Merck as an adverse event. *Id.* at pp. 20-21.

Merck first learned of Will's adverse reaction on May 21, 2002. *Id.* at p. 24. Before then, Merck did not include cerebellar ataxia as an adverse reaction in its product insert for VAQTA. *Id.* at p. 22. In the last quarter of 2003, Merck added cerebellar ataxia as an adverse reaction in its product insert for VAQTA. *Id.* Cerebellar ataxia meets the definition of a serious neurologic event. *Id.* at p. 26. Will's adverse reaction report qualified for rapid reporting to the FDA and other government agencies. *Id.* at p. 27. It qualified for rapid reporting because Will was hospitalized and "cerebellar ataxia" was not in the then-current package circular for VAQTA at the time of the report in May 2002. *Id.*

Will's adverse reaction report was the only report of cerebellar ataxia in the worldwide safety database Merck had. *Id.* at p. 28. There is a VAERS report of a hepatitis vaccination administered August 8, 1999, without stating the manufacturer, which was followed by ataxia. *Id.* at p. 70. The FDA database has an additional report of an adverse reaction of ataxia after

receipt of hepatitis A vaccine on January 3, 2002. *Id.* at p. 31. This adverse reaction was reported to the VAERS system. *Id.* Merck was the manufacturer of this hepatitis A vaccine. *Id.* There is a report of ataxia as an adverse event following hepatitis vaccine administered January 17, 2002, manufactured by Merck, without specifying whether it is hepatitis A or B. *Id.* at p. 70. There is an additional VAERS report of a Merck hepatitis vaccination, unspecified as hepatitis A or B, administered February 15, 2002 followed by ataxia. *Id.* at pp. 32-33. Some adverse event reports go directly to the FDA and others go directly to Merck. *Id.* at p. 39.

A Merck doctor telephoned Dr. Kane to seek additional information concerning Will, including obtaining the results of a PCR analysis. *Id.* at p. 38. In the Merck doctor's conversation with Dr. Kane, Dr. Kane stated that Will did not have encephalitis because his cerebrospinal fluid was negative. *Id.* at p. 49. There was no mention of a viral infection. *Id.* Dr. Kane said to the Merck doctor that he felt that Will's cerebellar ataxia was vaccine-related and he had a resident working with him whom he encouraged to publish Will's case in an anecdotal report. *Id.*

Merck informed the FDA of all available information about Will and, based on the information collected, Merck proposed changing the label for VAQTA. *Id.* at p. 51. Will had oligoclonal bands which were producing antibodies within his central nervous system. *Id.* at p. 57. Dr. Kane reported he had sent blood and spinal fluid for PCR analysis for hepatitis A. *Id.*

Attached to the exhibit of the Merck deposition is Will's VAERS, dated May 31, 2002, which Merck filled out after receiving information from Dr. Kane on May 21, 2002. MRK-STW 0055. Within days of Will's vaccination, he had significant neurological impairment. *Id.*

Also attached to the exhibit of the Merck deposition is Will's VAERS report, dated February 27, 2004, filled out by Merck. MRK-STW 0126. There is a question mark next to whether onset was on March 26, 2002. *Id.* The manufacturer received the report on February 19, 2004. *Id.* This report was a follow-up to reports previously submitted on May 31, 2002, June 18, 2002, September 17, 2002, December 31, 2002, August 5, 2003, October 21, 2003, and November 21, 2003. *Id.* In the description area, on page 2, the recorder states that Will received his hepatitis A vaccination on March 26, 2002 at 2:00 p.m.. *Id.* at 0127. There was "no illness at the time of vaccination." *Id.* On December 20, 2002, the physician reported that there was an insufficient amount of specimen to obtain results of the PCR analysis for hepatitis A. *Id.* "Colleagues of the physician agreed that acute cerebellar ataxia was 'the most likely diagnosis and believe there is a possible association with the vaccine.'" *Id.* at 0128.

As part of their prior civil suit against Merck, petitioners took the testimony of Barbara J. Kuter on January 13, 2006. Med. recs. at Ex. 30. Dr. Kuter was an executive director in policy, public health, and medical affairs. *Id.* at 8. Merck added cerebellar ataxia to the package information for hepatitis A vaccine (VAQTA) because the investigator (the reporting physician) deemed it vaccine-related and because it was a serious event. *Id.* at 112-13, 119. The WAES Adverse Experience Report reflects that Merck received information from a doctor concerning a two-year-old with no illness at the time, receiving hepatitis A vaccination, and, within days, experiencing significant neurological impairment. MRK-STW 0112. Merck's description of hepatitis A vaccine, inactivated (VAQTA) is that it is grown in cell culture in human MRC-5 diploid fibroblasts. It has a further serial passage of a proven attenuated strain. MRK-STW

0115. In June 2003, Merck applied to the FDA to add cerebellar ataxia to the post-licensure adverse reaction section. MRK-STW 0021.

TESTIMONY

William Stewart testified first for petitioners. Tr. at 6. He took both sons to the pediatrician on March 26, 2002 and both were well and happy. Tr. at 18. Adam is seven years older than Will. *Id.* Will was in nursery school and did not have an upper respiratory infection on March 26, 2002. Tr. at 9. Both boys received hepatitis A vaccine on March 26, 2002. Tr. at 10, 11.

That night, which was a Tuesday, they had a two-year birthday party for Will in anticipation of a family celebration on Sunday. Tr. at 10. The birthday party lasted from 6:30 p.m. to 9:00 p.m., which was an hour past Will's bedtime. Tr. at 11. Will had spaghetti and meatballs for dinner and a large cake with lots of frosting. He ate more frosting than cake. *Id.* Will played with Silly String, Playskool basketball, and jumped off and on the sofa easily so he could dunk. Tr. at 11, 12.

During the party, Will ran into the dining room wall at one point. Tr. at 12. When Will's parents went to Austin Regional Clinic on Sunday, March 31, 2002, Will's mother gave a history that she thought Will had been clumsy on Tuesday night, that he had run into a wall, and then, on Friday, March 29, 2002, both parents noticed he was a little unsteady walking. Tr. at 13. During the party, Will's mother saw him wheel around and run into the wall of the dining room. Tr. at 13-14. Will did not fall down. Tr. at 14.

Mr. Stewart was not aware of Will's having an upper respiratory condition. Tr. at 15. At the Emergency Room on April 1, 2002, Will had a green nasal discharge according to the

records, but Mr. Stewart did not see it. Tr. at 15-16. Mr. Stewart does not believe that Will's gait was unsteady on March 26, 2002. Tr. at 17. On Wednesday, March 27, 2002, there was nothing unusual. Tr. at 18. On Thursday, March 28, 2002, there was nothing unusual. *Id.* On Friday, March 29, 2002, after dinner, Will seemed unsteady on his feet. *Id.* They thought he might have an ear infection and discussed this on Saturday, March 30, 2002. Tr. at 19. They asked Will on Saturday, March 30, 2002, if his ear hurt. *Id.* On Sunday, March 31, 2002, Will was weaving noticeably when he walked. Tr. at 20. They took him to the clinic and saw Dr. Mouser, the pediatrician on call. *Id.* Will zigzagged down the hallway. The doctor checked his ears. Tr. at 21. Mr. Stewart was not aware of any upper respiratory symptoms. Tr. at 54.

On Monday, April 1, 2002, at 7:00 a.m., Will's hands were trembling. Tr. at 21. At the Emergency Department, Will's parents were pretty frantic and told the medical treaters there was a five-to-six-day history. Tr. at 55, 56. Dr. Kane was very thorough and seemed genuinely concerned. Tr. at 25. He asked a great many questions. *Id.* He was very professional. *Id.* Will may have stumbled more than once on the evening of his vaccination. *Id.*; tr. at 57. The symptoms Will exhibited on the weekend and his behavior on Tuesday night were different. By Monday, Will had significant issues with his gait, and the tremors were brand new. Tr. at 27. Will did bump into a wall on his birthday. Tr. at 60. In a statement he gave to the Texas Senate in May 2005, he stated that the onset of Will's cerebellar ataxia was 12 hours after his vaccination. Tr. at 65. He associated Will's clumsiness with the onset. Tr. at 66. However, twelve hours after vaccination, Will was asleep. Tr. at 66.

Will started to walk a little before his first birthday. Tr. at 33. In January 2002, he had a viral upper respiratory infection and otitis media. Tr. at 34. According to a neuropsychologic

record, he was bumping into furniture. At the day care, in the days following March 26, 2002, he was falling more frequently, but Mr. Stewart was not sure when. Tr. at 45. Will's condition deteriorated over three months. By June 2002, Will could not walk. Tr. at 46. He could not sit up either. Tr. at 50.

Dr. Donald H. Marks, an internist with a doctorate in microbiology and immunology testified next for petitioners. Tr. at 68. He studies neurologic reactions to Lyme disease vaccine and consults for vaccine companies. Tr. at 72. He is at a viral hepatitis clinic three times a week. Tr. at 73. Almost all his patients have hepatitis C. *Id.*

His opinion is that hepatitis A vaccine caused Will's acute cerebellar ataxia. Tr. at 78-79. He has a number of bases, the first being the temporal relationship. Tr. at 79. He accepts that the onset of Will's acute cerebellar ataxia occurred later in the week and not the evening of his vaccination. *Id.* Secondly, medical literature shows that hepatitis A virus can cause acute cerebellar ataxia. *Id.* Thirdly, hepatitis A vaccine is designed to induce an immune response that mimics hepatitis A infection, an infection known to cause cerebellar ataxia, which is consistent with causation. Tr. at 80. Fourthly, as respondent's Ex. D (the Connolly article) shows, other vaccines can cause acute cerebellar ataxia. *Id.* Fifthly, the mechanism is an immune-based central nervous system reaction. *Id.* Sixthly, Dr. Jeffrey Kane, Will's treating pediatric neurologist, stated that hepatitis A vaccine caused Will's acute cerebellar ataxia. *Id.* Seventhly, there is no plausible alternative explanation for Will's acute cerebellar ataxia. Tr. at 81. And lastly, hepatitis A vaccine, unlike hepatitis B vaccine or Lyme vaccine, each of which is a purified single protein, is not a recombinant vaccine. *Id.* Manufacturers grow hepatitis A in a tissue culture which contains a lot of proteins related to the cell line that the tissues grow in. *Id.*

The tissue culture is sliced, the cells broken, and the material centrifuged out and passed through a filter a few times. Tr. at 81-82. The material is then exposed to gallium or aluminum hydroxide, a metallic substance to which the proteins bind and, because of that binding, they have a stronger immune response when injected, which makes the vaccine more reactogenic. Tr. at 82. Hepatitis A vaccine is an inactivated whole virus vaccine, not a purified protein. It has thousands of proteins in the envelope surrounding the DNA. Tr. at 83. The hepatitis A vaccine is a relatively crude vaccine by modern standards. Tr. at 87-88.

Dr. Marks testified that a two-year-old is immunologically immature and his immune response could very well be abnormal. Tr. at 88. He does not regard Will's stumbling on the evening of the vaccination to be the onset of his acute cerebellar ataxia. Tr. at 89. Will had been eating cake for the prior three hours and it was 8:00 and 9:00 at night. He was tired and not feeling well due to the vaccination earlier. Tr. at 90. Dr. Marks does not think Will's walking into a wall was a symptom of anything. *Id.*

Will was not diagnosed with an upper respiratory infection at the time he got the vaccination when he was at a well-baby examination. *Id.* Will had numerous upper respiratory infections in the past without having cerebellar ataxia, but this was his first hepatitis A vaccination. Tr. at 97. The challenge to his immune system that triggered the cerebellar ataxia was the vaccine. *Id.* Hepatitis A vaccine was a substantial factor in causing Will's cerebellar ataxia. Tr. at 98. Will's underlying respiratory infection was a contributing factor to his acute cerebellar ataxia, but not a substantial factor. *Id.* Without the hepatitis A vaccine, Will would not have had acute cerebellar ataxia. Tr. at 99. Will had had colds before without getting

cerebellar ataxia. Without the added immunologic challenge of hepatitis A vaccine, Will would not have had cerebellar ataxia. *Id.*

If the onset of Will's ataxia were the night of the vaccination, Dr. Marks opined that Will would have had postinfectious cerebellitis rather than cerebellar ataxia. *Id.* But that is not what happened. Several days later, he started to develop the symptoms which resulted in his seeing Dr. Kane the next Monday. Tr. at 100. There was a time period between the vaccination and the development of the acute cerebellar ataxia which was sufficient to allow an aberrant immune response to occur. *Id.* If the ataxia had occurred the night of vaccination, Dr. Marks would be hard pressed to say it was vaccine-related. It would look more like an acute infectious process, but it did not happen that way. The timing was right. *Id.* An underlying mild viral infection may have been an initiating component, but had the vaccine not been given, Will would not have had cerebellar ataxia. Tr. at 100-01.

Dr. Kane filed a report with the Centers for Disease Control after doing a literature search, and finding reports of similar symptoms after hepatitis B vaccine and a single case report of cerebellar ataxia after a hepatitis A infection. Tr. at 102. Dr. Kane spoke to a friend who is an expert in neuroimmunology who contacted other colleagues and they agreed the vaccination was a possible cause. Tr. at 104-05. Dr. Kane, on Monday, April 1, 2002, wrote in his notes that Will had progressive ataxia over the prior four days which would put onset on Friday. Tr. at 108-09. Hepatitis A protein in the vaccine incited an immune response. Between two and 18 days is where 95% of the onset occurs after a known cause. Tr. at 111.

Dr. Marks has never treated a patient with cerebellar ataxia. Tr. at 112. Will's cerebellar ataxia does not look like it is a demyelinating ataxia. It looks more like an autoimmune

inflammatory reaction. Tr. at 123. Consistent with Will's having an immune-based reaction is that IVIG would improve his condition. Tr. at 124. Dr. Kane's doing research on the issue of vaccine causation was appropriate. Tr. at 126. Dr. Kane talked to an expert in neuroimmunology at the University of Texas. This is what doctors do when they have a question they need information about. Tr. at 126-27. Will's response to the hepatitis A vaccine was an immune response to primarily a single component, the hepatitis A protein in the vaccine. Tr. at 128.

In the Connolly article, the onset interval from vaccination to cerebellar ataxia was eight and 14 days, but that was based on just two cases (one after smallpox vaccine and the other after measles vaccine) and Dr. Marks stated that two cases is not large enough to give any kind of an estimate of the latency period. Tr. at 141-42. For those with cerebellar ataxia after viral infections, the latency period in the Connolly article was one day to 21 days. Tr. at 144-45.

The common presentation of cerebellar ataxia in children is between two and five years of age. Tr. at 160. William had an abnormal immunologic reaction to the vaccine, probably to a protein component of the vaccine. Tr. at 171. If he had a prior exposure to the protein in the vaccine, the onset should be four to five days. Tr. at 173-74. Dr. Marks referred to this as a memory response rather than a primary immune response. Tr. at 174. It is a reexposure: something in the vaccine was similar to something Will's body had encountered before. Tr. at 175. Will had an immune-mediated response. *Id.* Dr. Kane assumed Will had a vaccine-induced autoimmune ataxia. Tr. at 175-76.

Dr. Marks testified that, in order to have an autoimmune response, the body has to recognize either a cell protein or something that looks like a cell protein. Tr. at 176. When exposed to a vaccine, the body is exposed to an immune adjuvant (the aluminum) with the

vaccine protein, specifically designed to induce an immune response. *Id.* Will had relapses of cerebellar ataxia when he had intercurrent viral febrile illnesses. This is due to the viral infection suppressing the immune system, allowing the autoimmune cerebellar ataxia to progress. Tr. at 178-79. Vaccination on Tuesday with onset of cerebellar ataxia on Friday is the appropriate time frame (four days) to have an immunologic response from hepatitis A vaccine if there were prior exposure to some component in the vaccine. Tr. at 183-84.

Dr. John MacDonald testified for respondent. Tr. at 186. He teaches pediatric neurology and is board-certified in pediatric neurology. Tr. at 190, 191. He has seen patients with cerebellar ataxia. Tr. at 192. Chickenpox is a major cause of cerebellar ataxia. *Id.* He has five to six cases per year. *Id.* The majority of children with acute cerebellar ataxia get better. Tr. at 193. Cerebellar ataxia is assumed to be an immune reaction to a virus or other agent. Tr. at 194.

One can have cerebellar ataxia without demyelination. Tr. at 195. Will's cerebellar ataxia was not demyelinating. *Id.* Will had an intercurrent viral illness which had been going on for a while that affected his ears, his upper respiratory tract, and his sinuses. Tr. at 195-96. He may have had chronic ear disease based on his pediatrician's report that his eardrums were retracted, and on the MRI scan which showed he had chronic sinus disease. Tr. at 196.

The onset of Will's acute cerebellar ataxia was March 26, 2002 when his gait and balance changed though he maintained posture. Tr. at 197. The balance mechanism for a child is not fully developed at age two. Tr. at 198. A child can have a good day or a bad day before the age of eight in terms of balance. *Id.* Will's cerebellar ataxia fluctuated over many months. Tr. at 197. The course waxed and waned. *Id.* It would be consistent with acute cerebellar ataxia that it

would begin the evening of March 26, 2002, but Will would be totally normal on March 27th and 28th, yet he would worsen on the 29th, and steadily decline on the 30th and 31st. Tr. at 199.

Viral illness is the most common cause of cerebellar ataxia. Tr. at 200. If the vaccine had been the cause, according to the Connolly article which discusses two cases of vaccine-caused ataxia, the onset interval would be no earlier than eight days. *Id.* After first exposure, Dr. MacDonald would expect the onset of the illness to be more than four days. Tr. at 201. Dr. MacDonald asked why he should assume the rare chance occurrence (the vaccine) is the cause when the most common cause (a virus) is present in the case. *Id.*

Dr. MacDonald admitted the theoretical possibility that attenuated viral vaccines can cause cerebellar ataxia. Tr. at 205. If we had evidence of Will's prior exposure to a specific identifiable protein in the vaccine, he supposed there might be possible causation of the cerebellar ataxia from the vaccination. *Id.* Dr. MacDonald would admit to causation from the vaccine if there were signs of demyelination and a delay in the onset of ataxia, with no viral illness, and an altered mental status. Tr. at 206. Because Will tested positive for oligoclonal bands, we are safe in saying he had an insult to his nervous system. Tr. at 207-08.

Dr. MacDonald's opinion is that Will had what the vast majority of cases have: an infectious-mediated, viral infection-mediated acute cerebellar ataxia. Tr. at 209. Just because Will's prior upper respiratory infections did not cause acute cerebellar ataxia does not mean that this particular upper respiratory infection was not the cause of it because it was a different virus. *Id.*

On April 1, 2002, Will had a wide-based gait, but Dr. MacDonald did not find this out of range for a toddler. Tr. at 213. Will was not rapidly going downhill. *Id.* Acute cerebellar ataxia

can occur very early after a viral infection compared to after a vaccination, according to the Connolly article. Tr. at 222. We are limited in that the Connolly article discusses only two vaccine-related cases. Tr. at 223. Dr. MacDonald stated it was not unreasonable that cerebellar ataxia is an immune reaction. Tr. at 229. When Will received his vaccination, he was at a well-child examination without any sign of upper respiratory infection or ear infection. *Id.* Will had pink eye in early March 2002, a viral illness. His sinusitis indicates a chronic process. Tr. at 230. Regarding his patients, Dr. MacDonald posits a virus as the cause of cerebellar ataxia but, in over half the cases, he does not know the cause of the cerebellar ataxia. Tr. at 231-32.

DISCUSSION

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. Secretary of HHS, 418 F. 3d 1274, 1278 (Fed. Cir. 2005). In Althen, the Federal Circuit quoted its opinion in Grant v. Secretary of HHS, 956 F.2d 1144, 1148 (Fed. Cir. 1992):

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

In Capizzano v. Secretary of HHS, 440 F.3d 1317, 1325 (Fed. Cir. 2006), the Federal Circuit said "we conclude that requiring either epidemiologic studies, rechallenge, the presence of pathological markers or genetic disposition, or general acceptance in the scientific or medical

communities to establish a logical sequence of cause and effect is contrary to what we said in Althen...."

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

Without more, "evidence showing an absence of other causes does not meet petitioners' affirmative duty to show actual or legal causation." Grant, supra, at 1149. Mere temporal association is not sufficient to prove causation in fact. Hasler v. US, 718 F.2d 202, 205 (6th Cir. 1983), cert. denied, 469 U.S. 817 (1984).

Petitioners must show not only that but for the vaccine, Will would not have had acute cerebellar ataxia, but also that the vaccine was a substantial factor in bringing about his acute cerebellar ataxia. Shyface v. Secretary of HHS, 165 F.3d 1344, 1352 (Fed. Cir. 1999).

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

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

35 F.3d at 549.

As for epidemiological support for causation, the Federal Circuit in Knudsen ruled for petitioners even when epidemiological evidence directly opposed causation from a vaccine. In Knudsen, even though epidemiological evidence supported the opposite conclusion, i.e., that viruses were more likely to cause encephalopathy than vaccinations, the Federal Circuit held that that fact alone was not an impediment to recovery of damages. (Compare the instant action where Dr. MacDonald, respondent's expert, based his opinion against causation partly on the reason that it is more likely that a cold would cause cerebellar ataxia than a vaccine would.)

In Knudsen, the Federal Circuit stated:

> The bare statistical fact that there are more reported cases of viral encephalopathies than there are reported cases of DTP encephalopathies is not evidence that in a particular case an encephalopathy following a DTP vaccination was in fact caused by a viral infection present in the child and not caused by the DTP vaccine.

35 F.3d at 550.

The Federal Circuit stated in Althen, supra, at 1280, that "the purpose of the Vaccine Act's preponderance standard is to allow the finding of causation in a field bereft of complete and direct proof of how vaccines affect the human body."

The Federal Circuit in Capizzano emphasized the opinions of petitioner's four treating doctors in that case that the vaccine was the cause of petitioner's illness. 440 F.3d at 1326.

Here, we have the opinion of Will's treating pediatric neurologist Dr. Kane that his hepatitis A vaccination caused his acute cerebellar ataxia. This was Dr. Kane's conclusion after consulting with an expert neuroimmunologist who himself consulted with colleagues. Dr. Kane

also consulted the medical literature and an infectious disease specialist, Dr. Hauger, who opined Will might have encephalopathy due to hepatitis A vaccine and recommended a PCR test to look for hepatitis A.

Dr. Kane submitted a report interpreting Will's videotape of his birthday party the evening of vaccination and stated that it shows a normal two-year-old. He stated that Will did not have the onset of his acute cerebellar ataxia the evening of his vaccination, based on the videotape. Although the medical histories of onset vary, and the parents earnestly tried to provide every bit of information to the doctors that they could, Dr. Kane concludes, based on his observation of Will in the videotape, that his cerebellar ataxia did not begin the evening of the vaccination, Tuesday, March 26, 2002.

Dr. Kane saw Will during the week of December 27, 2006 and he notes in a letter that his opinion remains that hepatitis A vaccine triggered an autoimmune illness (very severe postinfectious ataxia) in Will based on the oligoclonal bands on his spinal fluid, his transient improvement on IVIG, his worsening with intercurrent infections, his clinical pattern, and the onset of his unusual immune response several days after he received hepatitis A vaccine.

The records are clear that Will's behavior was unremarkable on Wednesday, March 27, 2002, and on Thursday, March 28, 2002. The fourth day after hepatitis A vaccination (counting the day of vaccination as the first day) was Friday, March 29, 2002 when Will's condition became noticeable. He worsened over the weekend and Dr. Kane saw him on Monday, April 1st.

Although Dr. Kane initially thought that Will's cerebellar ataxia was due to a viral infection, he changed his mind when he realized that the course of Will's ataxia was lasting too long to be of the run of the mill type, the kind of ataxia Dr. Kane and his colleagues saw after

varicella (chickenpox) infection. Then, Dr. Kane explored the possibility that Will was having an autoimmune reaction to his hepatitis A vaccination. He contacted a friend who was an expert neuroimmunologist who himself contacted his colleagues and they agreed this could be the rare case of vaccine reaction. Dr. Kane looked at the medical literature and saw anecdotal reporting of ataxia following hepatitis A infection and ataxia following hepatitis B vaccination. And he realized that, if indeed Will had an autoimmune reaction to hepatitis A vaccine, then infusing him with immunoglobulin intravenously was the treatment of choice. Dr. Kane consulted with Dr. Hauger, an infectious disease specialist, who opined Will could have encephalopathy or encephalitis due to hepatitis A vaccination, and suggested IVIG therapy as well as testing by use of PCR for the presence of hepatitis A. She also noted that the presence of oligoclonal bands in Will's cerebrospinal fluid supported an immune response to the vaccine.

Will received three IVIG therapies and improved. Every decision Dr. Kane made concerning Will's diagnosis and treatment was right: (1) he realized he was not dealing with a postinfectious cerebellar ataxia because of the severity and duration of Will's cerebellar ataxia (once he saw Will was not better after almost a month); (2) he recognized the temporal importance of the hepatitis A vaccination; (3) he consulted the medical literature and an expert neuroimmunologist who consulted his colleagues, and also consulted Dr. Hauger, an infectious disease specialist with a strong knowledge of immunology, who confirmed the importance of three IVIG treatments and recommended testing for the presence of hepatitis A in Will; and (4) he came to the conclusion that Will had an autoimmune cerebellar ataxia due to the vaccine which required IVIG treatment.

Dr. Marks, petitioners' expert, listed all the reasons for his opinion that hepatitis A vaccine caused Will's acute cerebellar ataxia: the timing was right (assuming onset of four days with a prior exposure to a protein identical or similar to one in the vaccine), medical literature shows that hepatitis A virus causes acute cerebellar ataxia, hepatitis A vaccine contains hepatitis A virus in inactivated form, and medical literature shows that other vaccines cause acute cerebellar ataxia. Moreover, the Tuthill case report which respondent filed concludes that subclinical hepatitis A infection should be added to the list of documented causes of cerebellar ataxia.

Dr. MacDonald, for respondent, stated that the onset was the evening of the vaccination and, therefore, too short an interval for the vaccine to be the cause. He testified that Will's upper respiratory infection was the cause, based on Will's being diagnosed with an upper respiratory infection days after the vaccination. But, on March 26, 2002, Dr. Getman did not find Will to have a cold, throat, or ear problem. Dr. Getman diagnosed Will as a well child. His father did not give Dr. Getman a history of Will's having a cold. There is no factual support for Dr. MacDonald's insistence that Will had a cold on March 26, 2002. Dr. MacDonald pointed to an ear infection in early March and later MRI evidence of sinusitis, but he had no satisfactory explanation for Will's two-year examination on March 26, 2002 being perfectly normal. By Friday, March 29, 2002, Will had developed nasal congestion. By Monday, April 1, 2002, when Will's parents brought Will to the hospital, they gave a history that Will had had a cold for a week. This is not borne out by the medical records. This was an upsetting time, with Will seriously ill, and the undersigned does not fault Will's parents for being imprecise as to the onset

of Will's cold under the circumstances, but according to the medical records for March 26, 2002, Will did not have a cold.

Dr. Marks, for petitioners, testified that the cold which Will ultimately developed was not a substantial factor in Will's cerebellar ataxia, but that the hepatitis A vaccine was a substantial factor in causing Will's cerebellar ataxia. He also testified that but for the hepatitis A vaccine, Will would not have had cerebellar ataxia.

The undersigned notes that Dr. MacDonald's report following his watching the videotape of Will at his second birthday party the evening of vaccination does not support his assertion that onset of Will's cerebellar ataxia occurred that night. He describes Will's behavior in terms of possibility, not probability (the symptoms he saw may or may not indicate ataxia), and he admitted that the videotape did not confirm onset of ataxia on that day. Nevertheless, he concluded that his opinion is unchanged because ataxia can wax and wane. But the fact that ataxia can wax and wane is not relevant to when the ataxia begins. Because the videotape does not support, more likely than not, that Will's ataxia began on March 26, 2002, Dr. MacDonald should have changed his opinion, if he were being candid, because it does not support onset.

Dr. Kane, on the other hand, watched the same videotape and saw absolutely nothing abnormal about Will's behavior on the evening of his vaccination. Dr. Kane clarified the confusing series of notes in his records pertaining to onset of Will's cerebellar ataxia (based on what Will's parents had told him). Dr. Kane says that the videotape proves that onset of Will's cerebellar ataxia did not occur on March 26, 2002, but some time thereafter. (The evidence is uncontroverted that Will's behavior was normal on March 27 and 28, 2002.)

The undersigned finds from the records and Dr. Kane's letters that Dr. Kane is an objective, careful, and concerned pediatric neurologist. He reached his ultimate opinion that hepatitis A vaccine caused Will's cerebellar ataxia after considering the record (initially he thought Will had cerebellitis), consulting with an expert neuroimmunologist who himself consulted with colleagues, reviewing medical literature, and consulting with Dr. Hauger, an infectious disease specialist with immunologic training who also was one of Will's treating physicians. This all occurred before litigation. Dr. Kane, the expert neuroimmunologist, the neuroimmunologist's colleagues, and Dr. Hauger were not hired by anyone to testify for anyone's side. Dr. Kane's opinion in December 2006, which comes after litigation began, is consistent with his opinion in 2002 four years before litigation. In light of the Federal Circuit's emphasis in Capizzano on taking seriously the opinions of treating doctors, the undersigned finds that the opinions of Dr. Kane, the expert neuroimmunologist and his colleagues, and Dr. Hauger support Dr. Marks' opinion that Will had an autoimmune reaction to hepatitis A vaccine.

Although Dr. Marks agreed that his assumption that Will had prior exposure to a protein that was identical or similar to one in the vaccine was speculative (in order to have an onset of a mere four days), petitioner does not have the burden, according to the Federal Circuit in Knudsen, of proving a specific biologic mechanism. The Federal Circuit emphasizes in Knudsen, Althen, and Capizzano that petitioner's burden is to prove a plausible medical theory, a logical sequence of cause and effect, and an appropriate temporal interval between vaccination and illness.

The plausible medical theory for autoimmune cerebellar ataxia is that the body, sensing a protein to which it responds, misidentifies its own cells as a target for attack. The logical

sequence of cause and effect is that hepatitis A virus has been causally linked to cerebellar ataxia and the vaccine contains an inactivated form of the hepatitis A virus to which, in rare cases, individuals may respond with cerebellar ataxia. Medical literature links vaccines to cerebellar ataxia. The appropriate temporal framework for causation between viruses and cerebellar ataxia runs from 1 to 21 days, according to the Connolly article. Four days would be included in that span of time. If Will were exposed to a protein in the vaccine to which he was previously exposed, Dr. Marks testified that four days would be an appropriate interval for causation. Of particular interest in the Connolly article (R. Ex. D) is the statement that cerebellar ataxia was worse in children (57%) whose ataxia was due to varicella, Epstein-Barr virus, and vaccination than it was in children (31%) whose ataxia was due to unspecified viral illnesses. Will's ataxia was worse than the common garden-variety, prompting Dr. Kane to search for a more likely cause than a cold. The Nussinovitch article (R. Ex. G) lists hepatitis A virus as a cause of cerebellar ataxia. The vaccine contains inactivated hepatitis A virus.

Dr. MacDonald does not accept that attenuated viral vaccines can cause cerebellar ataxia, even though he concedes it is a theoretical possibility. He also admitted that it was not unreasonable to think that cerebellar ataxia is an immune reaction. Since we know from Dr. Getman's examination of Will on March 26, 2002 that he did not have a cold and was well, and we know that he received a hepatitis A vaccination, the question naturally occurs: to what was Will's cerebellar ataxia an immune reaction? Dr. MacDonald's conclusion is we do not know because over half the time, doctors do not identify the cause. Dr. Mark's, Dr. Kane's, Dr. Hauger's, and the expert neuroimmunolgist's and his colleagues' conclusion is that the hepatitis A vaccine caused Will's cerebellar ataxia.

It is unnecessary for the undersigned to determine whether the specific biologic mechanism is the presence of hepatitis A virus in inactivated form in the vaccine (akin to the subclinical hepatitis A virus in the Tuthill case report [R. Ex. C]) or prior exposure to a protein that is similar or identical to a component of the vaccine in order for petitioners to prevail, according to the Federal Circuit in Knudsen, since petitioners do not have the burden of proving the specific biologic mechanism.

On February 27, 2007, during a status conference, respondent expressed an interest in taking the testimony of Dr. Kane. This was three months after the hearing and nearly a year after petitioners had filed their petition on April 10, 2006, containing their expert Dr. Marks' report (Ex. 27) in which Dr. Marks recounts all the times Dr. Kane noted in the records that hepatitis A vaccine caused Will's cerebellar ataxia. Med. recs. at Ex. 27, pp. 1-6. In listing his reasons for causation in fact, Dr. Marks lists the opinions of treating physicians, including Dr. Kane. Dr. Kane's opinion and the fact that petitioners' expert Dr. Marks relied on Dr. Kane's opinion has been apparent from the first day of this litigation. On November 6, 2006, petitioners' counsel during a status conference stated that Dr. Kane would not be a witness at the hearing.

On March 2, 1007, respondent moved to take the testimony in person of Dr. Kane on the questions of onset and causation. The undersigned held a status conference on March 2, 2007 to discuss this motion, asking petitioners for their response.

On March 6, 2007, petitioners filed a response objecting to respondent's motion because respondent had ample opportunity to take Dr. Kane's testimony before the hearing and even call him as a witness during the hearing.

On March 12, 2007, respondent filed a 22-page response to petitioners' Motion for Decision on the Record, filed February 26, 2007.

Petitioners filed a reply on March 15, 2007. The undersigned agrees with petitioners that respondent's motion is unwarranted and would unnecessarily prolong disposition of this case.

It is clear from Dr. Kane's medical records that he based causation on his own medical literature search and his consultation with an expert neuroimmunologist who, himself, queried his colleagues about the issue of vaccine causation. Dr. Kane also consulted Dr. Hauger, an infectious disease specialist with training in immunology. As for onset, Dr. Kane explained the change in his opinion on onset in his letter interpreting the videotape of Will's second-year birthday party: he did not see Will manifest any signs of ataxia on the videotape and, therefore, Will's ataxia did not begin until after the evening of his vaccination. Dr. MacDonald does not opine that the videotape shows that Will probably had ataxia on that date either (although he does not change his opinion about the onset date).

The Vaccine Act, 42 U.S.C. §300aa-12(d)(3)(B), states that the special master "may require the testimony of any person ... as may be reasonable and necessary." The taking of testimony is discretionary with the special master. The undersigned finds it is neither reasonable nor necessary for respondent to take Dr. Kane's testimony, in light of his ample and numerous explanations for opinion on diagnosis based on his discussion in his medical records of how he reached his opinion that the vaccine caused Will's cerebellar ataxia and his explanation of his change of opinion on onset based on the videotape.

The undersigned finds that Dr. Marks' expert opinion on causation is more credible that Dr. MacDonald's. Dr. MacDonald was less than candid or credible for two reasons: (1) his

insistence that Will's cerebellar ataxia was due to a cold, when Will did not have a cold when he received the hepatitis A vaccine, according to Dr. Getman's medical record of that date; and (2) his adhering to an onset of cerebellar ataxia on the day of vaccination after viewing the videotape of Will's birthday party that night when he admitted in his report that the signs he saw were not sufficient to diagnose ataxia. Because of Dr. MacDonald's lack of credibility on these issues and respondent's failure to impeach Dr. Marks' testimony, petitioners have prevailed in this case.

This was always a strong case for petitioners and, in a June 6, 2006 Order, the undersigned suggested the parties attempt to settle the case. For whatever reason, that settlement did not occur. Nine months later, we are now in damages.

Petitioners have proved a prima facie case of causation in fact and proved that hepatitis A vaccine was a substantial factor in causing Will's cerebellar ataxia and, but for hepatitis A vaccine, Will would not have had acute cerebellar ataxia.

CONCLUSION

Petitioners have prevailed on the issue of entitlement. The undersigned encourages the parties to attempt to settle damages in this case and also offers alternative dispute resolution as a possible means of completing damages in this case. A telephonic status conference shall be set soon to discuss how to proceed with damages.

IT IS SO ORDERED.

_____ _____

DATE Laura D. Millman
Special Master