OFFICE OF SPECIAL MASTERS

Filed: December 13, 2005

MADISON RINDFLEISCH, by her mother and next friend LORI RINDFLEISCH,	*	
Petitioner,	*	No. 03-1952V
v.	*	CORRECTED COPY
SECRETARY OF HEALTH AND HUMAN SERVICES,	*	
Respondent.	*	

Ronald C. Homer, with whom was Sylvia Chin-Caplan, Boston, Massachusetts, for Petitioner.

Traci R. Patton, United States Department of Justice, Washington, D.C., for Respondent.

DECISION[1]

SWEENEY, Special Master

On August 19, 2003, Lori Rindfleisch, on behalf of her daughter Madison Rindfleisch ("Madison"), filed a petition for compensation under the National Childhood Vaccine Injury Act ("Vaccine Act"), 42 U.S.C. §§ 300aa-1 to -34 (2000 & Supp. II 2003). The petition alleges that Madison developed a variant of Guillain-Barré syndrome ("GBS")[2] as a result of diphtheria,

[1] The court encourages the parties to review Vaccine Rule 18, which affords each party 14 days to object to disclosure of (1) trade secrets or commercial or financial information that is privileged or confidential or (2) medical information that would constitute "a clearly unwarranted invasion of privacy."

[2] Guillain-Barré syndrome is otherwise known as acute idiopathic polyneuritis. Dorland's Illustrated Medical Dictionary 803 (30th ed. 2003). Acute idiopathic polyneuritis is:

> [a] rapidly progressive ascending motor neuron paralysis of unknown etiology, frequently after an enteric or respiratory infection. An autoimmune mechanism following viral infection has been postulated. It begins with paresthesias of the feet, followed by flaccid paralysis of the entire lower limbs, ascending to the trunk, upper limbs, and face and is attended by slight fever, bulbar palsy, absent or

tetanus, and pertussis ("DTP")[3] and inactivated polio virus ("IPV")[4] vaccinations administered on August 10, 2000, and/or measles, mumps, and rubella ("MMR")[5] and varicella[6] vaccinations administered on August 14, 2000.

The hearing in this matter was held in Boston, Massachusetts, on June 30, 2005. Testifying for petitioner was J. Ben Renfroe, M.D. Testifying for respondent was Arnold D. Gale, M.D. Posthearing briefing was completed on November 18, 2005.

I. FACTUAL HISTORY

Madison was born on November 9, 1994.[7] Pet. at 1. Ms. Rindfleisch's pregnancy was complicated by hypertension and labor was induced, but Madison encountered no problems in the neonatal period. Pet. Ex. 2 at 2. Up until August 2000, Madison was a healthy child except for the usual childhood ailments. Id. at 2-9; Pet. at 2; Pet. Ex. 1 at 5. In addition, Madison was up-to-date with her vaccinations. See Pet. Ex. 3 at 28.

> lessened tendon reflexes, and an increase in the protein of the cerebrospinal fluid without corresponding increase in cells.

Id. at 1482.

[3] The DTP vaccine is "a combination of diphtheria toxoid, tetanus toxoid, and pertussis vaccine; administered intramuscularly for simultaneous immunization against diphtheria, tetanus, and pertussis." Dorland's Illustrated Medical Dictionary, supra note 2, at 1998.

[4] The IPV vaccine is "a suspension of formalin-inactivated poliovirus . . . administered intramuscularly or subcutaneously for immunization against poliomyelitis." Dorland's Illustrated Medical Dictionary, supra note 2, at 2000.

[5] The MMR vaccine is "a combination of live attenuated measles, mumps, and rubella viruses, administered subcutaneously for simultaneous immunization against measles, mumps, and rubella." Dorland's Illustrated Medical Dictionary, supra note 2, at 1999.

[6] The varicella vaccination is "a preparation of live, attenuated human herpesvirus 3 (varicella-zoster virus) administered subcutaneously for production of immunity to varicella and herpes zoster." Dorland's Illustrated Medical Dictionary, supra note 2, at 2000. Varicella is commonly known as chickenpox. Id. at 2008. Herpes zoster, also called shingles, is "an acute infectious, usually self-limited, disease believed to represent activation of latent human herpesvirus 3 in those who have been rendered partially immune after a previous attack of chickenpox." Id. at 845.

[7] All references to the Petition shall be designated herein as "Pet. at __." All references to the pertinent Petitioner's Exhibit shall be designated herein as "Pet. Ex. __ at __."

On August 10, 2000, Madison had a well-child examination prior to her entry into kindergarten. Pet. at 2. Madison was declared a healthy child and given DPT and IPV vaccinations. Id.; Pet. Ex. 3 at 23, 28. Then, on August 14, 2000, Madison received MMR and varicella vaccinations after being declared healthy. Pet. at 2; Pet. Ex. 3 at 16, 28.

Madison began to show signs of a cold on September 2, 2000. Pet. at 2. After a couple of days, on September 4, 2000, Madison was taken to the urgent care facility at Sarasota Medical Center and diagnosed with an upper respiratory infection ("URI") and pharyngitis. Id. at 2-3; Pet. Ex. 12 at 1. She was given a prescription for Amoxicillin, an antibiotic. Pet. Ex. 12 at 1.

On September 9, 2000, Madison began to complain about neck pain and she was brought back to the urgent care center. Id. at 2; Pet. at 3. Madison was diagnosed with a URI and tonsillitis. Pet. at 3; Pet. Ex. 12 at 2. Madison's antibiotic prescription was changed to Zithromax. Pet. Ex. 4 at 3; Pet. Ex. 12 at 2. After this visit, Madison grew weaker through the rest of that weekend. Pet. at 3.

Madison returned to the urgent care center on September 11, 2000, due to the weakness and continuing cold symptoms. Id.; Pet. Ex. 12 at 3. Madison was diagnosed with a URI and an ear infection. Pet. at 3; Pet. Ex. 12 at 3. Her prescription was changed to another antibiotic, Ceclor, and Ms. Rindfleisch was told to observe Madison for a few days as Madison should improve. Pet. Ex. 4 at 3; Pet. Ex. 12 at 3.

Madison was brought to the emergency room at Sarasota Memorial Hospital on September 13, 2000, because she was dehydrated and her weakness increased such that she could no longer swallow, sit up, or walk. Pet. at 3; Pet. Ex. 4 at 3, 43-44, 53. The physician noted that Madison's mother had the same symptoms the prior week, but those symptoms resolved. Pet. Ex. 4 at 53. Madison was admitted to the pediatric unit for observation of her dehydration. Pet. Ex. 4 at 3, 8; Pet. at 3-4. In the pediatric admission records, the nurse noted that Madison got a cold that her mother had. Pet. Ex. 4 at 34. Ear, nose, and throat specialists ruled out an infectious cause for Madison's airway obstruction. Id. at 4. Computed tomography scans[8] of Madison's head and neck were normal and did not show any airway obstructions. Id. at 4, 10, 38-39; Pet. at 4.

[8] A computed tomography scan, more familiarly known as a CT scan, is a "recording of internal body images at a predetermined plane by means of the tomograph." Dorland's Illustrated Medical Dictionary, supra note 2, at 1919. A tomograph is "an apparatus for moving an x-ray source in one direction as the film is moved in the opposite direction, thus showing in detail a predetermined plane of tissue while blurring or eliminating detail in other planes." Id. In a CT scan, "the emergent x-ray beam is measured by a scintillation counter; the electronic impulses are recorded on a magnetic disk and then are processed by a mini-computer for reconstruction display of the body in cross-section on a cathode ray tube." Id.

On September 14, 2000, Madison had a lumbar puncture,[9] showing a white blood cell count of 32, which was elevated, with one poly, 99 monos, and four red blood cells.[10] Pet. Ex. 4 at 103. All of the white blood cells were mononuclear. Id. A consultation record from that same date indicates that both Madison and her mother had URI symptoms over the past several weeks. Id. at 47.

The physicians at Sarasota Memorial Hospital grew concerned about Madison's increasing neurological deficits and accompanying airway compromise. Id. at 4-5, 10; Pet. at 4. Specifically, on the morning of September 15, 2000, Richard A. Perez, M.D., noted:

> [Madison] was unable to lift her head from the pillow or turn it from side to side. She has full range of motion of her eyes. She has poor tone in her lower extremities. She has poor tone of the upper extremities with the inability to even lift her hands now. She is also complaining of muscle pain when she is handled or moved in any way. She is being suctioned from time to time by the nursing staff and the mother.

Pet. Ex. 4 at 5. Thus, in order to obtain a higher level of pediatric care for her worsening symptoms, Madison was transferred to All Children's Hospital ("ACH") on September 15, 2000. Id. at 5, 10, 51; Pet. at 4; Pet. Ex. 5 at 2-3.

Upon her arrival at ACH, Madison was examined by neurologist Joseph Casadonte, M.D. Pet. Ex. 6 at 10-12. After obtaining a history and performing a physical examination, Dr. Casadonte reported:

> Madison shows progressive weakness coincident with a URI infection. She has evidence of bulbar dysfunction,[11] that includes asymmetric motor weakness; deep tendon dependent reflexes are depressed. They are present in the ankles.

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[9] A lumbar puncture is "the withdrawal of fluid from the subarachnoid space in the lumbar region, usually between the third and fourth lumbar vertebrae, for diagnostic or therapeutic purposes." Dorland's Illustrated Medical Dictionary, supra note 2, at 1546.

[10] The medical records also contain results from cerebrospinal fluid tests dated September 15, 2000. Pet. Ex. 4 at 103-04. The specimen number differs from the one assigned to the tests performed on September 14, 2000. Id. at 103. No viruses were isolated from the sample. Id.

[11] The bulb, also known as the medulla oblongota or myelencephalon, is the part of the brain that "contains important collections of nerve cells that deal with vital functions, such as respiration, circulation, and special senses." Dorland's Illustrated Medical Dictionary, supra note 2, at 259, 1113.

> Sensation in intact and she has some hyperpathia.[12] I suspect she has an atypical presentation of Guillain-Barre. The differential includes brain stem encephalitis.[13]

Pet. Ex. 6 at 11 (footnotes added); see also Pet. at 5.

On September 15, 2000, Madison was tested for the presence of echovirus and coxsackie virus antibodies.[14] Pet. Ex. 6 at 93, 97. The tests revealed a slightly high level of echovirus type 11 and a high level of coxsackie A-9. Id. Four days later, she was tested again for echovirus antibodies, and types 4, 11, and 30 were high. Id. at 89.

Madison underwent a repeat lumbar puncture on September 16, 2000. Id. at 85-86, 99-100. The results of this lumbar puncture revealed two red blood cells and one white blood cell, but were negative for bacteria and viruses. Id. at 86, 99-100.

Also on September 16, 2000, Madison was placed on a ventilator to help her breathe. Id. at 2, 200; Pet. at 5. On September 20, 2000, Madison underwent a procedure to remove a foreign body (a tooth fragment) from her airway. Pet. Ex. 6 at 47-55, 73-75, 177. After this procedure, she was removed from the ventilator. Id. at 2, 174, 177.

Magnetic resonance images ("MRI")[15] of Madison's brain were normal on September 15 and 18, 2000. Id. at 1, 78, 83-84, 200. An MRI of Madison's cervical spine on September 15, 2000, revealed questionable fullness and questionable increased signal intensity at C3 through C6. Id. at 1, 83-84. The MRI report notes that the cervical spine findings were mild and could be normal. Id. at 84. An MRI of Madison's cervical spine on September 18, 2000, was normal. Id. at 1, 77.

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[12] Hyperpathia is the "abnormally exaggerated subjective response to painful stimuli . . . ." Dorland's Illustrated Medical Dictionary, supra note 2, at 885.

[13] Encephalitis is the "inflammation of the brain." Dorland's Illustrated Medical Dictionary, supra note 2, at 608.

[14] An antibody is "an immunoglobulin molecule that has a specific amino acid sequence by virtue of which it interacts only with the antigen that induced its synthesis . . . or with antigen closely related to it." Dorland's Illustrated Medical Dictionary, supra note 2, at 100.

[15] An MRI is "a method of visualizing soft tissues of the body by applying an external magnetic field that makes it possible to distinguish between hydrogen atoms in different environments." Dorland's Illustrated Medical Dictionary, supra note 2, at 908.

Madison was finally discharged from ACH on October 1, 2000, with a diagnosis of probable rhombomyelitis,[16] as she did not have the typical presentation of GBS. Pet. at 5-6; Pet. Ex. 6 at 1. The discharge summary from ACH, written by Mark Nichter, M.D., states:

> At the time of discharge, [Madison] had bilateral proximal upper extremity weakness with a virtually non existing shoulder shrug, she could march her fingers up and about her body and this was her method of moving her upper extremities. She had weak bilateral hand grip, but was able to grasp a suction catheter with both hands and manipulate it. She had proximal left lower extremity weakness greater than right lower extremity weakness. She had asymmetrical smile with mild weakness on the left side of her face. She could swallow although it was inefficient. There seemed to be asymmetry with weakness of the left side of the pharyngeal musculature.

Pet. Ex. 6 at 2. Dr. Nichter further wrote:

> It was Dr. Casadonte's feeling that this was a potentially polio like illness and was either due to a primary infectious cause of the brain stem and proximal spinal cord or apparent inflammatory antibody mediated response. No definite offending organism could be identified during this hospitalization although several antibody tests are pending at the time of discharge.

Id. at 3. Madison was being fed through a nasogastric tube at the time of her discharge and was slated to begin outpatient rehabilitation. Id. at 2-3.

Madison had a swallowing study performed at the Children's Hospital Medical Center of Akron on October 16, 2000. Pet. Ex. 7 at 15. Madison was still having difficulty swallowing, but could tolerate small sips of thin liquids. Id. She had another swallowing study performed on October 25, 2000. Id. at 16. Her swallowing ability had improved and she was permitted to have "[s]mall, judicious oral feeds (liquid/solid) on a daily basis." Id.

Madison also apparently underwent occupational and physical therapy at the Children's Hospital Medical Center of Akron from October through December 2000. Id. at 3-29. At Madison's initial evaluation, the occupational therapist noted that Madison had no active

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[16] Myelitis is the "inflammation of the spinal cord . . . ." Dorland's Illustrated Medical Dictionary, supra note 2, at 1209. The prefix "rhombo" likely refers to the rhombencephalon, which is the part of the brain that is comprised of the cerebellum, pons, and medulla oblongota. Id. at 1630. The pons and medulla oblongota are also parts of the brain stem. Id. at 246. In the discharge summary from ACH, Mark Nichter, M.D., indicated that Madison's brain stem and spinal cord were affected. Pet. Ex. 6 at 3. Another physician, Albert Saltiel, M.D., refers to the condition as rhomboencephalitis. Id. at 138, 156.

movement of her shoulders and right elbow, and minimal movement of her wrists, left elbow, and left hand. Id. at 20.

Madison underwent aquatic physical therapy from December 18, 2000, through April 11, 2001. Pet. Ex. 8 at 1-9.

Madison slowly made some improvements, but she continued to have very limited use of her right arm and had tight heel cords. Pet. at 7-8; Pet. Ex. 9 at 1-7. Madison continues to suffer the effects from her illness. Pet. at 8.

II. DISCUSSION

A. The Vaccine Act and Federal Circuit Precedent

Pursuant to 42 U.S.C. § 300aa-13(a)(1), the court shall award compensation if petitioner[17] proves, by a preponderance of the evidence, all of the elements set forth in § 300aa-11(c)(1)[18] of the Vaccine Act and that the illness is not due to factors unrelated to the administration of the vaccine.[19] A petitioner in the Vaccine Program can recover in one of two ways: either by proving an injury listed on the Vaccine Injury Table ("Table")[20] or by proving causation in fact.

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[17] Section 11(b)(1) requires that: (1) only the "person who sustained a vaccine-related injury . . . or the legal representative of any person who died as the result of the administration of a [Table vaccine] . . ." can bring an action for vaccine injury-related claims (so long as the requirements of subsection (c)(1) are satisfied) and (2) that no previous civil action was filed in the same matter. Petitioner, as Madison's mother, is the appropriate person to maintain this action.

[18] Subsection (c)(1) requires, inter alia, that the following elements be satisfied: (1) that the vaccine in question is set forth in the Vaccine Injury Table; (2) that the vaccine was received in the United States or in its trust territories; (3) that the injured person either sustained an injury as a result of the administration of a Table-designated vaccine for a period of more than six months after the administration of the vaccine, suffered illness, disability, injury, or condition from the vaccine which resulted in inpatient hospitalization and surgical intervention, or died from the administration of the vaccine; and (4) that the petitioner has not previously collected an award or settlement of a civil action for damages arising from the alleged vaccine-related injury or death.

[19] Of course, the petition must also be filed within the statutory period. 42 U.S.C. § 300aa-16(a). The petition in this case was timely filed.

[20] Petitioners can prove a Table injury by showing that they, or the injured person, received a vaccine listed on the Table and suffered an injury, or an acute complication or sequela of that injury, associated with that vaccine within the prescribed time period. 42 U.S.C.

In this case, petitioner cannot prove a Table injury because even though the DPT, IPV, MMR, and varicella vaccines are listed on the Table, Madison's alleged injuries are not. Thus, petitioner proceeded on a causation-in-fact theory.

In order to prevail under a theory of causation in fact, petitioner must show by a preponderance of evidence that the vaccine in question caused the injury. Bunting v. Sec'y of HHS, 931 F.2d 867, 872 (Fed. Cir. 1991). The Federal Circuit has explained what is required to meet that burden. Specifically, petitioner must establish that the vaccine can cause the injury in question, as well as show that the vaccine is in fact the cause of the injury alleged. Hines ex rel. Sevier v. Sec'y of HHS, 940 F.2d 1518, 1525 (Fed. Cir. 1991). To make the requisite showing, petitioner must offer "proof of a logical sequence of cause and effect showing that the vaccination was the reason for the injury." Shyface v. Sec'y of HHS, 165 F.3d 1344, 1353 (Fed. Cir. 1999) (quoting Grant v. Sec'y of HHS, 956 F.2d 1144, 1148 (Fed. Cir. 1992)). Although petitioner need not demonstrate her theory of causation to a medical or scientific certainty, Knudsen ex rel. Knudsen v. Secretary of HHS, 35 F.3d 543, 548-49 (Fed. Cir. 1994), causation in fact requires a reputable medical or scientific explanation supporting this logical sequence of cause and effect. Jay v. Sec'y of HHS, 998 F.2d 979, 984 (Fed. Cir. 1993) (quoting Grant, 956 F.2d at 1148). As Congress directed, "[E]vidence in the form of scientific studies or expert medical testimony is necessary to demonstrate causation" for a petitioner seeking to prove causation in fact. H.R. Rep. No. 99-908, at 15 (1986).

Without more, "evidence showing an absence of other causes does not meet petitioners' affirmative duty to show actual or legal causation." Grant, 956 F.2d at 1149. Petitioner must not only show that the vaccine was the but-for cause of the injury, but also that the vaccine was a substantial factor in bringing about the injury. Shyface, 165 F.3d at 1352. In essence, the special master is looking for a reputable medical explanation of a logical sequence of cause and effect (Grant, 956 F.2d at 1148), and medical probability rather than certainty (Knudsen, 35 F.3d at 548-49). As the Federal Circuit explained in Knudsen, medical probability means biologic credibility or plausibility: "Causation in fact under the Vaccine Act is thus based on the circumstances of the particular case, having no hard and fast per se scientific or medical rules." 35 F.3d at 547.

In a recent decision, the Federal Circuit instructed:

> Concisely stated, [petitioner's] burden is to show by preponderant evidence that the vaccination brought about her injury by providing: (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. If [petitioner] satisfies this burden, she is "entitled to recover unless the

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§§ 300aa-11(c)(1)(C)(i), -13(a)(1)(A). However, respondent can rebut the presumption by showing that a factor unrelated to the vaccine(s) caused the injury. Id. § 300aa-13(a)(1)(B).

> [government] shows, also by a preponderance of evidence, that the injury was in fact caused by factors unrelated to the vaccine." Knudsen v. Sec'y of Health & Human Servs., 35 F.3d 543, 547 (Fed. Cir. 1994) (alteration in original) (citation omitted).

Althen v. Sec'y of HHS, 418 F.3d 1274, 1278 (Fed. Cir. 2005). The Federal Circuit further explained that the "heavy lifting" required to establish causation by a preponderance of evidence in causation-in-fact cases should not be misconstrued to indicate that the burden is higher than that required by statute:

> While it may be true that proof of causation by preponderant evidence is not as "easy" as proof of causation by operation of law, neither Hodges nor Lampe instructs that the preponderance standard itself is to be made more onerous in vaccine cases. Nor is it to be made more difficult merely because our cases have referred to it as "heavy lifting."

Id. at 1280. Finally, the Federal Circuit explained that "close calls regarding causation are resolved in favor of injured claimants." Id. At hearing, petitioner was unable to prove that Madison suffers from atypical GBS. Nor did she present a logical sequence of cause and effect that demonstrated how Madison's DPT, IPV, MMR, and varicella vaccinations can cause and did cause her alleged atypical GBS.

B. Submitted Medical Literature

In support of her claim, petitioner filed Exhibit 18, consisting of seven articles from the medical literature.[21] Pet. Ex. 18 at Tabs A-G. Tab A is a three-page excerpt from the "National Childhood Encephalopathy Study." R. Alderslade et al., The National Childhood Encephalopathy Study, in Whooping Cough: Reports from the Committee on Safety of Medicines and the Joint Committee on Vaccination and Immunisation 79, 141-43 (1981). The authors note that reactions, including acute neurological reactions, to the measles vaccine occurred within seven to 14 days of inoculation due to delayed hypersensitivity. The risk of reaction is one in 87,000 immunizations.

Tab B is an article from the Canadian Pediatric Society/Health Canada Immunization Monitoring Program ("IMPACT"). Nicole LeSaux, M.D. et al., Decrease in Hospital Admissions for Febrile Seizures and Reports of Hypotonic-Hyporesponsive Episodes Presenting to Hospital Emergency Departments Since Switching to Acellular Pertussis Vaccine in Canada: a Report from IMPACT, 112 Pediatrics e348 (2003). The authors found a 79 percent decrease in febrile seizures following the introduction of the acellular pertussis vaccine, but no significant

[21] Althen confirmed that the Vaccine Act does not require a petitioner to provide medical literature to prove her case. 418 F.3d at 1280.

decrease in febrile seizures temporally related to the MMR vaccine six to14 days after inoculation.

Tab C is a chapter from a pediatric neurology textbook. Gerald M. Fenichel, Neurological Complications of Immunizations, in Pediatric Neurology: Principles and Practice 925 (Kenneth F. Swaiman ed., 1989). The author notes that "[n]eurological complications that are not ordinarily associated with natural measles infection are not likely to be caused by immunization." Id. at 928. Seizures may occur seven to 14 days after measles immunizations. Additionally, the author indicates that all children who were reported to have had encephalopathy during the second week after measles vaccination recovered without neurologic sequelae. Id.

Tab D is an article regarding the Australian Measles Control Campaign. Rennie M. D'Souza et al., Adverse Events Following Immunisation Associated with the 1998 Australian Measles Control Campaign, 24 Communicable Diseases Intelligence 27 (2000). The authors indicate that most reactions occurring within 30 days of an MMR vaccination were fainting, local reactions, and short-lived allergic reactions. The rate of encephalopathy was 0.06 per 100,000 administered doses, based upon one case that the authors categorized as possibly caused by the vaccine. Id. at 29. The individual reported as having encephalopathy developed stomach pain, anorexia, headache, ear infection, and aggressive behavior four days after vaccination. He recovered in one week and did not require hospitalization. The authors considered this a transient encephalopathy possibly related to the MMR vaccine. Id. at 30. The authors state that the incidence of encephalitis after measles vaccination is approximately one in 1,000,000 doses. Id. at 32.

Tab E is another article about Australian vaccinations. Glenda Lawrence et al., Surveillance of Adverse Events Following Immunization: Australia, 2000-2002, 27 Communicable Diseases Intelligence 307 (2003). Although the authors list illnesses as reactions, the illnesses are not linked to specific vaccines.

Tab F is a postlicensure surveillance study of the varicella vaccine. Robert P. Wise, M.D., M.P.H. et al., Postlicensure Safety Surveillance for Varicella Vaccine, 284 JAMA 1271 (2000). According to the authors, the most frequent reaction reported after varicella vaccine was rash. Pharyngitis and neurological syndromes were also reported. Three patients developed GBS. Id. at 1275.

Tab G is an article from a symposium entitled Pathobiology and Oligodendrocyte. Stephen A. Stohlman & David R. Hinton, Viral Induced Demyelination, 11 Brain Pathology 92 (2001). The authors contend that a diverse group of viruses can cause demyelination in people. They state, "Demyelinating lesions in humans may also occur rarely following systemic, most likely viral upper respiratory infections." Id. at 92. These infections include those caused by measles, mumps, varicella, and influenza viruses. Id. at 93. The process would be consistent with an autoimmune disease. Id. at 102.

Petitioner filed additional medical literature in support of her claim. Petitioner's Exhibit 24 is the entry for the Varivax vaccine from the Physicians' Desk Reference ("PDR"). Physicians' Desk Reference 2202-04 (56th ed. 2002). The entry lists the following adverse reactions for children ages one to 12, in decreasing order of frequency: upper respiratory illness, cough, irritability/nervousness, fatigue, disturbed sleep, loss of appetite, otitis (ear infection), headache, malaise, and nausea. Id. at 2204. In addition, the PDR lists the neurologic reaction of GBS, as well as pharyngitis. Id.

Petitioner's Exhibit 25 is a page from a pediatric textbook regarding the varicella-zoster virus. Martin G. Myers & Lawence R. Stanberry, Varicella-Zoster Virus, in Nelson Textbook of Pediatrics 973 (Richard E. Behrman et al. eds., unknown year). The authors note that in both the early and late parts of the incubation period, the varicella virus replicates in the respiratory tract. Symptoms of infection occur 14 to 15 days after exposure and constitute a rash, fever, malaise, anorexia, headache, and occasionally mild abdominal pain.

Respondent filed medical literature to contest petitioner's allegations. Respondent's Exhibit C is an article discussing the historical use of the term "poliomyelitis." James J. Sejvar, West Nile Virus and Poliomyelitis, 63 Neurology 206 (2004). The authors also discuss the association of West Nile virus and acute flaccid paralysis that resembles poliomyelitis.

Respondent's Exhibit D is an article concerning the evolution of new human viruses causing a paralytic poliomyelitis syndrome and rhomboencephalitis. Richard T. Johnson, Emerging Viral Infections of the Nervous System, 9 J. NeuroVirology 140 (2003).

Respondent's Exhibit E is an article that addresses the confusion over the term "poliomyelitis." Tom Solomon & Hugh Willison, Infectious Causes of Acute Flaccid Paralysis, 16 Current Opinion in Infectious Disease 375 (2003). The authors also discuss the importance of distinguishing between West Nile virus-caused acute flaccid paralysis and GBS. Anterior myelitis caused by poliovirus and West Nile virus is manifested by acute viral illness, then rapid onset of asymmetrical flaccid weakness, often with muscle tenderness. On the other hand, GBS is manifested by a gradual onset of ascending symmetrical weakness with sensory involvement, often involving the facial nerve, several weeks after viral infection or vaccination. In addition, the authors state that the second most common antecedent of GBS is cytomegalovirus, typically causing a URI. Id. at 377.

Respondent's Exhibit F is an article finding that acute flaccid paralysis may be caused by species B adenoviruses. Juliana P.R. de Azevedo et al., Characterization of Species B Adenoviruses Isolated from Fecal Specimens Taken from Poliomyelitis-suspected Cases, 31 J. Clinical Virology 248 (2004).

C. Hearing of June 30, 2005

The special master conducted a hearing in this matter on June 30, 2005, in Washington, D.C. Petitioner presented the expert testimony of J. Ben Renfroe, M.D. Respondent presented the expert testimony of Arnold D. Gale, M.D.

1. Testimony of J. Ben Renfroe, M.D.

Dr. Renfroe, a pediatric neurologist with a small percentage of adult patients, testified for petitioner.[22] Tr. at 4-5. His opinion is that the varicella, measles, and polio vaccines caused Madison's condition. Id. at 6. Wild varicella, varicella vaccine, and measles can result in autoimmune phenomena such as GBS, as well as transverse myelitis[23] and encephalitis. Id. at 7. Measles also can suppress the immune system, making a vaccinee more susceptible to the sequelae of these vaccines or the wild viruses. Id.

The temporal relationship between Madison's vaccinations (administered four days apart) and her illness was significant to Dr. Renfroe in forming his opinion. Id. Dr. Renfroe found Madison's clinical course fascinating and somewhat unique–she developed bulbar problems, throat pain, swallowing difficulties leading to her being on a ventilator, and weakness. Id. at 7-8.

On August 10, 2000, Madison received DPT and IPV vaccinations, followed by MMR and varicella vaccinations on August 14, 2000. Then, in the beginning of September 2000, she apparently had a URI with sore throat, discomfort, and cough. Id. at 8. Madison experienced an ongoing process, leading to paralysis of her ability to breathe and swallow. Id. Even though the paralysis was associated with the viral symptoms, Dr. Renfroe found it difficult to tell when the paralysis began. Id.

Madison had a lumbar puncture showing elevated white blood cells, which was otherwise normal. She was transferred from Sarasota Hospital to ACH, where she was placed on a ventilator. Id. at 10. Her lumbar puncture was repeated, showing not only elevated white blood cells, but also that the white blood cells were mononuclear cells. These cells were the only signs of inflammation. Id. Another lumbar puncture, performed in the next day or two, was perfectly normal. Id. Dr. Renfroe wondered if the Sarasota Hospital lumbar puncture was actually abnormal. Id.

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[22] All references to the Transcript of the June 30, 2005 proceedings shall be designated herein as "Tr. at __."

[23] Transverse myelitis is "the inflammation of the spinal cord . . . in which the functional effect of the lesions spans the width of the entire cord at a given level." Dorland's Illustrated Medical Dictionary, supra note 2, at 1209.

Dr. Renfroe's opinion is that Madison had a peripheral, not a central, nervous system pathology because he did not see any evidence of a brain lesion. Id. at 11. An MRI was performed that showed possible pathology. But afterwards, the MRI was normal. Id. at 10-11. And, initially, Dr. Casadonte, Madison's treating neurologist, diagnosed an unusual variant of GBS or rhombomyelitis. Id. at 12. "Rhombo" means the hind brain, which is the brainstem, including the pons and medulla, and cerebellum. Id. The diagnosis of rhombomyelitis is consistent throughout the medical records. Id. However, regarding the discharge diagnosis of probable rhombomyelitis, Dr. Renfroe stated: "As it flowed down, nobody ever went back and addressed that issue. The staff and attending physicians of the intensive care unit had simply placed rhombomyelitis on the chart and that stuck with the child." Id. at 39. He explained that the diagnosis remained in the medical records "for simplicity's sake." Id. at 12.

Dr. Renfroe disagrees with the diagnosis of rhombomyelitis or encephalitis, which are central nervous system conditions, because the MRI did not show a lesion. However, Dr. Renfroe had to admit that Madison did have a central nervous system pathology because her seventh cranial nerve[24] became weak two days after she was admitted to ACH. Id. at 12. But then, he discounted his statement because in cases where the seventh cranial nerve is affected, it is likely that the nearby sixth cranial nerve[25] is also affected. Id. at 12-13. Madison did not have palsy or eye movement abnormalities that one would see in a sixth cranial nerve pathology. Therefore, Dr. Renfroe suspected that Madison's seventh cranial nerve weakness was a peripheral problem. Id. at 13.

Dr. Renfroe claims that a central nervous system disease would not have caused the pattern of weakness exhibited by Madison. Id. at 12. Madison's weakness was flaccid or floppy, not spastic.[26] Id. at 13. In brain function, there is an upper motor neuron and a lower motor neuron. The upper motor neuron controls and suppresses the spinal cord. The lower motor neuron involves the anterior horn cells,[27] which are affected in amyotropic lateral sclerosis, spinal muscular dystrophy, and polio. Anything affecting below the lower motor neuron or anterior horn cells causes floppiness. Anything affecting above the lower motor neuron causes spasticity.

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[24] The seventh cranial nerve supplies the muscles of facial expression. Dorland's Illustrated Medical Dictionary, supra note 2, at 1237, 1239.

[25] The sixth cranial nerve supplies the lateral rectus muscle of the eye. Dorland's Illustrated Medical Dictionary, supra note 2, at 1237.

[26] Spasicity is the state of being "hypertonic, so that the muscles are stiff and the movements awkward." Dorland's Illustrated Medical Dictionary, supra note 2, at 1729.

[27] The anterior horn of the spinal cord is "the horn-shaped configuration presented by the anterior column of the spinal cord in transverse section . . . ." Dorland's Illustrated Medical Dictionary, supra note 2, at 419. Anterior horn cells are motor neurons "whose cell bodies are in the anterior horn of the spinal cord." Id. at 318.

Id. Madison has always been floppy. Dr. Renfroe considers a central nervous system problem to lead to spasticity and not floppiness. Id. at 14.

Dr. Renfroe believes that Madison had the peripheral nervous system injury of GBS. Id. at 16. GBS is an ascending paralysis. It is an autoimmune disease affecting the peripheral nerves both close to the spinal cord and distally. Id. at 14, 32. After some insult to the body occurs, whether trauma, viruses, or certain other organisms, the body forms an autoimmune response to the myelin[28] around the nerves, destroying the myelin and causing paralysis. Id. at 16. GBS has multiple clinical pictures. Id. at 15.

Campylobacter is an organism associated with GBS. Id. at 16. GBS has also been reported after measles and varicella infections. Id. Additionally, some cases of GBS are idiopathic and the cause is unknown. Id. In GBS, a protein is introduced into the body, prompting the body to form antibodies against it. That protein appears similar to a protein on the myelin sheath and, after the antibodies attack the virus, they attack the body. Id. at 17. A postinfectious disorder would be similar: an infection or stimuli causes the body to create antibodies against the protein. Once the infection is cleared, the body attacks proteins it finds that are similar in the nervous system. Id.

Dr. Renfroe stated that GBS is diagnosed mainly clinically, based upon a patient's symptoms and test results. Id. at 18. According to Dr. Renfroe, the problem in this case is that Madison's lumbar puncture was done too early and did not show the cytoalbuminologic dissociation[29] that is indicative of GBS. A physician needs to wait at least a week or two after the onset of neurologic symptoms before doing studies to confirm GBS. Id. at 19. However, Dr. Renfroe did admit that it was not premature to perform a lumbar puncture on September 14, 2000. Id. at 31-32. Dr. Renfroe would expect to see elevated proteins in a lumbar puncture of someone with GBS. Id. at 18. Dr. Renfroe cannot say that the battery of tests done on Madison ruled out a viral cause because there are many viruses and pathologies that Madison was not tested for. Id. at 20-21.

Dr. Renfroe stated that the varicella vaccine can lead to Madison's symptoms, as well as the symptoms of GBS. Id. at 21. To him, Madison's sore throat, rhinorrhea,[30] and stiff neck can be symptoms of a virus, but also can be part of her ongoing neurological illness. Id. at 21-22.

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[28] "Myelin is an electrical insulator that serves to speed the conduction of nerve impulses." Dorland's Illustrated Medical Dictionary, supra note 2, at 1689.

[29] Cytoalbuminological, also referred to as albuminocytological, means "pertaining to the level of protein as albumin in relation to the number of cells present in cerebrospinal fluid." Dorland's Illustrated Medical Dictionary, supra note 2, at 45.

[30] Rhinorrhea is "the free discharge of a thin nasal mucus." Dorland's Illustrated Medical Dictionary, supra note 2, at 1629.

According to the literature regarding the varicella virus, illness usually began 14 to 16 days after exposure, although incubation could range from ten to 21 days. Id. at 22. Madison developed her symptoms 19 days after vaccination, which would be within the incubation period for the wild virus. Id. at 23. Dr. Renfroe assumes that the incubation period for postvaccinal symptoms is the same as for exposure to the wild virus, reasoning that the varicella vaccine is made with a live, attenuated[31] virus, although he conceded that he is not an expert in this field. Id.

Nineteen days after receiving varicella vaccine, Madison had upper respiratory symptoms that one would see with any virus or cold. Several days later, she had neck stiffness, worsened cough, and, two days later, progression neurologically. Id. These are symptoms that may occur after varicella vaccination, as described in the PDR. Id. at 24. The PDR also states that GBS can follow varicella vaccination. Id.

Dr. Renfroe also believed that Madison's measles vaccination could have caused Madison's illness because GBS has been reported following both the measles vaccination and infection with the wild virus. Id. In addition, measles has a significant immunosuppressive effect on the vaccinee's ability to fight viral infection. Id. at 24-25. The immunosuppressive effects of measles usually begin within a week or so. Id. at 28. The effects escalate up to two to three weeks and then diminish. Id. Dr. Renfroe found it possible that the measles vaccine contributed to immunosuppressing Madison and so she had an unusual response to an otherwise benign exposure. Id. at 25. Her URI symptoms could have been caused by the measles vaccine, but any viral exposure could cause them. Id.

Dr. Renfroe believes that the URI could be associated with the vaccines and also then progress to a neurologic disorder. GBS caused by a wild virus takes about ten days to occur. But, Madison progressed fairly rapidly in a continuum of illness. Her bulbar failure may have begun prior to her diagnosis on September 19, 2000, because she was complaining of a stiff neck, cough, dysphasia,[32] and difficulty swallowing earlier than September 19. Id. at 25-26. He believes that the measles and/or varicella vaccine(s) caused Madison's neuropathy but is not certain of the "direct lineage." Id. at 26.

On cross-examination, Dr. Renfroe admitted that cytoalbuminologic dissociation of elevated proteins in the spinal fluid, without elevated white blood cells, is commonly found in GBS, but it develops over time and may not be discovered in an early lumbar puncture. Id. at 29. The lumbar puncture was performed over a week after Madison's URI symptoms and at least

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[31] Attenuation is "the reduction of the virulence of a pathogenic organism, usually by adaption to another host or to a different culture medium." Dorland's Illustrated Medical Dictionary, supra note 2, at 178.

[32] Dysphasia is the "impairment of speech, consisting in lack of coordination and failure to arrange words in their proper order, due to a central lesion . . . ." Dorland's Illustrated Medical Dictionary, supra note 2, at 576.

three days after her weakness began. Id. at 31-32. The physicians administered IVIG[33] to Madison, which is the treatment for GBS, transverse myelitis, and a number of other illnesses. She responded very rapidly to this treatment and so the doctors did not pursue a diagnosis. Id. at 31.

Dr. Renfroe maintained that Madison's presentation was atypical of GBS. He believes Madison's peripheral nervous system deteriorated, which he would call a variant of GBS. The symptoms began in her upper extremities. She then developed some bulbar signs. Her ankles were preserved, according to an examination by a medical resident, but several days later, her patella reflexes were zero. Id. at 32-33. However, even atypical reflexes can be gone for months or years in GBS. Id. at 33. Dr. Renfroe admitted that it was inconsistent with the diagnosis of classic GBS for Madison to never have lost her ankle reflexes, but reiterated that her presentation was unusual. Not only is her retention of ankle reflexes unusual for GBS, but the onset in the upper extremities asymmetry are also unusual. Id. at 33-34. Dr. Renfroe considers himself a "lumper" in diagnosis as opposed to a "splitter." Id. at 33.

Dr. Renfroe testifies that Madison's symptom of progressive flaccid paralysis, involving her left facial nerve and diaphragm, is consistent with GBS and polio. Id. at 35. Polio, a disease of the central nervous system, was never considered as a diagnosis in Madison's medical records.[34] Id. at 14, 36. Dr. Renfroe has discussed with petitioner's counsel the possibility that Madison had polio. Id. at 36; see also id. at 48. Dr. Renfroe does not know how to discern where in the structure of Madison's anterior horn cells her lesion is. Dr. Renfroe cannot tell if Madison had a viral response that affected her anterior horn cells as opposed to affecting the peripheral nerves coming from the anterior horn cells. Id. at 36-37.

Dr. Renfroe thinks that the elevated white blood cells in Madison's initial lumbar puncture were an acute stress response, not a real lab value, or a lab error. Id. at 37. The results of that lumbar puncture (high white blood cell count of 32 and absent proteins) are the opposite of what one would expect in GBS, even atypical GBS. Id. at 38. The lumbar puncture was repeated soon thereafter and was normal. Dr. Renfroe cannot explain why it would be normal so rapidly if it was an infectious process–it should have gotten worse. In addition, if it were an acute central nervous system process, it would have gotten worse. Id. Further, the results are inconsistent with GBS because they do not show a cytoalbuminologic dissociation. Id. Nor does the subsequent lumbar puncture show elevated proteins, which is also inconsistent with GBS. Id. at 41.

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[33] IVIG is an abbreviation for intravenous immunoglobulin, and is "a preparation of immune globulin suitable for intravenous administration; used in the treatment of primary immunodeficiency disorders." Dorland's Illustrated Medical Dictionary, supra note 2, at 778.

[34] Dr. Renfroe has never seen a case of polio. Tr. at 69.

Dr. Renfroe repeated that Madison had an adverse reaction to the measles vaccine, including immunosuppression. "Some entity at that point proceeded on to cause a significant neurologic injury in this child." Id. at 43. She had a fairly remarkable response to some insult and developed a profound, persisting neuropathy. Id. at 44. No laboratory data shows evidence of immunosuppression in Madison's case. Id. at 45. Dr. Renfroe could not point to anything in Madison's case, except her clinical course, that would transmute the biologic possibility of the MMR vaccine's having an immunosuppressive effect on Madison to the probability that this happened in Madison's case. Id. But, Madison had an unusual outcome to something. And, both wild measles and measles vaccine can lead to transverse myelitis or GBS. Id. at 46. Madison does not have transverse myelitis or typical GBS. Id. Further, Dr. Renfroe believes that rhombomyelitis is just another name for transverse myelitis. Id. at 47. He does not see any evidence that Madison had rhombomyelitis, but if one "goes with" rhombomyelitis, then the measles and varicella vaccine have been associated with myelitis, just as they have been with GBS. Id.

In addition, Dr. Renfroe does not think that Madison's clinical course was highly consistent with a naturally-acquired viral infection with gray matter[35] central nervous system involvement because that would require a very selective knock-out of these neurons. Id. at 48. However, Dr. Renfroe stated that the polio virus would present in a very similar fashion as Madison's case and is an infection of the anterior horn cells. Id. at 49. He checked whether Madison were given OPV, but had to assume she had IPV.[36] Id. If Madison had been given OPV, all would agree that this was classic polio. Id. at 50. He has never seen another viral infection causing clinical polio unless the child were immunocompromised. Id. He has difficulty calling this a lower motor neuron process because, while the seventh cranial nerve was affected, the sixth cranial nerve was not. Further, there was no evidence of inflammation on MRI. Id. Therefore, Dr. Renfroe concludes that Madison had a peripheral nerve process. But, from his standpoint, "it doesn't really matter." Id. Madison had an inflammatory process that was either central or peripheral and there are plenty of cases in which patients have both GBS and transverse myelitis. Id. at 51.

Dr. Renfroe thinks that the measles immunosuppression is less likely than Madison's having an adverse reaction to both the varicella and measles vaccines causing either a central or a

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[35] Gray matter is "the gray nervous tissue composed of nerve cell bodies, unmyelinated nerve fibers, and supportive tissue." Dorland's Illustrated Medical Dictionary, supra note 2, at 1782.

[36] The handwritten note in Madison's medical records is that she received IPV. The printed vaccine forms state solely OPV, or oral polio virus. Madison's mother filed an affidavit reporting that Madison had received IPV. Pet. Ex. 13 at 2. A risk of OPV, but not IPV, is poliomyelitis.

peripheral demyelination.[37] Id. If she experienced an anterior horn cell attack, she would have measles immunosuppression. Id.

One would not expect an acute illness occurring at the same time as GBS because GBS is a postinfectious process. Id. at 52. GBS is more consistent with exposure to the vaccines than to a concurrent URI. Id. The MMR and/or the varicella vaccine(s) may have caused an autoimmune neurologic disorder. Id. at 53. Dr. Renfroe thinks that the concurrent viral infection occurred in the time frame to be a postimmunization phenomenon, but is a benign issue. It could be from a wild virus which had a horrific course due to measles immunosuppression or it could have been a coincidence. Id. He does not know why Madison had URI symptoms. Id. at 54.

Dr. Renfroe does not know what to make of Madison's echovirus test results on September 19, 2000, because he is not an infectious disease specialist. Id. at 55. He is not sure if echovirus causes central nervous system infection, but presumes that it does. Id. at 56. Echovirus is fairly common. Id. Madison also tested high for coxsackie virus antibodies on September 15, 2000. Id. at 57. Dr. Renfroe would suspect that these are pathogenic viruses. He does not know their significance in this case. Id. at 58. He does not see evidence of an acute infection of Madison's central nervous system. Id. at 58-59. And, because the first lumbar puncture was done at 11:00 p.m., Dr. Renfroe stated:

> My concern about this from a physician's standpoint is that the guy doing this was a low man on the totem pole. He had the night shift. He's not got any seniority and he's sitting there with a little counter clicking these suckers off, trying to identify them. And he did the best he could. I just can't use this data much.

Id. at 60. However, Dr. Renfroe admitted that he had no evidence that the lumbar puncture was analyzed incorrectly. Id. Dr. Renfroe admitted that there were more white blood cells in the lumbar puncture than one should see with only four red blood cells. This exceeds what is acceptable for a bloody lumbar puncture so the 32 white blood cells are abnormal. Id. at 61. An elevated white blood cell count would be consistent with the stiff neck Madison had on September 9, 2000, if looked at in isolation, but Dr. Renfroe still found it important that a subsequent lumbar puncture had a normal result. Id. at 62-63.

Madison had a process that was inflammatory, and most likely implicated the peripheral nervous system. Even if it were most likely a central nervous system process, it still has the same cause. Id. at 68. She had a nervous system process somewhere up from the muscles either in spine or in the peripheral nerves. Id. Dr. Renfroe agreed that there is no affirmative evidence to tie the MMR vaccine to Madison's nervous system involvement. Id. at 72.

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[37] Demyelination is the "destruction, removal, or loss of the myelin sheath of a nerve or nerves." Dorland's Illustrated Medical Dictionary, supra note 2, at 488.

2. Testimony of Arnold D. Gale, M.D.

Dr. Gale, a pediatric neurologist, testified for respondent. Id. at 73. He is a Professor of Pediatrics and Neurology at the George Washington University School of Medicine and an Associate Clinical Professor of Pediatrics, Neurology, and Neurological Sciences at Stanford University. Id. at 74. He is board certified in pediatrics. Id.

Dr. Gale testified that Madison did not have GBS for six reasons: (1) her clinical presentation and the timing of her symptoms, i.e., she developed neurological symptoms while having a URI with fever and a stiff neck (signs of meningeal[38] irritation or central nervous system involvement); (2) her disorder did not ascend (almost all cases of GBS ascend); (3) her pattern of weakness was much more proximal than distal, which is the opposite of what happens in GBS; (4) her pattern of weakness was asymmetric (unequal on the left compared to the right side of her body), which would be unusual in GBS; (5) she never lost her distal deep tendon reflexes in her ankles; and (6) she never had elevated proteins in her lumbar punctures. Id. at 75.

The most atypical form of GBS is Miller-Fisher syndrome in which a patient develops paralysis of the eye muscles, ataxia,[39] and areflexia. Areflexia, or absent reflexes, develops early in that form of GBS and persists for months or even years. A patient must have areflexia or a physician cannot diagnose GBS. Id. at 76. Madison did not have GBS, classic or atypical. Id. At no point did she exhibit elevated proteins or the albuminocytologic dissociation, another hallmark of GBS. Id. at 76-77. The physicians did not perform her lumbar punctures too early to find elevated proteins. One does the lumbar puncture at the time of presentation when the patient is neurologically impaired. Id. at 77. By the time the patient has neurologic impairment and nonfunctional peripheral nerves, the patient has a lot of protein in his or her spinal fluid. Id. Madison did not, and her lumbar punctures were not too soon. Id.

Dr. Gale has treated patients with rhombomyelitis with involvement of the lower brain stem and upper spinal cord. Id. at 78. Madison's medical presentation was consistent with rhomboencephalomyelitis, which was her discharge diagnosis from the hospital. Id. "Rhomboencephalomyelitis" means inflammation and/or infection of the lower brain stem and spinal cord. Id. at 80. Based upon his education, training, and experience, Dr. Gale is convinced that Madison's symptomatology is entirely consistent with a diagnosis of rhomboencephalo-myelitis. Id.

Dr. Gale agrees with Dr. Renfroe that Madison's pattern of weakness looked more like lower motor neuron as opposed to upper motor neuron disease. Id. at 79. But, it is not the

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[38] The meninges are "the three membranes that envelop the brain and spinal cord . . . ." Dorland's Illustrated Medical Dictionary, supra note 2, at 1124.

[39] Ataxia is the "failure of muscular coordination." Dorland's Illustrated Medical Dictionary, supra note 2, at 170.

peripheral nerves the illness impacted. The disease acted instead on Madison's cell bodies or nuclei. Madison's illness involves the gray matter nuclei of her brain stem, as well as the uppermost portion of her spinal cord, also known as the anterior horn, in just the same way one sees in polio. Id.

The reason Dr. Gale knows Madison's nuclei are affected, rather than her peripheral nerves, is that she has pronounced flaccid paralysis, no sensory symptoms, an asymmetric pattern of weakness, and retained ankle reflexes. This is the exact pattern one sees in patients with poliomyelitis. Id. "Polio" means "gray" in Greek. Polio encephalomyelitis means brain and spinal cord inflammation. Encephalomyelitis means inflammation of only the gray matter. Id. at 80. All of Madison's involvement was with the gray matter–none of her white matter[40] was involved. Id.

Dr. Gale disagrees with Dr. Renfroe's opinion that Madison had an immune-mediated response to her measles and/or varicella vaccination(s) because an immune-mediated or postinfectious disorder is a bimodal illness: one has a naturally-occurring infection or an immunization, and at some later point, the boost to the immune system subsides and, when the person is no longer ill, he or she develops GBS. One does not have GBS with an ongoing illness. With GBS, you make antibodies to myelin because of an out-of-control immune response. Id. at 80-81. But, Madison's illness does not fit this analysis. She was acutely ill with a febrile illness affecting her upper respiratory tract at the same time she became neurologically impaired. That means that she did not have GBS or any other postinfectious or immune-mediated disorder. Id. at 81-82.

The second problem with Dr. Renfroe's analysis is that a postinfectious or immune-mediated disorder affects, almost invariably, the white matter in the nervous system. But Madison's case does not involve the white matter. Thirdly, a lumbar puncture on patients with postinfectious or immune-mediated disorders results in elevated cerebrospinal fluid proteins. But that never happened in Madison's case. Id. at 82. All of these factors strongly mitigate against diagnosing Madison with a postinfectious or immune-mediated disorder. Id. at 83.

Rhomboencephalomyelitis can be a postinfectious process if the white matter is affected, but it would not involve the gray matter. Id. Again, Madison did not have a white matter disorder. Id. at 84. If Madison had reacted directly, rather than in a postinfectious manner, to the MMR and/or varicella vaccine(s), she would have developed measles, mumps, rubella, or chickenpox first before developing encephalitis. Id. at 85. Madison did not have measles, mumps, rubella, or chickenpox. Id. Dr. Gale also disagreed with Dr. Renfroe's opinion that the measles vaccine suppressed Madison's immune system. Id. at 87.

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[40] White matter is "the white nervous tissue, constituting the conducting portion of the brain and spinal cord; it is composed mostly of myelinated nerve fibers arranged in anterior, posterior, and lateral funiculi." Dorland's Illustrated Medical Dictionary, supra note 2, at 1781.

Madison's first lumbar puncture with elevated white blood cells is entirely consistent with an acute inflammatory process caused by a virus, even though it cleared fairly quickly by the second lumbar puncture. Id. at 88. Madison's clinical presentation with fever, upper respiratory tract symptoms, stiff neck, and neurologic impairment–which was asymmetric, nonascending, and with proximal rather than distal weakness–together with the absence of elevated proteins in her cerebrospinal fluid, speak to an overwhelming probability of a brain stem disorder and upper spinal cord disorder involving the gray matter. Id. at 89.

Unlike Dr. Renfroe, who found the first MRI indicating inflammation of segments of Madison's cervical spinal cord to be unreliable in light of her normal second MRI, Dr. Gale thought the results consistent with Madison's clinical picture. The second MRI could reflect improvement or a change of mind. Id. at 90.

As for Madison's positive results for the presence of echovirus and coxsackie virus antibodies, Dr. Gale stated that echovirus can cause respiratory tract infection and even meningitis[41] (20 percent of cases). Madison had meningitis (stiff neck, fever, elevated white blood cells in her cerebrospinal fluid). Id. at 91. Dr. Gale was not disturbed, as Dr. Renfroe was, that the sixth cranial nerve was not affected with the involvement of the seventh cranial nerve because the nuclei (i.e., gray matter) of one could be affected alone. Id. at 92.

Not every case of brain stem or uppermost cord inflammation in gray matter is caused by poliovirus, although we can call it poliomyelitis because the gray matter is affected. Id. at 93. This inflammation can be caused by mycoplasma, echovirus, coxsackie virus, and Tadano virus. Id. at 94. Dr. Gale cannot point to a specific virus that made Madison ill but stated it was not the poliovirus and could have been an enterovirus. Id. at 99.

Madison had a central, not a peripheral, nervous system disorder. Id. at 95. Madison's shoulder shrug, indicative of the weakness one sees in the uppermost portion of the spinal cord and the lowermost portion of the brain stem, is also consistent with rhomboencephalomyelitis. Id. at 96. Madison's pattern of disease was clearly encephalitic. She was acutely ill with fever at the same time her mother was acutely ill with fever. Id. at 104. The measles vaccine and varicella virus have been associated with encephalitis. Id. An immune-mediated response can occur within three weeks. Id. at 106. However, this is irrelevant in Madison's case because she did not develop chickenpox first before getting encephalitis. Id. at 109. The time frame would be correct for Madison's developing the worst of her symptoms after measles vaccine if the vaccine suppressed her immune system. Id. at 115. There is more than one type of immune-mediated polyneuropathy. Id. at 116.

The number of white blood cells can diminish in the spinal fluid over time, but that does not mean that the results of Madison's first lumbar puncture were incorrect. Id. at 120. One only

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[41] Meningitis is the "inflammation of the meninges, usually by either a bacterium . . . or a virus . . . ." Dorland's Illustrated Medical Dictionary, supra note 2, at 1125.

sees cells increase when there is a strong meningeal component. In many cases of encephalitis confined to the anterior portion of the brain and spinal cord, one may not see cells at all in the spinal fluid. Id. at 121. Dr. Gale was surprised that the second MRI was normal. Id. at 122.

There is no evidence that Madison suffered immune suppression after her vaccinations or even before them. Id. at 123. All of the laboratory information provided in Madison's medical records is consistent with a central nervous system infection. Id. at 125-26. Making the correct diagnosis in Madison's case is essential because, if she has a relapse, a physician needs to know what she has in order to treat it. Id. at 127. No specific virus was found to have caused Madison's illness. Id. at 129-30.

D. Petitioner Has Not Met Her Burden

Petitioner has not met her burden because she failed to present a credible prima facie case that the MMR, varicella, IPV, and/or DTP vaccine(s) caused Madison's neurological disorder. Specifically, petitioner failed to overcome the findings in the medical records that Madison suffers from rhombomyelitis and failed to show by a preponderance of evidence that the vaccines implicated in this case can cause and did cause Madison's injury. Dr. Renfroe's testimony did not provide (1) a medical theory causally connecting the vaccines and the injury; (2) a logical sequence of cause and effect showing that the vaccines were the reason for the injury; and (3) a showing of a proximate temporal relationship between the vaccines and the injury. Moreover, respondent's expert's testimony effectively impeached petitioner's case. The special master finds Dr. Renfroe's testimony unconvincing because it did not address adequately the issues raised by the course of Madison's illness. Importantly, Dr. Renfroe's testimony that Madison had atypical GBS was unconvincing for several reasons.

First, the results of Madison's lumbar punctures argue against a diagnosis of GBS. While recognizing that it is typical for a GBS patient to have elevated proteins in the spinal fluid, Madison's medical records reveal no such evidence. The medical records confirm that neither lumbar puncture showed elevated protein levels. Although Dr. Renfroe conceded that a high white blood cell count, absent elevated proteins, was inconsistent with even atypical GBS, he believes that the first lumbar puncture was performed too early to get accurate results. Dr. Renfroe said that he would have repeated the lumbar puncture several days later. However, he did admit that it was not premature to perform a lumbar puncture on September 14, 2000.

To explain away test results that did not support his diagnosis, Dr. Renfroe claimed that Madison's initial lumbar puncture results were normal because she had an acute stress response from the lumbar puncture or, alternatively, that there was a laboratory error. Dr. Renfroe offered no evidence to support either assertion; they were mere conjecture. Indeed, when Dr. Renfroe elaborated on his speculation that a lab error occurred, he again offered nothing more than conjecture. In this vein, Dr. Renfroe argued that he did not trust the results of the first lumbar puncture because it was analyzed late in the evening, at 11:00 p.m., by a physician allegedly lacking in seniority. There is no objective evidence in the record that tests analyzed by

physicians working evening shifts are inherently untrustworthy and unreliable. Indeed, Dr. Renfroe admitted that he had no such evidence. Therefore, Dr. Renfroe's contention concerning the unreliability of Madison's lumbar puncture results is unpersuasive as it is grounded entirely on speculation.

Second, while maintaining that Madison suffered from atypical GBS, Dr. Renfroe acknowledged that her presentation of weakness in the upper extremities is unusual for GBS. He also admitted that Madison exhibited central nervous system pathology. Moreover, Dr. Renfroe conceded that Madison's symptoms were dissimilar to classic or atypical GBS because her ankles were preserved. But, his testimony implied that those findings also were unreliable because they were made by a resident.

Third, Dr. Renfroe's diagnosis is at odds with the diagnosis of Madison's treaters, who actually examined and cared for her during her hospitalization. Although Madison had been diagnosed initially with an unusual variant of GBS, Dr. Nichter's discharge diagnosis settled upon probable rhombomyelitis. Dr. Renfroe believed that once the diagnosis of rhombomyelitis was recorded in the medical records, Madison was stuck with it and it was never again addressed. There is no support for his position. Moreover, although recognizing that the diagnosis of rhombomyelitis is consistent throughout the medical records, Dr. Renfroe attempted to downplay this fact by contending that the physicians at ACH used that diagnostic label merely "for simplicity's sake." The special master rejects this contention. It is beyond dispute that when Madison was admitted to Sarasota Memorial Hospital, the attending physicians grew concerned about Madison's increasing neurological deficits and accompanying airway compromise. It was for those reasons that Madison was transferred to ACH on September 15, 2000. Clearly, Madison was a very sick child and it is not credible that Dr. Casadonte's diagnosis of suspected atypical GBS would be changed to probable rhombomyelitis if her physicians did not believe the change in diagnosis appropriate. Similarly, it is not believable that the change in diagnosis did not reflect a change in the physicians' medical opinion of Madison's condition based upon test results and their hands-on examination and treatment of Madison. Dr. Renfroe's testimony in this regard diminished his credibility. Thus, the medical records, which are replete with references to Madison's rhombomyelitis diagnosis, will not be set aside in favor of Dr. Renfroe's contention that Madison has atypical GBS.

It was noteworthy to the special master that at hearing, Dr. Renfroe discussed his disagreement with petitioner's counsel regarding Madison's diagnosis, to counsel's apparent discomfort. Much to counsel's chagrin, Dr. Renfroe explained at hearing that he believes Madison might have polio but that petitioner's counsel disagreed with him. He insisted that if Madison had received the OPV vaccine instead of the IPV vaccine, a hearing would have been unnecessary because everyone would agree that she had polio. Of course, polio is a disease of the central nervous system, unlike atypical GBS, which is a disease of the peripheral nervous system. These are two significantly different diagnoses. Obviously, petitioner's counsel was able to persuade Dr. Renfroe to opine on a diagnosis of atypical GBS, or else he would not have

testified to that fact. That an attorney could convince a medical expert to alter his diagnosis does not bode well for the credibility of the physician.

One final area where Dr. Renfroe's testimony was not convincing concerned his testimony relative to Madison's URI. Initially, Dr. Renfroe testified that the measles and/or varicella vaccine(s) caused Madison's URI. Dr. Renfroe also contended that the URI could not have caused Madison's GBS, which is a postinfectious disease, because there was not enough time occurring between the onset of Madison's URI and the onset of her neurological symptoms. However, when confronted on cross-examination with the evidence in the medical records that Madison and her mother had the same URI symptoms at the same time, and that Madison had tested positive for echovirus and coxsackie antibodies, Dr. Renfroe tried to side-step the issue. Rather than answer counsel's question head-on, Dr. Renfroe, having previously offered an opinion concerning the URI, now claimed he could not respond because he was not an infectious disease specialist. Dr. Renfroe further contended that Madison's URI was irrelevant since her purported GBS occurred concurrently with the infection. Dr. Renfroe's response to this line of questioning struck the special master as evasive.

In sum, Dr. Renfroe's testimony is result-oriented. The special master's unshakable impression is that Dr. Renfroe starts from the conclusion (a vaccine-caused illness) and works back from the conclusion in a multitude of ways, a number of which are contradictory. For example, when confronted again with evidence contradicting his opinion that Madison had atypical GBS, he said it did not matter whether Madison had a central or peripheral nervous system disease–whatever she had was caused by the measles and/or varicella vaccine(s). It is not a sufficient explanation to say that he is a "lumper" to justify diagnosing a peripheral neuropathy such as atypical GBS if the child actually has a central nervous system disease. It is not a sufficient explanation that, since the results of the first lumbar puncture make a diagnosis of GBS untenable, the results have to be wrong because they were interpreted by the physician who is the "low man on the totem pole." It is not a sufficient explanation that he is not an infectious disease specialist and, therefore, he can ignore evidence of echovirus and coxsackie virus infections in evaluating what role viral exposure may have played in Madison's neurological illness. Expert testimony must be "supported by appropriate validation." Daubert v. Merrell Dow Pharm., Inc., 509 U.S. 579, 590 (1993).

Respondent does not have the burden of proving Madison's diagnosis or what caused Madison's injuries, but the testimony of Dr. Gale is helpful in impeaching further Dr. Renfroe's credibility. Dr. Gale provides an evaluation of the total picture of Madison's medical records without cavalierly disregarding the results of tests on spinal fluid and blood because they weigh against a predetermined diagnosis.

Dr. Gale stated that Madison did not have GBS because of the timing of her symptoms (the existence of a concurrent URI with fever and a stiff neck), the descending pattern of her symptoms, the proximal rather than distal presentation of her weakness, the asymmetry of her

weakness, the preservation of her deep tendon reflexes in her ankles, and the absence of elevated proteins in her lumbar punctures. GBS is a postinfectious disorder that occurs at least one week after an infection or immunization, not simultaneously with an infection such as Madison experienced (and which her mother experienced at the same time as Madison). Moreover, GBS is a white-matter disease and Madison's symptomatology dictates that she had a gray matter disease, just like the poliomyelitis that Dr. Renfroe apparently was more persuaded she had. Poliomyelitis is a central nervous system disorder, not a peripheral neuropathy like GBS. It does not mean Madison had a poliovirus infection, but only that her brain stem and upper spinal cord were involved. Additionally, Madison's first MRI and lumbar puncture results are consistent with the diagnosis of a gray matter, central nervous system disease.

As Dr. Gale stated, based upon his review of the medical records, Madison never had a postinfectious or immune-mediated disease, both of which typically affect the white matter. Although he does not know the specific virus that caused her illness, and although he is not required to identify the specific virus, he is confident that some virus did.

Respondent's Exhibits C through F are illustrative of Dr. Gale's testimony and confirm his conclusions. Two articles discuss the relationship between viruses such as West Nile virus and adenovirus and acute flaccid paralysis that resembles poliomyelitis, such as experienced by Madison. One article even distinguishes between West Nile virus-caused acute flaccid paralysis and GBS. While West Nile- or poliovirus-caused anterior myelitis is manifested by acute viral illness with rapid onset of asymmetrical flaccid weakness, often with muscle tenderness, GBS is manifested by a gradual onset of ascending symmetrical weakness with sensory involvement several weeks after viral infection or vaccination. Another article notes the evolution of new human viruses causing a paralytic poliomyelitis syndrome and rhomboencephalitis, the same disease Madison suffers from.

All of respondent's articles serve to support Dr. Gale's opinion that Madison did not have an acute polyneuropathy involving the white matter of her peripheral nerves. Instead, Madison had a gray matter central nervous system disorder involving the lower brain stem and upper spinal cord in the context of a febrile illness, likely viral. Madison did not experience a postinfectious process because there was no white matter involvement. The medical records show that she developed neurological symptoms at the time of her URI, her pattern of weakness was more proximal than distal, her pattern of weakness was asymmetric, and she never lost her ankle reflexes.

There is no doubt that Madison and, by extension, her family, have endured great suffering; nevertheless, the requirements of the Vaccine Act must be satisfied before an award of compensation can be made. Here, petitioner has not carried her burden of proving, by a preponderance of the evidence, a medical theory connecting the vaccine(s) and Madison's injury, a logical sequence of cause and effect demonstrating that the vaccine(s) caused Madison's injury, and a proximate temporal relationship between the vaccine(s) and Madison's injury.

III. CONCLUSION

Petitioner's petition is dismissed with prejudice. In the absence of a motion for review filed pursuant to RCFC Appendix B, the clerk of the court is directed to enter judgment accordingly.[42]

IT IS SO ORDERED.

Margaret M. Sweeney
Special Master

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