OFFICE OF SPECIAL MASTERS
No. 04-455V
March 30, 2006
For Publication

ADAM GILBERT,	*	
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Petitioner,	*	
	*	
v.	*	Entitlement; hepatitis B vaccine
	*	and CIDP beginning as GBS
SECRETARY OF THE DEPARTMENT OF HEALTH AND HUMAN SERVICES,	*	
	*	
Respondent.	*	

Clifford J. Shoemaker, Vienna, VA, for petitioner.
James A. Reistrup, R. Lynn Harris, Alexis B. Babcock, Washington, DC, for respondent.

MILLMAN, Special Master

DECISION[1]

This case was one of four paradigm cases tried as part of the Hepatitis B-Neurological Demyelinating Omnibus Proceeding described in Stevens v. Secretary of HHS, No. 99-594V, 2006 WL 659525, at *1-*3 (Fed. Cl. Spec. Mstr. Feb. 24 2006). For an overview of the proceedings, please see the first three pages of Stevens. This case was to represent those

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

petitioners with chronic inflammatory demyelinating polyneuropathy (CIDP) who allege that hepatitis B vaccine caused their illness.

The undersigned intended to decide the Guillain-Barré Syndrome (GBS) case, Peugh v. Secretary of HHS, No. 99-319V, before deciding this CIDP case, but unfortunately Mr. Peugh died in 2005. His case is suspended, therefore, until his widow (the new petitioner) proves that his death from hypertension was related to his purported vaccine injury GBS. Petitioner's counsel in Peugh requested that the undersigned issue a ruling based on the evidence in the Omnibus proceeding whether hepatitis B vaccine can cause GBS and whether Mr. Peugh had GBS. In analyzing the instant case, Gilbert, the undersigned will issue a ruling on whether hepatitis B vaccine can cause GBS and will reserve to a future filing whether or not Mr. Peugh had GBS. In the instant action, Adam Gilbert (hereinafter, "Adam,") was initially diagnosed with GBS. When his symptoms worsened for more than two months, his treating physicians changed their diagnosis to CIDP, recognizing that the only positive factor in his history (i.e., possible etiology) was the hepatitis B vaccination he received three weeks before the onset of his symptoms.

Petitioner herein filed a petition on March 19, 2004, under the National Childhood Vaccine Injury Act, 42 U.S.C. §300aa-10 et seq., alleging that hepatitis B vaccine caused her son Adam to have CIDP. The case was assigned to Chief Special Master Gary Golkiewicz on March 19, 2004. He reassigned the case to former Special Master Margaret M. Sweeney on March 29, 2004. She held a hearing on October 13-15, 2004. Further motions and briefings are described in the Stevens decision. *See especially* Stevens, at *2. On December 14, 2005, former Special Master Sweeney was sworn in as a judge of the United States Court of Federal Claims.

On January 11, 2006, the case was reassigned to the undersigned. On March 28, 2006, petitioner moved to amend the caption to reflect that Adam was no longer a minor. The undersigned granted petitioner's motion. Adam is sole petitioner in this case.

FACTS

Adam was born on November 9, 1986. He has a history of attention deficit hyperactivity disorder (ADHD). Med. recs. at Ex. 2, pp. 14-15. He was on Ritalin and was normal neurologically. Med. recs. at Ex. 2, p. 17. Adam's speech had been somewhat delayed due to chronic ear infections. Med. recs. at Ex. 2, p. 32.

Adam received his first hepatitis B vaccination on May 11, 2001. Med. recs. at Ex. 13, p. 24. He received his second hepatitis B vaccination on August 8, 2001. Ex. 3, p. 15; also Ex. A attached to the petition with a cover sheet listing it as Ex. 1.

On September 4, 2001, Adam's father told Dr. C.E. Caraballo at the Neighborhood Family Practice that Adam had no equilibrium. He would stand up and then fall over. He had been normal six days previously. (That would put onset at 21 days after vaccination.) He denied drug use, infection, fever, vegetarian diet, abdominal pain, upper respiratory infection, or shortness of breath. He was unable to walk heel to toe . He was diagnosed with cerebellar ataxia. Med. recs. at Ex. 3, p. 16 (also Ex. 13, p. 22)..

On September 6, 2001, Dr. Heather Way at the Neighborhood Family Practice noted that Adam was not as strong on the right and had trouble getting up the stairs. He had been bumping into things for a week. He could not get off a blanket on the ground on Sunday (September 2nd). His mental status was clear as a bell. He was doing better than ever in school. He had no previous recent illness. Med. recs. at Ex. 3, p. 17.

The MRI done on Adam's brain on September 6, 2001 was normal. Med. recs. at Ex. 3, p. 31. On September 7, 2001, Dr. Way questioned whether Adam had GBS. Med. recs. at Ex. 3, p. 19. Adam saw Dr. Elie Rizkallah, a neurologist, at the MetroHealth System on September 7, 2001. There was no history of recent viral illness. Adam received hepatitis B booster vaccine one month prior to his feeling off balance and having gait difficulty. Med. recs. at Ex. 13, p. 6. Adam's deep tendon reflexes were absent in his lower extremities. Med. recs. at Ex. 13, p. 7. Dr. Rizkallah recommended admitting Adam for testing and wrote that his symptoms suggested GBS. *Id.*

Adam was admitted on September 7, 2001 with a history of being off balance for the past week with a tendency to fall. He did not have fever or a viral illness. He had hepatitis B vaccine one month previously. Med. recs. at Ex. 3, p. 49. Adam's nerve conduction studies on September 7, 2001 were supportive of a diagnosis of demyelinating polyneuropathy. Med. recs. at Ex. 3, p. 145. An Epstein Barr virus panel done on September 8, 2001 was negative. Med. recs. at Ex. 13, p. 23. His total protein in his cerebrospinal fluid (CSF) on September 8, 2001 was 192 mg/dl when the normal range is 15-45. Med. recs. at Ex. 13, p. 35. His eosinophil was elevated on September 8, 2001 at 1.55 when the normal range was 0.00-0.70. Med. recs. at Ex. 13, p. 45. Adam was discharged on September 16, 2001 with a diagnosis of GBS. Med. recs. at Ex. 3, p. 52.

On September 16, 2001, Adam saw Dr. Jaividhya Dasarathy at the MetroHealth System. Med. recs. at Ex. 13, p. 4. Adam had a history of being off balance for one week. Initially, his weakness was on the left side. Now he had unsteady gait. There were no associated visual symptoms, speech problems, sensory changes, fever, viral illness, diplopia, vertigo, swallowing

problems, chest pain, shortness of breath, or dizziness. He had difficulty climbing stairs and stumbled when he walked. His only positive history was a hepatitis B vaccination one month before. *Id.* Dr. Rizkallah, a neurologist, was a consultant on the case and felt Adam's CSF findings were consistent with GBS. Med. recs. at Ex. 13, p. 5. Adam received physical therapy from the MetroHealth Medical Center in September 2001. Med. recs. at Ex. 6

Adam saw Dr. Irwin B. Jacobs, a pediatric neurologist at the MetroHealth System, on October 3, 2001. Med. recs. at Ex. 13, p. 9. Dr. Rizkallah saw Adam on October 10, 2001. Med. recs. at Ex. 13, p. 11. Over the prior few days, Adam's gait had worsened. There were no intercurrent illnesses. *Id.* Dr. Rizkallah diagnosed GBS which had relapsed and recommended a second course of IVIG (intravenous immunoglobulin). It was too early to talk about a diagnosis of CIDP. Med. recs. at Ex. 13, p. 12.

Nerve conduction and EMG studies done on October 10, 2001 showed mild worsening of conduction velocities and decrease in motor amplitudes. The needle EMG showed evidence of Wallerian degeneration[2] in the tested muscles. Dr. Despande Huang's conclusion was the results were consistent with GBS with evidence of axonal loss and denervation. Med. recs. at Ex. 3, p. 169.

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[2] Wallerian degeneration is "the degenerative changes the distal segment of a peripheral nerve fiber (axon and myelin) undergoes when its continuity with its cell body is interrupted by a focal lesion." Stedman's Medical Dictionary, 27th ed. (2000) at 468.

On October 10, 2001, a VAERS[3] report was sent in. Adam was definitely weaker. Med. recs. at Ex. 3, p. 21. On October 11, 2001, Adam was admitted for one day to MetroHealth again with a diagnosis of acute infective polyneuritis. Med. recs. at Ex. 3, p. 174. He was weaker in his legs and unstable. He had difficulty climbing stairs. The admission was for repeated IVIG treatment. Med. recs. at Ex. 3, p. 176. Adam complained of decreased strength and unstable gait for seven days. *Id.*

On October 23, 2001, Dr. Rizkallah saw Adam again after his second course of IVIG. There were no signs of chronic GBS or CIDP. Med. recs. at Ex. 13, p. 14.

On October 31, 2001, Dr. Rizkallah noted clear regression in Adam's gait. Med. recs. at Ex. 13, p. 17. Eight weeks after Adam's diagnosis of acute inflammatory demyelinating polyneuropathy, Adam was showing relapse which is unexpected with GBS. Dr. Rizkallah then diagnosed CIDP and recommended a third course of IVIG. Med. recs. at Ex. 13, p. 18.

On November 8, 2001, Adam was admitted to the Cleveland Clinic Foundation with a two-month history of distal muscle weakness and gait disturbance. His history of loss of balance began in September. Med. recs. at Ex. 2, pp. 74, 75. He was initially diagnosed with GBS. His EMG showed decreased nerve conduction. He received intravenous immunoglobulin for five days without improvement. He was still wobbly with decreased lower extremity strength. Three weeks later, he got much worse. He then received IVIG for two days without change. Ten days

[3] "The Vaccine Adverse Event Reporting System (VAERS) is a national vaccine safety surveillance program co-sponsored by the Food and Drug Administration (FDA) and the Centers for Disease Control and Prevention (CDC). The purpose of VAERS is to detect possible signals of adverse events associated with vaccines." http://www.fda.gov/Cber/vaers/vaers.htm

prior to admission, he could not climb stairs and had even less strength in his lower extremities. His father noticed bilateral facial weakness. He received more IVIG for two days without change. The suspicion was that Adam had CIDP with a problem at the T4 (thoracic) level. *Id.*

Dr. N. Friedman, a pediatric neurologist, reviewed possible other etiologies on November 8, 2001. Med. recs. at Ex. 2, p. 51. Adam had been healthy before his CIDP with no predisposing fever but he received two doses of hepatitis B vaccine at a gap of three months. The last one occurred about a month back. He had no exposure to tick bite, toxic substances, sore throat, etc. The CIDP started with difficulty in walking fast, going upstairs, tiring easily, drifting to either side while walking, and feeling unsteady which worsened if his eyes were closed. *Id.* Adam's weakness progressed to be more severe but restricted to the lower extremities. The protein in his cerebrospinal fluid was elevated to 192. *Id.*

Adam was seen for CIDP and a new onset of papilledema[4] at the Cleveland Clinic Foundation from November 8 to 14, 2001. Med. recs. at Ex. 9, p. 16. His ANA (antinuclear antibody) was 2.7 with normal being less than 1.5. His Epstein Barr virus IgG was 305 with normal being less than18. He had a sedimentation rate of 26 and an increased gamma spike on protein electrophoresis. MRI of the thoracic spine on November 9, 2001 revealed a syrinx[5] at the level of T5-T8 with no evidence of cord enlargement. There was peripheral enhancement of the distal thoracic cord and lumbar nerve roots following contrast media, suggesting an inflammatory

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[4] Papilledema is edema of the optic disk. Stedman's Medical Dictionary, 27th ed. (2000) at 1307.

[5] Syrinx is a pathologic tubular cavity in the spinal cord. Stedman's Medical Dictionary, 27th ed. (2000) at 1775.

process. He had papilledema bilaterally. He was administered three days of Solu-Medrol[6] and had increased strength in his lower extremities. Med. recs. at Ex. 9, pp. 17, 22, 29, 30. Adam's CSF protein on November 12, 2001 was 198 with a normal range between 15-45. Med. recs. at Ex. 9, p. 28.

On November 23, 2001, Dr. Friedman found that Adam was 50% better from his day of admission on November 8, 2001, and 35% better from the day of discharge on November 14, 2001. He could now take a few steps without support. There was no bladder or bowel involvement. He was on Prednisone. His deep tendon reflexes were absent. Med. recs. at Ex. 2, p. 49.

On January 4, 2002, Dr. Friedman noted Adam was walking well without a walker. He used a treadmill for 20 minutes at two mph. He was in physical therapy three days a week. His plantar reflexes (upgoing toes) were positive (meaning a central nervous system problem) while his deep tendon reflexes were negative. His eyes were improving to near normal. Med. recs. at Ex. 2, p. 57.

On February 1, 2002, Dr. Friedman noted Adam had 80% strength increase in his upper extremities. He had 65% improvement in his lower extremities with left foot drop. Use of an AFO (ankle-foot orthosis) helped him walk in school. Med. recs. at Ex. 2, p. 60.

On May 31, 2002, Dr. Friedman noted that Adam's foot drop was improving. He was no longer on physical therapy but did exercises for muscle strengthening. Med. recs. at Ex. 2, p. 62.

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[6] Solu-Medrol is methyprednisolone sodium succinate used to treat inflammatory illnesses. Physicians' Desk Reference (2004) at 2788.

On June 9, 2003, an examination showed Adam to be normal neurologically apart from peroneal weakness in the lower extremities. He wore AFOs. Med. recs. at Ex. 9, p. 41. His CIDP was in remission. *Id.* On November 12, 2003, Adam had persistent foot drop. Med. recs. at Ex. 9, p. 47.

Other Submissions

Petitioner filed Ex. FFFF entitled "Inflammatory polyradiculoneuropathy with spinal cord involvement and let[h]al outcome after hepatitis B vaccination," by E. Sindern, et al., 186 *J Neurological Sci* 81-85 (2001). The authors describe a 36-year-old physician who had received three recombinant hepatitis B vaccinations without problem. His antibodies remained positive until 1997. He had a fourth injection. Nine days later, he had progressive weakness and numbness of his lower extremities. *Id.* at 81. He had no reflexes in his lower extremities. *Id.* at 82. His cerebrospinal fluid showed elevated protein of 107 mg/dl, rising to 181 mg/dl later. He had no recent infection with viruses or bacteria. Epstein Barr viral titer was negative. He had strong elevation of antibodies to hepatitis B surface antigen. The patient died of multiorgan failure and respiratory distress syndrome 17 weeks after vaccination. *Id.* On autopsy, he had inflammatory cell infiltrates in the gray matter, particularly in the anterior horns of the spinal cord. *Id.* at 83. The authors note that the patient did not meet the strong clinical criteria of GBS, even though he had ascending weakness, areflexia, and sensory impairment of the distal extremities with CSF albuminocytological dissociation, because the course of disease was progressive over four months until he died. *Id.* Neuropathological findings of inflammatory cell infiltrates in the spinal nerves and spinal ganglia with considerable loss of nerve fibers in the distal nerves confirmed the diagnosis of GBS. But the additional finding of inflammatory

cellular infiltrates in the anterior horn and in the long tracts of the spinal cord needed further consideration. *Id.*

The authors concede that they cannot conclude causation from the hepatitis B vaccination without epidemiologic support, but they state that causation "appears to be strongly supported by the close temporal relationship between vaccination and the onset of the symptoms, the strong increase of HBs [hepatitis B surface] antibodies within 3 weeks after vaccination, and the immune mediated nature of this manifestation. Furthermore, most other etiologies associated with this phenomena were excluded. In the course of hepatitis B infection, immune complexes that consist of HBsAg, anti-HBsAg and complement are formed." *Id.* at 85. They comment that deposition of such immune complexes occurs in diseases following hepatitis B viral infection. *Id.* They surmise that administration of the vaccine may cause a large amount of antigen and small amounts of antibodies in the serum which may induce the formation of soluble antigen-antibody complexes, initiating clinical disease. The illness appears to be autoimmune mediated. *Id.*

Petitioner's Ex. 16 is a compilation of articles upon which petitioner's expert, Dr. Carlo Tornatore, relies. The first article is entitled "Treatment of immune neuropathies," by P.A. van Doorne and M.P.J. Garssen, 15 *Current Opinion in Neurology* 623-31 (2002). P. Ex. 16, p. 1. The authors state that immune-mediated neuropathies may share immunological mechanisms and that GBS and CIDP "appear to be variants of one disorder, with very acute GBS patients at one end of the clinical spectrum and slowly progressive CIDP patients at the other." *Id.* They state in the section devoted to CIDP that CIDP may be considered a chronic variety of GBS with clear

clinical and immunological differences. It is sometimes difficult to distinguish between relapsing GBS and CIDP. *Id.* at 4.

The second article in petitioner's Ex. 16 is entitled "Pathogenesis of Guillain-Barré syndrome," by R.A.C. Hughes, et al., 100 *J Neuroimmunol* 74-97 (1999). *Id.* at 8. The authors discuss a recent reclassification of diseases underlying GBS and related disorders. *Id.* They state that arbitrarily defined diagnostic criteria separate GBS from subacute and chronic inflammatory demyelinating polyneuropathy. *Id.* at 9. They also state, "These more chronic diseases more probably represent members of a spectrum of disorders with a related pathogenesis." *Id.*

The third article in petitioner's Ex. 16 is entitled "Chronic Inflammatory Demyelinating Polyradiculoneuropathy. Clinical Characteristics, Course, and Recommendations for Diagnostic Criteria," by R.J. Baroha, et al., 46 *Arch Neurol* 878-84 (1989). *Id.* at 32. The authors state that they "believe that CIDP should also be considered a *syndrome*. One could in fact argue that the name CIDP is artificial." *Id.* at 37. Another alternate name for CIDP is "chronic GBS." *Id.*

Petitioner includes in Ex. 16 a chapter from P.J. Dyck's Peripheral Neuropathy, 3d ed., Vol. 2 (1993): chapter 81, "Chronic Inflammatory Demyelinating Polyradiculoneuropathy," by P.J. Dyck, et al.,, at 1498-1517. P. Ex. 16, pp. 42-60. The authors state that, only in modern times has CIDP been set apart from GBS. *Id.* at p. 42. The separation is due to their having different courses: CIDP evolves over weeks, months, or years and lasts years with incomplete improvement; GBS evolves over days or weeks and generally improves. *Id.* at 43. CIDP may follow a preceding infection, immunization, or receipt of biologic material within a few weeks or months of onset, but it is unclear if these occurrences are higher than in a control group. *Id.* at 45-46. The authors comment that GBS, CIDP, experimental autoimmune EAN (experimental

allergic neuritis produced by sensitizing animals to peripheral nerve myelin or P2 basic protein), and chronic EAN "bear a close resemblance to each other clinically and pathologically, suggesting that these are related diseases with a common pathogenesis. That the experimental diseases are autoimmune disorders is confirmed by the demonstration that T cells sensitized to P2 protein are necessary for the expression of the disease." *Id.* at 53. However, there are varying theories about the immune mechanism. *Id.* at 55. In animal models of CIDP, "antibodies appear to play an important pathogenic role." *Id.* at 56. "Another group of chemical mediators, the cytokines, clearly play a central role in inflammatory processes in general and in inflammatory demyelination in particular." *Id.* at 56.

Petitioner also filed in Ex. 16 an case note entitled "Relapsing Neuropathy due to Tetanus Toxoid. Report of a Case," by J.D. Pollard and G. Selby, 37 *J Neurol Sci* 113-25 (1978). P. Ex. 16, p. 76. The authors discuss a 42-year-old man who had three episodes of GBS after three vaccinations with tetanus toxoid over 14 years, leading to the inescapable conclusion that the vaccination caused his GBS. *Id.* at 80, 86. They cite literature showing that inoculations have been associated with both acute and chronic idiopathic demyelinating neuropathy. *Id.* at 83.

Petitioner filed in Ex. 16 a special communication from the Institute of Medicine (IOM) entitled "Adverse Events Associated With Childhood Vaccines Other Than Pertussis and Rubella. Summary of a Report from the Institute of Medicine," by K.R. Stratton, et al., 271 *JAMA* 1602-05 (1994), in which the IOM accepted, inter alia, that tetanus toxoid vaccine could cause GBS, citing the Pollard and Selby article. P. Ex. 16, pp. 92, 94, 95.

Petitioner filed in Ex. 16 an article entitled "Chronic inflammatory demyelinating polyneuropathy presenting with features of GBS," by K. Mori, et al., 58 *Neur* 979-82 (2002). P.

Ex. 16, p. 96. The authors describe five patients initially diagnosed with GBS whose symptoms persisted and became similar to CIDP in their chronic phase. *Id.*

Petitioner filed in Ex. 16 an excerpt from Guillain-Barré Syndrome by G.J. Parry (1993), in which the author states that an article about a group of CIDP patients states these patients initially received a diagnosis of GBS. *Id.* at 102, 108. In a chapter devoted to CIDP, the author states the major difference between GBS and CIDP is their temporal profiles. *Id.* at 110. Antecedent events are uncommon, but, in one study of CIDP, 32% of patients had had a preceding infection (usually cytomegalovirus) or vaccination. *Id.* at 113.

Respondent filed as Ex. I an article entitled "Hepatitis B vaccination and central nervous system demyelination: an immunological approach," by E. Piaggio, et al., 24 *J Autoimmunity* 33-37 (2005). The authors compare the T-cell response to hepatitis B surface antigen in patients with central nervous system demyelination or multiple sclerosis or other inflammatory or autoimmune diseases following hepatitis B vaccination with the T-cell response in healthy hepatitis B vaccinees. Their data showed no difference in T-cell proliferation or cytokine production between the two groups, thus not favoring a causal link between demyelinating illness and hepatitis B vaccine, although the result was not sufficient to exclude the causal link because the sample size, being quite small, limited the power of the study. *Id.* at 36.

TESTIMONY

The undersigned incorporates the general testimony described in Stevens, supra, at *10-*20, by reference, omitting the specific testimony applied to Ms. Stevens' case.

Dr. Vera S. Byers, an immunologist, testified for petitioner that, in 1983, there was a report of seven patients with CIDP who had active natural chronic hepatitis infection. They all

had hepatitis B surface antigen and the antibody complex. Tr. at 67-68. The IOM would expect that incidents of demyelinating diseases following the natural illness would not surprisingly follow the vaccination, although at a lower rate. Tr. at 68.

Dr. Carlo Tornatore testified for petitioner that, in animals, inducement of experimental allergic neuritis or EAN should be monophasic, as is GBS, but relapses may be seen after a single immunization. Tr. at 540-41. This lends support to the view that GBS and CIDP are the same type of process (inflammation of the peripheral nerves) with GBS being more acute and CIDP more indolent. Tr. at 541.

Dr. Tornatore testified that Adam had no equilibrium a little less than a month after receiving hepatitis B vaccine. Tr. at 541-42. Adam had a positive Romberg which means that, when he stood with his eyes closed and feet together, he swayed. Tr. at 542. That means he lost sensation in his feet. *Id.* Dr. Rizkallah documented weakness and diminished reflexes, and thought Adam had GBS. *Id.* Adam's EMG and nerve conduction tests were consistent with GBS. Tr. at 542-43. He had a complete white blood count, which was slightly elevated at 11.2. He had 13 percent eosinophils, where the normal range is zero to five. This indicates an allergic type of reaction. Tr. at 543. There were two other blood draws showing a high eosinophil count. One normally does not see this in GBS or CIDP. He received five days of IVIG and his eosinophil count dropped to 2.1. Tr. at 543-44. The immune response was now treated and was quieting down. Tr. at 544. The vaccination clearly could cause an allergic response. *Id.*

Dr. Tornatore testified that CIDP and GBS are both sequelae of wild hepatitis B infection. The timing fits within four to five weeks of vaccination. Tr. at 545. His opinion is that hepatitis B vaccine caused Adam's CIDP because the temporal relationship makes sense, it is biologically

plausible because we know that hepatitis B surface antigen can cause GBS, and Adam had eosinophilia, which is a marker of allergic response. Tr. at 547-48. If Adam had not received the vaccination, he would not have had CIDP. Tr. at 548.

Dr. Thomas P. Leist testified for respondent that hepatitis B vaccine did not cause Adam's CIDP. Tr. at 758. Adam's initial lumbar puncture had a protein of 192 and only three white cells. One potential diagnosis could be GBS. Tr. at 760. Adam's upgoing toes by October 31, 2001 indicate sensory nerve involvement, indicating an abnormality in the spinal cord. Tr. at 761. Adam's disease involved not only the peripheral nervous system but also the central nervous system. Tr. at 762. Dr. Friedman found papilledema. Tr. at 763. The eye disks were swollen due to a direct inflammatory process within the optic nerve or papilledema can indicate raised intercranial pressure. Adam also had facial weakness. Tr. at 763.

Dr. Friedman found a T4 sensory level. Tr. at 764. At the end of three days of steroids, Adam was better. Steroids can reduce cells in the cerebrospinal fluid and close or reduce the inflammatory process affecting the blood-brain barrier. Tr. at 765. Dr. Leist opined there was an inflammatory process going on in Adam's central nervous system because of the opening pressure of the lumbar puncture and 12 white cells in the fluid. Tr. at 766-67. There was also significant inflammation at the lower part of Adam's spine at the spinal roots. Tr. at 768, 769.

Initially, Adam's Epstein Barr virus titers were normal. Later on, they were positive. Tr. at 770. Dr. Leist is not saying that Adam had an Epstein Barr infection. *Id.* Possibly, these Epstein Barr virus antibodies came from the IVIG because the serum came from others. *Id.* An explanation of the positive Epstein Barr is passive transfer from a donor. *Id.*

It is uncommon in GBS and CIDP for there to be central nervous system involvement. Tr. at 772. Dr. Leist thinks Adam had a protracted monophasic process which abated under the influence of steroids. *Id.* at 774. Dr. Leist does not think Adam had GBS or CIDP. He called Adam's illness encephalomyelitis, involving inflammation of the brain, spinal cord, and nerve roots. *Id*. Dr. Leist does not know the cause. Adam could have acquired his Epstein Barr virus antibodies from the IVIG. At no point were hepatitis B surface antigen titers obtained. Tr. at 775. On cross-examination, Dr. Leist admitted that the nerves were also involved in Adam's case and therefore encephalomyeloradiculoneuritis would be a more accurate diagnosis. Tr. at 776-77. He admitted that encephalomyeloradiculoneuritis has been described as a complication of vaccinations. Tr. at 777.

In CIDP, we are looking at a case of GBS where the progression continues for at least two months. Tr. at 778, 779. Adam's illness continued to progress for at least two months. Tr. at 779. Upgoing toes can rarely be seen in CIDP. Tr. at 784, 785. Dr. Leist stated that the rare cases of CIDP can have optic and cranial nerve involvement. Tr. at 785, 786. Dr. Leist emphasized that Epstein Barr virus could have caused Adam's illness even though he agreed Adam's titers were initially negative for Epstein Barr and Adam could have had positive titers for Epstein Barr from donor transfer after he received IVIG. Tr. at 788, 789. Adam did not have any symptoms of Epstein Barr viral infection. Tr. at 791.

On rebuttal, Dr. Tornatore testified that Adam had a positive Epstein Barr virus titer only after he received IVIG treatment. Before IVIG, his Epstein Barr virus titer was negative. Tr. at 818. Dr. Tornatore opined this was probably a reflection of passive transfer of the viral antibody from a donor from the IVIG pool. Tr. at 818-19. Adam (unfortunately, the transcript has Dr.

Tornatore using the name "Justin") had no manifestations of Epstein Barr viral infection. One does not see an elevated eosinophil count in Epstein Barr viral infection. Tr. at 819. As for central nervous system involvement, one can see papilledema in about five percent of GBS cases. Tr. at 820. With vaccinations, any part of the neurologic axis can be involved. Tr. at 821.

DISCUSSION

This is a causation in fact case. To satisfy their burden of proving causation in fact, petitioners must offer "(1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of a proximate temporal relationship between vaccination and injury." Althen v. 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, __ F.3d __, 2006 WL 560660, at *7 (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...." Slip op. at 13-14.

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).

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

Close calls are to be resolved in favor of petitioners. Capizzano, supra, at *8; Althen, supra, at 1280. *See generally*, Knudsen v. Secretary of HHS, 35 F.3d 543, 551 (Fed. Cir. 1994).

In essence, the special master is looking for a medical explanation of a logical sequence of cause and effect (Althen, supra, at 1278; Grant, supra, at 1148), and medical probability rather than certainty (Knudsen, supra, 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, supra, at 549:

> 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.

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."

As the Federal Circuit stated in Knudsen, supra, at 548, "Causation in fact under the Vaccine Act is thus based on the circumstances of the particular case, having no hard and fast *per se* scientific or medical rules." The undersigned's task is to determine medical probability based on the evidence before the undersigned in this particular case. Althen, supra, at1281 ("judging the merits of individual claims on a case-by-case basis").

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. In Knudsen, Supra, at 550, 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.

The Federal Circuit in Knudsen, supra, at 549, also stated: "The special masters are not 'diagnosing' vaccine-related injuries." In the instant action, respondent's expert Dr. Leist opined that Adam had neither GBS nor CIDP but instead had encephalomyeloradiculoneuritis. Yet, on cross-examination, he admitted that the rare case of CIDP could include central nervous system manifestations.

A look at the Honorable Emily C. Hewitt's decision in Kelley v. Secretary of HHS, 68 Fed. Cl. 84 (Fed. Cl. 2005), is instructive not only in understanding the relationship of GBS and

CIDP, but also in realizing that the term used to describe the illness following vaccination is not dispositive of whether or not petitioner prevails. In Kelley, Judge Hewitt reversed the Chief Special Master's dismissal of a tetanus toxoid vaccination-CIDP petition.[7] Although the reversal of the Chief Special Master's dismissal was partly based on his use of legal criteria that were contrary to law (see the discussion in Althen, supra, as well as in the undersigned's Stevens case, supra, at *1-*2, *20-*22), Judge Hewitt's opinion in favor of Ryan Kelley was also based on Dr. Tornatore's opinion, buttressed by medical literature, that GBS and CIDP were on a pathological spectrum and that the cause of one was plausibly the cause of the other. Kelley, supra, at 90.

One of petitioner's exhibits in Kelley to support the view that tetanus toxoid can cause CIDP was a letter by Dr. Richard A.C. Hughes entitled, "Immunization and Risk of Relapse of Guillain-Barré Syndrome or Chronic Inflammatory Demyelinating Polyradiculoneuropathy," *Muscle & Nerve* 1230-31 (September 1996), which clarified together with other literature that the famed Pollard and Selby study[8] upon which the Institute of Medicine relied in its 1994 Report[9] to

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[7] Judge Hewitt's opinion in Kelley contrasts with her affirmance of the Chief Special Master's dismissal of the petition in Trojanowicz v. Secretary of HHS, 43 Fed. Cl. 469 (Fed. Cl. 1999), in which she found no abuse of discretion in the Chief Special Master's evaluation of the facts, the medical testimony, and the relevant medical literature in a pro se case in which petitioners alleged DPT caused their daughter's CIDP. The Chief Special Master's insistence on support from medical literature would not be consistent with the Federal Circuit's holdings in Althen (2005) and Capizzano (2006).

[8] Petitioner herein filed the Pollard and Selby article in P. Ex. 16, pp. 76-88.

[9] Adverse Events Associated with Childhood Vaccines. Evidence Bearing on Causality. The IOM discusses the 1978 Pollard and Selby article and concludes that if someone had GBS from five days to six weeks after tetanus toxoid vaccination, he was at greater risk for further GBS from future tetanus toxoid vaccinations, and since Pollard and Selby's article proves tetanus toxoid vaccine did cause GBS, the IOM concludes it can cause GBS. *Id.* at 89-90.

accept that tetanus toxoid can cause GBS did not actually involve GBS, but instead involved CIDP.

Another support for the rediagnosis of the Pollard and Selby patient with CIDP, not GBS, came from an article by Dr. Gerald M. Fenichel. Kelley, supra, at 93. Judge Hewitt concluded that whether Ryan Kelley proved he had GBS or CIDP was immaterial as long as he proved causation in fact. Kelley, supra, at 100. Therefore, in the instant action, whether Adam had encephalomyeloradiculoneuritis as Dr. Leist states, or GBS rediagnosed as CIDP as Adam's treating physicians and Dr. Tornatore state is not critical to petitioner's prevailing in this case.

The Federal Circuit in Capizzano emphasized the opinions of petitioner's four treating doctors in that case. 2006 WL 560660, at *7, *8. In the instant action, the treating doctors' diagnosis of Adam after his initial stage of neurologic illness was CIDP. Dr. Leist admitted that rare cases of CIDP can include central nervous system manifestations. The Sindern article that petitioner filed concerning a doctor who had clinically recognized GBS and who unfortunately died, reveals that the doctor's anterior horns of his spinal cord, nerve roots, and spinal ganglia were affected by cell infiltrates, prompting the authors to consider further their diagnosis. The undersigned doubts that medical diagnoses can always be clear cut. Dr. Leist's disagreement with the diagnosis of Adam's doctors and petitioner's expert Dr. Tornatore that Adam had CIDP is unpersuasive. The undersigned holds that Adam had CIDP. It is worthwhile remembering, however, that the actual name for the illness is, as Judge Hewitt stated in Kelley, not dispositive as to whether petitioner prevails. We are speaking here of a demyelinating illness that began a few weeks after vaccination which initially seemed to be GBS, was ultimately diagnosed as CIDP, and contained some central nervous system components.

Adam's CIDP began three weeks after his hepatitis B vaccination, constituting a strong temporal relationship to the vaccine since it is a time period in which an allergic reaction leading to demyelination and inflammation may reasonably occur, based on the medical literature and testimony in this case from Dr. Tornatore, and, generally, from Dr. Byers. The IOM's conclusion that tetanus toxoid vaccine can cause GBS from 5 days to six weeks later is consistent with concluding that the temporal relationship of three weeks between Adam's hepatitis B vaccination and the onset of his neurologic illness is appropriate for causation. The undersigned notes that no one has explained the specific biologic mechanism by which tetanus toxoid vaccine may cause GBS, although animal experimentation producing EAN yields some clues.

The medical community knows now that the patient in the Pollard and Selby case report actually had CIDP, not GBS, from communications from the authors to reputable neurologists such as Dr. Gerald M. Fenichel and Dr. Richard A.C. Hughes. These gentleman are well-known to the undersigned as being leaders in the field of neurology. The conclusion must be, therefore, that tetanus toxoid vaccine can and did (in the Pollard and Selby case report) cause CIDP, and no one to the undersigned's knowledge has yet pinned down that specific biological mechanism either. Yet we know causation occurred because of two positive rechallenges. What is of further interest for Adam's case is that the individual in the Pollard and Selby case report was obviously initially diagnosed with GBS, just as Adam was, and the conclusion was that the vaccine caused his GBS. It would be unfathomable in the light of two positive rechallenges for anyone to posit that the tetanus toxoid vaccine did not cause the Pollard and Selby patient's CIDP just because the diagnosis of his neurologic illness changed.

The medical theory that petitioner herein offers through his experts is that some kind of allergic response, here manifested in elevated eosinophils, occurred showing that Adam's body attacked itself in forming an immune reaction to hepatitis B surface antigen, resulting in demyelination of his nerves and inflammation that spread to his central nervous system (the upgoing toes, the papilledema). That petitioner cannot be more specific in describing the biologic mechanism is not dispositive of his prevailing in this case, according to the Federal Circuit in Knudsen. Animal studies mimic this process in the monophasic and recurring forms of EAN.

The article respondent filed as Ex. I to show no difference in T-cell proliferation or cytokine production among hepatitis B vaccinees who had demyelinating diseases and hepatitis B vaccinees who remained healthy is not dispositive because the authors admit their study was small and its power thereby reduced. In any event, the authors may have been looking for the wrong specific biological mechanism. That medical science still does not have the complete explanation for the causation of demyelinating diseases post-vaccination is legally irrelevant. *See* Knudsen, supra.

Petitioner has shown a logical sequence of cause and effect in his witnesses' testimony, the facts elicited from the medical records, and the medical literature. The undersigned notes that the medical records state repeatedly that Adam's only positive pre-illness factor was his hepatitis B vaccination. There was no other etiologic factor his doctors could find and they looked.

The undersigned finds Dr. Leist's attempt to blame Epstein Barr virus for Adam's CIDP not credible. Dr. Leist did not even believe it. He recognized that Adam's initial titers were

negative for Epstein Barr. That they became positive only after he received IVIG treatment is fully explained by both Dr. Tornatore and Dr. Leist as being due to donor transfer from IVIG.

Petitioner has prevailed in proving that hepatitis B vaccination caused his CIDP. Since Adam's initial diagnosis was GBS and the undersigned can find no reason based on the evidence including medical literature and testimony to distinguish between GBS and CIDP in terms of vaccine reaction, the undersigned recognizes that hepatitis B vaccine may also cause GBS. Petitioner has also proved that but for the hepatitis B vaccination, he would not have had CIDP.

CONCLUSION

Petitioner is entitled to reasonable compensation. The undersigned hopes that the parties may reach an amicable settlement, and will convene a telephonic status conference soon to discuss how to proceed to resolve the issue of damages.

IT IS SO ORDERED.

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DATE Laura D. Millman
Special Master