In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS
No. 99-608V
November 18, 2008
To be Published

HARILYN ADLER,	*	
Petitioner,	*	
v.	*	Entitlement; hepatitis B vaccine causing or significantly aggravating MS
SECRETARY OF THE DEPARTMENT OF HEALTH AND HUMAN SERVICES,	*	
Respondent.	*	

Ronald D. Homer, Sylvia Chin-Caplan, Boston, MA, for petitioner.
Lisa A. Watts, Washington, DC, for respondent.

MILLMAN, Special Master

RULING ON ENTITLEMENT[1]

[1] Vaccine Rule 18(b) states that all decisions of the special masters will be made available to the public unless they contain trade secrets or commercial or financial information that is privileged and confidential, or medical or similar information whose disclosure would clearly be an unwarranted invasion of privacy. When such a decision 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.

Petitioner filed a petition on August 4, 1999, under the National Childhood Vaccine Injury Act, 42 U.S.C. § 300aa-10 et seq., on her own behalf, ultimately alleging that hepatitis B vaccine administered on August 6, 1990 caused or significantly aggravated her multiple sclerosis (MS).

This case was one of the 65 cases transferred to the undersigned in January 2006 as part of the Omnibus hepatitis B vaccine-demyelinating injury cases, dealing with transverse myelitis (TM), Guillain-Barré syndrome (GBS), chronic inflammatory demyelinating polyneuropathy (CIDP), and MS.

In the four Omnibus paradigm decisions the undersigned issued[2] concerning hepatitis B vaccine and demyelinating diseases, the undersigned has held that the medically appropriate time frame between hepatitis B vaccine and the onset of GBS, CIDP, TM, or MS is between three and 30 days, based on the testimony of petitioners' expert Dr. Vera Byers and respondent's expert Dr. Roland Martin. Stevens v. Secretary of HHS, No. 99-594, 2006 WL 659525, at *12, *15 (Fed. Cl. Feb. 24, 2006).

The case went to hearing on May 27, 2008. Testifying for petitioner was Dr. Carlo Tornatore. Testifying for respondent was Dr. Martin A. Bielawski.

On August 4, 2008, petitioner filed a posthearing brief.

On September 4, 2008, respondent filed a post-hearing brief.

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[2] Stevens v. Secretary of HHS, No. 99-594, 2006 WL 659525 (Fed. Cl. Spec. Mstr. Feb. 24, 2006) (hepatitis B vaccine caused TM); Gilbert v. Secretary of HHS, No. 04-455V, 2006 WL 1006612 (Fed. Cl. Spec. Mstr. Mar. 30, 2006) (hepatitis B vaccine caused GBS and CIDP); Werderitsh v. Secretary of HHS, No. 99-310V, 2006 WL 1672884 (Fed. Cl. Spec. Mstr. May 26, 2006) (hepatitis B vaccine caused MS); Peugh v. Secretary of HHS, No. 99-638V, 2007 WL 1531666 (Fed. Cl. Spec. Mstr. May 8, 2007) (hepatitis B vaccine caused GBS and death).

On October 7, 2008, petitioner filed a reply to respondent's post-hearing brief.

The case is now ripe for a ruling on the issue of entitlement.

FACTS

Before the Vaccination

Petitioner was born on June 25, 1945.

On June 20, 1977, she saw Dr. Martin E. Liebling at the request of Dr. Martin Cohen. A year previously, she had fatigue and intermittent low grade fever of 101°. She had some cervical adenopathy which subsided. Several months previously, she had an enlarged inguinal node which was biopsied and found compatible with chronic lymphadenitis. In November 1976, she developed 4+ proteinuria and edema. She was diagnosed with nephrotic syndrome, etiology undetermined. She smoked two packs of cigarettes a day. Her father had severe myelofibrosis and myeloid metaplasia. Dr. Liebling was concerned about underlying lymphoma. Med. recs. at Ex. 6, p. 1.

Dr. Liebling notes on September 16, 1977 that petitioner had occult Hodgkin's disease and was on radiotherapy. Med. recs. at Ex. 6, p. 2.

On November 17, 1977, petitioner returned to Dr. Liebling and complained of back pain. Med. recs. at Ex. 6, p. 3.

Petitioner saw Dr. Liebling with tachycardia on January 3, 1978. She had been drinking five cups of coffee daily. Dr. Liebling told her to stop drinking coffee. Med. recs. at Ex. 6, p. 4.

Petitioner was admitted to Baptist Hospital on November 6, 1978 because of herpes zoster of the right side of her face. Med. recs. at Ex. 6, p. 6. She was discharged on November 9, 1978. Med. recs. at Ex. 6, p. 7.

On December 19, 1979, petitioner saw Dr. Liebling, complaining of bitemporal and frontal headaches for about three days. Med. recs. at Ex. 6, p. 9.

On April 6, 1981, petitioner saw Dr. Allan Herskowitz, a neurologist. She was well until 1977 when she developed fatigue, headache, and lymphadenopathy. She was diagnosed with nephrotic syndrome, prescribed Prednisone, and improved. Med. recs. at Ex. 3, p. 1. In late 1977 or early 1978, she was diagnosed with Hodgkin's disease, stage II-A, mainly confined to the neck and mediastinum. She had a splenectomy and underwent radiation. Her symptoms did not improve. She had chemotherapy. She did well afterwards without recurrence. *Id.* Petitioner felt well until 12 days prior to the April 6, 1981 visit when she noted some tingling dysesthesias and numbness of both feet. This gradually ascended to the mid-calf region and caused her occasionally to stumble or lose her balance because of inadequate sensation in her feet. *Id.* She had vague symptomatology in her hands on awakening, and her hands felt stiff. She had some right flank pain since a kidney biopsy. *Id.*

A year and one-half previously, she had herpes simplex involving the right side of her face. She had intravenous Vira-A therapy and improved. Her dietary habits were poor. *Id.* On examination, she had mildly diminished proprioception and vibration in both feet distally without loss of light touch or pinprick. *Id.* Dr. Herskowitz diagnosed a mild sensory polyneuropathy whose etiology was unclear. Med. recs. at Ex. 3, p. 2.

On April 20, 1981, Dr. Herskowitz wrote to Dr. Martin Liebling that petitioner still complained of dysesthesias in the lower extremities although she felt it had spread to involve her thighs. Her legs still felt weak and heavy at times. She no longer complained of her hands being stiff. Med. recs. at Ex. 3, p. 3.

On June 8, 1981, Dr. Herskowitz wrote Dr. Liebling that petitioner was doing better. The dysesthesias remitted except for the soles of her feet. Med. recs. at Ex. 3, p. 4. He wrote a similar letter on July 10, 1981. Med. recs. at Ex. 3, p. 5. However, on September 14, 1981, Dr. Herskowitz wrote Dr. Liebling that petitioner's symptoms increased over the prior month. She now had a numb sensation from her feet up to the mid-abdominal area. She felt her legs at times were weak as if they were going to collapse. She had difficulty with urination. She had one episode of questionable fecal incontinence. She noted some numbness over the fingertips of her left hand. Med. recs. at Ex. 3, p. 6. On physical examination, petitioner had significant impaired vibration and position sense in both feet distally to the mid-tibial region. Reflexes were clearly increased throughout (hyperreflexia). She had a positive Lhermitte's sign.[3] Dr. Herskowitz stated, "She has continued to display at this point a recurrence and progression of her symptoms which appear to be myelopathic in origin." *Id.* Her bladder problems were apparently recent. *Id.*

Petitioner was admitted to Baptist Hospital of Miami on September 20, 1981 for a complete myography to rule out any central nervous system involvement or recurrence of her primary lesion. Med. recs. at Ex. 6, p. 8. CT scan of the brain showed mild enlargement of the lateral ventricles. Med. recs. at Ex. 6, p. 9. She also had a prominent cisterna magna. Med. recs. at Ex. 3, p. 78. She was diagnosed with possible myelitis and peripheral neuritis of uncertain etiology, and trigonitis (bladder inflammation). Med. recs. at Ex. 3, p. 10. A cystourethroscopy did not reveal a neurogenic bladder. Med. recs. at Ex. 6, pp. 44, 45.

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[3] Lhermitte's sign is "the development of sudden, transient, electric-like shocks spreading down the body when the patient flexes the head forward, seen mainly in multiple sclerosis but also in compression and other disorders of the cervical cord." Dorland's Illustrated Medical Dictionary, 30th ed. (2003) at 1700.

On October 26, 1981, Dr. Herskowitz wrote Dr. Liebling that petitioner was still complaining of numbness in the mid-abdominal region and weakness of her legs. Dr. Herskowitz stated she might be having some time of autoimmune phenomenon. Med. recs. at Ex. 3, p. 11.

On November 2, 1981, petitioner returned, still complaining of tight band-like sensation in the upper thorax and stumbling when she walked due to inadequate sensation in her feet. She had some dysesthesias in her hand and electric shock down her spine when she flexed her neck. On examination, she had mildly to moderately impaired position and vibration sense distally in the feet up to the ankles. Med. recs. at Ex. 3, p. 12. There was a suggestion of bilateral Babinski signs (which would indicate central nervous system involvement). She had difficulty walking on heels or toes. She had a positive Lhermitte's sign. *Id.*

On February 3, 1982, petitioner returned to Dr. Herskowitz, still complaining of headaches which were mainly nocturnal. She also still had significant neck and back pain. Her neck was quite rigid. Med. recs. at Ex. 3, p. 13.

On March 22, 1982, petitioner returned to Dr. Herskowitz still having neck pain and headaches. The pain went from the base of her spine to the top of her head. She got three to four episodes a day. Her neck was quite stiff with hyperextension. Med. recs. at Ex. 3, p. 14.

On March 29, 1982, petitioner returned to Dr. Herskowitz. Over the past three days, she had fatigue, lethargy, double vision, and headaches. For the past several months, she had a generalized pruritis. She was in an automobile accident on January 12, 1982 and had a post-concussive syndrome, but her symptoms then were different than after the accident. The numbness in her feet was unchanged. She had unsteadiness in her walk over the prior several

days. On examination, there was some prominence to the globe on the right on inspection of her eyes. Dr. Herskowitz referred her to Dr. Eugene M. Eisner. Med. recs. at Ex. 3, p. 15.

Also on March 29, 1982, she saw Dr. Eisner and complained of double and blurred vision in her left eye. Med. recs. at Ex. 2, p. 3.

On April 2, 1982, petitioner saw Dr. Herskowitz. For the past week, when her double vision began, she had nausea with some weight loss due to inability to eat, occasional night sweats, dysequilibrium, and increased numbness in her feet. She did not feel well. On examination, she had mild right 6th nerve paresis which was brought out significantly with red glass testing of her extraocular muscles. Dr. Herskowitz felt petitioner might be having recurrent demyelinating episodes. Med. recs. at Ex. 3, p. 16.

On April 7, 1982, Dr. Herskowitz wrote to Dr. Liebling that petitioner developed right 6th nerve paresis and recently complained of some unusual sensation on the right side of her face. She had a very subtle right peripheral 7th nerve weakness as well. She complained of difficulty hearing localizing sounds on her right side. These symptoms presented more as focal demyelinating episodes. Med. recs. at Ex. 3, p. 18.

On April 15, 1982, petitioner had a CT scan of the brain which detected a possible Arnold-Chiari malformation, type I. Med. recs. at Ex. 3, p. 87.

On April 16, 1982, petitioner returned to Dr. Herskowitz, still complaining of some double vision to right gaze and numbness of the right side of her face. The day before, she had difficulty swallowing solids and felt as though her head were stuffy. On examination, she still had the right 6th nerve paresis but her right eye seemed to be moving laterally better. Med. recs. at Ex. 3, p. 19.

Dr. Herskowitz wrote Dr. Liebling on April 22, 1982 that petitioner's symptoms were gradually and slowly improving. She still had a right 6th nerve paresis, but this had improved as did her minimal facial weakness. Her appetite had improved and her bowel problems were less significant. Her spinal fluid protein electrophoresis showed an elevated IgG component which is consistent with either an autoimmune or demyelinating process. Med. recs. at Ex. 3, p. 20.

On May 3, 1982, petitioner returned to Dr. Herskowitz, having made considerable improvement. Her right 6th nerve paresis had almost completely cleared after three weeks on Prednisone. Spinal fluid gamma globulins were elevated, indicating this was a demyelinating episode. Med. recs. at Ex. 3, p. 21.

On June 3, 1982, petitioner returned to Dr. Herskowitz with significant improvement. Her double vision looking to the right was only minimal. She still had some complaints of dysesthesias of the feet. Med. recs. at Ex. 3, p. 22.

On October 1, 1982, Dr. Herskowitz wrote Dr. Liebling that petitioner had been doing quite well until about a month previously when she began feeling a sensation of heat in the soles of her feet and increasing numbness. She also had no energy generally and had intermittent leg cramps. Med. recs. at Ex. 3, p. 23.

She still had diplopia on January 23, 1983. Med. recs. at Ex. 2, p. 83. This continued in 1984. Med. recs. at Ex. 2, p. 5.

On August 2, 1990, petitioner saw Dr. Jerry Rosenbaum, a rheumatologist, complaining about discomfort about her right shoulder for the past month with associated diminished range of motion, morning stiffness, nocturnal pain, and referred pain to her upper arm. Med. recs. at Ex. 9, p. 29. She received radiation and chemotherapy for Hodgkin's 12 years previously. *Id.*

Physical examination revealed diminished internal rotation about her right shoulder with guarding and a mildly tender subdeltoid bursa. Dr. Rosenbaum's impression was capsulitis. *Id.*

After the Vaccination

Petitioner alleges she received a hepatitis B vaccination on August 6, 1990 although she has not provided documentation of vaccination. However, in a letter dated September 15, 1999, Dr. Edward J. Feller, a gastroenterologist, wrote a letter to petitioner's counsel's paralegal stating that petitioner had worked for the medical group for at least 20 years, but unfortunately they purge their records after seven or eight years and her vaccine record from 1990 would have been destroyed. He continues:

> I clearly do remember however that she was vaccinated for hepatitis B in so far [sic] as it was recommended that anyone who worked in a medical office who had direct patient contact be vaccinated against hepatitis B. I know that she received the vaccine. It was possible that it was on or about the date that she has stated.

Med. recs. at Ex. 5, p. 1.

On August 12, 1990, Dr. Eisner diagnosed her with retrobulbar neuritis. Med. recs. at Ex. 2, p. 7.

On August 13, 1990, petitioner underwent a brain MRI with gadolinium. It was normal. Med. recs. at Ex. 3, p. 88.

Dr. Herskowitz wrote a letter dated August 13, 1990 to Dr. Eugene Kafka. He stated that 8-10 years previously, he had seen petitioner for peripheral neuropathy secondary to Hodgkins which apparently resolved. She was left with a mild residua of dysesthesias in her feet which had been nonprogressive and stable. She was doing well until one week previously (which would be

August 6, 1990) when she noted left hemicranial retro-orbital pain which persisted for about five days and then, on August 11, 1990, noticed a big black spot in front of her left visual field. The pain in her eye increased with eye movement. She saw Dr. Eisner and had a full work-up which was normal except for a central scotoma (lost or depressed vision) and a left Marcus Gunn pupil. He put her on Prednisone. There had been no change in her vision. Dr. Herskowitz diagnosed petitioner with left retrobulbar neuritis. About one week prior to this, she received a heptavax injection. (Petitioner alleges vaccination on August 6, 1990, the date her eye problems began, according to Dr. Herskowitz's record.) Med. recs. at Ex. 3, p. 26.

A visual evoked response done on August 15, 1990 was abnormal due to prolonged latency in the left eye. Med. recs. at Ex. 3, p. 89.

On August 20, 1990, Dr. Herskowitz wrote Dr. Kafka that petitioner was much improved. The vision in her left eye was significantly better. She no longer had a Marcus-Gunn pupil in the left eye. Petitioner asked Dr. Herskowitz if hepatitis B vaccine could have precipitated this and he told her she did have an altered immune system. Med. recs. at Ex. 3, p. 28.

On August 27, 1990, Dr. Herskowitz wrote Dr. Kafka that petitioner was doing much better. She noticed some minor paresthesias in her feet. Med. recs. at Ex. 3, p. 29.

On September 7, 1990, Dr. Herskowitz wrote Dr. Kafka that petitioner saw Dr. Eisner the day before and he told her that her vision was normal. She complained of increasing numbness in her feet up to the midcalf. She had this in 1981. On examination, she had impaired vibratory and position sense in both feet and decreased ankle reflexes. She had mild weakness of her right foot. Med. recs. at Ex. 3, p. 30.

Nerve conduction studies conducted on October 2, 1990 were normal. Med. recs. at Ex. 3, p. 90. Visual evoked response done on October 2, 1990 was abnormal due to prolongation of the left optic tracks. Med. recs. at Ex. 3, p. 91. Somatosensory evoked responses were abnormal in both lower extremities on October 2, 1990. Med. recs. at Ex. 3, p. 92.

On March 14, 1991, Dr. Herskowitz wrote Dr. Kafka that petitioner had an automobile accident on March 6, 1991. She immediately started complaining of neck pain, bilateral shoulder pain, and headache. She had an automobile accident six years previously with neck injuries that never got completely better. After examining petitioner, Dr. Herskowitz's impression was cervical sprain. She still had a left Marcus-Gunn phenomenon. She did not have any pathologic reflexes. She had normal strength. Med. recs. at Ex. 3, p. 31.

A cervical spine x-ray done on March 14, 1991 showed slight narrowing of the C5-6 and C6-7 discs. Med. recs. at Ex. 3, p. 93.

On April 25, 1991, Dr. Herskowitz wrote Dr. Kafka that physical therapy did not improve petitioner. She still had neck pains, and limited head rotation, flexion, and extension. Med. recs. at Ex. 3, p. 33.

An MRI of the cervical spine done May 1, 1991 showed nothing remarkable except the narrowing of the disc space at C5-6 and C6-7. Med. recs. at Ex. 3, p. 94. There was no evidence of any root encroachment at any level. *Id.*

Dr. Herskowitz noted on June 24, 1991 that an MRI of petitioner's spine did not show any significant herniated disks. Med. recs. at Ex. 3, p. 35.

On January 15, 1992, Dr. Herskowitz wrote an attorney that petitioner was still having significant neck discomfort with limitation of range of motion. She still had spasm of the

paracervical and trapezius muscle. Dr. Herskowitz felt this was a permanent injury, mainly soft tissue. Her disability was in the range of 5-6%. Med. recs. at Ex. 3, p. 42.

On May 27, 1994, petitioner saw Dr. Liebling. She stated she had been depressed for months without any specific reason. Med. recs. at Ex. 6, p. 12. Dr. Liebling wondered if she could have a collagen disorder with anemia, vague athralgias, vague headaches, and elevated sedimentation rate. Med. recs. at Ex. 6, p. 11.

On June 12, 1994, petitioner saw Dr. Rosenbaum, who had not seen her since 1990. She had a positive antinuclear antibody (ANA) with a titer of 1:160, and a hemoglobin of 11.6 with an elevated MCV. Med. recs. at Ex. 9, p. 21. She had classical tender areas of fibromyalgia. Med. recs. at Ex. 9, p. 22.

On June 15, 1994, Dr. Herskowitz wrote Dr. Kafka, noting that petitioner had a normal MRI of the brain in August 1990. In September 1990, she had numbness extending to the mid-calf in both feet and a mild grade 4/5 weakness in the right foot. Med. recs. at Ex. 3, p. 43. In October 1990, nerve conduction studies were done of both lower extremities and were normal despite her complaints of numbness. She stated that for about a year (which would be June 1993), she has noticed that her legs felt weak and had slowly been getting weaker. Her balance had not been good over the prior several months. Over the last two weeks, she had increasing lower back pain. She had a mild frontal headache. She has been feeling generally sick, weak and exhausted over the past month. She had night sweats without fever and recurrent herpes lesions of the face. Over the past month, she had joint pains in her knees and less in her shoulders. On examination, fundoscopic exam was normal. Visual fields were full. Med. recs. at Ex. 3, p. 44.

Dr. Herskowitz's conclusion was that petitioner might have a systemic or inflammatory process. Lupus was a possibility. Med. recs. at Ex. 3, p. 45.

On June 21, 1994, petitioner had an MRI done on her lumbar spine. There was no evidence of compression or abnormal enhancement on gadolinium administration. Med. recs. at Ex. 3, p. 95. On June 21, 1994, petitioner had an MRI done on her brain which showed changes consistent with MS of moderate severity. There was associated dilatation of ventricles and sulci. This could be a transient effect of steroid therapy if she were on it. If she were not on it, it would suggest atrophy. Med. recs. at Ex. 3, p. 97.

Dr. Herskowitz wrote Dr. Kafka on June 27, 1994 that petitioner still had a very mild paraparesis 4+/5 in both lower extremities. The MRI of her lumbar spine was normal. The MRI of her brain showed hyperintense periventricular signals consistent with demyelinating disease. She did not have a clear case of MS. Perhaps she had a mixture of lupus and MS. Med. recs. at Ex. 3, p. 46.

On July 13, 1994, Dr. Herskowitz wrote Dr. Kafka that petitioner was unchanged. She complained of being unsteady when she walked with weakness of her legs. She had some mild urinary incontinence. The numbness in her legs to midcalf had been present since 1981. This most likely represented residual neurologic deficit from myelitis at that time. He thought petitioner most likely had MS. He did not think her complaints about her eyes and poor vision were related to MS. She was depressed. Med. recs. at Ex. 3, p. 47.

Dr. Herskowitz wrote Dr. Kafka on August 10, 1994 that petitioner made a nice recovery from her last bout of paraparesis. She had only minimal grade 4+/5 weakness in her proximal muscles in her legs. Dr. Eisner examined her eyes and found only that her prescription was a

little bit worse than before. She had nocturnal cramps in her calves and feet which she had had for many years. Med. recs. at Ex. 3, p. 49.

Dr. Herskowitz wrote Dr. Kafka on November 4, 1994 that petitioner complained of an increase in fatigue, heaviness, and weakness of her legs. Her calf cramps resolved spontaneously. She was neurologically unchanged. She had a positive Lhermitte's sign. Dr. Herskowitz thought she was in relative remission from her MS. She saw Dr. David Racher for a second opinion and he agreed with the diagnosis of MS. Med. recs. at Ex. 3, p. 50.

On November 22, 1994, petitioner saw Dr. Rosenbaum, complaining of morning stiffness lasting one to two hours, pain in both knees and hips, and moderate fatigue. Med. recs. at Ex. 9, p. 4. She was diagnosed with connective tissue disease. *Id.*

In a note dated December 12, 1994, Dr. Herskowitz states that Dr. Rosenbaum did not feel petitioner had lupus but had some component of it. She still complained of weakness of her legs and pain in her knees. Med. recs. at Ex. 3, p. 52.

On January 11, 1995, Dr. Herskowitz noted that petitioner was significantly better. She walked better and her legs were stronger. She broke out with herpes simplex on the right side of her face which had been recurrent for years. She seemed in remission neurologically. Med. recs. at Ex. 3, p. 53.

On May 7, 1995, Dr. Herskowitz saw petitioner who was doing better. She was less dizzy and no longer had difficulty walking after getting up. She felt her legs were stronger and she had fewer headaches. The MRI was unchanged since 1994. Dr. Eisner found no change in her visual exam from prior visits several years ago. Dr. Liebling did not see recurrent adenopathy. Neurologically, she was stable. She had minor bladder leaking several weeks prior,

but this cleared up. Dr. Herskowitz reassured her that her MS was stable. Med. recs. at Ex. 3, p. 62.

On September 22, 1995, she was having light flashes in her left eye. Med. recs. at Ex. 2, p. 10.

On September 26, 1995, Dr. Herskowitz wrote that petitioner had questionable optic neuritis in the left eye in the past and, three weeks previously, had a very transient five-minute episode of loss of vision or white-out in her right eye. She saw Dr. Eisner who found no abnormalities. Neurologically, she was unchanged. She still had impaired vibratory and position sense in both feet distally to the knees. Med. recs. at Ex. 3, p. 54. Nerve conduction studies were normal, just as in June 1994. Med. recs. at Ex. 3, p. 99. Petitioner had a combination of significant physical and emotional problems. Med. recs. at Ex. 3, p. 55.

On October 17, 1995, Dr. Herskowitz noted that petitioner was still complaining of weakness in her legs and now of cramps in the left hamstring. Her neurologic examination was unchanged. Med. recs. at Ex. 3, p. 56.

On November 17, 1995, Dr. Herskowitz noted petitioner was still the same. She complained of headaches which had cleared and continued to complain of proximal leg weakness. She had diffuse leg cramps. Neurologically, she was unchanged over the past year. Neither the cramping nor the joint pain was due to MS. Med. recs. at Ex. 3, p. 57.

On February 20, 1996, petitioner saw Dr. Liebling. She had been diagnosed with MS and also with a lupus-like crossover syndrome. He suggested to petitioner that her diseases may be interrelated in that she now had three immune diseases: (1) nephrotic syndrome with her original Hodgkin's disease; (2) MS; and (3) a lupus-like syndrome. Med. recs. at Ex. 6, p. 13.

On April 2, 1996, petitioner saw Dr. Howard L. Zwibel, a neurologist. Petitioner had her first major neurological symptoms in 1981 when she had numbness in her lower extremities. Dr. Herskowitz treated her with steroids. In 1983, petitioner had an episode of diplopia, again treated with steroids. In 1990, petitioner had an episode of visual loss in the left eye which was felt to represent optic neuritis. Her current complaints were weakness in her lower extremities and some degree of pain in her lower back and legs. She had a diagnosis of both MS and lupus. Her significant past history included Hodgkin's disease and a nephrotic syndrome. Her brain MRI of 1994 showed white matter disease consistent with a diagnosis of demyelinating disease. Med. recs. at Ex. 9, p. 12. Dr. Zwibel found petitioner's symptoms most compatible with the diagnosis of relapsing-remitting MS. Her titers suggested lupus. Med. recs. at Ex. 9, p. 13.

On August 2, 1996, petitioner saw Dr. Jeffery S. Ritter, a rheumatologist, complaining of pain in her left shoulder. In 1994, her ANA was 1:640, followed by ANAs of 1:16, 1:6, and 1:80. Med. recs. at Ex. 9, p. 48. Neurological examination revealed no focality. Med. recs. at Ex. 9, p. 49. Dr. Ritter diagnosed her with left shoulder tendinitis. Dr. Ritter did not believe petitioner had a systemic collagen vascular disease such as a lupus-like syndrome. While her ANA was positive once, it was negative on subsequent occasions. Her DNA antibodies had been up and down. A lot of her symptoms may have been related to fibromyalgia. *Id.*

On April 7, 1997, Dr. Herskowitz noted he had not seen petitioner for the past year. She complained that, for the past six months, when she rose from a sitting position, she had trouble walking. For the past several months, she had lightheadedness and some headaches with vague visual symptoms. She had retired on disability. The neurologic examination was basically unchanged from September 1995. Med. recs. at Ex. 3, p. 61.

On April 15, 1997, an MRI was done of petitioner's brain, showing bilateral multifocal lesions, but no worsening of her MS since the prior MRI of June 21, 1994. Med. recs. at Ex. 2, p. 16; Ex. 3, p. 101.

On April 18, 1997, petitioner saw Dr. Liebling. Her MS was a little bit progressive. She recently had frequent episodes of dizziness and lightheadedness intermittently. She had occasional stress incontinence. She told Dr. Liebling that her rheumatologist finally felt that she did not have lupus. Med. recs. at Ex. 6, p. 14.

On April 18, 1997, Dr. Eisner wrote to Dr. Alan Herskowitz that he found no significant change in petitioner's eye examination from her visit on September 22, 1995. She had slight optic atrophy in the left eye due to old optic neuritis related to her MS. This had no relationship to her lightheadedness, dizzy spells, and headaches. Med. recs. at Ex. 2, p. 13.

On April 6, 1998, petitioner returned to Dr. Herskowitz. She had been stable until the prior several months. A lot of her old symptoms returned. She had brief scotomata in her left eye. Her lower extremities became progressively weaker. She again had difficulty rising and walking. Her neurologic examination was basically unchanged. She had a positive Lhermitte's sign. Med. recs. at Ex. 3, p. 64.

On October 14, 1998, petitioner saw Dr. Antonio F. Muina. She was recently diagnosed with MS and started taking beta interferon but was concerned it might affect her platelet count. She had multiple petechiae and purpura. Dr. Muina diagnosed thrombocytopenia, most likely secondary to beta interferon. Med. recs. at Ex. 6, p. 15.

On November 8, 1999, petitioner saw Dr. Bhupinder S. Mangat, a neurologist. In 1980, petitioner started having numbness in her feet without paralysis. In 1990, she received hepatitis

B vaccine. A few days later, she had optic neuritis. She had deteriorating vision in her right eye and was treated with steroids. In 1994, she had a brain MRI and MS was diagnosed for the first time. Med. recs. at Ex. 11, p. 19. Her main complaint was low back pain. She got spasms in her lower extremities and had deteriorating vision in her right eye. A large grayish spot came and went, lasting from 10 to 15 minutes without pain. She also had headaches, mostly at night. She gave a history of deteriorating memory and clumsiness with her hands. Her hands and feet were weak and she lost her balance. On examination, there was pallor of the optic discs, more on the left than on the right. Med. recs. at Ex. 11, p. 20. Her upper extremities were not weak. Romberg's sign was positive. Med. recs. at Ex. 11, p. 21.

On December 29, 1999, petitioner underwent an MRI of her brain. White matter changes and symmetrical ventricular dilatation were not significantly changed since her MRI of April 15, 1997. Med. recs. at Ex. 11, p. 18.

On January 25, 2000, petitioner saw Dr. Howard E. Gross, a cardiologist. She had mild to moderate aortic insufficiency. Med. recs. at Ex. 12, p. 1.

On August 10, 2000, petitioner saw Dr. Mangat. She had a history of memory deficit and loss of balance. In 1994, after an MRI of her brain, she had a diagnosis of MS for the first time. She complained of visual disturbance in her right eye. On examination, there was pallor of the optic discs, more on the left than on the right. Med. recs. at Ex. 11, p. 15.

On December 14, 2000, petitioner saw Dr. Mangat. She did not have any recent history of double vision, blurred vision, numbness in the face, difficulty swallowing or talking, or numbness, weakness, or any paralysis of the arms and legs. She sometimes got extremely weak

and tired. Dr. Mangat found no deterioration in her demyelinating disorder. Med. recs. at Ex. 11, p. 13.

On December 18, 2000, petitioner saw Dr. Gross. Petitioner was asymptomatic. Med. recs. at Ex. 12, p. 4.

On August 2, 2001, petitioner complained to Dr. Mangat of slightly blurred vision and transient face numbness. Med. recs. at Ex. 11, p. 10. She did not have numbness in the lower extremities. *Id.*

On October 5, 2001, petitioner saw Dr. Mangat. She had antiphospholipid syndrome. She complained of weakness in the arms and legs, and extreme fatiguability. Med. recs. at Ex. 11, p. 8.

An upper GI series performed on April 2, 2002 showed large, spontaneous gastroesophageal reflux. Med. recs. at Ex. 13, p. 58.

A Lupus Anticoagulant Assay ordered by Dr. David F. Fernandez on April 6, 2002 proved negative. There was no evidence of lupus anticoagulant. Med. recs. at Ex. 13, p. 31.

On April 1, 2003, petitioner saw Dr. Mangat, complaining of extreme vertigo and extreme loss of balance. An MRI of her brain would be done to see if there were a worsening of her MS. Med. recs. at Ex. 11, p. 6.

On April 14, 2003, petitioner underwent an MRI of her brain with and without contrast. Med. recs. at Ex. 11, p. 4. Dr. Paul A. Goldberg described areas of abnormal white matter signal predominantly periventricular and compatible with MS. There were no enhancing lesions and no evidence of a recent cerebrovascular accident. Med. recs. at Ex. 11, p. 5.

Additional Filed Material

Respondent filed an article entitled "Diagnostic Criteria for Multiple Sclerosis: 2005 Revisions to the 'McDonald Criteria,'" by C.H. Polman, et al., 58 *Ann Neurol* 840-46 (2005). R. Ex. C. The authors state that, in 2001, the International Panel on the Diagnosis of Multiple Sclerosis presented new diagnostic criteria under its chairman Dr. W. Ian McDonald which formally incorporated MRI into the well-established diagnostic workup. *Id.* at 840. The panel reconvened in March 2005 to review progress since the adoption of the original criteria. The authors state that objective findings are required to make the diagnosis. *Id.* at 841. They prefer "rigorous demonstration of dissemination in time" to dissemination of lesions in space. *Id.* at 842. T2 lesions on MRI demonstrate dissemination in time. *Id.* The authors caution that a negative MRI means that "extreme caution needs to be taken before making a diagnosis of MS." *Id.* at 845 n.5.

TESTIMONY

Dr. Carlo Tornatore, a neurologist, testified for petitioner. Tr. at 3. He is the director of Georgetown Hospital's Multiple Sclerosis Clinic, and follows 1,500 patients there. Tr. at 4. In 1977 or 1978, petitioner had Hodgkin's disease and received radiation, chemotherapy, and splenectomy. Tr. at 5. In 1981, she complained of tingling and numbness. *Id.* Her neurologist Dr. Hershkowitz diagnosed it as peripheral neuropathy secondary to Hodgkin's. Tr. at 6.

About six months later in 1981, petitioner had intermittent numbness in the mid-abdominal area. Tr. at 7. The final diagnosis was possible myelitis and peripheral neuritis of uncertain etiology. *Id.*

In March 1982, petitioner developed a sixth nerve palsy. The sixth nerve is a peripheral nerve. Tr. at 8. Petitioner was stable for eight years, leading Dr. Tornatore to conclude that she was not experiencing an inflammatory illness, such as MS. Tr. at 12.

In 1990, petitioner received her first hepatitis B vaccination. *Id.* When the undersigned asked Dr. Tornatore if petitioner's pre-vaccination neurological condition were do to her lymphoma, he said it probably was since lymphoma can cause peripheral neuropathy as can chemotherapy. Tr. at 14. There was no evidence of myelitis in the cervical or thoracic spinal areas on MRI. *Id.* She had no evidence of brain abnormality in her first MRI in 1990. Tr. at 15. If she had had MS as the cause of her sixth nerve palsy, it should have showed up on MRI. *Id.* Moreover, the brain MRI in 1990 showed no atrophy, which is a central component of MS. *Id.* The McDonald criteria for MS states specifically that if there is a normal brain MRI, one has to be extremely careful in diagnosing MS. Tr. at 16.

Petitioner had two neurologic episodes without anything showing up in her brain or spinal cord, and no atrophy in her brain or spinal cord nine years later even though her symptoms continued. Tr. at 18. Dr. Tornatore does not diagnose petitioner as having relapsing, remitting MS before the hepatitis B vaccination. Tr. at 20.

After petitioner receives her vaccination, she develops optic neuritis in her left eye and has a brain MRI which was normal. Tr. at 21. Dr. Tornatore's opinion is that the vaccine clearly triggered petitioner's optic neuritis. But he is unsure if it triggered a de novo autoimmune response or if petitioner had a low grade autoimmune process related to her lymphoma and then the vaccine triggered the optic neuritis. *Id.* He called this difficult. *Id.*

In 1994, petitioner complained of more neurologic symptoms and her MRI, four years after the optic neuritis following the vaccination, was grossly abnormal which was consistent with moderately severe MS. *Id.* She had associated dilatation of her ventricles and sulci. *Id.* From 1982, when she had her first symptoms, to 1990, she had a normal brain MRI. Tr. at 21-22. Then she received hepatitis B vaccination, had optic neuritis, and within four years, her brain MRI showed a lot of inflammation and incredibly active MS. The tempo of the symptoms or at least the MRI findings dramatically changed. Tr. at 22. Something happened here. Dr. Tornatore stated that even if he accepted that petitioner had a pre-vaccination low grade inflammation that may have caused some pre-vaccination symptoms, the vaccination clearly was a trigger on much more significant MRI findings. *Id.*

Dr. Tornatore did not know if petitioner had inflammation due to a neurologic disease or an autoimmune disease like lupus. *Id.* Dr. Tornatore opined the vaccine caused significant aggravation if petitioner had previous inflammation but, if she did not, it was an initiator of her MS. Either way, if not for the vaccine, petitioner would not have had these MRI changes in 1994. Tr. at 23.

Dr. Tornatore did not believe that petitioner's pain in her left eye on the day of vaccination was too soon to have the vaccine cause it. Tr. at 23-24. Within a day of vaccination, a vaccinee may feel flu-like and have some kind of constitutional symptoms. Tr. at 24. The immune system is turned on and the white blood cells secrete chemokines and cytokines. *Id.* These irritate different muscles and soft tissues. *Id.* The pain in petitioner's eye on the day of vaccination was not necessarily due to demyelination but just to the irritation of her soft tissue or the optic sheath (the covering of the optic nerve). *Id.* Subsequently, demyelination happens. *Id.*

Dr. Tornatore testified that the vaccine changed the tempo of petitioner's neurologic problem. Tr. at 25. She did not have demyelinating peripheral neuropathy before she received hepatitis B vaccine. Dr. Tornatore presumed she had a sensory or small fiber polyneuropathy before the vaccination. Tr. at 26. He thinks this pre-vaccination polyneuropathy was unrelated to her MS because her symptoms persisted, her spinal MRIs were normal, and she previously had lymphoma and chemotherapy. *Id.* In 1990, nine years after the onset of her symptoms, Dr. Herskowitz felt petitioner had residual sensory neuropathy. *Id.*

If the hepatitis B vaccination did not significantly aggravate petitioner's pre-existing autoimmune disease, her post-vaccination course was of a second neurologic illness, i.e., MS, which had nothing to do with her pre-vaccination small fiber polyneuropathy. Tr. at 27. In 1982, petitioner had an elevated IgG in her cerebrospinal fluid which indicates some type of inflammation. But that does not make it MS. *Id.* Something lupus-like was going on, but it changed when she was vaccinated. *Id.*

On cross-examination, Dr. Tornatore stated he would not disagree that petitioner's 1981 symptoms sounded like myelitis. Tr. at 30. But if there was myelitis that was significant, the doctors would have seen something on a subsequent MRI of her cervical and thoracic spine. *Id.* Both petitioner's April and September 1981 episodes involved the lower extremities. However, a new symptoms was the numbness coming up to her midabdomen. Tr. at 31. She also had difficulty with urination and a positive Lhermitte's sign. *Id.* These were new symptoms. *Id.* Any irritation of the spinal cord, not just MS, can lead to Lhermitte's sign. Tr. at 31-32. Dr. Tornatore does not disagree with respondent's expert Dr. Bielawski that these symptoms sound like myelopathy. Tr. at 32. Petitioner had a lot of disk disease in her spine. Tr. at 34. That

could be the cause of her Lhermitte's sign. *Id.* But if she had pre-vaccination myelitis, Dr. Tornatore would like to have seen something on her spinal MRI. *Id.*

Either way–whether she had pre-vaccination myelitis or myelitis only post-vaccination–Dr. Tornatore attributes petitioner's significant worsening to the vaccination. Tr. at 34. His reason is that petitioner's brain MRI shortly after vaccination was normal but, within four years, it changed significantly. Tr. at 35. Dr. Tornatore adheres to Dr. John Kurtzke's five-year rule, i.e., that how someone is after five years of MS sets the tone for how he or she will be the rest of his or her life. *Id.*

In April 1982, petitioner had fatigue, lethargy, double vision, and headaches. Tr. at 36. At best, petitioner had a sixth nerve palsy. Dr. Bielawski brings in the fifth and seventh nerves as well in his report. Tr. at 37. Dr. Tornatore stated that, if there had been a lot of inflammation in the fifth, sixth, and seventh nerves, then on brain MRI eight years later, petitioner should have had a very significant degree of inflammation, but she did not. Tr. at 38. Dr. Herskowitz, her treating physician, thought petitioner had an inflammatory condition. She was unsteady and had loss of sensation in her feet. Tr. at 39. There were no MRIs in 1982. Tr. at 40. But once there were MRIs, there was no significant lesion and you would expect it. *Id.* The McDonald criteria state to use extreme caution in diagnosing MS when, although there are two episodes, there is a negative MRI. Tr. at 42. Dr. Tornatore thought it unbelievable that petitioner would have three symptoms of myelitis in 1981 and 1982 and nine years later, have a normal MRI. Tr. at 44.

Dr. Tornatore could not give a cause for petitioner's pre-vaccination eye symptoms. *Id.* The records were difficult to read, but there is one that said petitioner's eye exam was normal. Tr. at 45. She had a number of infections. *Id.*

Dr. Tornatore admitted that there was no evidence of the vaccination on August 6, 1990 although a letter from petitioner's employer stated that he did not doubt she received it. Tr. at 47. But petitioner did tell Dr. Herskowitz that she received it. *Id.* Petitioner gave Dr. Herskowitz a history that one week before she saw him, she received heptavax vaccine. Tr. at 48. Dr. Tornatore considers petitioner's onset of symptoms after vaccination to be medically appropriate. Tr. at 48-49. Six days after vaccination, petitioner was diagnosed with lateral retrobulbar neuritis on August 12, 1990. Tr. at 49. This neuritis began an inflammatory process resulting in a brain MRI four years later showing a lot of plaque and disease. *Id.* For those four years, petitioner was untreated for MS but did not have any events. Tr. at 50. This shows that something major happened during this period of time, and this was the vaccination. *Id.*

Interpreting petitioner's first symptom of eye pain post-vaccination, Dr. Tornatore stated that inflammation starts in the blood vessels and then enters the nervous system. The dura and optic nerve have blood vessels that go from one to the other. Tr. at 53. The pathology of MS is perivenular demyelination. The inflammatory cells in the blood vessels leak out and cause inflammation in the optic nerve. *Id.* Petitioner's change in vision five days post-vaccination is the evidence of demyelination. Tr. at 54. The eye pain is not evidence of demyelination. *Id.*

Petitioner did not develop demyelination post-vaccination immediately. She had an inflammatory period and then developed demyelination. Tr. at 55. Even if her demyelination had occurred immediately after vaccination, Dr. Tornatore opined that this would only mean that petitioner had T cells that were already primed to myelin basic protein. Tr. at 57. If he accepted that petitioner had a prior demyelinating disease or MS, his proof of significant aggravation of her MS from the vaccination is her brain MRI in 1994. Tr. at 57, 58. Petitioner's optic neuritis

in August 1990 resolved by September or October 1990. Tr. at 58. She had sensory complaints from her feet to her midcalf, but she had those symptoms before the vaccination. *Id.* From 1990 to 1992, petitioner's sensory symptoms appeared to abate. Tr. at 59.

Petitioner's loss of vision in 1990 is a neurological sign. Tr. at 60. The pain before the loss of vision is not a neurological sign. *Id.* The loss of vision occurred with an appropriate time relationship with the vaccination. Tr. at 61. Petitioner's normal brain MRI in 1990 means she had no prior evidence of demyelination within the neuraxis.[4] Tr. at 65. If the doctors had made thin cuts of MRI through the eye orbit, they might have seen inflammation. Tr. at 65-66.

Dr. Martin A. Bielawski testified for respondent. Tr. at 67. He is a neurologist with a subspeciality in neurophysiology. Tr. at 67, 69. His opinion is that hepatitis B vaccine did not injure petitioner. Tr. at 70. Petitioner had three distinct neurological events with objective findings before she was vaccination: (1) in April 1981 when she had ataxia, sensory symptoms of the legs, and dimensional deficiency, pointing to a problem in the posterior columns of the spinal cord; (2) in September 1981, when she again had leg symptoms, sensory symptoms and symptoms up to the midabdomen, diminished vibration, Lhermitte's sign, indicating spinal cord irritation, positive Babinski signs indicating upper motor neuron dysfunction, indicating myelitis; and (3) in March and April 1982, when she had fatigue, double vision, headache, facial numbness, right sixth nerve problem, unsteady gait, indicating a problem in the brain stem, and on CT scan, dilated ventricles. Tr. at 70-71.

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[4] Neuraxis is "the central nervous system." Dorland's Illustrated Medical Dictionary, 30th ed. (2003) at 1252.

Dr. Bielawski disagreed with petitioner's treater Dr. Herskowitz's diagnosis of polyneuropathy in 1981. Tr. at 71-72. His reason is that petitioner had diminished position of vibration sense, but this could be caused by chemotherapy. She did not have change in her reflexes or light touch sensation. Tr. at 72. Her EMG was normal, but this can result in a very small fiber neuropathy. *Id.* He thinks petitioner's symptoms beginning in 1981 indicates a central nervous system disorder. *Id.* He also thinks that petitioner's symptoms before 1990 fulfill the criteria for a diagnosis of MS. *Id.* Those criteria are that the person has two or more attacks and objective findings indicating lesions in time and space. Tr. at 73. Petitioner had a cerebrospinal fluid test in 1982 showing elevated IgG which can be seen with inflammatory disease and postinfectious disease. Since she did not have a postinfectious disease or lupus, there was no other inflammatory condition that could have caused her elevated IgG. *Id.*

Petitioner had chemotherapy in 1977 for Hodgkin's. *Id.* If she were to have a peripheral neuropathy related to her chemotherapy, it would have occurred before 1981. He also did not think chemotherapy played a role in her neurological symptoms. Tr. at 74. When asked how he could diagnose MS without an abnormal MRI, Dr. Bielawski responded that part of the revised McDonald criteria indicates that two or more attacks with objective clinical evidence of two or more regions is sufficient for a diagnosis of MS. *Id.* Even though her brain MRI in August 1990, a week post-vaccination was normal, Dr. Bielawski opined she had MS because she still had fulled the criteria for diagnosing MS. *Id.* He has seen patients with MS lesions on MRI that come and go. If theorized that if MRIs had been available in 1981 and 1982, petitioner perhaps would have shown a demyelinating lesion which could have gone by the time she had a brain MRI in 1990. *Id.*

Dr. Bielawski said he would not have expected her abnormal brain MRI in June 1994 because her clinical symptoms did not change from 1990 to 1994. Tr. at 75. She had the same symptoms in 1994 (paresthesias, leg numbness, ataxia, diplopia, facial numbness and weakness, fatigue, Lhermitte's sign, Babinskis) that she had in 1990. *Id.* He stated that MRI findings do not have to correlate clinically with the severity of the disease. *Id.* He attributes her retrobulbar neuritis in 1990 to another attack of MS. Tr. at 75, 76. Petitioner had eye pain either the day of or the day after hepatitis B vaccination. Tr. at 76. The pain was related to the inflammation of the optic nerve sheath. He could not see the relationship to the vaccine because this was her first hepatitis B vaccination and she did not develop systemic inflammatory symptoms such as fever or myalgia. *Id.* He believed the process was more of an inside out than an outside in process, beginning within the optic nerve tissues with microglia,[5] and then cytokines released which then went to the blood brain barrier, attracting more cytokines and T cells, and then demyelination. Tr. at 77. The attack on the optic nerve tissue (the microglia) causes the inflammation and demyelination, causing pain in the optic nerve sheath. *Id.* Thus, petitioner's eye pain on the day of or day after hepatitis B vaccination means there was demyelination on that day. *Id.*

Dr. Bielawski's opinion is that petitioner's vaccination is coincidental to her eye pain and optic neuritis. Tr. at 78. Petitioner had relapsing, remitting MS. Her neurological symptoms after her optic neuritis are typical of that condition. *Id.* She accumulated brain lesions from 1990 to 1994. One of the mysteries of MS is that she did not have any clinical manifestations of those

[5] Microglia are "small, non-neural, interstitial cells of mesodermal origin that form part of the supporting structure of the central nervous system." Dorland's Illustrated Medical Dictionary, 30th ed. (2003) at 1152.

lesions. Tr. at 79. Dr. Bielawski does not believe that hepatitis B vaccine significantly aggravated petitioner's pre-existing MS. *Id.*

Dr. Bielawski agreed there is a five-year rule that indicates the course of someone's MS is what occurred during five years, but there are patients whose experiences differ from that. Tr. at 98. He thinks that petitioner had a relatively benign course of MS from 1982 to 1990. Tr. at 99. But even patients with benign forms of MS have flareups. *Id.* He does not consider optic neuritis to be a benign flareup. *Id.* Dr. Bielawski agreed that MS can be an immune-mediated disorder and that six to seven days between cause and immune response was an appropriate time frame. Tr. at 99-100.

DISCUSSION

This is a causation in fact case. To satisfy her burden of proving causation in fact, petitioner must offer "(1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of a proximate temporal relationship between vaccination and injury." Althen v. Secretary of HHS, 418 F. 3d 1274, 1278 (Fed. Cir. 2005). In Althen, the Federal Circuit quoted its opinion in Grant v. Secretary of HHS, 956 F.2d 1144, 1148 (Fed. Cir. 1992):

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

In Capizzano v. Secretary of HHS, 440 F.3d 1274, 1325 (Fed. Cir. 2006), the Federal Circuit said "we conclude that requiring either epidemiologic studies, rechallenge, the presence of pathological markers or genetic disposition, or general acceptance in the scientific or medical

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

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

Petitioner must show not only that but for the vaccine, she would not have had either onset or significant aggravation of her MS, but also that the vaccine was a substantial factor in bringing about the onset or significant aggravation of her MS. Shyface v. Secretary of HHS, 165 F.3d 1344, 1352 (Fed. Cir. 1999).

The Federal Circuit in Capizzano emphasized that the special masters are to evaluate seriously the opinions of petitioner's treating doctors. 440 F.3d at 1326. In Capizzano, four of petitioner's treating physicians opined that hepatitis B vaccine caused her rheumatoid arthritis.

Close calls are to be resolved in favor of petitioners. Capizzano, 1440 F.3d at 1327; Althen, 418 F.3d at 1280. *See generally*, Knudsen v. Secretary of HHS, 35 F.3d 543, 551 (Fed. Cir. 1994).

Congress defined "significant aggravation" as "any change for the worse in a preexisting condition which results in markedly greater disability, pain, or illness accompanied by substantial deterioration of health." 42 U.S.C. § 300aa-33(4).

Although respondent challenges whether petitioner ever received hepatitis B vaccine, the undersigned accepts that she did because of: (a) the letter from her employer that she did receive

it (he is a doctor and hepatitis B vaccine was required for his staff) and (b) her mention of having received heptavax when she went to Dr. Herskowitz with eye pain within a week of vaccination.

In Werderitsh v. Secretary of HHS, No. 99-319V, 2006 WL 1672884, at *24 (Fed. Cl. Spec. Mstr. May 26, 2006), which was one of the four paradigm cases in the Omnibus proceeding concerning hepatitis B vaccine and demyelinating diseases, the undersigned referred to petitioner's expert Dr. Vera Byers who stated that "if someone with the phenotype of MS that is relapsing/remitting were to allege that hepatitis B vaccine worsened his or her MS, the undersigned might find it impossible to determine whether the vaccine played any role in the course of an illness that, by itself, is episodic."

The Werderitsh case concerned whether hepatitis B vaccine causes MS. At issue in that case was also whether petitioner already had a mild case of MS pre-vaccination which hepatitis B vaccine significantly aggravated. Dr. Tornatore, petitioner's expert in the instant action, was also petitioners' expert in the Omnibus proceeding. He testified that if Mrs. Werderitsh had MS by the time she received hepatitis B vaccine, the vaccine significantly aggravated it. *Id.* The undersigned discussed the Omnibus testimony as follows:

> All the experts herein agree that Mrs. Werderitsh has a genetic propensity for MS. All the experts involved in the study of MS agree that in order for a patient to have MS, that person also needs an environmental component. But what that component is (virus? vaccination?) and when it should occur (puberty? post-puberty?) is unclear. Petitioner's expert Dr. Tornatore believes that hepatitis B vaccine is the environmental component.

Id.

In Werderitsh, the undersigned ruled for petitioner, holding that hepatitis B vaccine caused or, in the alternative, significantly aggravated petitioner's MS. 2006 WL 1672884, at *26. The undersigned stated:

> It appears that she had a decade's worth of visual disturbance that was similar to her visual problem a few days to a week after the first hepatitis B vaccination, which Dr. Hoyer opined could be optic neuritis. ...
> A month after Mrs. Werderitsh's second hepatitis B vaccination, she lost the ability to use her left leg and to vacate her bladder. MRIs identified brain lesions, at first two and then later four. Although the spinal MRIs never revealed abnormalities, Mrs. Werderitsh's clinical symptoms underscore the correctness of the diagnosis of MS (which no expert in this case doubted in any event).

2006 WL 1672884, at *26-*27.

The parallels between Werderitsh and the instant case are clear. Both petitioners had symptoms pre-vaccination that may be consistent with MS lasting for a decade. An argument could be made, just as Dr. Byers described in the Omnibus proceeding, that in a case of relapsing-remitting MS, it is hard to decide if the up and down course of the disease is due to the nature of the disease or the effect of an antigenic challenge.

The instant action has a considerable amount of mystery, but then, as respondent's expert Dr. Bielawski said, MS is a disease of mystery. The most striking mystery is why petitioner's brain MRI in 1994 was markedly abnormal when her symptomatology from 1990 to 1994 was stable, i.e., she continued to have symptoms, but not worse symptoms. Moreover, if the undersigned accepts Dr. Bielawski's opinion that petitioner had pre-existing MS beginning in 1981, why was her first brain MRI in 1990 normal? This is the primary reason that Dr. Tornatore opined she did not have MS for nine years before vaccination. Of note, petitioner's treating Dr.

Herskowitz attributed her pre-vaccination neurological symptoms to the effect of chemotherapy after she had Hodgkins, an opinion with which Dr. Tornatore agreed but Dr. Bielawski disagreed. The Federal Circuit in Capizzano emphasizes that the special masters are to take seriously the opinions of treating doctors. If petitioner's pre-vaccination neurologic symptoms were due to chemotherapy, then she did not have pre-vaccination MS. But the difficulty remains that many of her symptoms persisted for years and can be consistent with MS.

The undersigned cannot offer more explanation than the experts in this case about the mysterious course of petitioner's MS. What we do know is that the first brain MRI showing lesions was in 1994, four years after a prior normal MRI in 1990 (which was done soon after the onset of optic neuritis). Moreover, besides agreeing with the treater Dr. Herskowitz's diagnosis of peripheral neuropathy pre-vaccination, Dr. Tornatore emphasized that the McDonald criteria for diagnosing MS require extreme caution when an MRI is negative. Petitioner's brain MRI in 1990 was negative. Dr. Bielawski's explanation for this normal brain MRI is that lesions come and go.

Dr. Tornatore also emphasized the Five-Year Rule, i.e., the course of MS is set by what occurs during five years of symptoms. Thus, if the onset of petitioner's MS were in 1981, rather than in 1990, she should have continued with a normal brain MRI instead of having a significantly abnormal one in 1994. But, if the onset of her MS was in 1990 after the hepatitis B vaccination, then her abnormal brain MRI in 1994 was within the Five-Year Rule and would explain her worsening MS in future.

The undersigned can appreciate Dr. Bielawski's opinion that it is reasonable to diagnose petitioner's pre-vaccination symptoms as MS because the McDonald criteria for diagnosing MS

are that petitioner have separate lesions in space and time. Although there were no MRIs in existence during the time period of 1981-1990, she had symptoms suggesting different problems at different times. But the undersigned can also appreciate Dr. Tornatore's opinion that it is reasonable not to diagnose petitioner's pre-vaccination symptoms as MS because the McDonald criteria advise extreme caution for diagnosing MS when objective testing such as MRI is negative, such as petitioner's first brain MRI in 1990. Dr. Bielawski circumvented the McDonald criteria cautionary language by pointing to the positive IgG in petitioner's cerebrospinal fluid before she received hepatitis B vaccine. But there are various conditions that can cause an elevation of IgG in the spinal fluid and its presence did not impress Dr. Tornatore with diagnostic value.

In the final analysis, as Dr. Tornatore stated, we are in the same place. If petitioner had a pre-vaccination onset of MS, rather than chemotherapy-induced polyneuropathy, then hepatitis B vaccine significantly aggravated it. If petitioner did not have a pre-vaccination onset of MS but experienced the onset of her MS with her optic neuritis post-vaccination, then the vaccine caused it. Dr. Tornatore emphasized that there was nothing else challenging petitioner's immune system at this point that could result in her abnormal brain MRI in 1994.

Following the Federal Circuit's instruction in Althen and Capizzano that, when dealing with close cases, special masters should rule in favor of petitioners, the undersigned rules that petitioner has satisfied her burden of proof in showing that hepatitis B vaccine caused her MS or, in the alternative, significantly aggravated it and, without her having received the vaccine, she would not have had the onset or significant aggravation of her MS. The biologically plausible medical theory is the same as in Werderitsh and the other paradigm cases in the Omnibus

proceeding: (1) an environmental challenge (the vaccine) affected petitioner's immune system so as to cause demyelination; (2) the logical sequence of cause and effect was petitioner's eye pain (showing inflammation) leading to retrobulbar optic neuritis (demyelination); although she recovered from optic neuritis, other symptoms occurred; and (3) the timing between vaccination and onset of optic neuritis was appropriate for causation of an immune-mediated disease, as both experts agreed.

CONCLUSION

Petitioner has made a prima facie case of entitlement. The undersigned and counsel for the parties will engage in a telephonic status conference soon to discuss damages.

IT IS SO ORDERED.

November 18, 2008
DATE

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