In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS
No. 99-432V
July 13, 2009
To be Published

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JACINDA S. FISHER,	*	
	*	
Petitioner,	*	
	*	
v.	*	Entitlement; hep B vaccine;
	*	two months after second
SECRETARY OF THE DEPARTMENT OF	*	vaccination, optic neuritis
HEALTH AND HUMAN SERVICES,	*	and MS; one week after third
	*	vaccination, optic neuritis and
Respondent.	*	leg weakness
* *		

Clifford J. Shoemaker, Vienna, VA, for petitioner.
Chrysovalantis P. Kefalas, Washington, DC, for respondent.

MILLMAN, Special Master

RULING ON ENTITLEMENT[1]

Petitioner filed a petition on July 2, 1999, under the National Childhood Vaccine Injury Act, 42 U.S.C. §300aa-10 et seq., alleging that she received hepatitis B vaccine on July 13, 1992, August 13, 1992, and January 23, 1993, causing her an adverse reaction. Petition, ¶ 2. Proof of vaccination was filed as petitioner's exhibit 13. Her adverse reaction was ultimately described

[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.

as multiple sclerosis (MS), whose onset was presumably in October 1993, two months after her second hepatitis B vaccination, when she was diagnosed with optic neuritis.

On July 2, 1999, this case was assigned to special master Richard Abell.

On August 3, 1999, chief special master Gary Golkiewicz assigned the case to himself along with 73 other cases asserting hepatitis B vaccine caused a demyelinating illness.

On August 13, 1999, the chief special master issued an Order in this and 80 other cases stating that documents such as medical records, affidavits, and expert reports were missing and shall be filed by November 5, 1999.

On December 8, 1999, instead of filing said documents in these cases, petitioners' counsel moved to designate one case as a master file so that filings would occur only in that one case. As for the other cases (including the instant action), counsel asserted he was accumulating records and would scan and file them.

On January 5, 2000, respondent filed a response to petitioner's motion to designate one case as a master file, saying petitioner's motion should be denied. Petitioner's counsel in the instant action represented petitioners in 137 of 282 claims for injuries allegedly related to hepatitis B vaccine, involving 39 different attorneys and 22 pro se petitioners.

On February 14, 2000, the chief special master denied as premature petitioners' counsel's motion to designate a master file until he had filed medical records in all the cases. This order included all 137 cases in which petitioner's counsel herein was counsel.

On May 16, 2000, petitioner filed a status report saying she was still collecting records in the case.

On August 21, 2000, almost one year after filing her petition, petitioner filed a status report saying she was still collecting records in the case.

On December 12, 2000, petitioner filed a status report saying she was still collecting records in the case.

On March 13, 2001, petitioner filed a status report saying she was still collecting records in the case and working with potential experts.

On April 5, 2001, this case was transferred to the undersigned.

On May 16, 2001, the undersigned issued an Order directing 84 petitioners, including the petitioner in this case, to file hard copies of their medical records.

On July 31, 2001, petitioner filed an application for issuance of subpoenas to obtain records.

On August 7, 2001, the undersigned granted petitioner's application. More than two years had passed since petitioner filed her petition and she still had not filed any medical records.

On August 29, 2001, the undersigned issued an Order stating that petitioner had never filed a single medical record since she filed her petition over two years earlier and, if she did not file a single medical record by March 8, 2002, the case would be dismissed for lack of prosecution.

On February 8, 2002, petitioner filed exhibits 1-15, the first of her medical records.

On March 21, 2002, respondent filed a status report, requesting from petitioner an affidavit, current medical records, a legible vaccine record, and an expert opinion in support of her claim.

On March 29, 2002, petitioner filed a legible copy of exhibit 13 which was her vaccination record.

On September 13, 2002, petitioner filed copies of subpoenas she had sent to providers.

On December 5, 2002, the chief special master reassigned this case to himself again.

On May 7, 2003, the chief special master reassigned this case and 36 others to then–special master Margaret M. Sweeney to comprise a hepatitis B vaccine-neurological demyelinating Omnibus proceeding..

On January 6, 2004, former special master Sweeney issued an order concerning the Omnibus hepatitis B vaccine-demyelinating diseases proceeding and the designation of four cases (not the instant action) to represent four demyelinating diseases at issue: transverse myelitis (TM), Guillain-Barré syndrome (GBS), chronic inflammatory demyelinating disease (CIDP), and multiple sclerosis (MS). There were 65 cases encompassed within the Omnibus proceedings.

The Omnibus proceeding was held before former special master Sweeney from October 13-15, 2004. At the end of 2005, former special master Sweeney left to become a judge on the United States Court of Federal Claims.

On January 11, 2006, the chief special master transferred the instant action and all the 65 hepatitis B vaccine-demyelinating disease cases that were part of the Omnibus proceeding to the undersigned.

The first responsibility of the undersigned after the Omnibus cases were transferred to her was to rule in the four paradigm cases upon which the testimony and exhibits focused at the Omnibus proceeding. The undersigned held that hepatitis B vaccine can cause demyelinating

diseases (including MS, the disease at issue in the instant action) if the onset was between three days and one month based on the Omnibus 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).[2]

In Pecorella v. Secretary of HHS, No. 04-1781V, 2008 WL 4447607 (Fed. Cl. Spec. Mstr. Sept. 17, 2008), the undersigned ruled that an appropriate onset between hepatitis B vaccine and a demyelinating disease could be up to two months because in Pecorella, respondent elected not to defend when there was a two-month onset. In Pecorella, the disease was transverse myelitis. Thus, subsequent to the September 17, 2008 decision, the undersigned has accepted that a two-month interval between hepatitis B vaccination and a demyelinating disease is a medically appropriate time interval consistent with causation.

A hearing was held in this case on September 23, 2008. Testifying for petitioner was Dr. Carlo Tornatore, a neurologist, who opined that petitioner's second vaccination caused her optic neuritis two months later, and her third vaccination caused further eye problems and leg weakness one week later, resulting in a diagnosis of MS. Testifying for respondent was Dr. Subramaniam Sriram, a neurologist, who opined that petitioner's MS occurred before she received hepatitis B vaccine and was unaffected by her vaccinations.

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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; onset was12 or 13 days after first vaccination with recovery; onset of TM was one week after second vaccination); 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; onset was 21 days after second vaccination); Werderitsh v. Secretary of HHS, No. 99-310V, 2006 WL 1672884 (Fed. Cl. Spec. Mstr. May 26, 2006) (hepatitis B vaccine caused MS; onset was one month after second vaccination); 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; onset of GBS was eight days after fourth vaccination).

Were it not for respondent's expert's defense in this case that MS had preceded petitioner's hepatitis B vaccination, there would have been no reason for a hearing in this case since petitioner's first symptom of MS (according to petitioner's expert) occurred two months after vaccination, which was the onset interval in Pecorella in which the undersigned held two months was an appropriate time frame for causation based on respondent's decision in that case not to defend.

FACTS

Petitioner was born on November 9, 1957.

On November 6, 1981, petitioner went to Orthopedic Associates of Waynesboro because she fell and hurt her leg at work on October 30, 1981. Med. recs. at Ex. 17, p. 11. Dr. Ronald W. Rau diagnosed her with a strained right knee. Med. recs. at Ex. 17, p. 24.

On October 8, 1982, petitioner complained to her doctor of having pains in all her joints, including her back, behind her neck and down the spine, for about eight months. Med. recs. at Ex. 14, p. 3. On examination, she was tender over the C7 and down the upper thoracic vertebrae. She was also tender over the joints in her hands, but without swelling. She was tender over the ankles, but without swelling. *Id.*

On November 13, 1986, petitioner complained of a sensation of numbness along the outside of her foot with some soreness in her foot. She had been having some achiness down in the low back at the time. Med. recs. at Ex. 4, p. 5. She had some very minimal tenderness down the lumbosacral junction and over the left sacroiliac area. The reflexes in her legs were all normal. She had a decreased pinprick sensation along the lateral aspect of her left foot compared with the inside of her right foot and the lateral aspect of her right foot. She did not have motor

deficits. She continued to have some tenderness across the dorsum of the left foot and some over the Achilles tendon area but no definite swelling or erythema. *Id.* The doctor thought petitioner's left foot pain was due to a combination of a mild local tendinitis as well as lumbar radiculopathy.[3] *Id.*

On November 14, 1986, petitioner saw Dr. Kenneth A. Boatright, an orthopedist, complaining of pain and numbness involving her left heel for the past month or so. Med. recs. at Ex. 2, p. 2. She had been doing a lot of standing at the time. The pain was localized into the plantar aspect of the heel and was exacerbated by first getting up on the foot after sitting or lying for any prolonged period of time. *Id.* There was associated numbness involving the lateral aspect of the foot. Physical examination showed point tenderness along the medial aspect of the calcaneal tuberosity at the plantar fascial insertion. Petitioner had pain with stretching of the plantar fascia. She also had some numbness along the lateral aspect of the foot. The reflexes at the knees and ankles were both 2+. Dr. Boatright detected no motor or sensory abnormalities. His impression was that petitioner had plantar fasciitis but he could not completely explain the numbness along the lateral border of the foot. He wondered if she had radicular pain. *Id.*

On November 28, 1986, petitioner saw Dr. Boatright, complaining of left heel pain. She was diagnosed with plantar fasciitis. Although she was injected, she noted no significant improvement. The pain was actually worse. Med. recs. at Ex. 17, p. 38. She still had pain along the plantar fascial insertion into the calcaneal tuberosity and pain along the lateral aspect of the

[3] Radiculopathy is "[d]isorder of the spinal nerve roots." Stedman's Medical Dictionary 27th ed. (2000) at 1503.

foot. Her Achilles reflexes were both 2+ and her knees both 2+. Dr. Boatright wanted her to have a CT scan to check her left L5-S1 disc. *Id.*

On July 1, 1987, petitioner saw her doctor with severe pains in her back radiating around into her chest. She was tender directly over the spine and over some of the paraspinous muscles. The doctor thought this was more of an inflammatory process. Med. recs. at Ex. 14, p. 5. X-rays at Waynesboro Hospital were negative except for a few degenerative disks. *Id.*

On November 2, 1987, petitioner saw her doctor, complaining of low back pain and some pain down her left buttock and leg since the day before. She had had back pain before but stated it had never been quite this sharp or severe. Med. recs. at Ex. 17, p. 26. She said she bent over to brush her teeth the other morning and then the pain started developing. It hurt especially to sit or change positions and was better if she stood still or lay down. *Id.* On examination, petitioner's back revealed some tightness and spasm, especially at the left sacroiliac joint area and down in the left buttock area. Deep tendon reflexes were equal and symmetrical, but slightly decreased bilaterally. The doctor diagnosed petitioner with acute low back strain with left sciatica. Fairly recent thoracic and lumbosacral spine x-rays did not show any significant disk problem. He prescribed back instructions with later exercise, Centrax for muscle spasms, and Darvocet for pain. *Id.*

On November 14, 1987, petitioner went to Waynesboro Community Hospital with a complaint of fluttering in her chest. Med. recs. at Ex. 15, p. 78. Her history was a lot of back pain over the last four to five years. She was told this was due to arthritis. She also had pain in her hands, feet, and knees. *Id.*

On November 16, 1987, petitioner saw Dr. Thomas J. Spicuzza of Neurological Rehabilitation Associates with complaints of pain and paresthesias which began about a year earlier. They started as a numbness laterally in the left foot followed by pain in the sole of the foot. Med. recs. at Ex. 7, p. 4. Dr. Spicuzza identified that as coming from the sacral 1 level to the lumbar 5 level of the spine. The foot pain subsided, but the numbness persisted. A couple of weeks ago, while bending over, petitioner experienced severe pain radiating down the left side of her lower back into her buttocks and down over the posterior thigh. A CT scan of the low back with contrast was said to be normal. Additionally, the pain extended upward and probably had some cervical component. In the past, there was a question of rheumatoid arthritis. *Id.* On physical examination, reflexes on the left upper extremity were diminished compared to the right, but the lower extremity reflexes were symmetrical and well preserved at both ankles. Dr. Spicuzza thought petitioner had probable degenerative spine disease. Med. recs. at Ex. 7, p. 5.

On November 27, 1987, petitioner saw her doctor. Med. recs. at Ex. 14, p. 10. She had been in the hospital because of chest pain and with tachycardia. She had some pain in the epigastric area and in the substernal area. Her left arm had gone to sleep or felt numb. She had good range of motion in her extremities and her reflexes were okay. She might have an ulcer or a viral syndrome. *Id.*

On December 4, 1987, petitioner went to Waynesboro Community Hospital, complaining of severe abdominal cramping. Med. recs. at Ex. 15, p. 89. Her history was back, knee, and ankle pain in the past. *Id.* Her symptoms were probably more compatible with osteoarthritis than rheumatoid arthritis. Med. recs. at Ex. 15, p. 90. On examination, her extremities were essentially normal. She was essentially normal neurologically. *Id.*

On January 6, 1989, petitioner went to King's Daughter's Hospital. Med. recs. at Ex. 12, p. 2. She had very limited range of movement in her neck and was diagnosed with acute cervical strain. *Id.*

On January 10, 1989, petitioner saw her doctor. Med. recs. at Ex. 14, p. 13. She had had an automobile accident on January 6th and now had a cervical collar in place. She had back injuries but no fracture. On examination, she was tender over the lumbosacral, sacroiliac joint areas. *Id.*

On January 14, 1989, petitioner went to Waynesboro Community Hospital complaining of falling down a flight of stairs after slipping on ice with resulting arm, rib, and hip pain. Med. recs. at Ex. 17, p. 29.

On April 12, 1989, petitioner saw Dr. Charles F. Andersen of Orthopedic Associates of Waynesboro, stating she had been in a car accident in January and had multiple bruises. Med. recs. at Ex. 17, p. 23. On January 14, 1989, she fell down a flight of stair and landed on her right arm. *Id.*

On November 28, 1989, petitioner saw her doctor. Med. recs. at Ex. 14, p. 15. At work, she had lifted a patient the wrong way and had a lot of back pain as if her back were ripped apart. Since then, she had had a lot of back pain making it very difficult to move around or bend and lift. On examination, she was tender over the paraspinous muscles on both sides of the back but worse on the right side, which radiated down to the right leg. Straight-leg raising caused pain on the right side. Deep tendon reflexes were hypoactive bilaterally. *Id.*

On January 10, 1990, petitioner saw her doctor, complaining of some aching down in the low back and right flank area with a tender area on her right foot. Med. recs. at Ex. 14, p. 16.

The doctor diagnosed petitioner with a small area of superficial phlebitis[4] of the right foot and a urinary tract infection. *Id.*

On January 15, 1990, petitioner returned to her doctor with an inflamed vein in the right foot just in the instep, extending over the medial side of the foot. She said her whole leg became numb over the prior 24 hours. But there was a good pulse and she had good sensation to feel. Her legs were not swollen. *Id.*

On January 18, 1990, petitioner returned to her doctor. Her foot felt better but now she had a tender area behind her right knee. The doctor diagnosed superficial phlebitis of the right leg. *Id.*

On January 26, 1990, petitioner returned to her doctor. She continued to have some soreness along the instep of her right foot, although the previous lump she had there was clear. The area of soreness she had behind her right leg was better. Med. recs. at Ex. 14, p. 20.

Petitioner received hepatitis B vaccine on July 13, 1992, August 13, 1992, and January 23, 1993.

On February 15, 1993, petitioner saw Dr. Gerry D. Martin, with poor vision in her left eye which could possibly be optic neuritis. She had a definite papillitis or inflammation of the left optic disc. He discussed the possible relationship of the inflammation with a demyelinating process. Med. recs. at Ex. 5, p. 2.

On February 15, 1993, petitioner saw her doctor, complaining of pain and cramps in her left leg for about two weeks. Med. recs. at Ex. 14, p. 24. The leg cramped up at night and had

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[4] Phlebitis is "inflammation of a vein." Dorland's Illustrated Medical Dictionary 30th ed. (2003) at 1423.

been weak and gave way over the prior two weeks intermittently. Petitioner had lost sight in her left eye a few weeks previously, went to see Dr. Gillespie who gave her some drops and then went back and he gave her more drops. She went to Dr. Martin for a second opinion and he told her she had optic neuritis. Her vision had come back gradually. Now she was beginning to get a few symptoms in the right eye as well. She continued to be weak in the left arm and left leg. *Id.*

On February 16, 1993, petitioner returned to her doctor. She had gotten out of the bath tub that morning and her left leg gave way. The doctor then spoke to Dr. Martin, the ophthalmologist, about petitioner's eye "and he said when he did check it in October [1992], her left eye had elevated disc with what he considered to be probably optic neuritis and vision was 2200." She also had a pupil that did not react (Marcus Gunn pupil), which had resolved. The doctor made an appointment for petitioner to see a neurologist (Dr. Spicuzza) on March 8, 1993 and also to have a head MRI. Med. recs. at Ex. 14, p. 25.

On February 17, 1993, petitioner had a brain MRI after she experienced possible optic neuritis in her left eye which was transient, and left leg weakness. P. Ex. 1, p. 22. Petitioner had two or three small focal areas of increased signal on the first and second echo T2 images in the deep white matter primarily in the left hemisphere and one in the periventricular region. Dr. James E. Nathe stated that these findings were subtle and minimal at best, but could be associated with demyelinating disease, such as MS. As for the optic nerves, on the right side in one section only, there was a little increased signal intensity in the right optic nerve. Dr. Nathe suspected this was due to partial volume effect rather than a true focal enhancement of the right optic nerve, and, therefore, the optic nerves were very likely within normal limits. *Id.*

On March 9, 1993, petitioner returned to Neurological Rehabilitation Associates. Med. recs. at Ex. 7, p. 8. Petitioner complained of visual problems and weakness. She gave a history of having visual loss about a year previously which now affected her right eye and cleared up. She had left hand numbness and weakness. A brain MRI a week earlier showed multiple plaques. On physical examination, she had an increase in left-sided reflexes and decreased left hand strength as compared to right. The impression was probable MS. *Id.*

On March 22, 1993, Dr. Spicuzza wrote a letter to petitioner, stating that the tests on her spinal fluid were compatible with MS. Med. recs. at Ex. 7, p. 12.

Other Submitted Materials

Petitioner filed an article entitled "A study of molecular mimicry and immunological cross-reactivity between hepatitis B surface antigen and myelin mimics" by D-P Bogdanos, et al., 12 Clinical & Developmental Immunology 3:217-24 (Sept. 2005), as exhibit 28. The authors found that people who received hepatitis B vaccine were more likely to have reactivity to at least one of the small hepatitis B virus surface antigens than controls did. However, none of the vaccinees reported symptoms of demyelinating disorders and most lost their cross-reactivity at six months after vaccination.

After the hearing, petitioner filed exhibits 30-37 consisting of articles. The first article, exhibit 30, is entitled "Encephalitis after hepatitis B vaccination. Recurrent disseminated encephalitis or MS?" by A. Tourbah, et al., 53 Neurology 396-401 (1999). The authors studied eight patients with confirmed inflammation occurring less than 10 weeks after hepatitis B vaccination, with a mean interval of 4.4 weeks. *Id.* at 396, 398. The authors admit that a "direct causal, triggering, or precipitating association between hepatitis B vaccination and encephalitis

cannot be demonstrated in this study." *Id.* at 400. They advise patients to avoid hepatitis B vaccination if they have a personal or family history of symptoms suggesting inflammatory or demyelinating central nervous system disease. *Id.*

The second article, exhibit 31, is entitled "Epidemiology of Autoimmune Reactions Induced by Vaccination," by R.T. Chen, R. Pless, and F. DeStefano, 16 Journal of Autoimmunity 309-18 (2001). The authors conclude that science is still lacking in evidence to support that vaccinations cause autoimmune disease. The pathogenic mechanism or mechanisms for most autoimmune diseases are not known. *Id.* at 309. Table 1 lists evidence for or against a determination of causation. *Id.* at 310. Included on that table is hepatitis B vaccine. Under the category of "biologic plausibility" of causation, the authors list Guillain-Barré syndrome and central nervous system demyelinating diseases and state that biologic plausibility of causation has been demonstrated. *Id.* However, they could not determine if there were case reports, case series, and uncontrolled studies, and there were no data on whether there were controlled studies and controlled clinical trials showing causation. *Id.* The authors state:

> MS is a disease of the central nervous system characterized by the destruction of the myelin sheath surrounding neurons. It is generally believed to be an autoimmune disease that occurs in genetically susceptible people. Unknown environmental factors are also suspected to be involved in its pathogenesis. Environmental factors, such as vaccines, could be involved in actually causing the disease, resulting in an overall excess of MS in the population, or as possible triggers for the clinical expression of MS in genetically susceptible individuals, without causing an excess in disease incidence.

Id. at 313.

The third article, exhibit 32, is entitled "Hepatitis B Vaccination and First Central Nervous System Demyelinating Event: A Case-Control Study," by E. Touzé, et al., 21

Neuroepidemiology 180-86 (2002). The authors conducted a hospital-based case-control study of 236 patients with first central nervous system demyelination and 355 matched controls, and came up with an odds ratio of 1.8 for the first central nervous system demyelinating event within two months after hepatitis B vaccination. If they restricted their analysis to MS cases, the odds ratio was 2.0. They concluded that the data ruled out a strong association between hepatitis B vaccine and subsequent demyelinating event, and did not clearly indicate a moderate risk of the same. *Id.* at 180, 183. The authors state "the vaccination may be a trigger for the onset of the disease, but not cause the disease." *Id.* at 183. They also state:

> Because vaccination, as is the case for natural infection, constitutes a strong antigen challenge, an association between HB vaccine and MS is not implausible. Two major mechanisms have been suggested linking antigenic reaction due to infection or vaccination to autoimmune CNS diseases: (1) molecular mimicry relying on sequence similarities between the exogenous antigen and a self-antigen ..., (2) antigen-independent activation of quiescent autoreactive T cells by a bystander phenomenon, probably mediated by proinflammatory cytokines produced in the microenvironment....

Id. at 185.

The fourth article, exhibit 33, is a case report entitled "Development of Multiple Sclerosis after Hepatitis B Vaccination: An Immunologic Case Report," by B. Gran, et al., 54 Neurology A164 (April 2000; Suppl 3). The authors found cross-recognition of hepatitis B surface antigen and a proteolipid protein-derived peptide by a T-cell line isolated from the peripheral blood of a patient who developed MS three months after hepatitis B vaccination. This finding suggested to the authors that molecular mimicry warranted further investigation as a possible trigger of autoimmune demyelination after hepatitis B vaccination. *Id.*

The fifth article, exhibit 34, is entitled "Vaccinations and multiple sclerosis" by O. Gout, 22 Neurol Sci 151-54 (2001). Gout admits that epidemiologic studies have not demonstrated that hepatitis B vaccine causes MS, but it "could be a triggering factor in susceptible individuals in the same manner as infections." *Id.* at 153. Gout posits three possible pathogenic mechanisms: (1) molecular mimicry between hepatitis B vaccine proteins and myelin components; (2) indirect immunologic stimulation by the large quantity of exogenous hepatitis B surface antigen; and (3) direct or indirect immunologic toxicity of vaccine contaminants. *Id.*

The sixth article, exhibit 35, is a case report entitled "Two Episodes of Leukoencephaliits Associated with Recombinant Hepatitis B Vaccination in a Single Patient" by D. Konstantinou, et al., 33 Clinical Infectious Diseases1772-73 (2001). The authors describe positive rechallenge in a patient who experienced right homonymous hemianopia (demyelinating lesion in her brain) four weeks after receiving her second hepatitis B vaccination, and left hemiparesis and deterioration of vision 11 days after receiving her third hepatitis B vaccination. *Id.* at 1772. Brain MRI revealed a new, large lesion in the right parieto-occipital region which had the same characteristics that the prior lesion had. *Id.* at 1883. The authors state this is the first instance of rechallenge from hepatitis B vaccination. *Id.*

The seventh article, exhibit 36, is entitled "Recombinant hepatitis B vaccine and the risk of multiple sclerosis. A prospective study" by M.A. Hernán, et al., 63 Neurology 838-42 (2004). By performing a case-control study of recombinant hepatitis B vaccination and MS, the authors conclude that the incidence of MS increased within three years of vaccination. *Id.* at 840.

The eighth article, exhibit 37, is entitled "Guillain-Barre Syndrome Following Vaccination in the National Influenza Immunization Program, United States, 1976-1977" by

L.B. Schonberger, et al., 110 American Journal of Epidemiology 2:105-23 (1979). The authors examined the incidence of GBS among swine flu vaccinees and concluded there was a higher incidence up to nine or 10 weeks following vaccination compared to baseline. *Id.* at 112.

Subsequent to petitioner's post-hearing filing of exhibits 30-37, respondent filed Dr. Sriram's supplemental expert report as exhibit C, and five articles (exhibits D-H). Dr. Sriram went through each of the articles petitioner filed after the hearing and commented on their contents. In the first, exhibit 30, the Tourbah article, the authors were cautious not to state there was direct causation of MS from hepatitis B vaccine, and only four of their eight patients really showed connection of the onset of MS after hepatitis B vaccination. Dr. Sriram concluded there is no reputable scientific evidence to support the conclusion that hepatitis B vaccine causes demyelinating disease. *Id.* at 1.

In response to exhibit 31, the Cohen article, Dr. Sriram concludes with the authors that studies do not show an increased risk of relapse of MS in the two-month period following hepatitis B vaccination. *Id.* at 2.

In response to exhibit 32, the Touzé article, Dr. Sriram said the study was small and the number of cases within the first two months was small. Any relationship between hepatitis B vaccine and MS was weak. *Id.*

Dr. Sriram then moves to exhibit 36, the Hernán study, noting that most of the MS cases appeared after one year post-vaccination. The editorial accompanying the article cautions that hepatitis B vaccine in the United Kingdom was administered particularly to high-risk patients. *Id.*

Dr. Sriram then examines exhibit 35, the Konstantinou article, and notes that the patient did not have MS. He regards the relationship of her demyelinating illness to hepatitis B vaccination as uncertain. *Id.* at 2-3.

Dr. Sriram then analyzes exhibit 33, the Gran poster presentation, about a single case study performed on someone who developed MS after hepatitis B vaccination. Dr. Sriram states it is unknown if MS patients who were not vaccinated against hepatitis B have proteolipid peptide reactive lines that crossreact with hepatitis B antigen, as did the patient in the study. *Id.* at 3.

Dr. Sriram does not discuss exhibit 34, the Gout article, and exhibit 37, the Schonberger article, in his supplemental report until the end of his report when he cites Gout for the idea that no one knows if vaccination induces or worsens MS. *Id.* He states that epidemiological articles which are attached to his supplemental report show no higher incidence of MS among hepatitis B vaccinees, including a reanalysis of the Touzé study. He also states, "While a possible connection between an acute worsening of MS occurring in a temporal context with immunization can have a biological probability, similar to the known association between acute worsening of MS and infection, there is no evidence to suggest either the induction of MS or the progression of MS is more likely than not mediated or influenced by vaccination." *Id.*

The first article (exhibit D) attached to Dr. Sriram's supplemental report is entitled "Hepatitis B Vaccination and the Risk of Multiple Sclerosis" by A. Ascherio, et al., 344 N Engl J Med 5:327-32 (2001). The authors did a nested case-control study of two large cohorts of nurses and found no association between hepatitis B vaccination and the development of MS. They note in reference to a French passive surveillance of adverse drug effects that most cases of

demyelination in the central nervous system occurred within two months of exposure. *Id.* at 331-32. They found plausible that the vaccine "could cause an acute autoimmune reaction in susceptible persons soon after administration," but thought that hypothesis inappropriate with MS because many MS patients have lesions preceding the onset of their clinical symptoms by weeks or months as detected on MRI. *Id.* at 332.

The second article (exhibit E) attached to Dr. Sriram's supplemental report is entitled "Vaccinations and the Risk of Relapse in Multiple Sclerosis" by C. Confavreux, et al., 344 N Engl J Med 319-26 (2001). The authors did a case crossover study (which does not involve controls as the patients serve as their own controls) of 643 patients with relapses of MS, 15% of whom reported prior vaccination within 12 months. The authors found no increase in the relative risk of relapse associated with exposure to tetanus, hepatitis B, or influenza vaccination. *Id.* at 324. The authors assumed for the purpose of the study that the risk of relapse remained the same after each vaccination. *Id.* at 324-25. Recall bias was a potential problem, but the authors thought it was minimal. *Id.* at 325. The authors chose only a two-month risk period in which vaccination might have triggered a relapse based on data from the literature and on expert opinion. *Id.*

The third article (exhibit F) attached to Dr. Sriram's supplemental report is a poster presentation entitled "Demyelinating Disease and Hepatitis B Vaccination: Survey of 735 Patients Seen at MS Clinic" by M. Coustans, et al., 54 Neurology A165 (April 2000 Suppl 3). The authors studied the rate of incidence of MS or relapse among patients with MS after hepatitis B vaccination among their patients and concluded that hepatitis B vaccine might not increase the relapse rate. However, two of their patients had a first central nervous system

episode after receiving hepatitis B vaccine and then had two relapses shortly after receiving a second hepatitis B vaccination. For those two MS patients, the authors state that the patients' course raises an argument favoring hepatitis B vaccination as the cause of the central nervous system episode. Since the vaccinees among their patients were younger than the general MS population, the authors thought that hepatitis B vaccine might precipitate MS in genetically predisposed patients. *Id.*

The fourth article (exhibit G) attached to Dr. Sriram's supplemental report is entitled "Hepatitis B vaccination and first central nervous system demyelinating events: Reanalysis of a case-control study using the self-controlled case series method" by M.N. Hocine, et al., 25 Vaccine 5938-43 (2007). The authors reanalyzed case data from the case-control study of Touzé (petitioner's exhibit 32) and arrived at a lower odds ratio by including an additional 53 unmatched cases that Touzé had omitted. The authors agree with Touzé that there is no strong association between hepatitis B vaccine and a first episode of central nervous system demyelinating disease. *Id.* at 5942. Also, like Touzé, they cannot exclude a weak association between hepaitis B vaccine and central nervous system demyelinating disease. *Id.* They were unable to confirm Hernán's finding (petitioner's exhibit 36) of an increased risk of multiple sclerosis up to three years post-vaccination against hepatitis B. *Id.* They found little evidence of an effect up to 2.29 years after vaccination. *Id.*

The fifth article (exhibit H) attached to Dr. Sriram's supplemental report is an editorial commenting on the Hernán article (petitioner's exhibit 36) and is entitled "Does the hepatitis B vaccine cause multiple sclerosis" by R.T. Naismith and A.H. Cross, 63 Neurology 772-73 (2004). Although the authors found it hard to argue with Hernán's results, they questioned

whether his study of 11 cases of MS in the article can be generalized to the general population. *Id.* at 772. They posit there might be unrecognized bias in the Hernán paper because high-risk patients were targeted for vaccination. *Id.* They query why, if hepatitis B vaccine can cause MS, hepatitis B infection is not linked with MS onset or worsening in the literature. *Id.* at 773.

TESTIMONY

Dr. Carlo Tornatore, a neurologist specializing in MS, testified for petitioner. Tr. at 5. His opinion is that petitioner's hepatitis B vaccinations from July 1992 to January 1993 caused her MS. Tr. at 8. Prior to October 1992, petitioner never had any vision problems or any other symptom that petitioner can now recognize as MS. *Id.* (Dr. Tornatore had a conversation with petitioner on the day of the hearing. *Id.*) After petitioner's second vaccination on August 13, 1992, she went to an ophthalmologist who noted that, in October 1992, two months after the second vaccination, she had decreased vision in her left eye. Tr. at 9-10. She also had headaches and tingling for about a year. Tr. at 10. In October 1992, the acuity in petitioner's left eye was 20/100. *Id.* There was also a depression of her vision in the middle called an apparent pupillary defect or a Marcus Gunn pupil. Tr. at 11. There was also elevation of the left optic nerve and the papillary area without hemorrhage. The ophthalmologist concluded that petitioner had a definite papillitis or inflammation of the left optic disc, indicating optic neuritis. *Id.* Whether the onset was six or 10 weeks after the second hepatitis B vaccination made no difference to Dr. Tornatore because both intervals were appropriate for causation. Tr. at 12.

When one administers vaccines, the first vaccination is not enough to produce the T-cell and humoral responses. Tr. at 13. After the second vaccination, the immune system takes that antigen and presents it to different cells so that they develop memory against it. It takes about a

month to three months for that effect to maximize. *Id.* The nerves could be affected before clinical symptoms occur. Tr. at 17.

Petitioner recovered from her October 1992 optic neuritis after about two weeks. Tr. at 26. Then she received her third hepatitis B vaccination on January 23, 1993. Three weeks later, she went to her doctor on February 15, 1993 complaining of pain and cramps in her left leg for about two weeks. *Id.* The onset interval between her third hepatitis B vaccination and her leg weakness was one week. *Id.* She also lost sight in her left eye a few weeks earlier around the same time as her leg weakness. *Id.* The following day, February 16, 1993, she could not walk on her left leg after soaking in a tub of hot water, which is a challenge for MS patients. Tr. at 27. Dr. Tornatore referred to petitioner's reacting to her third hepatitis B vaccination faster than after her second vaccination (one week compared to two months) as an anamnestic response and also rechallenge. Tr. at 29. Petitioner got an MRI showing multiple lesions and the diagnosis of MS was made. Tr. at 30.

Dr. Tornatore said this pattern of events was a logical sequence of cause and effect, had a plausible biological mechanism, and reasonable timing (two months after the second vaccination and one week after the third). Tr. at 31. Dr. Tornatore described the medical theory underlying his opinion: the vaccine contains a series of proteins that cause the immune system to become overactive. *Id.* But in rare cases, the immune system recognizes not only the vaccine proteins, but also proteins found on myelin or in nerves that resemble the vaccine proteins, and the immune system becomes directed against those as well as the vaccine proteins. Tr. at 32. Then, the vaccinee has an autoimmune response. *Id.*

Dr. Tornatore described the concept of molecular mimicry where a protein meant to look like one thing may look like another and the immune response becomes directed at both. Tr. at 33.

As for the logical sequence of cause and effect, Dr. Tornatore stated that petitioner had two separate events after her second and third hepatitis B vaccinations that would validate the logical sequence of the vaccine's causing her demyelinating episodes. *Id.* In addition, the timing of these events is appropriate for causation. Tr. at 33-34.

Dr. Tornatore believes that if petitioner had never received hepatitis B vaccine, she would not have had MS. Tr. at 34. The basis for his opinion is that petitioner had no evidence before the first hepatitis B vaccination of anything abnormal in her central nervous system. *Id.* She did have foot numbness prior to vaccination, but petitioner told Dr. Tornatore during their conversation that she was told she had plantar fasciitis, and after she received an injection of steroids, the pain was better. *Id.* Dr. Tornatore stated the pain would not have been better if the numbness were due to central nervous system problems. *Id.*

If, however, Dr. Tornatore were to assume that petitioner had mild MS symptoms before she received hepatitis B vaccine, his opinion would then be that the vaccine significantly aggravated her MS based on her second and third vaccinations leading to recurrent neurologic symptoms. Tr. at 35. Respondent's expert, Dr. Sriram, stated in his expert report that he believed petitioner's MS occurred before her vaccinations. *Id.* The undersigned asked Dr. Tornatore if, assuming petitioner had pre-vaccination MS, why would not the first hepatitis B vaccination, rather than only the second and third vaccinations, have induced a significant aggravation of her MS. Tr. at 36. He responded that the first vaccination may not stimulate the

immune system to trigger a T-cell mediated response which is why vaccination is repeated. *Id.* Once petitioner received the second vaccination, her T-cell repertoire was more primed for a response and symptoms began to appear. *Id.* Dr. Sriram thought in his report that the first clinical sign of petitioner's MS was her left foot numbness initially thought to be either plantar fasciitis or lumbosacral disc disease which occurred five years before she received hepatitis B vaccine. Tr. at 37-38.

To Dr. Tornatore, whether petitioner's left foot numbness five years before vaccination was MS and the hepatitis B vaccine significantly aggravated it or whether the doctors were correct in diagnosing petitioner with plantar fasciitis and she did not have MS until after the hepatitis B vaccinations did not matter because we end at the same place, which is a vaccine-related injury. Tr. at 38.

Dr. Sriram said in the same report that petitioner's rapid resolution of her numbness suggests that MS was the cause of her numbness. Tr. at 39. He also states that a history given in March 1993 of visual loss occurring a year earlier would put onset of MS before her first hepatitis B vaccination July 1992. *Id.* Dr. Tornatore thought that the ophthalmologist was just being a little sloppy in his notation and that this was really a reference to petitioner's October 1992 visual problems. Tr. at 40. He does not agree with Dr. Sriram that petitioner's onset of MS occurred in 1986 when she had pain and numbness of her left foot because a local injection helped her. Tr. at 41.

On cross-examination, Dr. Tornatore was informed that the steroid injection did not help petitioner's plantar fasciitis. Tr. at 43. But Dr. Tornatore stated he was relying on petitioner during her conversation with him prior to trial in recounting the result of the steroid injection. *Id.*

Dr. Tornatore was asked if petitioner had right leg numbness on January 15, 1990. Tr. at 47. He said that she had an inflamed vein in her right foot extending up over the medial side of her foot. She had phlebitis (inflammation of the vein). Tr. at 47-48. Dr. Tornatore thought she had a clot. Tr. at 48. Petitioner was prescribed an antibiotic and anti-inflammatory. Tr. at 49-50. Someone could have numbness with phlebitis. Tr. at 50. Dr. Tornatore agreed that petitioner had relapses of MS after her diagnosis with MS and these relapses were not preceded by vaccinations. Tr. at 60.

Dr. Subramaniam Sriram, a neurologist specializing in MS, testified for respondent. Tr. at 64. His opinion is that petitioner's onset of MS occurred before her first hepatitis B vaccination, and her visual and other problems subsequent to her vaccinations are independent of them and purely temporal in relationship. Tr. at 67-68. He denied petitioner had any significant aggravation of her MS, noting that she had done remarkably well for an MS patient. Tr. at 68.

Dr. Sriram stated that petitioner's alleged plantar fasciitis before her first hepatitis B vaccination was actually MS because sensory abnormalities are very common in MS. Tr. at 69. Forty-six percent of MS patients present with sensory abnormalities in their hands or feet. *Id.* Numbness in the feet is a common MS presentation. *Id.* His reading of the medical literature does not indicate that plantar fasciitis is associated with numbness. *Id.* Usually, with plantar fasciitis, recovery takes time, whereas a mild attack of MS may resolve spontaneously. Tr. at 69-70. He thinks petitioner, at the age of 29, was too young to have plantar fasciitis. Tr. at 70.

Petitioner had optic neuritis after her second hepatitis B vaccination. Optic neuritis is the second most common manifestation of MS after sensory symptoms. *Id.* Petitioner's presentation, which was inflammation of the optic disc, was somewhat unusual. *Id.* She had complete

resolution. Tr. at 71. Petitioner may also have had an MS symptom when she had a numb leg with phlebitis. *Id.* Dr. Sriram thought a two-month interval between vaccination and MS symptom was too long to be causal. Tr. at 74. He stated that the American Academy of Neurology does not prevent MS patients from being vaccinated. Tr. at 76. All the epidemiological studies show there is no proof that vaccinating an MS patient worsens the MS. *Id.*

Dr. Tornatore offered at that point that petitioner has relapsing or remitting MS. Tr. at 79. Petitioner informed him that she has not had a relapse in about five years. *Id.* She is probably moving into the secondary progressive phase. Tr. at 80.

Dr. Sriram said that there is no evidence that hepatitis B could stimulate the immune system and cause an MS attack. Tr. at 81. There is no evidence clinically, experimentally, or in animal studies. Tr. at 81-82. He believes that petitioner had her first MS attack in 1989 when she was 29 years old. Her condition is not substantially worse than what it would have been had she not received hepatitis B vaccine. Tr. at 82.

On cross-examination, Dr. Sriram agreed that the development of optic neuritis would be an acute worsening of MS. Tr. at 84. Petitioner was a nurse's aide. Tr. at 85. She sprained her back while bending over a few weeks after she had plantar fasciitis. *Id.* Dr. Sriram did not know petitioner had a history of back problems. *Id.* He admitted there is no evidence of demyelination of petitioner's spinal cord in 1987 when she had plantar fasciitis. Tr. at 93. He thinks however that petitioner's experience of severe pain radiating down the left side of her lower back when she bent down was very typical of MS. *Id.* It can also be a sign of nerve impingement in the area, but Dr. Sriram wants to be parsimonious in putting petitioner's case together. *Id.* He thinks

petitioner was describing Lhermitte's sign in 1993 where someone with MS has sudden shooting pain down his or her back into the legs when bending the neck or back. *Id.* Dr. Sriram admitted someone could have pain in the lower spine and still have a normal CT scan, as petitioner did. Tr. at 95.

Dr. Sriram explained what he meant when he said he wants to be parsimonious in putting petitioner's case together. Tr. at 96. He stated there must be some frugality in assessing multiple symptoms so that a unitary diagnosis is obtained. For every symptom, doctors do not assume a different diagnosis. Thus, for petitioner's situation, her left foot numbness and back pain does not mean she had MS. She had fasciitis and lumbosacral disc disease and MS. But to put this all together gently would probably mean she has one disease with different manifestations. *Id.*

The undersigned asked Dr. Sriram to comment on petitioner's doctors not considering she had MS or a demyelinating disease before she received hepatitis B vaccine. Tr. at 96-97. Dr. Sriram answered it happens all the time. Tr. at 97. When petitioner had her symptoms in 1987, the MRI which came into use in 1984 or 1985 was not sufficiently advanced in use to diagnose MS. *Id.* At that time, MS was essentially a clinical diagnosis. Tr. at 98. Moreover, Dr. Sriram said that petitioner did not see a neurologist at that time. Instead, she saw a podiatrist and a number of family practitioners. *Id.* He described the 1980s as a nihilistic period because there was no treatment for MS "and so it was not something on the radar screen of many physicians because okay, you make the diagnosis, so what, was sort of the psyche at that time." *Id.* In the last 15 to 20 years, there is more awareness about MS because we have treatment options unavailable in the mid-1980s. *Id.*

Petitioner's counsel corrected Dr. Sriram in calling to his attention that Dr. Thomas Spicuzza whom petitioner saw in the 1980s was a neurologist working in rehabilitation. Tr. at 99-100. Dr. Spicuzza wrote a letter diagnosing petitioner with probable degenerative spine disease as the cause of her symptoms. Tr. at 100. In 1993, Dr. Spicuzza wrote to petitioner that her studies and spinal fluid were compatible with MS. *Id.* This is the same Dr. Spicuzza that petitioner had been seeing since 1987. *Id.*

On January 15, 1990, petitioner had an inflamed vein in the right foot and numbness and was diagnosed with phlebitis. Tr. at 103. Dr. Sriram thought that it was possible petitioner had both MS and phlebitis which, petitioner's counsel called to his attention, would not be parsimonious as it would involve two diagnoses. Tr. at 104.

Dr. Sriram agreed that there is a biologically possible theory causally connecting hepatitis B vaccine and MS. Tr. at 116. He would not agree that any theory petitioner's counsel proposed was biologically plausible. Tr. at 118. He agreed that evidence of positive rechallenge was strong evidence of causation in certain situations. Tr. at 121. He thought positive rechallenge taking the form of allergic reactions would be related to immunizations, but separate events which might be random are not necessarily connected. *Id.* He agreed that if someone had CIDP three times after three tetanus vaccinations, as described in the Pollard and Selby article,[5] that would be evidence of causation. Tr. at 123. He agreed that the timing of petitioner's optic neuritis after her third hepatitis B vaccination would fit within an accepted temporal relationship for causation. Tr.

[5] J.D. Pollard and G. Selby, "Relapsing neuropathy due to tetanus toxoid," 37 Journal of Neurological Science 113-25 (1978). This article was not submitted into evidence. However, the parties, the experts, and the undersigned are well aware that the article showed repeated onsets of peripheral neuropathy in a recipient after each of a series of tetanus toxoid vaccine.

at 129-30. Dr. Sriram agreed that MS is a disease with multiple factors as causative agents including a genetic propensity and an environmental trigger. Tr. at 137. Those triggers can include viruses or pathogens. Tr. at 137-38.

On redirect, Dr. Sriram stated that there is no evidence that hepatitis B vaccine causes MS. Tr. at 142. Hepatitis B vaccine is still recommended for MS patients. *Id.* He does not think that petitioner's onset of optic neuritis one week after her third hepatitis B vaccination when she already was diagnosed with MS constituted significant aggravation because MS patients will have attacks. Tr. at 143. If vaccines causing MS was really a biologic phenomenon, Dr. Sriram said we should be seeing a lot more attacks in the MS patient populations, and we do not. Tr. at 144. Since the peripheral nervous system reacts sooner than the central nervous system, GBS would occur earlier than MS. But optic neuritis, which involves the central nervous system, is an eloquent part of the nervous system and if petitioner had reacted to the second hepatitis B vaccination with optic neuritis, it would not have taken two months, but would have occurred earlier. Tr. at 145-46.

On recross, Dr. Sriram admitted that MS patients have attacks from viral illnesses and other stressors, and that a vaccine is a stressor. Tr. at 149. It could take three days or 30 days for someone to have an attack of optic neuritis after a viral illness because the potency of the viral infection is different in two different individuals. Tr. at 150. But a protein has a calibrated amount of protein given to every vaccinee. *Id.* It is possible that genetic susceptibility may dictate how quickly a person responds. *Id.* The status of the person's immune system may also affect his response time to an illness. *Id.* Dr. Sriram agreed that there is nothing in the medical records to suggest that petitioner was seen for MS symptoms for the two years prior to1992 when

she had her first hepatitis B vaccination. Tr. at 152. He said it was classic for MS to be in remission. *Id.*

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. *Id.* at 1148.

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

Here, respondent's defense is that petitioner's MS preceded her hepatitis B vaccinations because the numbness accompanying her plantar fasciitis and her right leg phlebitis were really symptoms of an undiagnosed MS. Moreover, respondent's expert Dr. Sriram stated that petitioner's worsened symptoms of optic neuritis two months after her second hepatitis B vaccination and her optic neuritis and leg weakness one week after her third hepatitis B vaccination were unrelated to her vaccinations.

Respondent's counsel also asked petitioner's expert Dr. Tornatore in cross-examination if petitioner's subsequent relapses of MS after she was diagnosed with MS followed vaccinations. The answer was no. The implication, the undersigned takes from this approach, is that if hepatitis B vaccine did not cause every MS relapse petitioner experienced, then hepatitis B vaccine could not be the cause of her MS.

Another point which respondent's expert Dr. Sriram made is that hepatitis B vaccine could not cause MS when the public health community advises MS patients to receive this vaccine. A discussion of these points follows.

The undersigned is aware that Dr. Sriram, respondent's expert, uses the principle of parsimony to justify his assumption that petitioner's numbness in the context of plantar fasciitis and phlebitis must be related to pre-vaccination MS rather than plantar fasciitis or phlebitis. But, on being questioned how Dr. Spicuzza, a neurologist specializing in rehabilitation, who saw petitioner before and after her hepatitis B vaccinations, could miss diagnosing petitioner with MS

before the vaccinations, Dr. Sriram's reply was that missing a diagnosis happens all the time. Frankly, to explain the absence of an MS diagnosis or even a work-up to determine if a patient has MS equals missing that the patient has MS does not persuade the undersigned that petitioner's MS began before her vaccinations. Moreover, petitioner was examined for neurologic abnormality and none was found. Dr. Spicuzza, the neurologist, found petitioner normal neurologically and diagnosed her numbness as probably due to degenerative spine disease.

Dr. Sriram thought petitioner was too young for plantar fasciitis and, besides, plantar fasciitis is not accompanied by numbness. Dr. Boatright, the orthopedist who diagnosed petitioner with plantar fasciitis knew how old petitioner was. Her youth did not dissuade him from diagnosing petitioner with plantar fasciitis.

The Federal Circuit in Capizzano emphasized the special masters' taking into serious consideration the opinions of treating doctors. 440 F.3d at 1326. The undersigned thus takes seriously Dr. Spicuzza's opinion that petitioner was normal neurologically before she received hepatitis B vaccinations and that her complaints were probably due to degenerative spine disease. The undersigned also takes seriously Dr. Boatright's opinion that petitioner had plantar fasciitis.

Before her hepatitis B vaccinations, petitioner made numerous visits to doctors because of back sprains, an automobile accident, and degenerative disks. She was tested neurologically and no one found her to be neurologically abnormal. It is one thing to diagnose someone with the wrong neurological disease. It is quite another for a whole collection of doctors, including the neurologist Dr. Spicuzza, to miss MS entirely.

The salient feature of this case is positive rechallenge or what Dr. Tornatore called an anamnestic response, meaning each exposure to the hepatitis B surface antigen resulted in a

worsening of symptoms. His theory is that petitioner's immune system was primed with her first hepatitis B vaccination. When she had the second hepatitis B vaccination, two months later she developed optic neuritis. Two months may seem too long to Dr. Sriram, but respondent in Pecorella decided not to defend against that interval and the undersigned has accepted it as an appropriate temporal interval for causation ever since.

Petitioner recovered from her optic neuritis. When petitioner had the third hepatitis B vaccination, one week later, she had optic neuritis again plus leg weakness. As in the Konstantinou article and the unsubmitted Pollard and Selby article, this case strongly suggests the presence of challenge, sometimes known as positive rechallenge, which confirms causation. In Konstantinou the vaccinee had the same problem with brain lesions after her second and third hepatitis B vaccinations. In Pollard and Selby, the vaccinee has peripheral neuropathy after each of three vaccinations against tetanus.

Even assuming arguendo that petitioner's leg numbness accompanying her plantar fasciitis was not due to radicular problems (problems with the nerve roots coming from her spine due to degenerative disks) but in essence was a mild symptom of MS, her symptoms post-vaccination were considerably worse. Thus, as Dr. Tornatore stated, if petitioner had MS before the vaccinations, the vaccinations significantly aggravated it. The same can be said for the numbness accompanying phlebitis.

But the undersigned is not persuaded that petitioner had MS before her hepatitis B vaccinations merely because of isolated symptoms of numbness. Not all numbness is due to MS. The fact that she had MS after her vaccinations does not mean that any numbness before her vaccinations is symptomatic of MS. The symptom of numbness by itself and undiagnosed as MS

does not signify that it is a symptom of MS without objective testing or evidence of lesions occurring over space and time. The undersigned is particularly unwilling to accept that isolated episodes of numbness signify MS when petitioner's contemporaneous doctors did not diagnose or even consider whether she had MS. This is particularly so in light of her testing as normal neurologically before vaccination.

As for Dr. Sriram's reliance on the principle of parsimony (which petitioner's counsel identified as Occam's razor),[6] there is no way to be parsimonious in this case, i.e., no one can put all the symptoms into one disease. Phlebitis is an inflammation of a vein. It has nothing to do with MS. An inflammation of the plantar fascia has nothing to do with MS. We end up with multiple diagnoses no matter whether petitioner had a quiescent form of MS before vaccination or her MS began after vaccination.

Dr. Sriram acknowledged the biological theory underlying Dr. Tornatore's opinion, but then shied away from it. When Dr. Sriram testified that "While a **possible** connection between an acute worsening of MS occurring in a temporal context with immunization can have a biological **probability** [emphasis added]," he combined possible with probable in the same sentence. It cannot be both possible and probable. All things are possible. Not everything is probable. The undersigned has the impression that Dr. Sriram was almost where Dr. Tornatore was, but resolutely turned away because of his concern about vaccination as good public policy and the stringent requirements of causation that exist in the world of medicine, rather than under the Vaccine Program.

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[6] Occam's razor is "[t]he principle of parsimony. William of Occam (14th century) stated it thus: 'The assumptions introduced to explain a thing must not be multiplied beyond necessity.'" Stedman's Medical Dictionary 27th ed. (2000) at 1250.

The idea respondent's counsel proposed in cross-examining Dr. Tornatore that in order for the vaccine to cause MS, petitioner would have had to have been vaccinated before every worsening of her MS is not persuasive. Both parties know that MS is an episodic disease. Once any immune-mediated disease such as MS begins, the individual with that disease becomes sensitized to all immune challenges, including colds and viruses. In a recent decision, Hawkins v. Sec'y of HHS, No. 99-450V, 2009 WL 711931 (Fed. Cl. Spec. Mstr. 2009), the undersigned noted that once petitioner in that case had acute disseminated encephalomyelitis (ADEM) or, in the alternative, acute MS, petitioner told her treating physicians that whenever she had an infection or another vaccination, her old symptoms recurred. 2009 WL 711931, at *6. This was also noted in the testimony. 2009 WL 711931, at *14-15. As the undersigned wrote, at *22, "Whenever petitioner gets sick, she has a relapse." The idea that only a vaccine can cause a worsening of symptoms of MS or any other type of immune-mediated disease is just not borne out in the experience of the undersigned. See also Larive v. Sec'y of HHS, No. 99-429V, 2004 WL 1212142, at *1 (Fed. Cl. Spec. Mstr. 2004), in which petitioner had focal segmental glomerulosclerosis (FSGS), a form of nephrotic syndrome, after hepatitis B vaccine, and had subsequent relapses of FSGS after a cold and after receiving MMR vaccine.

The undersigned respects Dr. Sriram's conservative viewpoint as the medical professional he is. He wants epidemiological proof, animal experimentation, and in vitro testing in order to be persuaded that hepatitis B vaccine can cause MS. The Federal Circuit does not require this in order for petitioner to prevail. Knudsen, Althen, Capizzano. The many articles that both parties submitted discuss a biologically plausible theory for causally connecting hepatitis B vaccine and MS. Dr. Tornatore's testimony does the same. There is a logical sequence of cause and effect

here in that rechallenge shows a causal relationship. The timeframes of two months after the second vaccination and one week after the third vaccination fit within the parameters of causation.

As for Dr. Sriram's argument that doctors recommend hepatitis B vaccinations to their MS patients which they would not do if there were the risk of exacerbating their MS, public vaccination policy is not an area in which the undersigned has any role to play. The Federal Circuit has clarified in three cases (Knudsen, Althen, and Capizzano) the criteria petitioners must fulfill. These criteria do not include considering what vaccine policy doctors promote for their patients. That doctors still recommend hepatitis B vaccine to their MS patients does not make this advise harmful because there is a rare risk of causing or exacerbating MS. Doctors recommend the influenza vaccine to people who, before receiving the vaccine, sign informed consent forms warning them of the rare occurrence of Guillain-Barré syndrome as an adverse reaction. None of the special masters decides against petitioners who bring flu vaccine-GBS cases in the Vaccine Program merely because the public health community still recommends flu vaccinations each flu season. It would not be reasonable to assume that in a particular case, flu vaccine did not cause GBS merely because the public health community recommends receipt of flu vaccine. We are talking apples and oranges here with the argument that because neurologists recommend hepatitis B vaccine to their MS patients, the vaccine cannot cause or worsen MS in rare cases.

Petitioner has prevailed in proving that hepatitis B vaccine caused her MS.

CONCLUSION

Petitioner is entitled to reasonable compensation. The undersigned hopes that the parties may reach an amicable settlement, and will set up a status conference soon to discuss further proceedings in this case.

IT IS SO ORDERED.

July 13, 2009
DATE

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