

In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

No. 04-1781V

September 17, 2008

To be Published

REGINA PECORELLA, *

Petitioner, *

v. *

SECRETARY OF THE DEPARTMENT OF HEALTH AND HUMAN SERVICES, *

Respondent. *

John F. McHugh, New York, NY, for petitioner.

Alexis B. Babcock, Washington, DC, for respondent.

Entitlement: hepatitis B vaccine;
two months later, TM; temporal
association; MS diagnosis two
years later

MILLMAN, Special Master

RULING ON ENTITLEMENT¹

The issue in this case is whether a 60-day interval between vaccination and transverse myelitis is an appropriate interval so as to find for petitioner in a causation in fact case.

Petitioner filed a petition dated December 22, 2004, under the National Childhood Vaccine

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

Injury Act, 42 U.S.C. §300aa-10 et seq., alleging that hepatitis B vaccine administered on January 9, 2002 caused her injury. ¶ 3. On January 12, 2002, three days after vaccination, petitioner's liver enzymes were slightly elevated, a condition her gynecologist attributed to the vaccination but of no great concern. ¶ 4. According to petitioner's affidavit, filed with her petition, the onset of her pain was March 16, 2002, over two months after her hepatitis B vaccination. Affidavit, ¶ 6. Petitioner was diagnosed with transverse myelitis (TM) and two years later with 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 TM, Guillain-Barré syndrome (GBS), chronic inflammatory demyelinating polyneuropathy (CIDP), and MS.

In the four Omnibus paradigm decisions the undersigned issued² 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).

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 was 12 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).

Petitioner in the instant action filed a report on December 22, 2004 from her treating internist Dr. Harry S. Jacob in support of her allegations. Med. recs. at p. 27. The undersigned issued the four decisions in the paradigm cases of the Omnibus proceeding starting in 2006.

Respondent filed an expert report from Dr. Benjamin M. Greenberg, a neurologist, on March 31, 2008. R. Ex. A.

On June 25, 2008, petitioner filed the expert report of Dr. Yehuda Shoenfeld, an immunologist.

On July 29, 2008, respondent filed a Request for Ruling on the Record. Respondent states that compensation is not appropriate under the terms of the Vaccine Act, but that respondent “will not expend further resources to defend the case.” Request at p. 2.

Experts

Dr. Harry S. Jacob

Petitioner filed the letter of Dr. Harry S. Jacob, an internist, in support of her allegations. Med. recs. at p. 27. Dr. Jacob has been a treating physician for petitioner since December 14, 1995. He states, after recounting petitioner’s history, “It appeared that she had had a reaction to the vaccine, possibly an autoimmune reaction.” *Id.* Dr. Jacob reviewed the adverse reactions reported in the Physicians’ Desk Reference and found that TM was one of them. He concludes:

It is my opinion that the hepatitis b vaccine injection was a precipitating cause of her transverse myelitis and the development of the multiple sclerosis. There was no other factors [sic] or illnesses that may have contributed to these events. The medical literature does support a links [sic] between hepatitis vaccines and neurological events.

Id.

Dr. Benjamin M. Greenberg

Respondent filed Dr. Benjamin M. Greenberg's expert report after petitioner filed her expert report from Dr. Harry S. Jacob, but before petitioner filed her expert report from Dr. Shoenfeld. R. Ex. A. His disagreement with the Hernán article, as described below, constitutes the bulk of his report. Dr. Greenberg ignores petitioner's initial diagnosis of TM two months after her vaccination and fails to comment on her elevated liver enzyme results three days after vaccination. He also does not address the relationship of petitioner's TM to her ultimate diagnosis of MS. He submits three articles in support of his opinion.

Dr. Yehuda Shoenfeld

Petitioner's expert Dr. Yehuda Shoenfeld is an immunologist. He states in his report that three days after petitioner received hepatitis B vaccine on January 9, 2002, she went to her physician for a routine examination which included blood chemistry tests. These showed elevated liver enzymes attributed to hepatitis B vaccine. Rep. p. 1 (petitioner did not give an exhibit number for this report). One month after vaccination, on February 11, 2002, petitioner complained of right abdominal pain. *Id.* Eight weeks after vaccination, petitioner had two days of pelvic pain and right flank pain. On March 17, 2002, she was admitted to Long Island Jewish Hospital because of severe stabbing back pain radiating to both legs for five days. *Id.* Her liver enzymes had reached five to six times the normal limit. Rep. p. 2.

On March 18, 2002, petitioner complained also of urinary retention and her worsening continued to paralysis of both legs. *Id.* MRIs of the brain and spine were unremarkable. *Id.* On March 22, 2002, petitioner was diagnosed with TM. *Id.* On December 3, 2002, petitioner had her second brain MRI which revealed two small nodular foci of hyperintensity on T2 and FLAIR

images in the left hemisphere with a minimal area of increased signal in the left frontal region with gadolinium contrast. *Id.* Her symptoms were still attributed to TM. *Id.*

On April 21, 2003, petitioner was diagnosed with subacute left hemisensory disturbances and weakness of unclear etiology. Rep. p. 3. The neurologist thought the signal change on brain MRI suggested the presence of an underlying demyelinating illness among other possible diagnoses. *Id.* On May 19, 2004, petitioner was diagnosed with MS. *Id.* On June 30, 2004, she was diagnosed with relapsing-remitting MS. *Id.* She also had a prominent pain syndrome. *Id.*

Dr. Shoenfeld opines at page 3 of his report that petitioner suffered from both acute hepatitis and a neurological illness (TM), recognized as adverse effects of hepatitis B vaccine. Her brain MRIs showed dynamic changes from normal to two small nodular foci of hyperintensity on T2 and FLAIR images in the left hemisphere with increased signal on gadolinium contrast. Rep. p. 4.

Dr. Shoenfeld then discusses at length alternative biologically plausible medical theories (molecular mimicry, polyclonal activation of B lymphocytes, epitope spreading, bystander activation, and superantigen binding) to explain how hepatitis B vaccine can cause autoimmune diseases, of which TM and MS are examples. Rep. pp. 7-9.

Dr. Shoenfeld relies on studies that have analyzed hepatitis B vaccination and TM to conclude that most cases of TM have occurred within a period of seven to 60 days after vaccination. Rep. at p. 11. He also states that TM may be the presenting or first symptom of MS. Rep. at p. 12. Patients with a focal central nervous system demyelination, such as TM or optic neuritis, whose brain MRI scans show demyelinating lesions have an 83% chance of being

diagnosed with MS in the following decade compared with 11% of such patients with normal brain MRI scans. *Id.*

Dr. Shoenfeld states that petitioner's TM evolved within two years to a full-blown demyelinating disease compatible with MS. Rep. p. 15. He regards petitioner's history as a classic case of vaccine-induced autoimmunity which began within two months of receiving her first hepatitis B vaccination and evolved to MS within two years. *Id.* He attaches 86 articles in support of his opinion.

Medical Literature

On pages 726-28 of petitioner's medical records, petitioner attached the Hernán article: "Recombinant hepatitis B vaccine and the risk of multiple sclerosis. A prospective study," 63 *Neurology* 838-42 (2004). Hernán and his associates analyzed 163 MS cases and 1,604 matched controls. *Id.* at 839. They concluded that an increased risk lasted for three years post-hepatitis B vaccination. *Id.* at 840. Petitioner herein claims that the Hernán article substantiates a long-onset cause of MS from hepatitis B vaccine. ¶ 20.

In a subsequent article, filed with respondent's expert Dr. Greenberg's report (Ex. A), entitled "Hepatitis B vaccination and multiple sclerosis: the jury is still out," the same Hernán and co-author S.S. Jick, in 15 *Pharmacoepidemiology & Drug Safety* 653-55 (2006), state that the association between hepatitis B vaccine and MS has not been convincingly demonstrated but an absence of an association has not been established either. *Id.* at 653. Hernán and Jick support another author's "conclusion that there is not enough evidence to establish the existence of an increased risk of MS associated with hepatitis B vaccine in adults. However, we also believe that there is not enough evidence to establish the absence of an increased risk of MS associated with

hepatitis B vaccine. Only additional, fully prospective data will help us escape from this deadlock.” *Id.* at 655.

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, 956 F.2d 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 TM and MS, but also that the vaccine was a substantial factor in bringing about her TM and MS. Shyface v. Secretary of HHS, 165 F.3d 1344, 1352 (Fed. Cir. 1999).

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

Furthermore, to require identification and proof of specific biological mechanisms would be inconsistent with the purpose and nature of the vaccine compensation program. The Vaccine Act does not contemplate full blown tort litigation in the Court of Federal Claims. The Vaccine Act established a federal “compensation program” under which awards are to be “made to vaccine-injured persons quickly, easily, and with certainty and generosity.” House Report 99-908, *supra*, at 3, 1986 U.S.C.C.A.N. at 6344.

The Court of Federal Claims is therefore not to be seen as a vehicle for ascertaining precisely how and why DTP and other vaccines sometimes destroy the health and lives of certain children while safely immunizing most others.

35 F.3d at 549.

The Federal Circuit in Capizzano emphasized the importance of the special masters’ heeding the opinions of petitioner’s four treating doctors in that case. 440 F.3d at 1326.

The undersigned has already ruled in the Omnibus paradigm case Stevens that hepatitis B vaccine can cause TM. Any of the theories that Dr. Shoenfeld propounded (molecular mimicry, bystander activation, epitope spreading, etc.) in his report are biologically plausible. The Federal Circuit in Knudsen expressly stated that petitioner does not have to prove the specific biological mechanism in order to prevail. Petitioner has satisfied the first Althen criterion that there is a

biologically plausible medical theory relating hepatitis B vaccine to her TM and subsequent MS. That TM can be the first sign of MS is not an issue. In Werderitsh, another Omnibus paradigm case, in which the undersigned ruled that hepatitis B vaccine could cause MS, petitioner's initial symptoms were diagnosed as either TM or MS.

There is a logical sequence of cause and effect that hepatitis B vaccine, which plausibly can lead to TM and MS, did lead to petitioner's TM and MS in this case. Petitioner has satisfied the second Althen criterion of a logical sequence of cause and effect.

The major issue in this case has been whether the two months between vaccination and onset of TM is a medically appropriate temporal interval. Until now, the undersigned has relied upon the Omnibus testimony of Dr. Vera Byers for petitioners and Dr. Roland Martin for respondent that the appropriate time interval for causation (if Dr. Martin were to accept causation of demyelinating disease from hepatitis B vaccine) was from three to 30 days. The instant action is the first case in which the undersigned has reached a decision, based on Dr. Shoenfeld's expert report, that two months is an appropriate temporal interval.

Dr. Shoenfeld's 120-page curriculum vitae was attached to his expert report. He is both a researcher and author in the field of immunology. He has been on 37 editorial and/or advisory boards. He teaches, has patents, writes monographs and chapters, edits textbooks, and has 1,288 articles listed in his CV. His analysis of the immunological literature and theories in his expert report posits the knowledge that no other doctor in this case has disputed: the temporal sequence of petitioner's symptoms fits within immunologic probability as being related to the vaccination.

The Federal Circuit in Capizzano has stressed the special masters' heeding the opinions of treating doctors. Here, petitioner's treating doctor, Dr. Jacob, wrote a report in favor of

causation of petitioner's TM and MS from the hepatitis B vaccination. This is further support for the undersigned's reliance on Dr. Shoenfeld's opinion in finding in favor of petitioner.

Respondent, after petitioner filed Dr. Shoenfeld's expert report, decided not to expend any further resources in defending this case, asked for a ruling on the record, but maintained that the case is not compensable. If respondent were willing to dispute the two-month interval between vaccination and onset of TM beyond the claims of the initial Hernán article, respondent could have filed a supplemental report from Dr. Greenberg addressing Dr. Shoenfeld's expert report, his description of immunologic theory, and his conclusion that two months was an appropriate temporal period. Since Dr. Greenberg dealt only with Dr. Jacob's letter and the Hernán article in his report, it would have been reasonable for respondent to file a supplemental report from Dr. Greenberg addressing Dr. Shoenfeld's report. That respondent failed to do so and asked for a ruling on the record is telling.

Petitioner has satisfied the third Althen criterion of proving a medically appropriate time frame between vaccination and injury. Petitioner has proved causation in fact.

CONCLUSION

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

IT IS SO ORDERED.

DATE

Laura D. Millman
Special Master

