In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS
No. [redacted]V
October 18, 2007
To be Published

JANE DOE/06,	*	
	*	
Petitioner,	*	
	*	
v.	*	Entitlement; flu vaccine caused small fiber sensory neuropathy; respondent's expert agrees
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SECRETARY OF THE DEPARTMENT OF HEALTH AND HUMAN SERVICES,	*	
	*	
Respondent.	*	

David L. Terzian, Richmond, VA, for petitioner.
Glenn A. MacLeod, Washington, DC, for respondent.

MILLMAN, Special Master

RULING ON ENTITLEMENT[1]

Petitioner filed a petition, dated October 12, 2006, under the National Childhood Vaccine Injury Act, 42 U.S.C. §300aa-10 et seq., alleging that a flu vaccination administered on October 23, 2003 caused her serum sickness and small fiber neuropathy. Although there is no

[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. Petitioner so moved and the Ruling on Entitlement is redacted.

vaccine record in the medical records, her medical histories in the weeks following October 23, 2003 refer to said vaccine and there is a bill for the influenza vaccination at Ex. 7, p. 2.

Four treating physicians, i.e., Dr. Robert P. McGovern, Dr. Robert B. Steinberg, Dr. Emilio Melchionna, and Dr. Kenneth C. Gorson, concurred that petitioner experienced serum sickness and small fiber neuropathy as a consequence of her flu vaccination. The medical theory proposed is that something in the vaccine was antigenically similar to her dorsal root ganglia.

At a telephonic status conference held on October 3, 2007, respondent asked the undersigned to rule on the record.

FACTS

Petitioner, a psychiatrist, was born on July 1, 1950.

She received flu vaccine and pneumococcal vaccine on October 23, 2003. Med. recs. at Ex. 7, p. 2.

On November 3, 2003, petitioner saw Dr. John A. Egelhofer with stinging pain in her lower arms and legs. On November 4, 2003, she had fever and a red rash. Dr. Egelhofer diagnosed petitioner with arthralgia, myalgia, and a rash caused by a viral exanthem. Med. recs. at Ex. 7, p. 11.

On November 5, 2003, petitioner saw Dr. Robert P. McGovern, an allergy specialist. Med. recs. at Ex. 8, p. 1. Two weeks previously, she received influenza vaccine and pneumococcal vaccine. She was fairly well until three days previously when she noticed a rash on her arms and itching. For the prior two nights, she could not sleep and her arms burned and itched as did her ankles. She had some swelling of her joints. She had pain when she walked or moved. Petitioner noticed her left arm swelling where the influenza vaccine was administered.

The swelling resolved in the next three or four days. She had no problem in the arm where the pneumococcal vaccine was administered. She had a history of allergic rhinitis. Her father had a history of serum sickness and her mother had allergic rhinitis and rosacea. Dr. McGovern diagnosed petitioner with serum sickness. *Id.*

On April 1, 2004, petitioner saw Dr. Emilio M. Melchionna, a neurologist. Med. recs. at Ex. 11, p. 1. Around November 4, 2003, petitioner developed diffuse joint pain, chest pressure, and a fine pigmentous rash over the medial lateral surfaces of her fingers, as well as allodynia, and burning pain in the feet and hands which gradually progressed upward to involve her whole body. Dr. Melchionna diagnosed petitioner with a small fiber sensory polyneuropathy. He noted that her onset was quite acute and most likely related to an autoimmune phenomenon. He also noted that Guillain-Barré syndrome is a well-known complication of influenza vaccine and Dr. Melchionna wondered if petitioner had a similar type of autoimmune mechanism resulting in this acute neuropathy. Med. recs. at Ex. 11, p. 2.

On December 6, 2004, petitioner saw Dr. Robert B. Steinberg, a pain management specialist. Med. recs. at Ex. 10, p. 8. Dr. Steinberg describes petitioner as developing serum sickness in conjunction with vaccinations, complicated by neuropathic pain affecting initially her entire body. *Id.*

On December 2, 2005, petitioner saw Dr. Kenneth C. Gorson, a neurologist who specializes in neuromuscular diseases. Med. recs. at Ex. 12, p. 1. Ten to 12 days after receiving vaccination, petitioner developed an acute illness most consistent with serum sickness. She developed an uncomfortable small fiber painful neuropathic syndrome with burning, stinging, and electrical pain, and a sunburned sensation over the feet and legs, thighs, forearms, shoulders,

hands, and chest wall. *Id.* Dr. Gorson's impression was presumable post-vaccine-associated serum sickness with onset of small fiber ganglionitis. Med. recs. at Ex. 12, p. 2. He wrote to Dr. Melchionna that he completely concurred with Dr. Melchionna's assessment and believed that petitioner's condition must be associated in some fashion with an immunologic reaction to the vaccine given the close temporal course. The most likely explanation would be molecular mimicry where her antibody response to the vaccine must have interacted inadvertently with the antigen on her dorsal root ganglion cells which supply small nerve fibers, given her prominent neuropathic pain syndrome in the absence of ataxia, areflexia, or more prominent nerve conduction abnormalities. *Id.*

Medical Reports

On February 26, 2007, respondent filed a Rule 4(c) Report, contesting liability, together with a report from Dr. Thomas P. Leist, a neurologist, stating that parvovirus B19 caused her small fiber polyneuropathy and that Pneumovax, which she received at the time of her flu vaccination, lists serum sickness in its package insert for adverse experiences reported in clinical trials and/or during post-marketing experience after administration of the vaccine. He also linked metronidazole, which petitioner had been using for rosacea, with serum sickness although that generally occurs after oral administration, not the topical administration of metronidazole that petitioner was using. Dr. Leist concluded that epidemiologic studies do not support serum sickness after either flu vaccine or Pneumovax, petitioner probably did not have serum sickness, and another plausible explanation for her symptoms was parvovirus B19. R. Ex. A. Dr. Leist is a neuroimmunologist and specialist in multiple sclerosis. R. Ex. B.

On May 8, 2007, petitioner filed an expert report from Dr. David S. Younger, chief of neuromuscular diseases at NYU Medical Center and St. Vincent's Catholic Medical Center. P. Ex. 16. Petitioner had a history of seasonal, food, and preservative allergies, asthma, and autoimmune thyroid disease. P. Ex. 16, p. 2. She received influenza vaccine and pneumococcal vaccine in separate areas of her upper arms on October 23, 2003. *Id.* Later that evening, she noted formation of a welt in the area where she received flu vaccine which lasted a few days. *Id.* Eleven days later, on November 3, 2003, petitioner noted shooting pain in the injected arm, followed by restlessness of her legs, pressure, electrical and painful burning sensations and numbness throughout her whole body from her face to her feet, with weakness and, later, sleep apnea and urinary incontinence. *Id.* Her father had had serum sickness and her mother had had allergies. *Id.*

Dr. Younger examined petitioner on March 26, 2007. *Id.* She had distal high stocking and high glove sensory loss to vibratory stimulation, proprioception, and cold temperature sensation, weakness of the right tibialis anterior muscle to firm resistance with imbalance on tandem gait and in erect stance with her eyes closed, with generally intact cognition, cranial nerves, and tendon reflexes. P. Ex. 16, pp. 2-3.

Dr. Younger had petitioner undergo EMG and nerve conduction studies of the legs on March 26, 2007. P. Ex. 16, p. 3. The results showed reduced amplitudes of bilateral peroneal sensory nerve action potentials (SNAP), more on the left, with mild right-sided slowing of velocity; slowing of the left sural nerve velocity with normal SNAP amplitude. Punch skin biopsy showed neuropathy. *Id.*

Dr. Younger stated that flu vaccine caused petitioner debilitating serum sickness and immunologically-mediated peripheral neuropathy presented as acute body burning. *Id.* The red rash on her left arm was where she had received flu vaccine. Where she received the pneumococcal vaccination, she did not have any reaction. *Id.* She was ultimately diagnosed with post-vaccination small and large fiber neuropathy, serum sickness, and acute burning body syndrome. P. Ex. 16, p. 4. On March 16, 2007, petitioner had a blood study reporting petitioner had a parvovirus B19 IgG of 6.3, which was high, and a normal IgM value, indicating past exposure to the virus. P. Ex. 16, p. 8.

Dr. Younger then discussed neurological adverse effects associated with influenza vaccine which include peripheral nerve disorders such as Guillain-Barré syndrome (GBS), which is autoimmune in causation, related to acquired heightened antibody-mediated humoral immunity, similar to experimental allergic neuritis (EAN), an animal model of inflammatory demyelination of the peripheral nervous system. *Id.* EAN occurs after active immunization with the P2, P0 peptide, specific T-cell lines, and CD+ T-cells, autoreactive to the non-neural antigen ovalbumin analogous to influenza vaccine preparation. *Id.* Small fiber neuropathy is a subtype of neuropathy predominantly or exclusively affecting small diameter fibers, myelinated and unmyelinated, sensory and autonomic. *Id.* Dr. Younger noted that parvovirus infection is not a reported cause of painful small fiber neuropathy (in answer to Dr. Leist's report). P. Ex. 16, p. 9.

To Dr. Younger, the most logical sequence of cause and effect in this case is that the flu vaccination led to an acquired heightened immunity in petitioner similar to GBS and EAN as a result of her exposure to either inactivated vaccine viral particles or the preservative in the vaccine. This led to the development of generalized painful, small fiber neuropathy and

ganglionopathy. The temporal relation between the flu vaccination and her neurologic injury to the peripheral nervous system conformed to the usual pattern for such post-vaccination reactions. *Id.* Dr. Younger's opinion was that petitioner developed small fiber sensory neuropathy, ganglionopathy, and dysautonomia due to flu vaccine. *Id.*

Petitioner also filed the report of treating neurologist Dr. Emilio M. Melchionna, dated April 23, 2007. P. Ex. 28. He first saw petitioner on April 1, 2004 on referral from her primary care physician. Petitioner received a flu vaccination in the left deltoid region on October 23, 2003, followed by a localized erythematous reaction measuring 6 cm. By November 4, 2003, petitioner developed diffuse joint pain, chest pressure, and recurrent rash. Most prominent was a diffuse burning pain and allodynia, worse in the hands and feet, involving her whole body. P. Ex. 28, p. 1. Petitioner's diagnosis was of a sensorimotor, small fiber polyneuropathy whose etiology was consistent with an autoimmune phenomenon. *Id.* Dr. Melchionna's working diagnosis was of an autoimmune polyneuropathy triggered by influenza vaccination not unlike the more acute inflammatory demyelinating polyneuropathy called GBS. P. Ex. 28, pp. 1-2. Petitioner was referred to a neuromuscular specialist, Dr. Kenneth Gorson, due to the autoimmune nature of her condition. Dr. Gorson characterized her neuropathy as consistent with a small fiber ganglionopathy which he attributed to serum sickness secondary to the influenza vaccination she received on October 23, 2003. P. Ex. 28, p. 2. Dr. Melchionna states, "The causal connection was never in doubt since my first visit with [petitioner]." *Id.* Dr. Melchionna stated petitioner had a known history of allergic tendencies. She developed a significant localized autoimmune reaction to the vaccination. Within two weeks, she had the acute onset of symptoms including rash, arthralgia, and neuropathy. *Id.* Similar to GBS which flu vaccine can

cause, the temporal relation to the vaccination fit perfectly for an autoimmune reaction due to molecular mimicry which consists of the flu vaccine antigen stimulating the immune system to attack its own tissue, in this case the dorsal root ganglia. P. Ex. 28, pp. 2-3. Petitioner's autonomic fibers are involved as well. P. Ex. 28, p. 3. Petitioner filed Dr. Younger's and Dr. Melchionna's reports on May 8, 2007.

At a telephonic status conference on June 22, 2007, respondent asked for and received the opportunity to have an expert neuromuscular physician review the case and submit a report. On September 21, 2007, respondent filed the expert report of Dr. Ahmet Höke, Director of the Neuromuscular Division, Department of Neurology, Johns Hopkins Hospital, dated September 9, 2007. R. Ex. D. Dr. Höke's practice focuses on peripheral nerve disorders. R. Ex. D, p. 1. His opinion is that petitioner has non-length-dependent small fiber sensory neuropathy. R. Ex. D, p. 2. She could as well have small fiber sensory ganglionopathy. Dr. Höke finds the distinction academic. *Id.* The medical community suspects that most of these non-length dependent small fiber sensory neuropathies are autoimmune in nature because of the temporal course and pattern of involvement. R. Ex. D, p. 3. Most patients with non-length dependent small fiber sensory neuropathies have other autoimmune diseases, as does petitioner. This strengthens the likelihood that non-length-dependent small fiber sensory neuropathies are likely autoimmune. *Id.*

Dr. Höke notes a large body of medical literature associating flu vaccine with GBS, another autoimmune peripheral neuropathy. More recent studies show a definite increase in risk of GBS for patients receiving flu vaccine. *Id.* Dr. Höke states, "Given this association and the fact that the non-length-dependent small fiber sensory neuropathy is likely to be autoimmune in nature, it is plausible that the plaintiff's symptoms may have been initiated by the vaccinations

she had on October 23rd, 2003. The temporal course of symptom onset within 2 weeks fits with other neurological complications of vaccinations." *Id.*

Dr. Höke entertained the possibility that a viral exanthem could have independently caused petitioner's non-length-dependent small fiber sensory neuropathy, which her primary care physician, Dr. Egelhofer, assumed on November 4, 2003. Dr. Höke stated he did not believe a viral exanthem could have been responsible for the non-length-dependent small fiber sensory neuropathy: "The rash and other constitutional symptoms started ... at the same time that she had painful paresthesias, so the temporal course of viral exanthem preceding the non-length-dependent small fiber sensory neuropathy by 2-4 weeks could not have been possible." *Id.* Dr. Höke concludes that petitioner's neuropathy is relatively rare. "Based on associations with flu vaccination and other autoimmune peripheral neuropathies, it is likely that the vaccines may have initiated her neuropathy, but we cannot be sure." *Id.*

DISCUSSION

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 1317, 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...."

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).

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. Hasler v. US, 718 F.2d 202, 205 (6th Cir. 1983), cert. denied, 469 U.S. 817 (1984).

Petitioner must show not only that but for the flu vaccine, she would not have had serum sickness and small fiber neuropathy, but also that the flu vaccine was a substantial factor in bringing about her serum sickness and small fiber neuropathy. 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.
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> 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 stated in Althen, 418 F.3d at 1280, that "the purpose of the Vaccine Act's preponderance standard is to allow the finding of causation in a field bereft of complete and direct proof of how vaccines affect the human body."

The Federal Circuit in Capizzano emphasized the opinions of petitioner's four treating doctors in that case. 440 F.3d at 1326.

As the Federal Circuit stated in Knudsen, 35 F.3d at 548, "Causation in fact under the Vaccine Act is thus based on the circumstances of the particular case, having no hard and fast *per se* scientific or medical rules." The undersigned's task is to determine medical probability based on the evidence before the undersigned in this particular case. Althen, 418F.3d at1281 ("judging the merits of individual claims on a case-by-case basis").

The Federal Circuit in Knudsen, 35 F.3d at 549, also stated: "The special masters are not 'diagnosing' vaccine-related injuries."

As for epidemiological support for causation, the Federal Circuit in Knudsen ruled for petitioners even when epidemiological evidence directly opposed causation from a vaccine.

In Knudsen, even though epidemiological evidence supported the opposite conclusion, i.e., that viruses were more likely to cause encephalopathy than vaccinations, the Federal Circuit held that that fact alone was not an impediment to recovery of damages. In Knudsen, the Federal Circuit stated:

> The bare statistical fact that there are more reported cases of viral encephalopathies than there are reported cases of DTP encephalopathies is not evidence that in a particular case an encephalopathy following a DTP vaccination was in fact caused by a viral infection present in the child and not caused by the DTP vaccine.

35 F.3d at 550.

The timing here is appropriate for an immune response. The pathological process described in the medical literature and in the reports of Dr. Younger, Dr. Melchionna, and Dr. Höke is consistent with what happened to petitioner clinically, and shows a biologically plausible medical theory (autoimmune reaction), a logical sequence of cause and effect (a vaccinee with prior autoimmune problems reacts adversely to another antigen, producing serum sickness and small fiber neuropathy), and a medically appropriate time frame (two weeks). Dr. Leist, respondent's neurologic expert, decries the lack of epidemiologic support, but the Federal Circuit does not require petitioner to provide it (Knudsen, Althen), although in this case, Dr. Younger comments that the more recent medical literature does support that flu vaccine causes GBS and that GBS is another peripheral neuropathy whose pathogenesis is autoimmune, just as petitioner has a peripheral neuropathy whose pathogenesis is autoimmune.

Here, four of petitioner's treating physicians, including her neurologist Dr. Melchionna and a neurologist specializing in neuromuscular disease, Dr. Gorson, opined that flu vaccine

caused her serum sickness and small fiber neuropathy. See Capizzano. Respondent's own neuromuscular medical expert Dr. Höke opined that the flu vaccine likely caused petitioner's small fiber sensory neuropathy although he said he could not be sure. Petitioner's standard of proof is not certainty, but probability. See Knudsen. Because of Dr. Höke's opinion in favor of causation in fact, respondent asked for a ruling on the record.

Dr. Leist's opinion is not credible in light of the opinions of Dr. Younger, Dr. Melchionna, and Dr. Höke (who also eliminated the possible alternate cause of a viral exanthem, which had been Dr. Egelhofer's initial diagnosis). Dr. Younger explains why parvovirus B19 (Dr. Leist's alternate cause) would not have caused petitioner's illness. Dr. Leist opined that pneumococcal vaccine would be more likely the cause of serum sickness. But the site where petitioner received pneumococcal vaccine was not inflamed unlike the site where she received influenza vaccine. Therefore, her reaction could not be attributed to the pneumococcal vaccine. Moreover, the medical literature associates acute peripheral neuropathy with influenza vaccine. In light of the opinions of Dr. Younger, Dr. Melchionna, and Dr. Höke, which fully and convincingly explain the effect of the flu vaccination on petitioner, the undersigned cannot accept Dr. Leist's opinion as credible.

The undersigned has previously held that measles vaccine caused serum sickness: Stansfield v. Sec'y of HHS, No. 93-172V, 1995 WL 737530 (Fed. Cl. Spec. Mstr. November 29, 1995), and that hepatitis B vaccine caused GBS: Gilbert v. Sec'y of HHS, No. 04-455V, 2006 WL 1006612 (Fed. Cl. Spec. Mstr. March 30, 2006). That medical literature supports that flu vaccine causes a higher incidence of GBS, that GBS is an acute neuropathy as is small fiber sensory neuropathy, that petitioner's treating doctors recognized her serum sickness as a

consequence of her flu vaccination with a secondary effect of small fiber sensory neuropathy, and that three experts in neuromuscular diseases (the treating Dr. Gorson, petitioner's expert Dr. Younger, and respondent's expert Dr. Höke) plus the treating neurologist Dr. Melchionna all opine that flu vaccine caused petitioner's serum sickness and small fiber sensory neuropathy lead the undersigned to conclude that petitioner has proved that influenza vaccine caused her injury,

Petitioner has prevailed in proving that influenza vaccine caused her serum sickness and small fiber sensory neuropathy.

CONCLUSION

Petitioner is entitled to reasonable compensation. The undersigned hopes that the parties may reach an amicable settlement. A telephonic status conference is set for January 16, 2008, at 10:30 a.m. to give petitioner's counsel, at his request, enough time to consult with an economist.

IT IS SO ORDERED.

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DATE Laura D. Millman
Special Master