

In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

No. 07-20V

December 17, 2009

To be Published

LOUISE SCHMIDT, *

Petitioner, *

v. *

SECRETARY OF THE DEPARTMENT OF HEALTH AND HUMAN SERVICES, *

Respondent. *

Carol L. Gallagher, Somers Point, NJ, for petitioner.
Glenn A. MacLeod, Washington, DC, for respondent.

Entitlement: influenza vaccine and possible URI; acute transverse myelitis

MILLMAN, Special Master

RULING ON ENTITLEMENT¹

Petitioner filed a petition on January 12, 2007 under the National Childhood Vaccine Injury Act, 42 U.S.C. §300aa-10 et seq., alleging that influenza vaccine she received on November 22, 2005 caused her transverse myelitis (TM) whose onset was December 19, 2005.

On January 12, 2007, this case was assigned to special master George L. Hastings.

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 constitute a clearly 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.

Medical records and expert reports were subsequently filed.

On January 7, 2009, this case was reassigned to the undersigned. More expert reports were filed.

On April 29, 2009, a hearing was held to take the testimony of Dr. Ralph Costa, petitioner's treating family practitioner, and of petitioner. On May 5, 2009, the hearing continued in order to take the testimony of Dr. Marcel Kinsbourne, petitioner's expert neurologist, and of Dr. Benjamin Greenberg, respondent's expert neurologist.

Subsequent to the hearing, petitioner filed medical literature (Exs. 44-45) on May 11, 2009.

On July 15, 2009, petitioner filed her posthearing brief.

On August 17, 2009, respondent filed her posthearing brief.

On August 31, 2009, petitioner filed her response to respondent's posthearing brief.

FACTS

Petitioner was born on February 14, 1957.

On November 22, 2005, she received influenza vaccine.

On Monday, December 19, 2005, petitioner had a consultation with Dr. Ricardo Y. Mabanta. Earlier that week, she had developed a cold, but no fever. She entered West Jersey Hospital Voorhees which diagnosed her with transverse myelitis and postviral infection. Med. recs. at Ex. 7, pp. 10, 75.

On December 25, 2005, petitioner had a consultation with Dr. Ellen K. Turner at West Jersey Hospital Voorhees. Two weeks earlier, petitioner had an upper respiratory infection with a runny nose and some sore throat, but no fever. She also had a flu shot at that time. Two weeks

later, she had an unusual sensation in her lower extremities characterized by numbness, weakness, and inability to walk. She had a positive ANA. Her serum herpes simplex virus antibody type 1 was positive. She had a positive IgG consistent with past exposure. Med. recs. at Ex. 7, pp. 81, 83.

Other Submitted Material

Petitioner filed as Ex. 27 an article entitled “A primary care guide to transverse myelitis” by A.D. Middleton, B. Greenberg (respondent’s expert in the instant action), and W. Foliaco, Patient Care, Primary Care Topics in Neurology & Psychiatry 18-23 (Sept. 2007). On page 18, the authors state that potential causes of myelitis may include infectious diseases, postvaccination adverse event, systemic autoimmune diseases, multiple sclerosis, acute disseminated encephalomyelitis, and neuromyelitis optica. On page 20, the authors state:

Many patients report a recent viral illness (involving fever, headache, nausea, vomiting, diarrhea, respiratory symptoms, or muscle pain) in the weeks preceding the onset of TM symptoms. Other patients, particularly children, may have had a recent vaccination. Some case reports have demonstrated a close temporal relationship between vaccinations such as influenza or hepatitis B and the onset of TM; however, conclusive evidence is still lacking. [citations omitted.]

Petitioner filed as Ex. 28 a case report entitled “Acute Transverse Myelitis After Influenza Vaccination: Magnetic Resonance Imaging Findings” By R. Bakshi and J.C. Mazziotta, 6 J Neuroimaging 248-50 (1966). The authors state that acute transverse myelitis (ATM) is an inflammatory disorder associated with an antecedent or intercurrent factor, such as infection, but also has been reported following vaccinations, including influenza. *Id.* at 248. The case report concerned a woman who had the onset of transverse myelitis one month after receiving inactivated influenza vaccine. She had no antecedent illnesses. *Id.* The authors state

that MRI findings in postvaccination acute transverse myelitis have not been well described. The only other report of MRI findings postvaccination to date in the literature described acute transverse myelitis after hepatitis B vaccination. *Id.* They mention that a few cases of acute transverse myelitis have been reported in the literature after flu vaccination. *Id.* They state with reference to the woman whose MRI findings form the subject of their case report:

This association of ATM following the influenza vaccination does not prove cause and effect. However, because no other known causes of ATM were identified, a postvaccination syndrome was diagnosed by exclusion.

Id. at 250.

Petitioner filed as Ex. 29 a case report entitled “Acute Disseminated Encephalomyelitis Associated with Influenza Vaccination” by J.H. Cheong, et al., 35 J Korean Neurosurg Soc 223-25 (2004). The authors describe an acute disseminated encephalomyelitis (ADEM) that either an upper respiratory infection or an influenza vaccination may have caused. Two weeks before admission to the hospital, a girl received influenza vaccine followed by mild fever and sore throat. *Id.* at 223.

Petitioner filed as Ex. 30 an article entitled “Neurological Complications of Immunization” by F.M. Fenichel, 12 Ann Neurol 119-28 (1982). In the section on acute transverse myelitis (ATM), Dr. Fenichel notes that there were two reports in the medical literature of ATM following influenza immunization, one with an onset interval of seven days and the other with an onset interval of 29 days. *Id.* at 122.

Petitioner filed as Ex. 33 a case report entitled “Myelopathy following influenza vaccination in inflammatory CNS disorder treated with chronic immunosuppression” by A.J. Larner and S.F. Farmer, 7 European J Neurology 731-33 (2000). The vaccinee was on

immunosuppressive therapy when he received influenza vaccine. Two days later, he had onset of acute cord syndrome. *Id.* at 731, 732. The authors state, “The rarity of neurological complications following influenza vaccination makes it impossible to establish a definite causal relation....” *Id.* at 732. They also state that a number of factors in this case indicate the flu vaccine caused the man’s myelopathy: the temporal relation between the two events, the absence of prior cord symptoms or signs, and the anatomical concordance of the cord lesion and the injection site. *Id.* at 733.

Petitioner filed as Ex. 36 two case reports entitled “Neurologic Complications Associated with Influenza Vaccination: Two Adult Cases” by N. Nakamura, et al., 42 Internal Med 191-94 (2003). The second case concerned a man with paraplegia seven days after influenza vaccination which was diagnosed as transverse myelitis. *Id.* at 191. The authors state that this second case had acute myeloneuropathy caused by an allergic reaction. *Id.* at 193. They note that in Japan, from 1972 to 1996, about 70 cases with neurologic complications after influenza vaccination were reported. Two of those cases were myelitis and eight were acute disseminated encephalomyelitis. *Id.* They posit an underlying immunological status produced such an allergic neurologic reaction. *Id.* at 194.

Petitioner filed as Ex. 43 an article entitled “Immunopathogenesis of acute transverse myelitis” by D.A. Kerr and H. Ayetey, 15 Current Opinion in Neurology 339-47 (2002). The authors state that acute transverse myelitis (ATM) “exists on a continuum of neuroinflammatory disorders that also includes Guillain-Barré syndrome (GBS), multiple sclerosis (MS), acute disseminated encephalomyelitis and neuromyelitis optica (NMO).” *Id.* at 339. “[C]linical and pathological studies support the notion that there are many common features of the inflammation

and neural injury.” *Id.* They mention that several reports of ATM following vaccination had been published and “it is widely reported in neurology texts that ATM is a post-vaccination event.” *Id.* at 340. They discuss a couple of case reports, one of a man with ATM two days after flu vaccination and another with myelopathy nine days after hepatitis B vaccination. *Id.* They advise viewing such case reports with caution because “it is entirely possible that two events occurred in close proximity by chance alone” and extensive data shows overwhelmingly that vaccinations are safe. *Id.* at 341. They note that in 30-60% of idiopathic ATM cases, there was an antecedent respiratory, gastrointestinal, or systemic illness. *Id.* They posit that the mechanisms of causation may be molecular mimicry or superantigen-mediated immune activation. *Id.* at 342.

Petitioner filed as Ex. 45 an article entitled “IL-6 induces regionally selective spinal cord injury in patients with the neuroinflammatory disorder transverse myelitis” by A.I. Kaplin, et al., 115 J Clin Invest 10:2731-41 (2005). The authors posit the theory that IL-6, a glycoprotein cytokine that mediates signal transduction between immune cells, is a trophic factor under some circumstances which, when elevated, causes central nervous system destruction in transverse myelitis (TM) patients. *Id.* at 2731, 2732. They state at p. 2738:

We found in pathological spinal cord specimens from patients with TM that astrocytes were the predominant source of IL-6 production. Astrocytes have been shown to produce IL-6 in response to direct stimulation by proinflammatory cytokines (e.g., TNF- α and IL-1 β), viral and bacterial pathogens, and neurotransmitters. What triggers the initial biosynthesis of IL-6 in astrocytes is currently being investigated, but potential candidates include an immune response following vaccination or an antecedent infection that could involve mechanisms such as molecular mimicry or superantigen-mediated inflammation. Why some individuals mount a dramatic elevation of their IL-6 levels that results in the pathophysiological injury seen in TM is still

unknown, but the potential contribution of genetic differences to CNS [central nervous system] IL-6 production has been previously described. [citations omitted.]

TESTIMONY

Dr. Ralph Costa testified first for petitioner. Tr. at 4. His office administered the flu vaccine to petitioner on November 22, 2005. Tr. at 10. It was not normal practice at his office to administer flu vaccine if a patient was showing signs of an upper respiratory infection. *Id.* He has a note meaning petitioner took Sudafed on December 17th (Saturday) to go to a party. Tr. at 16. Sudafed is a short-acting drug. Dr. Costa did not think it could have an impact on petitioner's transverse myelitis two days later. *Id.* He did not see anything in petitioner's medical records to indicate a cause for her transverse myelitis other than the flu vaccine. Tr. at 17. There is nothing positive about petitioner's physical examination at the hospital indicative of an upper respiratory infection or cold. Tr. at 19, 21. One of the causes of transverse myelitis that Dr. Greenberg lists in an article respondent filed in which Dr. Greenberg is a co-author is vaccinations. Tr. at 24.

Dr. Costa's opinion is that petitioner's November 22nd flu vaccination is the only hard fact that is able to be documented as the cause of petitioner's transverse myelitis. Tr. at 25. Nothing on physical examination or in the laboratory reports substantiates a cold. *Id.* Her white blood count was not even elevated. *Id.* We do not know if there really was a respiratory infection. *Id.* In Dr. Costa's opinion, the flu shot is the most likely contributor or trigger to petitioner's transverse myelitis. Tr. at 26. The timing is medically appropriate. Tr. at 27.

Petitioner previously had a flu shot on December 1, 2003. *Id.* This would presensitize her to the 2005 flu vaccination. Tr. at 28. The first vaccination creates a memory immune

response. The second introduction of the allergen triggers the prior response. *Id.* Petitioner had seen Dr. Costa for years and had very ordinary medical issues prior to the vaccination. Tr. at 30. Dr. Costa is still petitioner's treating physician. *Id.* She is his only patient to have transverse myelitis. Tr. at 31. She is the only transverse myelitis patient he has had for whom he has done primary care. *Id.* He did not treat petitioner in the hospital. *Id.*

On December 15, 2006, someone provided Dr. Costa with the information that petitioner had an upper respiratory infection after the flu shot. Tr. at 33. Probably petitioner told him. *Id.* He believes that petitioner diagnosed herself with an upper respiratory infection rather than a physician. *Id.* Someone with sinusitis can confuse it with an upper respiratory infection. Tr. at 35. In many cases, the congestion of sinusitis is indistinguishable from viral-caused congestion. Tr. at 36. Sudafed is a decongestant. Tr. at 39. Sudafed is used for congestion from any cause. *Id.* The treating physicians at the hospital ascribed petitioner's transverse myelitis to a virus and not to her flu vaccination. Tr. at 42.

Dr. Costa believes that petitioner's transverse myelitis is due to her flu vaccination because the time frame of 27 days is appropriate to have a significant antibody response to the flu vaccine. Tr. at 50. There was no other cause for her transverse myelitis. Tr. at 51. In addition neurologic and autoimmune conditions have been documented with a response from various vaccines. Tr. at 53. When you have a hard fact, such as the vaccination, versus coincidence, the hard fact predominates in discussing causation. Tr. at 55. Dr. Costa said that even if petitioner had an upper respiratory infection at the time she received flu vaccine, it would not change his opinion that the vaccine caused her transverse myelitis. Tr. at 59, 65. Flu vaccine itself can give a vaccinee flu-like symptoms. Tr. at 64. In his written report, Dr. Costa stated

that if petitioner had not had flu vaccine, she would not have had transverse myelitis. Tr. at 67. He considers the flu vaccine to be a substantial factor causing petitioner's transverse myelitis. Tr. at 71.

On May 5, 2009, the hearing resumed. Dr. Marcel Kinsbourne testified for petitioner. Tr. at 92 (the page numbers continue from the first transcript). He is a neurologist. Tr. at 93. His opinion is that influenza vaccine caused, precipitated, or triggered petitioner's transverse myelitis 27 days later. Tr. at 99. This is within a medically reasonable time frame for precipitating factors of an immune-mediated disorder such as transverse myelitis. *Id.* It is quite a complex process where certain chemicals release other chemicals which activate certain cells. Tr. at 111.

Dr. Kinsbourne stated that transverse myelitis is an immune-mediated disorder, meaning some provocative event featuring a protein called an antigen elicited from someone's immune system an overwhelming maladaptive response causing self-injury. Tr. at 100. The person's immune system not only reacted in defense against the antigen in question, but also had additional unwanted effects on some part of the body, in this case, of the nervous system. *Id.* The injury is inflicted not by an invading organism or the vaccine itself, but rather by the body's reaction to the invading organism or the vaccine. *Id.*

One mechanism which might cause this reaction is molecular mimicry. *Id.* The immune system does not react to a whole organism or whole virus, but only to antigens on the surface of the virus or bacterium. Tr. at 101. If some part of the surface antigen is structurally similar to a component of the person's body, such as his or her nervous system, the antibody or cellular response against that epitope on the surface of the organism also recognizes a similar structure in

the nervous system. *Id.* In a case of transverse myelitis, some component of the myelin sheath which wraps around the lengthy nerve fibers in the spinal cord becomes the focus of attack, causing a demyelinating disorder. *Id.*

There is also another mechanism to describe the immune-mediation involved in transverse myelitis, which is that interleukin (IL)-6 has a particular affinity for the spinal cord. The transverse myelitis group at Johns Hopkins University opined that transverse myelitis is largely if not completely due to an attack of the IL-6 on the tissue of the cord. Tr. at 101-02. Vaccinations work by generating polyinflammatory cytokines such as IL-6 and others in order to render an immune response. Tr. at 102. Proinflammatory cytokines are chemical substances released when inflammation occurs. *Id.* Their job is to cause inflammation as part of the defensive action of the innate immune system. *Id.* The other immune system is the adaptive immune system which specifically targets something like influenza or hepatitis B but cannot work if the innate immune system is not working. Tr. at 103. There is a cascade of events from the injury to the inflammation, the release of cytokines, causing inflammation, which is a defensive reaction to bring cells to the injured area. Tr. at 103-04. Secondary to that is the adaptive immune system determining the invader's specific nature and producing antibodies against it and T-cells specifically against that. Tr. at 104. Molecular mimicry is the action of the adaptive immune system. *Id.*

Flu vaccine can cause inflammation in the peripheral nervous system when someone gets Guillain-Barré syndrome from it. *Id.* In this case, flu vaccine has similarly acted in the central nervous system, i.e., the spinal cord, engendering immunity by producing IL-6. *Id.* Every vaccine, in order to be effective in causing an immune response, will have cytokines mediating

the response, one of which is IL-6, which Johns Hopkins has recently identified as the attacker in transverse myelitis. Tr. at 105. Dr. Kinsbourne would call this second theory a cytokine attack. Tr. at 106.

Dr. Kinsbourne mentioned that the medical records in the instant action refer to petitioner's having a postinfectious disorder. That means the doctors did not expect an organism, whether a bacterium, a virus, or vaccine, to be there. Tr. at 109. What they would expect was activation of the immune system which cleared the organism; but after the infection, the damage was done. *Id.* He believes that petitioner's doctors were not indicating that the only cause of petitioner's transverse myelitis was either a bacterium or a virus when they used the term "postinfectious." He also believes that term could encompass post-vaccinal. *Id.*

Dr. Kinsbourne said that myelopathy can have multiple causes. *Id.* You cannot tell what petitioner was reacting against from the medical records. Tr. at 110. Petitioner was healthy on November 22, 2005 when she received influenza vaccine. Tr. at 112. The Emergency Medical Service noted the morning of the onset of transverse myelitis that petitioner described having sinus congestion for which she took Sudafed. Tr. at 113.

Dr. Kinsbourne said that if petitioner had had a cold on December 17, 2005, that would have been a "very very" short interval to her transverse myelitis two days later. Tr. at 116. Dr. Kinsbourne does not see petitioner as having an acute infection. Tr. at 118. He does not think that something that comes in a day or two is a viable causative factor. *Id.* If petitioner had had a cold a couple of days before her onset of transverse myelitis, it might have provided a further trigger to the immune process that the flu vaccine set up a month before. *Id.* Dr. Kinsbourne

opined that if petitioner had not received flu vaccine, she would not have contracted transverse myelitis. Tr. at 120.

Dr. Kinsbourne did not see anything in the Cherry Hill Fire Department EMS or emergency room records that showed objective evidence of an upper respiratory infection on December 19, 2005. Tr. at 121. But an upper respiratory infection and a vaccination can both work together to provide an immunologic challenge to the body affecting the myelin sheath in the spinal cord. Tr. at 123. Both are substantial factors in causing the transverse myelitis. Tr. at 126, 154.

On cross-examination, Dr. Kinsbourne admitted that the clinical signs of an upper respiratory infection are not the first day that the person has the virus. Tr. at 136. He does not believe that a cold will cause transverse myelitis. *Id.* He thinks someone would definitely have to have fever and other signs that there was an infection able to elicit a generalized immune response. *Id.* He is unimpressed with the severity of petitioner's alleged runny nose, believing it insufficient to have an effect on her immune system. Tr. at 137. Transverse myelitis is a rare event, and vaccine-associated transverse myelitis is even rarer. Tr. at 138.

Dr. Benjamin Greenberg testified for respondent. Tr. at 164. He is a neurologist who is director of the transverse myelitis program at the University of Texas Southwestern. Tr. at 165. Previously, he was co-director of the transverse myelitis program at Johns Hopkins. *Id.* He teaches a course on multiple sclerosis and demyelinating disease. Tr. at 166. He has authored or co-authored articles specifically on transverse myelitis. *Id.* He has special competence in transverse myelitis, multiple sclerosis, and central and peripheral demyelinating diseases. Tr. at 167. His opinion is that petitioner's influenza vaccination did not play a role in her transverse

myelitis. Tr. at 168. His basis is that there is limited scientific, epidemiologic, and medical evidence substantiating a relationship between influenza vaccine and demyelinating disease. Moreover, in the instant action, there is a very clearly identifiable and documented better explanation for petitioner's transverse myelitis, i.e., her preceding infection. Tr. at 169.

The lack of documentation of symptoms of a viral infection or upper respiratory infection does not change his opinion at all. *Id.* On more than four occasions, doctors noted the presence of an upper respiratory infection that the petitioner reported when she arrived at the hospital. Tr. at 170. He does not think that the day someone takes Sudafed is an accurate way to date when he or she had a cold. Tr. at 172. Dr. Greenberg thinks that molecular mimicry is the process by which a viral infection causes transverse myelitis. Tr. at 174-75. Biologically, molecular mimicry with an active infection is more likely than with a killed virus vaccine because in an active infection, the virus is replicating compared to a fixed antigen. Tr. at 175.

Flu vaccinations are recommended for people with chronic debilitating diseases. Tr. at 176. Dr. Greenberg distinguishes between Guillain-Barré syndrome and transverse myelitis predominantly in the different chemical nature of the myelin in the peripheral and central nervous systems. Tr. at 177. The immune system and the peripheral nervous system have no barrier between them and immune cells flow in and out of these areas of nerves and myelin constantly. Tr. at 178. But there is a very tight blood-brain barrier preventing this constant communication with the immune cells in the central nervous system. *Id.* Many people have autoantibodies that recognize antigen in their central nervous system, but they do not necessarily get disease. *Id.* Thus, there is a difference between what can trigger GBS and transverse myelitis. *Id.*

Epidemiologic evidence substantiates that flu vaccine can cause GBS, but not that flu vaccine can cause transverse myelitis. Tr. at 180. People with multiple sclerosis already have a breached blood-brain barrier, but there are no epidemiologic studies showing a relapse rate after they receive influenza vaccine. *Id.*

Dr. Greenberg stated that even if there were no upper respiratory illness in this case, he would be skeptical of the flu vaccine causing petitioner's transverse myelitis. Tr. at 184. He would regard it as coincidence. Tr. at 185. There is no animal model or epidemiology to support anything more than coincidence. *Id.* There is no increased rate of transverse myelitis during flu season when flu vaccines are administered. Tr. at 186. It is incredibly difficult to identify a preceding infection as a trigger of the immune system. Tr. at 187. Between 30 and 60 percent of transverse myelitis cases are preceded by an upper respiratory infection or gastroenteritis. *Id.* Dr. Greenberg agrees there is no objective evidence of clinical signs of petitioner's having an upper respiratory infection in the medical records. Tr. at 188. This supports his view that petitioner's upper respiratory infection preceded her onset of transverse myelitis by weeks. Tr. at 189. The appropriate time frame for postinfectious transverse myelitis is a few days to four weeks after the infection. *Id.* There have been cases out to six weeks depending on the organism. Tr. at 190.

In order for Dr. Greenberg to agree that flu vaccine can cause transverse myelitis, he would want an analysis of a patient's spinal fluid to see if there were antibodies or cells there that recognized both spinal cord and flu vaccine. *Id.* It would necessitate putting flu vaccine in a dish and a slice of spinal cord in a dish, but this has never been done and was not done in this case. *Id.* That would be one type of direct evidence and another would be an animal model. Tr.

at 191. He is unaware of any medical article showing that mice received flu vaccine and developed central nervous system demyelination. *Id.* That would be a direct relationship biologically although not in humans. *Id.*

Dr. Greenberg discussed his own article, which petitioner filed as Ex. 27, entitled “A Primary Care Guide to Transverse Myelitis,” in which on page 18, he says one cause of transverse myelitis is vaccination. Tr. at 192. He explained he meant that there are certain vaccines, such as simple rabies vaccine, which have been linked to central nervous system demyelinating events. This does not apply to flu vaccines. Tr. at 193. The simple rabies vaccine had nervous system tissue in it and people developed an autoimmune reaction to that tissue, but not necessarily to the viral components. *Id.*

In the same article, Dr. Greenberg and his co-authors mentioned that case reports drew a relationship between influenza vaccine and transverse myelitis as well as hepatitis B vaccine and transverse myelitis, but they found conclusive evidence lacking. Tr. at 194.

As for both an upper respiratory illness and flu vaccine being substantial factors in causing petitioner’s transverse myelitis in the instant action, Dr. Greenberg stated that “it is probably not needed and not a factor.” *Id.* He bases his opinion on the biology showing postinfectious rates have much more probability. *Id.*

Dr. Greenberg agreed that there is something different in how petitioner recognizes self versus not self, but we do not know if her myelin is different or it just presents a unique feature that is similar to an antigen on an infection. Tr. at 206. The odds are that it is a one-time event. Tr. at 207. He agrees that petitioner’s immune system is not the standard, normal immune system. *Id.*

Dr. Greenberg said that a viral infection invades the tissue which the immune system has to invade in order to clear it out unlike a vaccination which deposits pieces of the vaccine in a lymph node that activates the immune cells, but the immune system does not have to clear it out. Tr. at 216-17. Flu vaccine is a killed virus vaccine which means it does not replicate. Tr. at 222. He would not expect the same response to nonreplicating proteins as occurs to replicating proteins. Tr. at 223. Dr. Greenberg's understanding of the word "postinfectious" does not include a reaction to vaccines. Tr. at 225. Postinfectious means an actual primary infection. *Id.*

DISCUSSION

To satisfy her burden of proving causation in fact, petitioner must prove by preponderant evidence "(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. . . ." Such an approach is inconsistent with the use of circumstantial evidence. *Id.* 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.”

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. *Id.* at 1148.

Petitioner must show not only that but for the influenza vaccine, she would not have had transverse myelitis, but also that the vaccine was a substantial factor in bringing about her transverse myelitis. 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 that the special masters are to evaluate seriously the opinions of petitioner's treating doctors since "treating physicians are likely to be in the best position to determine whether a logical sequence of cause and effect show[s] that the vaccination was the reason for the injury." 440 F.3d at 1326. See also Andreu v. Secretary of HHS, 569 F.3d 1367, 1375 (Fed. Cir. 2009).

As for epidemiological support for causation, the Federal Circuit in Knudsen v. Secretary of HHS, 35 F.3d 543, 551 (Fed. Cir. 1994), ruled for petitioners even when epidemiological evidence directly opposed causation from DPT vaccine. The case concerned the cause of a baby's encephalopathy after a vaccination. Respondent provided evidence that more encephalopathies are caused by viruses than by vaccines, convincing the special master to rule against petitioners. But the Federal Circuit thought the epidemiologic evidence should not bar petitioners from prevailing. Even though epidemiological evidence supported respondent's view 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.

Both parties in the instant action agree on a significant number of issues. They agree that petitioner had acute transverse myelitis (ATM) as a reaction to something: a cold (respondent) or a flu vaccination (petitioner) or to both if the undersigned holds that petitioner did have an upper respiratory infection (petitioner). They agree that there is a biologically plausible medical theory—molecular mimicry—which explains how an infection (respondent) and/or a vaccination (petitioner) can cause ATM. Respondent’s expert Dr. Greenberg disagrees that vaccines can cause ATM, but Dr. Greenberg and his co-authors wrote in an article giving primary care advice to other doctors with ATM patients that ATM may be an adverse reaction to vaccines, without stating that the vaccinations had to contain nerve tissue, such as the rabies vaccine used to contain.

The medical literature, including that authored by Dr. Greenberg’s former colleague at Johns Hopkins Medical Center transverse myelitis center, Dr. Douglas A. Kerr, indicates that influenza vaccine can cause central nervous system disease, of which one is ATM, as well as peripheral nervous system disease, such as Guillain-Barré syndrome (GBS). Dr. Kerr writes in an article petitioner filed as Ex. 43, “Immunopathogenesis of acute transverse myelitis,” that ATM is on a spectrum of neurological disorders, including both the central and peripheral nervous systems, that may be caused by vaccination:

[The authors state that acute transverse myelitis (ATM)] “exists on a continuum of neuroinflammatory disorders that also includes Guillain-Barré syndrome (GBS), multiple sclerosis (MS), acute disseminated encephalomyelitis and neuromyelitis optica (NMO).” “[C]linical and pathological studies support the notion that there are many common features of the inflammation and neural injury.” [They mention that several reports of ATM following vaccination had been published and] “it is widely reported in neurology texts that ATM is a post-vaccination event.”

The undersigned is cognizant of the fact that Dr. Kerr and his co-author do not conclude that vaccines, including influenza vaccine, cause ATM. But Dr. Greenberg's statement at trial that one must separate central nervous system disorders from peripheral nervous system disorders in distinguishing the plausibility of vaccine adverse reaction because the former retain a blood-brain barrier and the latter do not and, therefore, in the case of an inactivated viral vaccine, there cannot be a breach of the blood-brain barrier in order to cause ATM cannot be unique to testimony in a court hearing but never receive discussion in the medical literature. Yet this distinction is not made in any of the medical articles respondent filed. And Dr. Kerr writes that central nervous system demyelinating disorders are on a spectrum with peripheral nervous system demyelinating disorders, having common features of inflammation and neural injury, that ATM fits on this disease spectrum, and that ATM is widely reported in medical textbooks as a post-vaccination event.

In Mouille v. Sec'y of HHS, No. 05-1204V, 2009 WL 4456207 (Fed. Cl. Spec. Mstr. 2009), the undersigned held that both influenza vaccine and a cold or sinusitis were substantial factors in causing the vaccinee's meningoencephalitis, a central nervous system disease. Respondent's pediatric neurological expert testified the sole cause was the sinusitis. 2009 WL 4456207, at *9. Respondent's second expert, specializing in pediatric infectious disease, testified that inactivated flu vaccine does not get into the central nervous system to stimulate this type of response, similar to Dr. Greenberg's testimony in the instant action. He too thought the cold was the cause of the meningoencephalitis. 2009 WL 4456207, at *10. The treating physician in Mouille, just as the treating physician in the instant action, testified for petitioner. The undersigned found petitioner's experts to be persuasive.

Based on a Shyface analysis, the undersigned in Mouille held that both the upper respiratory infection and the flu vaccine were substantial factors in causing Maurice Mouille's meningoencephalitis. 2009 WL 4456207, at *14. The undersigned cited to other cases in which the vaccinee had both an infection and a vaccination as substantial factors in causing acute transverse myelitis (three cases) or meningitis (one case; meningitis is also a central nervous system disease): Herkert v. Sec'y of HHS, No. 97-518V, 2000 WL 141263 (Fed. Cl. Spec. Mstr. 2000) (acellular DPT and cytomegalovirus caused transverse myelitis); Nash v. Sec'y of HHS, No. 00149V, 2002 WL 1906501 (Fed. Cl. Spec. Mstr. 2002) (whole-cell DPT and pneumococcus caused meningitis); Camerlin v. Sec'y of HHS, No. 99-615V, 2003 WL 22853070 (Fed. Cl. Spec. Mstr. 2003) (HiB vaccine and otitis media caused transverse myelitis); and Pearson v. Sec'y of HHS, No. 03-2751V, 2008 WL 5093378 (Fed. Cl. Spec. Mstr. 2008) (upper respiratory infection and hepatitis B vaccine caused transverse myelitis).

The undersigned does not actually know if petitioner in the instant action had an upper respiratory infection (URI) a week or two before the onset of her acute transverse myelitis. The only proof that she did is the history she gave to various hospital treaters. But assuming she did have a URI, it occurred within the same appropriate time period for causation from the influenza vaccine. As Dr. Kinsbourne testified, if the undersigned holds that petitioner did have a URI within the appropriate time frame, both are substantial factors in causing petitioner's transverse myelitis. The undersigned finds Dr. Kinsbourne's testimony persuasive.

Respondent is well aware that petitioner does not have the burden of providing epidemiologic studies in support of petitioner's allegations. Knudsen, Althen, and Capizzano. Petitioner also does not have the burden of proving the specific biologic mechanism explaining

how the vaccine caused the injury. Knudsen. Dr. Greenberg wants direct proof in order to be convinced that influenza vaccine can cause ATM. He wants an analysis of petitioner's spinal fluid to see if there were antibodies or cells there that recognize both spinal cord and flu vaccine. This would necessitate putting flu vaccine in a dish and a slice of petitioner's spinal cord in a dish, which was never done. That would be one type of direct evidence and another would be an animal model. He is unaware of any medical article showing that mice received flu vaccine and developed central nervous system demyelination. These are all fine ideas in the world of investigative medicine. They have nothing to do with the burden of proof of petitioners in the Vaccine Program and the Federal Circuit has specifically rejected that petitioners have to provide direct evidence in order to prevail.

In his own primary care guide for taking care of transverse myelitis, Dr. Greenberg and his co-author mention that vaccinations have been associated with transverse myelitis, although they say there is no conclusory evidence. At the hearing, Dr. Greenberg stepped back from his statement that vaccines have been associated with transverse myelitis to imply that he meant only simple rabies vaccines and other vaccines that contain nerve tissue. But the literature (which has been filed in this case) does not mention simple rabies vaccine; it does mention flu vaccine (as well as other vaccines). The point is not that there is conclusory proof from case reports, but that in the medical literature and, according to Dr. Kerr, who is Dr. Greenberg's former colleague at the transverse myelitis center of Johns Hopkins, also in the medical textbooks, doctors have connected vaccinations and acute transverse myelitis. As Dr. Kerr wrote, "it is widely reported in neurology texts that ATM is a post-vaccination event." No one, including Dr. Greenberg, has inserted the caveat in the literature that this association of

vaccination with ATM applies only to vaccines that contain nerve tissue, such as simple rabies vaccine.

The Federal Circuit in Capizzano and Andreu emphasized that the special masters should consider the opinions of the treating doctors. Here, petitioner's treating family physician, Dr. Costa, testified on her behalf. Respondent stressed through cross-examination of petitioner's doctors as well as direct examination of Dr. Greenberg that none of the hospital treaters identified the cause of petitioner's ATM as the flu vaccine and they wrote instead that she had postinfectious or postviral ATM. Thus, in this case, either there is a stalemate between Dr. Costa and petitioner's hospital treaters, or the undersigned has to pick one side as persuasive. The undersigned notes that Dr. Costa wrote that petitioner was to receive no more flu vaccinations and it was his office that gave her the flu vaccination at issue. That Dr. Costa would alter his practice's procedures based on what occurred in this case is of substance to the undersigned because he is still her treating physician. It is small surprise that treaters who were never going to see petitioner again for ATM would write what is commonly known: that URIs are frequently associated with ATM.

The undersigned finds that both Dr. Costa's and Dr. Kinsbourne's opinions on causation are persuasive. Dr. Costa testified as a fact witness. Therefore, the undersigned bases her analysis primarily on Dr. Kinsbourne's testimony. The flu vaccine together with a URI can set up a process called molecular mimicry which involves stimulating the production of an elevated level of interleukin (IL)-2 (according to Johns Hopkins) which causes the vaccinee's immune system to attack the myelin in a section of her spinal cord. This is a biologically plausible medical theory connecting the vaccine to the injury, fulfilling the first prong of Althen.

In the instant action, petitioner's flu vaccine, together with a URI that either occurred briefly thereafter or a couple of weeks later (depending on which history one accepts), caused her immune system to attack a section of her spinal cord myelin. This is a logical sequence of cause and effect, fulfilling the second prong of Althen.

The timing of one month between vaccination, URI, and onset of ATM is medically appropriate for an immune-mediated injury, fulfilling the third prong of Althen.

Petitioner has prevailed in proving a prima facie case of causation in fact. Dr. Kinsbourne testified that but for petitioner's receiving influenza vaccine, petitioner would not have had acute transverse myelitis

CONCLUSION

Petitioner is entitled to reasonable compensation. A telephonic status conference will be set to discuss how to resolve damages.

IT IS SO ORDERED.

December 17, 2009
DATE

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