OFFICE OF SPECIAL MASTERS

No. 99-0219V

(Filed: July 27, 2000)

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HILLARY JOHNSON, by and through her Parents and Next Friends, MARY JOHNSON and VERNON JOHNSON,	*	
Petitioners,	*	**TO BE PUBLISHED**
v.	*	
SECRETARY OF HEALTH AND HUMAN SERVICES,	*	
Respondent.	*	
* *		

Douglas Q. Meystre, Worcester, MA, for petitioners.
Vincent J. Matanoski, Washington, DC, for respondent.

DECISION

MILLMAN, Special Master

On April 9, 1999, petitioners filed a petition on behalf of their daughter, Hillary Johnson (hereinafter, "Hillary"), for compensation under the National Childhood Vaccine Injury Act of 1986[1] (hereinafter the "Vaccine Act" or the "Act"). Petitioners have satisfied the requirements for a prima facie case pursuant to 42 U.S.C. § 300aa-11(c) by showing that: (1) they have not previously collected an award or settlement of a civil action for damages arising from the alleged vaccine injury; and (2) tetanus-diphtheria (Td) vaccine was administered to Hillary in the United States.

[1] The National Vaccine Injury Compensation Program comprises Part 2 of the National Childhood Vaccine Injury Act of 1986, 42 U.S.C.A. §300aa-1 et seq. (West 1991), as amended by Title II of the Health Information, Health Promotion, and Vaccine Injury Compensation Amendments of November 26, 1991 (105 Stat. 1102). For convenience, further references will be to the relevant subsection of 42 U.S.C.A. § 300aa.

Petitioners allege that Td was a substantial factor in causing in fact Hillary's acute disseminated encephalomyelitis (ADEM). Respondent denies Td caused in fact Hillary's ADEM.

The court held a hearing in this case on April 6, 2000. Testifying for petitioners was Dr. Spencer G. Weig. Testifying for respondent was Dr. Subramaniam Sriram.

FACTS

Hillary was born on December 25, 1981. On May 18, 1995, she saw Dr. Brian O'Sullivan with a complaint of a chronic cough. She coughed predominantly with exercise. He had diagnosed her with exercise-induced asthma four years previously. Both sides of her family have a history of asthma and allergies. Her 12-year-old brother coughs with prolonged exercise. Her mother smokes cigarettes in the house. Med. recs. at 73.

On April 12, 1996, when Hillary was 14 years old, she received a Td vaccination. Med. recs. at 11. On May 2, 1996, she saw Dr. Stjepan Kereshi, a neurologist. Her chief problem was headache. A couple of years previously, she had had a bout of headaches, but they improved. Over the prior week (approximately April 25, 1996, 13 days after vaccination), she started to have a mild headache which had gradually gotten worse and was now severe. She had vomited twice. She did not have photophobia. Her headache was usually located in her forehead and stayed there. Hillary described it as a pressure type of pain. She had been taking Compazine and Fiorcet, but they did not help much. She felt light-headed and also looked pale. Hillary did not have a history of head injury. She denied she was under stress. Just before the headaches started, she did some strenuous physical activity in the gym which she had not done much of before. Hillary also complained of some numbness in both feet and legs below the knee. Her mother had headaches as a young child. Med. recs. at 83.

From May 9 to 16, 1996, Hillary was at the University of Massachusetts Hospital. The discharge diagnosis was ADEM. An MRI of her spinal cord showed disseminated demyelination, widened cervical spinal cord at C5 to C6, and no masses. An MRI of the brain showed intraventricular white matter lesions. Hillary gradually gained increased control over her bladder function. She had episodes of incontinence only when sleeping and when her mind was distracted. She had upgoing Babinskis bilaterally. Med. recs. at 88, 92, 93, 284, 285.

Dr. Paula McEvoy's neurological assessment of Hillary at the hospital was that her ADEM was probably triggered but not caused by her recent immunization. Supportive features of this assessment were the acute onset, her age, and the preceding immunization. Her seizures most likely were not secondary to an infectious etiology although immunization may have triggered the immunogenic process. Med. recs. at 145, 146.

Hillary has sequela of a neurogenic bladder (no spontaneous normal bladder contraction). Med. recs. at 314, 344.

Written Submissions

Petitioners submitted medical articles in support of the allegations of their petition. The first submission was "Relapsing Neuropathy Due to Tetanus Toxoid. Report of a Case."[2] The authors describe a 42-year-old man who had an episode of Guillain Barre syndrome (GBS), a peripheral demyelinating neuropathy, after each of three injections of tetanus toxoid over a period of 14 years. The theory behind causation is that the antecedent event triggers an immune response against the nerves in the patient. *Id.* at 113. In his first two episodes, the interval between vaccination and onset

[2] By J.D. Pollard and G. Selby, *J Neurol Sciences* 37:113-25 (1978).

was two weeks. In his third episode, the interval between vaccination and onset was 10 days. *Id.* at 114.

Pollard and Selby had little doubt that the tetanus toxoid caused the three clinical episodes of demyelinating neuropathy. *Id.* at 117. They cite the collection of literature from 1954 which lists all of the neurologic sequelae of typhoid-paratyphoid vaccination and states that 40% of patients had signs of central nervous system (CNS) disorder. *Id.* In explaining their causative thesis, the authors refer to the cell-mediated immune system which vaccinations affect. *Id.* at 122.

Petitioners also filed "Relapsing acute encephalopathy: a complication of diphtheria-tetanus-poliomyelitis immunization in a young boy."[3] A 7-year-old boy developed relapsing acute encephalitis after receiving two DPT vaccinations. The boy first manifested acute disseminated encephalitis. In the second episode, he had optic neuritis. The authors conclude that the vaccinations caused both these demyelinating episodes. The onset after the first DPT was two weeks. The onset after the second DPT was 10 days. *Id.* at 137. The authors state that both demyelinating diseases (the acute disseminated encephalomyelitis and optic neuritis) are immunomediated. *Id.* "Neurological complications due to an immuno-allergic mechanism do not differ clinically from those following viral infections." *Id.* at 138.

Petitioners lastly submitted "Encephalomyelitis-associated antimyelin autoreactivity induced by streptococcal exotoxins"[4] in support of their allegation that a bacterial infection, not just viruses, may cause ADEM. The authors used test tube (in vitro) testing to prove that streptococcus pyogenes (S. pyogenes) caused ADEM in a child. They state:

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[3] By J. Mancini, et al., *Eur J Pediatr* 155:136-38 (1996).

[4] By P.G. Jorens, et al., *Neurology* 54:1433-41 (2000).

> Acute disseminated encephalomyelitis (ADEM) is an autoimmune demyelinating disorder of the CNS, usually preceded by immunization or by a viral or bacterial infection. ... Once activated, autoreactive T-cells migrate rapidly into the CNS, and may become reactivated by myelin antigens in the brain and initiate the pathogenic autoimmune cascade.

Id. at 1433-34.

A three-year-old child had an ear infection for six weeks caused by S. pyogenes followed by ADEM. The authors state that the patient's massive demyelination is possibly related to pathogenic autoreactivity against myelin antigens which the S. pyogenes exotoxins triggered. *Id.* at 1439. In addition, the authors isolated myelin basic protein (MBP)-reactive T-cell clones which crossreacted with substances from the S. pyogenes. The authors conclude that their study "directly implicates *S. pyogenes* as an etiologic agent in encephalomyelitis. Many of the data presented are compatible with in vivo activation of immune cells by superantigens of this *S. pyogenes* strain." *Id.* at 1440.

Respondent submitted an excerpt from Adverse Events Associated with Childhood Vaccines. Evidence bearing on Causality.[5] R. Ex. A. The IOM states:

> There is biologic plausibility for a causal relation between vaccines and demyelinating disorders. The reports in the literature that describe a possible association between demyelinating diseases of the CNS (ADEM, transverse myelitis, and optic neuritis) are case reports. ... The case reports describe the demyelinating disease that occurs within the biologically plausible latency period of 5 days to 6 weeks, ... No population-based incidence rates for ADEM or optic neuritis were identified. This question [of causation] is difficult at best for rare adverse events and can be answered only if both good *age-specific* background rates for the specific disease in question are known and aggressive surveillance of adverse events is carried out or if large observational studies are done. None of this specific information is available when considering the relation between tetanus toxoid, DT, or Td and the occurrence of ADEM, transverse myelitis, or optic neuritis.

[5] Edited by K.R. Stratton, et al. (1994) 85-86. This is under the aegis of the Institute of Medicine (IOM).

> The evidence is inadequate to accept or reject a causal relation between tetanus toxoid, DT, or Td and demyelinating diseases of the CNS (ADEM, transverse myelitis, and optic neuritis).

Respondent also submitted "Risk of Serious Acute Neurological Illness After Immunization With Diphtheria-Tetanus-Pertussis Vaccine."[6] This study examines whether there is a statistically significant risk of serious acute neurological illness within seven days of vaccination of children younger than two years of age with DPT and finds there is not. It does not examine risk beyond the seven days. None of the children had ADEM. The authors agree that to rule out any possibility of an association between previous vaccination and neurological events, a study would have to be several times larger than theirs and would be extremely expensive. *Id.* at 40.

Respondent lastly submitted "Acute Disseminated Encephalomyelitis in Childhood: Report of 10 Cases."[7] The authors discuss ten children with ADEM, eight of whom had a preceding event of either an infection or vaccination. The authors state:

> Acute disseminated encephalomyelitis is an immunologically mediated inflammatory demyelinating disease of the central nervous system principally affecting the white matter. It is usually preceded by a viral infection or vaccination ....

Id. at 198.

Case number seven in the article involved an 11-year-old boy who had received 21 doses of nonhuman rabies vaccine for a dog bite one month previously. *Id.* at 199. The authors state that ADEM usually follows infections and has also been reported after MMR vaccine. *Id.* at 200.

TESTIMONY

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[6] By J.L. Gale, et al., *JAMA* 271:37-41 (1994).

[7] By R.A. Apak, et al., *J Child Neur* 14:198-201 (1999).

Dr. Spencer Weig testified first for petitioners. Tr. at 4. He is board-certified in pediatrics, neurology with a specialty in child neurology, and electroencephalography. Tr. at 5. He is the section head for the division of child neurology at Albany Medical Center and a full-time faculty member there. *Id.* He took care of Hillary when he was a full-time faculty member at the University of Massachusetts Medical Center from 1990-97. *Id.* He had a team working with him. Tr. at 6.

On May 9, 1996, Hillary's previous history was that she had been well. *Id.* On April 29, 1996, she saw her family physician with a five-day history of frontal, severe headaches. *Id.* The doctor ordered a head CT scan and neurological consultation. *Id.* The neurologist who saw her on May 2, 1996 felt her condition was most likely a prolonged migraine. Tr. at 7.

On May 9, 1996, Hillary was admitted to the University of Massachusetts Medical Center. *Id.* Over the preceding three to four days, she had more specific neurological symptoms: since May 6th, tingling, numbness in her hands and feet; since May 7th, difficulty getting up; and on May 8th, double vision and incontinence. *Id.* Hillary was first seen in the emergency room. *Id.* Dr. Weig saw her within her first several hours at the hospital. Tr. at 8. Hillary was scared, but she had normal mental status and speech. *Id.*

Her physical examination showed early swelling of the optic nerve heads, weak legs, some weakness in her arms, positive Babinski responses, hyperreflexia, and an abnormal sensory examination (sensation was cut off at mid-chest, indicating spinal cord difficulty). *Id.* They did an emergency MRI of her spinal cord, which was abnormal with at least two areas of inflammation: the neck or cervical area, and the thoracic area. Tr. at 9. Her spinal tap (LP) showed a mild increase in pressure of the spinal fluid and an inflammatory response. *Id.* She was diagnosed with at least myelitis. *Id.*

On May 10, 1996, a further MRI of the brain showed areas of inflammation. *Id.* The diagnosis was ADEM. Tr. at 9-10. Dr. Weig's plan was to treat Hillary with large doses of corticosteroids, i.e., oral prednisone. Tr. at 10. Dr. Paula McEvoy was the resident in pediatrics assigned to Hillary. Tr. at 11.

Within several days, Hillary made early improvement and could move her legs. *Id.* She was discharged from the University of Massachusetts on May 16, 1996 to a rehabilitation setting. Tr. at 11-12. Dr. Weig saw Hillary once or twice after discharge. Tr. at 12. Dr. Pamela Follett, a resident in pediatric neurology, followed her case. *Id.* Hillary's last visit to Dr. Weig was October 1996. *Id.* She has regained most of her neurological functions, but her residuum is bladder dysfunction. *Id.* She has incontinence and voiding problems (enuresis) which ADEM caused. Tr. at 12-13. A urologist is handling these problems. Tr. at 13.

Dr. Weig testified that ADEM is acute (having a relatively acute onset), disseminated (widespread in the CNS) encephalomyelitis (inflammation of the brain and spinal cord). *Id.* The mechanism of causation is unclear. *Id.* ADEM is usually not a random event, meaning there is a preceding event which triggers the inflammatory process. Tr. at 13-14. Over the last year, there has been a flare up with six children having ADEM in Albany, New York. Tr. at 14. In the past 12 - 18 months, the six children in Albany and most others he has seen in the past had an identifiable immunological challenge, usually an infection, one to two weeks before onset of their symptoms. Tr. at 14-15. The Apak article confirms this. Tr. at 15.

Dr. Weig stated that Hillary's immunological challenge was the tetanus vaccination she received on April 12, 1996. *Id.* She did not have any other exposures or infections. Tr. at 15-16. The doctors tested her for Lyme's disease and other infectious agents, which were negative. Tr. at 16. Dr. William Durbin, the infectious disease section head at the University of Massachusetts,

stated on May 9, 1996 that Hillary's epidemiology was essentially negative: no ill contacts, no animal exposures, no travel, no tick or animal bites, no tuberculosis, and no preceding illness. Tr. at 16-17. He doubted she had any primary active infectious cause of her syndrome. Tr. at 17-18.

ADEM need not follow a virus or live virus vaccine to have a causative relationship with a preceding infection or antigen. Tr. at 19. Mycoplasma pneumonii infection has been documented at his hospital and linked to ADEM. Tr. at 19-20. This is not a virus or a bacterium either, but it is known in literature and in his experience to cause ADEM. *Id.* It is treated with antibiotics. Tr. at 20. ADEM occurred 10 days into the course of an upper respiratory infection. Tr. at 21-22. This is consistent with common experience in child neurology: most children with ADEM are recovering from a preceding illness. Tr. at 22.

Dr. Weig does not distinguish between trigger and cause as Dr. McEvoy did in her notation in the medical records concerning tetanus vaccination and Hillary's ADEM. Tr. at 23-24. There are multiple viral and bacterial agents and vaccines associated with ADEM. Tr. at 24. Dr. Weig holds his opinion of causation from the tetanus vaccination more likely than not. Tr. at 25.

On cross-examination, he stated there is no clinical test to prove that tetanus vaccine caused Hillary's ADEM. Tr. at 26-27. He relies on timing, no alternate explanation, and the occurrence of an immunization. Tr. at 27. An immunization is the appropriate type of event to elicit ADEM. Tr. at 28. Tetanus toxoid and diphtheria toxoid vaccine is a potent trigger of the immune system. *Id.* The aim is to induce the immune system to produce antibodies to particular agents. *Id.* The immune system may be activated in a more general sense. *Id.*

ADEM is not an autoimmune disease. Tr. at 29. It is an immunologically-mediated disease. *Id.* Its actual pathology is mediated by the body's immune system. *Id.* It is also a postinfectious

process, consisting of the misfiring of the immune system. *Id.* ADEM is monophasic. Tr. at 30. The prodrome is the preceding event linked causally to the subsequent illness. Tr. at 31. The lesions are areas of inflammation and demyelination. *Id.* There is no known direct crossreactivity between tetanus toxoid and the central nervous system. Tr. at 32. There is also no laboratory analysis. *Id.*

Dr. Weig is a clinician. *Id.* An autoimmune disease, such as lupus erythematosis, is chronic and ongoing. Tr. at 33-34. An immune-mediated disease process is monophasic and post-infectious, such as ADEM and GBS. *Id.* Most chapters in textbooks list ADEM as a post-infectious syndrome and not as an autoimmune disease. Tr. at 34. He is aware of experimental allergic encephalomyelitis or EAE. *Id.* It is monophasic and called autoimmune. Tr. at 35. Multiple sclerosis is not monophasic. *Id.* Part of EAE is "allergic." Tr. at 36. Hillary's ADEM is the only case he has seen that he would attribute to a vaccination. Tr. at 37. In Dr. Weig's other cases, other than mycoplasma pneumonii (which is both viral and bacterial) or acute upper respiratory infection, he does not recall if he figured out a specific agent other than knowing the child had previously been ill with a virus. Tr. at 37-38.

The medical literature describes a child who received two diphtheria, tetanus, and poliomyelitis vaccines five years apart and had recurrent bouts of ADEM after each. Tr. at 38-43. Dr. Weig could not distinguish whether diphtheria or tetanus vaccine is the potential agent here. Tr. at 45. No literature points to either as the cause of ADEM. *Id.* Theoretically, ADEM could occur coincidentally post-vaccination. Tr. at 46.

When asked how to distinguish coincidence from cause, Dr. Weig responded that the time line for Hillary's illness was typical of other ADEM cases with a preceding illness or immunological challenge. *Id.* He looks at the big picture. *Id.* He does not know the background rate for ADEM. Tr. at 49. If Hillary had had an upper respiratory infection at the time she had her vaccination, Dr.

Weig could not determine which of the two was the cause of her ADEM. Tr. at 50-51. With any infection or immunization, Dr. Weig would look at what occurred 10 to 21 days before onset. Tr. at 55. Beyond that, there would be no causal relationship. *Id.* The appropriate immunologic event is the one with the right timing and challenge. Tr. at 56.

Dr. Subramaniam Sriram testified for respondent. Tr. at 57. He is an internist and neurologist whose specialty is immune-mediated demyelinating processes. Tr. at 58. He defined ADEM as an immune-mediated disorder directed against antigens, resulting in inflammation and damage to the myelin sheath. Tr. at 58-59. It is believed to be autoimmune because it is directed against cell antigens. Tr. at 59. The medical literature does not indicate that either tetanus or diphtheria toxoid causes ADEM. *Id.* There are only anecdotal case reports. Tr. at 59-60. The IOM states that the evidence is inadequate to accept or reject a causal relationship between Td vaccine and ADEM. Tr. at 60-61.

Dr. Sriram also stated that there is no background rate for ADEM. Tr. at 61. Moreover, there are no known sequence homologies, i.e., similarities between an antigen and the proteins in amino acids, between tetanus toxin and neural antigens which would create molecular mimicry and lead to an autoimmune response. Tr. at 62-63.

Dr. Sriram runs the largest multiple sclerosis (MS) clinic in Tennessee, sees patients in the morning, and does research in the afternoon. Tr. at 67. He has seen one or two ADEM patients a year for 20 years. *Id.* He can always find a preceding upper respiratory infection or cough, but no cultured virus (no increase in antibody response). Tr. at 67-68. He has never had a vaccination antecede ADEM. Tr. at 70. Treatment, not the cause, of ADEM was of interest to Dr. Sriram. Tr. at 71.

Dr. Sriram testified that it was insignificant if there was no known antecedent in Hillary's case because in 50 percent of cases, there is no antecedent infection. Tr. at 72. The Apak article reported a high (40 percent) incidence of relapse of ADEM. Tr. at 73. Dr. Sriram wondered if these were actually childhood MS cases. *Id.* He thought the diagnosis of ADEM in the Apak paper questionable. *Id.* He has teenage MS patients. *Id.* Twenty percent do not have antecedent infections. Tr. at 73-74. Dr. Sriram admitted that Hillary does not have MS. Tr. at 74.

In most cases of ADEM, an infectious cause cannot be ascertained. Tr. at 75-76. Ascertainment would depend on identifying a definite organism by culture or a rising titer. Tr. at 76. A weak viral infection can be subclinical followed by severe ADEM and, conversely, a strong viral infection can be followed by a weak ADEM. Tr. at 76-77. (Dr. Weig agreed with this.) Tr. at 77. For a structure to have homology, the amino acid of the infectious agent must be similar to the MBP of the nervous system. Tr. at 75.

Postvaccinial encephalomyelitis has been related to smallpox or vaccinia vaccine. Tr. at 78-79. The term now has been used to refer to all vaccines, which Dr. Sriram regards as a mistake. Tr. at 79. Rabies vaccine and smallpox vaccine have been shown to cause ADEM. *Id.* However, rabies used to be made in the spinal cord. Tr. at 80. Pasteur grew rabies vaccine in the spinal cord of dogs. *Id.* His vaccinees contracted ADEM. *Id.* Later, duck embryo was used to make the Semple rabies vaccine, which also caused ADEM. *Id.* There is no ADEM following Td vaccine to his knowledge. Tr. at 87.

Smallpox vaccine causes ADEM, but we do not know the mechanism or the homology of causation, that is, evidence and epidemiology in support of that conclusion. Tr. at 81. There may be molecular mimicry in other viruses. Tr. at 84-85. The reason smallpox vaccine causes ADEM is that the components of the vaccine contain something similar to the human nervous system. Tr.

at 83. The Pollard and Selby study that found that Td vaccine caused GBS has nothing to do with Td causing ADEM. Tr. at 86-87.

Dr. Sriram agreed that Hillary's neurogenic bladder is due to her ADEM. Tr. at 88-89. He also agreed that much about ADEM is unknown. Tr. at 89. He said we will never understand how smallpox vaccine causes ADEM. *Id.*

Dr. Sriram agreed that Hillary's Td vaccination on April 12, 1996 was an immunological challenge to her body and that she did not have another immunological challenge such as an infection. Tr. at 90. However, because a lot of infections may be subclinical, Dr. Sriram could not exclude the possibility that Hillary had a subclinical infection. Tr. at 91. The medical literature does not associate Td and ADEM. Tr. at 92. It associates ADEM with viral syndromes, rabies vaccine, and smallpox vaccine. *Id.* Dr. Sriram would pick an unknown or idiopathic cause of Hillary's ADEM over the Td vaccine because of the weak evidence in support of causation. Tr. at 93-94.

DISCUSSION

Petitioners are proceeding on a theory of causation in fact. To satisfy their burden of proving causation in fact, petitioners must offer "proof of a logical sequence of cause and effect showing that the vaccination was the reason for the injury. A reputable medical or scientific explanation must support this logical sequence of cause and effect." Grant v. Secretary, HHS, 956 F.2d 1144, 1148 (Fed. Cir. 1992). Agarwsal v. Secretary, HHS, 33 Fed. Cl. 482, 487 (1995); see also Knudsen v. Secretary, HHS, 35 F.3d 543, 548 (Fed. Cir. 1994); Daubert v. Merrell Dow Pharmaceuticals, Inc., 509 U.S. 579 (1993).

Without more, "evidence showing an absence of other causes does not meet petitioners' affirmative duty to show actual or legal causation." Grant, supra, 956 F.2d at 1149.

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

In essence, the special master is looking for a reputable medical explanation of a logical sequence of cause and effect (Grant, supra, 956 F.2d at 1148), and medical probability rather than certainty (Knudsen, supra, 35 F.3d at 548-49). To the undersigned, medical probability means biologic credibility or plausibility rather than an 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.

Although the United States Supreme Court in Daubert v. Merrell Dow Pharmaceuticals, Inc., 509 U.S. 579 (1993), listed various criteria for federal district court judges to follow in their role as gatekeeper for the admission of scientific and medical evidence, such criteria are merely aides in evaluation, rather than prescriptions, for the Office of Special Masters. Even in federal district courts, "Daubert's list of specific factors neither necessarily nor exclusively applies . . . in every case . . . [and its] list of factors was meant to be helpful, not definitive." Kumho Tire Co., Ltd. v. Carmichael, 526 U.S. 137, 141, 151 (1999).

In the Office of Special Masters, even the Federal Rules of Evidence are not required.[8] Invariably, consistent with the legislative intent in creating the Vaccine Program, the special masters admit most evidence. But see, Domeny v. Secretary, HHS, No. 94-1086V, 1999 WL 199059 (Fed. Cl. Spec. Mstr. March 15, 1999), aff'd, (Fed. Cl. May 25, 1999) (unpublished), aff'd, No. 99-5130 (Fed. Cir. Apr. 11, 2000) (rejecting proffer of dentist's testimony for diagnosis of a neuropathy).

As the Federal Circuit stated in Knudsen, supra, 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." Thus, the task before the undersigned is not to delineate how petitioners' evidence does or does not satisfy the Daubert litany of support in peer-reviewed medical literature, concurrence among a majority of physicians in the field of immunology and/or neurology, and confirmative testing of methodology. Rather, the task is to determine medical probability based on the evidence before the undersigned in this particular case.

The evidence in this case is very much a battle of the experts. Dr. Weig, Hillary's treating pediatric neurologist, opined that Hillary's Td vaccination was the immunological challenge that produced her ADEM two weeks later. The timing is crucial in understanding the nature of an immune-mediated disease. The medical literature, particularly the article showing that streptococcus pyogenes, a bacterial infection, caused ADEM in a child, shows that bacterial infection, not only viruses and viral vaccines, cause ADEM.

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[8] CFC Rules, Vaccine Rule 8(b) Evidence. "In receiving evidence, the special master will not be bound by common law or statutory rules of evidence. The special master will consider all relevant, reliable evidence, governed by principles of fundamental fairness to both parties."

Dr. Sriram, for respondent, on the other hand, relies heavily on the Institute of Medicine's position of neutrality on causation and his own experience with animal studies dealing with models of multiple sclerosis. He is willing to accept that smallpox vaccine causes ADEM without understanding the mechanism or homology that permits it to do so (and says we will never know). However, he is unwilling to accept that Td vaccine can cause ADEM and the reason he is unwilling is that we do not know the mechanism or homology. If the absence of that knowledge does not foreclose his accepting that smallpox vaccine causes ADEM, why should the same absence foreclose his accepting that Td vaccine caused Hillary's ADEM? Dr. Sriram's lack of consistency is not assuring in the search for credibility here.

Moreover, Dr. Sriram posits that he prefers to believe that a subclinical infection is the cause of Hillary's ADEM rather than the known immunological challenge, i.e., the Td vaccine. This position is also not reassuring to the undersigned. A subclinical infection and no infection have the same visible effect: no symptoms. Hillary seemed perfectly healthy. For the special master to assume Hillary had a subclinical infection in order to conclude that Td vaccine was not the only immunological challenge to her system would require an unsubstantiated evidentiary leap. Dr. Sriram's final position on causation is that he would pick an unknown or idiopathic cause over the Td vaccine. The undersigned gets the sense that Dr. Sriram would not accept Td vaccine as the cause under any circumstance because that is not his role for respondent.

The medical note which Dr. Paula McEvoy wrote assumed that Td probably triggered Hillary's ADEM. Hillary's treating pediatric neurologist Dr. Weig testified that he agreed that Td vaccine probably caused her ADEM. His reasoning shows a clear logical sequence of cause and effect, to wit, that Td vaccine, for whatever reason, provoked an immunological reaction in Hillary at just the right time sequence (about two weeks) that one would look for an immunological

challenge. This is not a situation where the testimony relies solely on temporal association, which by itself would be legally insufficient to support affirmatively petitioners' burden of proof. Where an immunological process requires a certain number of days or weeks to manifest itself (as it does here) and the challenge and effect are so linked temporally, that process is sufficient legally to support an expert opinion of causation.

But there is more evidence than just an appropriate temporal process in Hillary's case. The medical literature submitted herein is replete with causal relationships between vaccinations and illness. The intervals in the Pollard and Selby paper were two weeks after tetanus toxoid for the first two episodes of GBS, and 10 days for the last episode. The onset interval of acute relapsing encephalomyelitis in the Mancini article was two weeks after the first DPT and 10 days after the second DPT. Obviously, neither tetanus toxoid nor DPT is a viral vaccine. These articles plus the Jorens article on streptococcus pyogenes causing ADEM show that non-viral antigens can result in immune-mediated illnesses such as ADEM.[9]

Petitioners have satisfied their burden of showing a logical sequence of cause and effect between Td vaccine and Hillary's ADEM because: (1) the medical personnel who treated Hillary agreed that her Td vaccination caused her ADEM; (2) the medical literature is supportive that vaccinations are a known cause of ADEM (and includes the occurrence of bacterial infection causing ADEM); and (3) the whole sequence of immunological challenge and illness occurred within the proper temporal framework to allow for the demyelination process,.

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[9] Respondent's literature submissions were the IOM report (which was neutral), the Gale article which examined serious illness only within 7 days of vaccination and, not surprisingly because the interval was so short, did not deal with ADEM; and a submission stating that ADEM is usually related to a viral infection or vaccination, and in one case with a prior vaccination, the onset interval was one month.)

Respondent's expert was willing to accept that smallpox vaccine causes ADEM without understanding the mechanism or the homology to explain it. The undersigned is similarly willing to accept that Td vaccine was a substantial factor causing Hillary's ADEM without understanding the mechanism or homology. The Federal Circuit in Knudsen specifically does not require more.

Moreover, the Federal Circuit does not require that epidemiological proof support petitioners' allegations. That there is no background rate for ADEM and thus no way to determine if Td vaccinees contract ADEM at a higher rate than background is legally irrelevant. In Knudsen, the Federal Circuit rejected the prior holding that because epidemiology shows that more individuals have encephalopathy after viral infections than after DPT vaccine, therefore, a virus and not DPT had to have caused petitioners' child's encephalopathy, stating:

> 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.

Petitioners' evidence herein shows a logical sequence of cause and effect based on reputable medical opinion, medical literature, and understanding of immunological processes. Td vaccine was a substantial factor in causing in fact Hillary's development of ADEM.

CONCLUSION

Petitioners are 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 the filing of life care plans, unless the parties agree on a joint life care plan. The parties should be aware that alternate dispute resolution is available to them as well, and if they choose ADR, they

should contact the undersigned. Should the parties not be able to settle this case, the undersigned will hold a damages hearing.

IT IS SO ORDERED.

_____ _____

DATE Laura D. Millman
Special Master