OFFICE OF SPECIAL MASTERS

October 29, 2003

ALEXANDER CAMERLIN, by his Mother and Next Friend, KIMBERLY CAMERLIN,	*	
Petitioners,	*	No. 99-615V PUBLISHED
v.	*	
SECRETARY OF THE DEPARTMENT OF HEALTH AND HUMAN SERVICES	*	
Respondent.	*	

Ronald C. Homer, Sylvia Chin-Caplan, Boston, MA, for petitioner.
Vincent J. Matanoski, Washington, DC, for respondent.

DECISION

MILLMAN, Special Master

On August 4, 1999, petitioner filed a petition on behalf of her son, Alexander Camerlin (hereinafter, "Alexander"), for compensation under the National Childhood Vaccine Injury Act of 1986[1] (hereinafter the "Vaccine Act" or the "Act"). Petitioner has satisfied the requirements for a prima

[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.

facie case pursuant to 42 U.S.C. § 300aa-11(c) by showing that: (1) he has not previously collected an award or settlement of a civil action for damages arising from the vaccine injury; and (2) HiB vaccine was administered to Alexander in the United States.

Petitioner alleges that HiB was a substantial factor in Alexander's contraction of acute transverse myelitis (TM) and/or acute disseminated encephalomyelitis (ADEM). Respondent concedes that Alexander had ADEM/TM but states that HiB was not its cause.

The court held a hearing in this case on July 1, 2003. Testifying for petitioner were Dr. Elizabeth C. Dooling and Dr. Ralph Shapiro. Testifying for respondent were Dr. Robert S. Daum and Dr. John T. Sladky.

FACTS

Alexander was born on April 23, 1990. On January 3, 1991, he saw the doctor for irritability since 4:30 a.m. His right eye was swollen and his right hand was puffy. He had been screaming for two hours and had a temperature of 101°. Med. recs. at Ex. 5, p. 60. On January 5, 1991, he went to the doctor with left otitis media and was prescribed Augmentin. Id.

Eleven days later, at nine months of age, he received HiB vaccine on January 16, 1991. On January 18, 2001, he was back to the doctor, having developed a fever of 105° that morning. He was twitching and sent to the ER. He was floppy and toxic-appearing. Med. recs. at Ex. 5, p. 59. An MRI showed slightly enlarged lateral ventricles. He had some swelling in the C1-C8 sections of his spinal cord with increased signal on T2-weighted MRI. His Babinskis were upgoing with slightly increased tone. Alexander was diagnosed with cervical TM. Med. recs. at Ex. 2, p. 1.

Alexander was admitted to Baystate Medical Center on January 18, 1991 and discharged on February 13, 1991. Med. recs. at Ex. 13, p. 184. Dr. L. Nordstrom, Alexander's pediatrician, wrote the admission history stating that Alexander was in his usual state of good health until 12 days prior to admission when he developed otitis media and was treated with Amoxicillin. He received HiB vaccine and, within 36 hours, started to develop temperatures up to 105° and became lethargic. Dr. Nordstrom sent him to the ER. On physical examination, Alexander was extremely lethargic, almost somnolent at times, and had a high temperature. Neurologically, he showed little spontaneous movement. On January 21, 1991, he appeared much weaker and floppy. He was diagnosed as having cervical TM. On January 22, 1991, Alexander developed salt-wasting syndrome, cerebral in nature. Med. recs. at Ex. 13, p. 185.

Other Submissions

Petitioner filed Exhibit 21, Tab A, "Autoimmunity through infection or immunization," by M. Regner and P.-H. Lambert, 2 *Nature Immunology* 3:185-88 (2001). The authors discuss inducing an encephalitis model in animals with a peptide taken from a *Haemophilus influenzae* protein–which shares 6 of 13 amino acids with proteolipid protein. Infection with this virus also caused disease. Id. at 186. In discussing various disease models and the possibility that molecular mimicry and trigger factors might work in tandem, the authors state that viral infections might subclinically prime autoreactive T cells without causing clinical disease at the time of infection but, later, after an appropriate time interval, nonspecific stimuli may activate these T cells. Experiments on mice using this methodology caused white matter lesions in the central nervous systems of these mice. Id. at 186.

Respondent filed Exhibit F, a chapter on HiB by Dr. Daum. (It is chapter 193 of Nelson's Textbook of Pediatrics, 16th ed., pp. 833-37 [2000].) Dr. Daum describes otitis media in his chapter:

> Acute otitis media is one of the most common infectious diseases of childhood. It is thought to result from the spread of bacteria from the nasopharynx through the eustachian tube into the middle-ear cavity. Usually because of a preceding viral upper respiratory tract infection, the mucosa becomes hyperemic and swollen, resulting in obstruction and an opportunity for bacterial multiplication in the middle ear.

Id. at 837.

Dr. Daum states:

> Noninvasive *H. influenzae* infections such as otitis media... usually caused by nontypable strains, probably gain access to sites such as the middle ear and sinus cavities by direct extension from the pharynx. The factors facilitating spread from the pharynx include eustachian tube dysfunction and antecedent viral infections of the upper respiratory tract.

Id. at 834.

TESTIMONY

Dr. Elizabeth C. Dooling testified first for petitioner. She is a board-certified pediatric neurologist, an Associate Professor of Neurology at Harvard, and a staff neurologist and staff pediatrician at Massachusetts General Hospital. Her specialty is developmental anomalies and brain tumors. Tr. at 6, 7.

Dr. Dooling saw Alexander for a second opinion in April 1991. Tr. at 8. He had been fussy the evening of his HiB and given Tylenol. Eleven days previously, he had otitis media (OM) and was on antibiotics. Id. At 4:30 a.m., the morning after the vaccination, he was spread-eagled and moaning. Tr. at 9. He was taken to the Emergency Room at Bay State Hospital. His fever reached 105° and he

was very irritable, lethargic and toxic. Id. His spinal fluid tap showed an elevated white blood cell count (36 white cells of which 51% were polys, and a mildly elevated protein of 36). His glucose was normal as were his cultures. The diagnosis was an acute encephalitic process. He had no movement of his legs and arms. He was irritable and somnolent. Tr. at 10. The MRI showed swelling and a postinfectious process. Tr. at 11.

Dr. Dooling's opinion is that the HiB was a substantial factor in this process. Alexander had been vaccinated three times before his HiB vaccination without any adverse event. Tr. at 12. Medical literature shows that vaccines, including HiB vaccine, can lead to demyelinating disorders. Tr. at 13. It is very uncommon for a child under one year of age to have an acute encephalomyelitis or a transverse myelitis. Tr. at 15. There can be a latent period that can be as short as one day. Tr. at 17-18. Alexander had periventricular changes in his brain, but not multiple lesions within the brain parenchyma. Tr. at 19-20.

Alexander had been a healthy boy the day before his vaccination. Tr. at 20-21. There was no evidence of bacterial or viral infection in Alexander. His cultures were negative. Tr. at 22. Dr. Dooling also opined that Alexander's OM was another substantial factor in his TM. Tr. at 24. He was recovering from the OM when he received HiB vaccination which affected his immune responses, making him more vulnerable. Id. These two substantial factors shortened the onset interval in Alexander's case. Tr. at 25.

Dr. Dooling consulted with Dr. Donald Medearis, Chief of Children's Service and an infectious disease specialist, on this case. Tr. at 26. Dr. Medearis consulted a doctor at CDC. There were two reports of adverse events following HiB with TM or encephalitis in late 1991. Tr. at 28. (Alexander's

case was reported to the CDC, according to respondent's counsel. Tr. at 38. It is one of three reported to the Institute of Medicine. Tr. at 39.)

Dr. Dooling stated that there is a synergy between infecting organisms in the medical literature such that when one is recovering from an infection, the immunologic response alters, and a second provoking agent produces a more florid response, aggravating or magnifying it. Tr. at 29.

Dr. Dooling opined that if Alexander had not received HiB vaccine, he would not have contracted TM subsequent to his ear infection. Tr. at 32. Alexander had finished his antibiotic regimen when he received HiB. Tr. at 42. On January 16, 1991, Dr. Nordstrom checked his ears. Id. In the hospital, all of Alexander's mucous membranes were inflamed and his ears were red. Tr. at 43. Dr. Dooling said that, even though the ears may have been clear when he received his HiB vaccination, we do not know if his immune system had recovered completely. Tr. at 44. Any upper respiratory tract infection, including OM, can lead to TM. Tr. at 45. She would not vaccinate someone who had recently recovered clinically from a prior infection. Tr. at 53-54.

Dr. Ralph S. Shapiro testified next for petitioner. He is board-certified in pediatrics and pediatric hematology and oncology. He also practices clinical immunology. Tr. at 57. His area of interest is developing therapeutic interventions for immunologic diseases and autoimmune diseases. Tr. at 58.

Dr. Shapiro was struck by Alexander's catastrophic event immediately after vaccination. He was also struck by Alexander's swelling of his eye and arm at the time he had OM. Tr. at 59. In most OM, one does not get swelling of the eye and arm. Id. Alexander may have had haemophilus B infection at the time because of his swelling. It is a very aggressive organism and causes cellulitis,

meningitis, and pneumonia because it has the ability to invade tissue. Tr. at 60. Alexander was in the recovery phase just at the time he received HiB vaccine. Tr. at 60-61.

Dr. Shapiro stated there is a lag-time for the body's immune system to recover homeostasis after infection, which may take up to one month. Tr. at 62. In the majority of cases, there should be no problem vaccinating someone with a mild infection. Tr. at 63.

Transverse myelitis or any inflammatory central nervous system disease caused by an immune response requires a priming event and then some type of triggering event. Tr. at 67. The priming event sensitizes the effector cells, which are most often T cells. T cells have to recognize something present in the cells they attack in order to damage them. He assumes that the myelin was attacked. Id. The cells proliferated and released inflammatory proteins to increase tissue damage and swelling. Dr. Shapiro believes the priming event occurred prior to Alexander's vaccination which was the trigger. Tr. at 67-68. There is scientific evidence that haemophilus has a protein that shares some of the sequences of myelin basic protein complement, that is, proteolipid protein. Because of the enormity of Alexander's reaction to HiB vaccine, he believes that Alexander had haemophilus influenza beforehand. Tr. at 68. Within 36 hours of vaccination, he had enough inflammation to spike fevers as high as 105° and progress to a critical state. Id.

It may have been because of Alexander's prior exposure to this infection within a critical time frame that the vaccine rechallenged him with a similar antigen and he had a lot of activated cells already challenged. Tr. at 69. These cells are primarily T cells, positive and negative subsets, which draw in neutracils, and other inflammatory cells. Id. Sensitization occurs reaching a certain threshold of immune reaction before the magnitude of response develops the clinical demyelinating disorder. Tr. at 70.

Animal models show this clearly–antigenic challenge causing priming and a trigger within a critical time frame. Id.

Alexander's vaccination was at a critical time because 10 to 11 days beforehand, he had an antigenic challenge and the vaccination accelerated his immune reaction. That period of time is when T cells are at their peak of reactivity. Tr. at 71. Dr. Shapiro does not know what the first sensitization event was, but it activated Alexander's T cells to attack his myelin or he would not have had TM. Tr. at 72. Conjugated haemophilus B vaccine, because it contains a protein to trick the baby into responding, is a very profound stimulus to his immune system. Tr. at 74. The child does not make a good antibody response to the first vaccination, but he does make a T-cell response. Tr. at 75. That is the reason for doing the priming at a young age so that the child will make a better antibody response later. Id. T cells regulate a lot of immune reaction. Tr. at 76-77. There is a bystander effect as well where other immune cells become activated. Tr. at 77.

Cytokines will make the blood-brain barrier more permeable. Tr. at 78. The DeStefano article[2] which concludes that certain vaccines do not cause demyelinating illness applies to adults. Tr. at 80. Children are more vulnerable to adults to have their blood-brain barriers breached, plus they are exposed to different types of antigenic insults. Id.

Haemophilus B influenza has protein-sharing homology with proteolipid protein. Tr. at 83. It may trigger an immune reaction in the nervous system which may be harmless unless the cells get in the

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[2] "Vaccinations and Risk of Central Nervous System Demyelinating Diseases in Adults," by F. DeStefano, et al., 60 *Arch Neurol* 504-09 (2003) (R. Ex. V). The authors conclude after conducting an epidemiologic analysis that vaccination against hepatitis B, influenza, tetanus, measles, or rubella is not associated with an increased risk of multiple sclerosis or optic neuritis.

brain or spinal cord. Tr. at 84. Host susceptibility plays a role in autoimmunity. Tr. at 84-85. Timing of events is important because there is a critical time to have a disease. Tr. at 85. Infection with one organism and then a second infection elicits inflammatory cytokines in animal models. Tr. at 86. In Alexander, T cells had to have been present that were reactive against myelin before the clinical event took place and he assumes that this happened with the OM, but OM is not the only way it could have happened. When Alexander received the vaccine, this accelerated the immune response leading to TM. Tr. at 89.

Doctors do not give the same vaccine in the same month because they are more likely to get an exaggerated response if they do. Tr. at 91. HiB vaccine was a substantial and a critical factor in this case because, without it, Alexander would not have developed TM. Tr. at 92. Haemophilus infection primed Alexander and the HiB vaccine acted as the trigger. Tr. at 96, 106. The vaccine was an accelerant or adjuvant to a subclinical process. Tr. at 107.

Dr. Robert Daum testified for respondent. He is a pediatric infectious disease specialist at the University of Chicago. Tr. at 110. He participated in nine clinical trials of HiB vaccines and has authored or co-authored 36 original articles on HiB disease or vaccine. Id. Conjugated HiB vaccine's protective antigen is a carbohydrate or sugar molecule, either a long version called a polymer, or a short version called an oligomer, both taken from the type B polysaccharide. Tr. at 112. Because the molecule is not particularly protective in young children, it is hooked to a protein carrier to cause recipients to be immunogenic. Id.

The HiB that Alexander received is recommended to be administered in four doses, with brisk antibody response after the third dose, but not after the first. Tr. at 114. The T cells recognize that the vaccine has been administered, but there is no massive inflammatory response. Tr. at 115.

Dr. Daum testified that Dr. Shapiro's theory does not make sense because if Alexander's prior OM were caused by haemophilus B infection, he would have been sensitized to haemophilus B protein, but the HiB does not contain haemophilus protein. Tr. at 117. If Alexander's OM were caused by HiB infection, T cells would respond to the protein antigen in the HiB, but HiB vaccine does not contain HiB protein. Tr. at 116-17.

Dr. Shapiro responded that HiB vaccine did not stimulate the exact same pool of cells directly but rather accelerated the immune reaction that was going on in other cells. Tr. at 118. The vaccine has the carbohydrate which stimulates cells through the T cells in the milieu of inflammatory cytokines. Tr. at 119-20. Dr. Daum stated there is no evidence for this. The first vaccination does not cause non-specific T-cell polyclonal stimulation. Tr. at 120. A carbohydrate is not a non-specific activator of T cells. Id. Dr. Shapiro responded that there is evidence of lymphoproliferative response with tetanus toxoid. Tr. at 121. Dr. Daum stated this is not relevant to HiB because tetanus is a very potent T-cell activator, unlike a carbohydrate antigen. Tr. at 122. Dr. Shapiro responded that it does not matter what the stimulant is. The body responds to carbohydrate as if it were a protein when the vaccine is conjugated. Tr. at 123. Dr. Daum stated he had not seen this type of immune response. Id.

When Alexander saw his doctor on January 3, 1991 with a fever, swollen right eye, and puffy right hand, he did not have OM and his temperature was normal. He was prescribed an antihistamine for an allergic reaction, and he got better by himself. Tr. at 124. If HiB had caused his OM, Alexander

would have been seriously ill at that time and not gotten better, and the prescription would not have been Benadryl. Tr. at 124-25. On January 5, 1991, Alexander returned to the doctor with left OM. There was no mention of his eyelid or hand. The vast majority of haemophilus influenza strains that cause OM do not have carbohydrate and are unencapsulated strains, sometimes called untypable strains. Tr. at 126. HiB is an infrequent cause of OM. Id. The doctor prescribed two antibiotics (Augmentin). Tr. at 127. On January 16, 1991, Alexander's OM was fully resolved and it was appropriate to inoculate him with HiB vaccine. Id.

Dr. Daum testified that OM does not challenge our immune system, but is a localized infection. Id. Our immune system is active all the time. Tr. at 128. Alexander's swollen and puffy eyelid and hand are not symptoms of an infectious disease because they resolved in two days. Id. Dr. Daum does not know what caused them. Tr. at 129. (He was reminded that, on January 3, 1991, Alexander had also been screaming for two hours and had nasal discharge and a fever of 101.° Tr. at 133.) Dr. Daum's opinion is that Alexander did not have a reaction to HiB vaccine and he does not know the cause of his TM. Tr. at 138. HiB is one of the least reactive vaccines although vaccinees can get fever, but not 105°--usually a low-grade 101°. Tr. at 138, 139. Even if a child has a mild infection, the doctor should vaccinate him. Tr. at 135, 147.

Dr. Daum stated that Alexander's fever on January 3, 1991 could have been due to many things, e.g., response to an infection, but not an immune response (although it could be). Tr. at 147, 148. A mild febrile illness can develop into an OM. Tr. at 154. Dr. Daum does not know if Alexander had both meningitis and TM. Tr. at 160-61. He concludes by the results of the spinal tap (a few inflammatory cells) that Alexander did not have HiB meningitis when he was hospitalized. Tr. at

161, 162. He had a mild meningeal response. Tr. at 162. A temperature of 105° is a very brisk response to an inflammatory process. Id. In the pre-vaccine era, HiB infection caused OM in rare cases. Id. Dr. Daum disagrees that if one gives vaccinations close in time, one amplifies the immune response. He testified that vaccinations given close in time dampen the immune response. Tr. at 164. He does not know what causes TM. Tr. at 165. In Dr. Daum's opinion, neither Alexander's OM nor his HiB vaccine caused his TM. Id.

Dr. John T. Sladky testified next for respondent. He is a board-certified pediatric neurologist and chief of the department at Emery University. Tr. at 168. He wrote the chapter on pediatric inflammatory neuropathies for Swaiman's textbook on pediatric neurology. Tr. at 169. He has seen 32 cases of ADEM/TM in the last six years. Tr. at 170.

TM is uncommon in children under two years of age. Id. In half the cases, there is an antecedent, usually gastroenteritis. Tr. at 171. In the medical literature, there is an antecedent in 60% to 70% of the cases. Id. In his practice, he has not seen OM as the antecedent event nor is it in the medical literature, although infections and fever are. Tr. at 172.

Dr. Sladky agreed with Dr. Dooling that, because Alexander was encephalopathic, he probably had acute disseminated encephalomyelitis or ADEM, but it did not really make any difference for the purpose of the discussion if it were ADEM or TM. Tr. at 174-75. Alexander had both demyelination and Wallerian degeneration or axonal destruction because he did not recover. Tr. at 178. If it were just demyelination, he would have recovered. Id.

Dr. Sladky testified that Alexander had a non-specific viral syndrome on January 3rd. Tr. at 181. Because Alexander had a runny nose and a history of fever, it is not unreasonable to suppose he

had a cold. Tr. at 182. That OM would develop in the context of an upper respiratory infection is not surprising. Tr. at 181-82. Dr. Sladky testified that antibiotics cleared up Alexander's OM which did not cause his ADEM/TM after his vaccination. Tr. at 182.

There is no evidence that haemophilus influenza infection is related to central nervous system demyelination. Id. OM does not lead to central nervous system demyelination. Id. There is no evidence that HiB vaccine leads to ADEM or TM. Tr. at 182-83. If he has a child come in with ADEM, he always asks if he had a recent immunization. Tr. at 183. The presence of an antecedent event does not necessarily mean causality. Tr. at 184. The timing here between vaccination and onset of disease is ridiculously short. Tr. at 185. It takes ten days between exposure to an antigen and the onset of the disease in experimental animal models. Tr. at 186.

Dr. Sladky testified that a process began some time before immunization which was destined to become ADEM/TM. He does not see how the vaccine could have played a causal role. Tr. at 188. The immune process probably began seven to 21 days prior to his first clinical signs. Tr. at 189. The possible causes of TM are gastroenteritis or upper respiratory infection. Id. The most likely explanation is a post-infectious or para-infectious phenomenon. Tr. at 190.

There are three possible scenarios. The first is that there is a subclinical infection or immune stimulus which we do not understand. Tr. at 190-91. Secondly, there are antecedent infectious events: gastroenteritis, cough, cold, fever, flu. Tr. at 191. Thirdly, there are children who have concurrent infection at the time of their neurologic dysfunction when the antecedent events were brief and self-limited, and then, after a period of latency, the neurologic dysfunction follows. Id. Some chronic infections may last for weeks and initiate an immunologic response and an immune-mediated attack on

the central nervous system at the same time the immune system is attempting concurrently to fight off the infection. Id.

One needs a latency period of one to two weeks from the initial immune stimulus, but infectious symptoms might not develop until after an incubation period. Tr. at 192. The immune system is certainly activated and it is an autoimmune phenomenon attacking the central nervous system in this case. Tr. at 193. The immunization is another antigen. Tr. at 194. If a child has a serious infection with fever, one does not immunize him because one wants him to recover. Id.

There is a difference in the blood-brain barrier in an infant and in an older child. Tr. at 200. But, at nine months of age, a child's blood-brain barrier is intact, comparable to an adult, and does not change. Tr. at 200-01. He would expect that if HiB vaccine caused ADEM/TM, we would see more cases. Tr. at 203.

For autoimmunity, it is a hypothesis that one needs host-susceptibility, environmental factors, and timing, and may be true in some cases. Tr. at 206, 207. Alexander's rhinitis and OM occurred within the appropriate time interval for a post-infectious process, if ADEM or TM were post-infectious. Tr at 208. Dr. Sladky testified that the HiB immunization did not make Alexander's immune system more active. Id.

In some haemophilus B protein, there is an overlap in amino acids and protein fragments may be involved. Tr. at 209-10. Vaccine can be a non-specific stimulus, differing from the original stimulus, according to Dr. Shapiro. Tr. at 213. In HiB vaccine, antigen is a surface coated polymer (oligosaccharide). Tr. at 216. Dr. Daum stated that HiB is covered with a capsule and there is no

protein, just carbohydrate. Tr. at 217. He stated that molecular mimicry cannot happen because the protein is not HiB. Tr. at 219. There is very little immune response to the first dose. Tr. at 220.

Dr. Shapiro testified that molecular mimicry is only one process to explain what happened. Id. HiB has sugar (polysaccharide, carbohydrate) on the surface. Tr. at 221. The protein carrier is not part of the HiB itself, but a detoxified altered version of diphtheria toxoid, according to Dr. Daum. Tr. at 223. Dr. Daum stated that, in this age group, the response to HiB infection is minimal even if the recipient gets an infection and meningitis. Tr. at 224. From three months to three years of age, there is no response immunologically to HiB, which is why unconjugated vaccines do not work. Tr. at 225. Dr. Shapiro replied that this was correct for an antibody response, but not for a T-cell response. Tr. at 225-26. One gets a T-cell response to protein. Tr. at 225. Dr. Daum stated it was not much of a T-cell response although there is some. Tr. at 226. Dr. Shapiro testified that there are co-stimulatory factors and a whole range of response. Alexander had an explosive immune response after vaccination which stimulated his immune system. He had both 105° fever and an inflammatory response. The vaccine was a significant contribution. Tr. at 227.

Dr. Sladky replied that there was no explosive response. Tr. at 228. This was the culmination of an autoimmune response manifested clinically by the breakdown of the blood-brain barrier, invasion of the spinal cord, demyelination, axonal degeneration, and inflammation in the meninges. Tr. at 228-29. It was the culmination of a mechanism of injury affecting the nervous system. Tr. at 229-30.

DISCUSSION

Petitioner is proceeding on a theory of causation in fact. To satisfy her burden of proving causation in fact, petitioner 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.

Petitioner must not only show that but for the vaccine Alexander would not have had the injury, but also that the vaccine was a substantial factor in bringing about his 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 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 the 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, ___, 119 S. Ct. 1167, 1171, 1175 (1999).

In the Office of Special Masters, even the Federal Rules of Evidence are not required.[3] Invariably, consistent with the legislative intent in creating the Vaccine Program, the special masters admit most evidence.

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 petitioner's evidence of immunomodulation 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.

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[3] 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."

The testimony of Drs. Dooling, Shapiro, and Sladky is that Alexander had some post-infectious or para-infectious process for a week or two which culminated in his TM (or ADEM and the witnesses said it does not make any difference which it is). Where they disagree is whether the HiB vaccine was the trigger for the explosive culmination in clinical signs within 36 hours of administration: 105° fever, limpness, lethargy, encephalopathy, transverse myelitis.

Petitioner's experts Dr. Dooling, his treating pediatric neurologist, and Dr. Shapiro, an immunologist, opined that HiB vaccine was a trigger because it stimulated T cells that had been previously stimulated by the underlying infection. Dr. Shapiro testified that the prior infectious process accounted for Alexander's screaming for two hours, low-grade fever, puffy hand, and swollen eyelid on January 3, 1999, and his left OM on January 5, 1999, and could even have been haemophilus influenza infection (although it could have been some other infectious process). His immune system having been primed by this prior infectious process, Alexander's HiB vaccine triggered the onset of clinical symptoms and, therefore, was a substantial factor in Alexander's ADEM/TM. But for the HiB vaccine, Alexander would have fought off the prior infection and not had the catastrophic developments that followed vaccination.

It is insignificant to the undersigned whether Alexander's prior underlying infectious process was haemophilus influenza or not. As Dr. Sladky, respondent's neurologist, testified, there had to have been some cause which led to the breach of his blood-brain barrier, demyelination, TM, and axonal destruction. Alexander's January 3rd runny nose, fever, two hours of screaming, puffy eyelid, and swollen hand and his January 5th left otitis media suggested to Dr. Sladky that Alexander had a viral

infection and that the January 3rd upper respiratory infection led to the OM. The latency period from these events to his clinical onset of ADEM/TM was appropriate for causation.

The undersigned is unimpressed that the first dose of HiB vaccine (normally administered to a two-month-old whereas, here, Alexander was nine months old) does not provoke antibody response. As Dr. Shapiro testified, it is the immune challenge and the spurring of T-cell activity that occurred here. It is obvious that no one would inoculate a child if it had no response whatsoever. The undersigned finds that respondent's experts' denial of a substantial role for the vaccine in this case is not credible because it makes no sense to ignore the T-cell response merely because antibody response would be minimal (if it would be minimal in a nine-month-old). The undersigned finds Dr. Daum's recitation that Alexander's blood-brain barrier was just as sturdy as an adult's (and therefore would be impermeable to attack) directly contradicts Dr. Sladky's testimony that whatever infectious process Alexander had must have breached his blood-brain barrier in order for him to have encephalopathy.

This case is reminiscent of Herkert v. Secretary of HHS, No. 97-518V, 2000 WL 141263 (Fed. Cl. Spec. Mstr. Jan. 19, 2000), in which John Henry Herkert was fighting off cytomegalovirus (CMV) when he received acellular DPT. That night, he became warm and, by the next morning, he was limp as a dishrag. He had cervical TM. The undersigned accepted petitioner's evidence that the vaccination modulated his immune system so that he could no longer fight off the CMV.

Similarly, in the instant action, Alexander experienced a slight fever the evening of vaccination. He had had a prior infection which appeared clinically over, but which Dr. Shapiro testified was in its latency. The HiB vaccination triggered an autoimmune response which manifested in his being spread-

eagled and moaning at 4:00 a.m. the next morning, with fevers reaching 105°. This is indeed a logical sequence of cause and effect which both Drs. Dooling and Shapiro cogently explained.

As respondent's experts, Drs. Daum and Sladky, testified, it is highly unusual to ascribe any causative role to the HiB vaccine. (It is also highly unusual for a child under two years or even five years of age to have ADEM/TM.) Drs. Daum and Sladky relied on the DeStefano article, an epidemiological analysis, showing no causation of demyelinating diseases in adults from certain vaccinations in support of their opinion of no causation. However, the undersigned is not bound by the lack of epidemiological support, as the Federal Circuit made clear in Knudsen, supra (even though viruses more often cause encephalopathy than do vaccines, that did not prevent petitioners from prevailing in their suit that vaccination caused their child's encephalopathy):

> 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.

This case is also reminiscent of Nash v. Secretary of HHS, No. 00-149V, 2002 WL 1906501 (Fed. Cl. June 27, 2002) (DPT significantly aggravated child's latent meningitis, resulting in encephalopathy, seizure disorder, developmental delay, and deafness). James Nash received his first DPT vaccination when he had a low-grade fever and a stuffy nose. After the vaccination, he had a higher fever and was vomiting. He returned to his doctor two days after vaccination with a supple neck and soft fontanelle. By the time he went to the ER that same day, he had not only fever, but also lethargy and bulging fontanels. He was diagnosed with acute meningitis, most likely bacterial.

In contrast to the instant action where petitioner's expert Dr. Shapiro testified that Alexander's underlying infection was ending and his immunological recovery (or homeostasis) was just beginning, in James Nash's case, the streptococcus pneumoniae infection that led to his meningitis was just beginning. One of the factors persuading James Nash's expert immunologist that his vaccination was a substantial factor in causing his meningitis was his rapid decompensation after vaccination, but before meningitis was fulminant. By modulating his immune system, the vaccine made it more difficult for James to fight the underlying streptococccal pneumoniae.

The undersigned agrees with Drs. Dooling and Shapiro in the instant case that what happened to Alexander post-HiB vaccination was catastrophic and indicates an underlying infectious process which the vaccination, normally harmless according to Dr. Daum, provoked into a vicious state. This explains the shortened interval between vaccination and neuropathy, a mark of all three cases (Herkert, Nash, and the instant action). In those individuals who are unfortunately susceptible to an autoimmune attack, the combining of an infectious process within the appropriate time frame to the onset of clinical symptoms with an immunization just before clinical signs can lead to disastrous consequences and did in these cases.

As in Shyface, supra, there are two substantial factors in this case: the first is the underlying infectious process (a non-specific virus, according to Dr. Sladky who connected the symptoms of fever, screaming, puffy eyelid, and swollen hand on January 3rd with the OM on January 5th into one infectious process, probably an upper respiratory illness) and the second is the HiB vaccination. In Shyface, the vaccinee suffered an extremely high fever due to receipt of DPT while at the same time having the beginning of an E. coli infection. Testimony showed that the infection was not at a sufficient

level to have alone caused such a high fever, which led to Cheyenne Shyface's encephalopathy and death. The Federal Circuit held that because the vaccine played a substantial factor in Cheyenne Shyface's encephalopathy and death and but for the vaccination, Cheyenne would not have experienced the injury and sequela, petitioners must prevail. The vaccine's being a substantial factor is sufficient to entitle petitioners to compensation. 165 F.3d at 1353.

The vaccine here, as in Shyface, was a substantial factor in causing his ADEM/TM from which he still suffers today, and but for the HiB vaccination, Alexander would not have suffered from ADEM/TM but would have successfully fought off his underlying infectious process and recovered a normal immune state.

There are cases dealing with other vaccines in other courts in which TM plaintiffs have prevailed: Toner v. Lederle Laboratories, a Division of American Cyanamid Co., 828 F.2d 510, modified, 831 F.2d 180 (9th Cir. 1987), cert. denied sub nom., Lederle Laboratories, Division of American Cyanamid Co. v. Toner, 485 U.S. 942 (1988) (vaccine manufacturer's negligence proximately caused infant's TM); Unthank v. U.S., 732 F.2d 1517 (10th Cir. 1984) (swine flu vaccination caused adult's TM); Guillory v. St. Jude Medical Center, 675 So.2d 1198 (5th Cir. Ct. App. LA 1996) (amended to increase attorney's fees and affirmed workers' compensation decision that hepatitis B vaccine triggered adult TM); cf. Wyeth Laboratories, Inc. v. Fortenberry, 530 So.2d 688 (Sup. Ct. MI 1988) (decision against vaccine manufacturer in adult TM reversed because package warning was adequate). The undersigned has ruled in this program that MMR vaccine caused TM, Tufo v. Secretary of HHS, No. 98-108V, 2001 WL 286911 (Fed. Cl. Spec. Mstr. Mar. 2, 2001),

and that tetanus vaccine caused ADEM: Johnson v. Secretary of HHS, No. 99-0219V, 2000 WL 1141582 (Fed. Cl. Spec. Mstr. July 27, 2000).

Others have also ruled that vaccines caused ADEM: Althen v. Secretary of HHS, No. 00-170V, 2003 WL 21439669 (Fed. Cl. Sept. 30, 2003) (tetanus vaccine); Kuperus v. Secretary of HHS, No. 01-0060V, __ WL __ (Fed. Cl. Spec. Mstr. Oct. 23, 2003) (DTaP vaccine).

The issue here is not whether the vaccine alone caused Alexander's ADEM/TM, but whether it was a substantial factor in causing his ADEM/TM. Dr. Shapiro's testimony about the effect of the vaccine on Alexander's already-burdened immune system is medically probable, being a logical sequence of cause and effect based on a reputable medical opinion, satisfying the standard that the Federal Circuit created in Grant, supra. Dr. Dooling's testimony is consistent with Dr. Shapiro's. Even Dr. Sladky's opinion is consistent except for depicting the HiB vaccine as a substantial factor because he confirmed the role of the underlying infectious process starting on January 3rd and leading to OM on January 5th.

Petitioner has proved a prima facie case of causation in fact that HiB vaccine was a substantial factor in causing Alexander's ADEM/TM and that, but for his vaccination, he would not have endured his catastrophic illness.

CONCLUSION

Petitioner is entitled to reasonable compensation. The undersigned hopes that the parties may reach an amicable settlement, and will convene a telephonic status conference soon to discuss the filing of life care plans, unless the parties agree on a joint life care plan. 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