OFFICE OF SPECIAL MASTERS

No. 99-429V

(Filed: May 12, 2004)

MATTHEW Z. LARIVE, Petitioner(s),	*	**TO BE PUBLISHED**
v.	*	
SECRETARY OF THE DEPARTMENT OF HEALTH AND HUMAN SERVICES, Respondent.	*	

Clifford J. Shoemaker, Vienna, VA, for petitioner.
Heather L. Pearlman, Washington, DC, for respondent.

DECISION

MILLMAN, Special Master

On August 4, 1999, petitioner (hereinafter, "Matthew") filed a petition on his own behalf 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 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

[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.

a civil action for damages arising from the vaccine injury; and (2) hepatitis B and MMR vaccines were administered to him in the United States.

Petitioner alleges that hepatitis B vaccine was a substantial factor in his contraction of, and MMR a substantial factor in worsening, focal segmental glomerulosclerosis (FSGS), a form of nephrotic syndrome. Respondent concedes that Matthew has FSGS, but states that hepatitis B vaccine was not its cause and MMR did not worsen it.

The court held a hearing in this case on February 27, 2004. Testifying for petitioner was Dr. Joseph A. Bellanti. Testifying for respondent was Dr. M. William Schwartz.

FACTS

Matthew was born on July 29, 1974. He received hepatitis B vaccinations on June 12, 1996, July 10, 1996, and December 10, 1996. Med. recs. at Ex. 10, pp. 6, 9.

On March 4, 1997, which was a Tuesday, Matthew saw Dr. Rasheed Siddique, complaining of swelling of his ankles that began on Thursday, February 27, 1997. He had scrotal edema which started on Monday, March 3, 1997. He denied any history of fever, trauma, shortness of breath, or chest pain. He denied any urinary symptoms, and had normal bowel habits. He had been working with plastics for three years. Med. recs. at Ex. 1, p. 10. Dr. Siddique referred Matthew to Dr. M.A. Bashir.

On March 12, 1997, Matthew went to Dr. Bashir, complaining of a two-week history of marked peripheral edema and some shortness of breath. A work-up revealed severe nephrotic syndrome with 9.7 grams of protein and a creatinine clearance of 79 cc's per minute. Clinically, Matthew had significant edema (3+) and diminished breath sounds (indicating pleural effusion).

The diagnosis was minimal change disease and focal segmental glomerulosclerosis. Med. recs. at Ex. 1, p. 21.

Matthew had had symptoms of a cold one week prior to development of swelling. In 1996, he had had an episode of peripheral edema that lasted for one week. He did not have a history of hypertension or diabetes and had no other significant medical history. Med. recs. at Ex. 4, p. 16.

An electron microscopy was done on tissue collected March 17, 1997. There were no inflammatory cellular infiltrates in the cells. Med. recs. at Ex. 10, p. 4.

Matthew received MMR vaccine on July 30, 1998. Med. recs. at Ex. 10, p. 9. At the end of August, he had a relapse of his FSGS, developing edema of his scrotum and of his lower extremities. He was hospitalized from September 3 to 8, 1998 for an intravenous diuretic. Med. recs. at Ex. 2, pp. 3, 19, 22.

Other Submissions

Petitioner submitted Exhibit 17, consisting of a number of items in the medical literature. The first is a letter entitled "Nephrotic syndrome after recombinant hepatitis B vaccine," by F. Macdrio, et al., 43 *Clin Nephrology* 349 (1995). They report a case of a 40-year-old nurse who had nephrotic syndrome, manifested by generalized edema, after her second hepatitis B vaccination. She had two relapses in the following eight months as steroid treatment was reduced.

The second item in P's Exhibit 17 is a case report entitled "Large Artery Vasculitis Following Recombinant Hepatitis B Vaccination: 2 Cases," by A. Zaas, et al., 28 *J Rheumatology* 5:1116-20 (2001). The first case concerned a 19-year-old woman who received hepatitis B vaccine in March, April, and September 1995, and gradually developed fatigue and malaise in the summer of 1995. In October 1995, she developed severe headaches and hypertension. After starting treatment, she

developed acute renal failure. Anticardiolipid IgG, IgM, and IgA were negative. She was put on steroids. The second case concerned a 61-year-old woman who, the night after receiving her first hepatitis B vaccination, experienced fatigue, myalgias, and eye pain, which resolved. After her second dose of hepatitis B vaccine in October 1997, she developed fatigue, low-grade fevers, anorexia, and headache. By November 1997, she had lost 30 pounds and had hypertension. Renal angiograms in November 1998 showed arteritis. She was treated with steroids but experienced renal failure and had a renal transplantation in November 1999. The authors ponder, at 1119, whether "patients with immunologic dysfunction may be more susceptible to developing vasculitis following vaccination."

The third item is a letter entitled "Hepatitis B vaccine side-effect" by Y. Carmeli and R. Oren, 341 *Lancet* 250-51 (Jan. 23, 1993). The authors describe a 21-year-old man who experienced acute glomerulonephritis six weeks after receiving his third hepatitis B vaccination.

The fourth item is a letter entitled "Glomerulonephritis After Recombinant Hepatitis B Vaccine" by M. Pennesi, et al., 21 *Ped Infectious Dis J* 2:172-73 (Feb. 2002). A 12-year-old girl developed glomerulonephritis two weeks after her second hepatitis B vaccine. She had a similar episode two weeks after her first hepatitis B vaccine, which was self-limiting. The association between the hepatitis infection and glomerulonephritis is well-known.

The fifth item is a letter entitled "Nephrotic syndrome following hepatitis B vaccination" by I Islek, et al., 14 *Ped Nephrology* 1:89-90 (Jan. 2000). A 4-year-old boy experienced nephrotic syndrome 8 days after receiving his third hepatitis B vaccination. He had generalized edema. The authors thought the dominant cell in the immunopathogenesis of minimal change nephrotic

syndrome was the T cell. They thought the timing of the illness after the vaccination "strongly favors an immune-mediated side effect of vaccination." Id. at 89.

The sixth item is a case report entitled "Suspected Hepatitis B Vaccination Related Vasculitis" by C. Le Hello, et al., 26 *J Rheumatology* 1:191-94 (1999). The authors describe three cases of vasculitis after receipt of hepatitis B vaccine. The first case concerns a 16-year-old girl who developed purpura on her arms 20 days after vaccination, followed 15 days later by purpura on her legs, and abdominal pain, arthalgias, and myalgias. The second case also concerned a 16-year-old girl who developed purpura 7 days after vaccination. The third case concerned a 19-year-old woman who had arthralgias and unstable gait 7 days after her third vaccination.

The seventh item is an article entitled "Rheumatic disorders developed after hepatitis B vaccination" by J.F. Maillefert, et al., 38 *Brit Soc for Rheumatology* 978-83 (1999). The authors conclude from a study of 22 patients that hepatitis B vaccine might trigger the onset of underlying inflammatory or autoimmune rheumatic diseases. One of the various diseases described occurring after hepatitis B vaccine is nephrotic syndrome.

The eighth item is an article entitled "Hepatitis B vaccine and neurotoxicity" by M. Pirmohamed and P. Winstanley, in an unidentified journal. They describe a 35-year-old man who developed cranial nerve palsies following hepatitis B vaccination.

The ninth item is a short communication entitled "Major adverse reactions to yeast-derived hepatitis B vaccines–a review," by I. Grotto, et al., 16 *Vaccine* 4:58-63 (1998). Among other reactions, they describe vasculitis and glomerulonephritis.

The tenth item is a letter entitled "Churg-Strauss vasculitis with brain involvement following hepatitis B vaccination" by L. Beretta, et al., in an unidentified journal.

The eleventh item is an article entitled "Immune-mediated pathology following hepatitis B vaccination. Two cases of polyarteritis nodosa and one case of pityriasis rosea-like drug eruption" by F. De Keyser, et al., 18 *Clinical & Experimental Rheumatology* 81-85 (2000).

The twelfth item is an article entitled "A review of hepatitis B vaccination" by M.R. Geier, et al., 2 *Expert Opin Drug Saf* 2:113-22 (2003).

Petitioner submitted Exhibit 20, "Acute Glomerulonephritis Associated With Normal Serumβ1C-Globulin," by L.U. Tina, et al., 115 *Amer J Dis Child* 29-36 (Jan. 1968).

He submitted Exhibit 21, containing two letters. The first is entitled "Measles Vaccination and the Nephrotic Syndrome," by J.A. Kuzemko,4 *BMJ* 665-66 (1972). The author discusses two children who developed nephrotic syndrome after receiving measles vaccine. The second letter is entitled "MMR and the nephrotic syndrome" by A.S. Ahuja and M. Wright, *BMJ* 796 (1989). The child developed nephrotic syndrome two weeks after receiving MMR vaccine. She developed swelling 6 days after the vaccination.

Petitioner submitted Exhibit 22, chapter 82 in a book entitled Pediatric Primary Care. A Problem-Oriented Approach, 3d ed., ed. by M.W. Schwartz [respondent's expert], et al. (1997). The chapter is entitled "Nephrosis" by T.L. Kennedy. On page 567, Dr. Kennedy lists the types of nephrotic syndrome, including focal segmental glomerulosclerosis, which accounts for 5% to 10% of cases of nephrotic syndrome. Dr. Kennedy writes that one of the types of nephrotic syndrome is associated with exogenous agents such as immunizations. He states that relapses of children with nephrotic syndrome precipitated by immunizations are reported but uncommon. Id. at page 570.

Petitioner submitted Exhibit 23, which is Figure 20-1 depicting immunologically mediated diseases. There are three columns entitled: non-specific (primary), specific (secondary), and tissue-

damaging (tertiary). The non-specific shows an inflammatory response called phagocytosis. The specific immune response has cell-mediated immunity and antibody elaboration. The tissue-damaging process describes four types, of which the fourth is delayed hypersensitivity.

Petitioner submitted Exhibit 24, which is petitioner's VAERS report, filed February 3, 1999. A VAERS follow-up was obtained on April 19, 1999, noting that petitioner had a previous reaction and positive rechallenge. Ex. 24, at unpaginated page 3.

Attached to petitioner's Prehearing Memorandum and Witness List and Exhibit List are nine more exhibits. The first is an order from a case dealing with hepatitis B vaccine and rheumatoid arthritis.[2] The second is an excerpt (pages 48 and 53) from the IOM's Adverse Effects of Pertussis and Rubella Vaccines, National Academy Press (1991) (see R's Ex. H which contains pages 32 - 64). On page 48, the Institute of Medicine or IOM states, "An increasing severity of the event with increasing dose number would tend to support a causal interpretation." This same point is reiterated on page 53:

> *Dose-Response Relation* The existence of a dose-response relation–that is, an increased strength of association with increased exposures or other appropriate relation–strengthens an inference that an association is causal.

In discussing temporal relationship, the IOM states, at the same page:

> The committee ... considered whether the adverse event occurred within a time interval following vaccination that was consistent with current understanding of its natural history.

Petitioner's third exhibit is a one-page excerpt (p. 21) from the IOM's Adverse Events Associated with Childhood Vaccines–Evidence Bearing on Causality, National Academy Press

[2] Capizzano v. Secretary of HHS, No. 00-759V, 2003 WL 2143586 (Spec. Mstr. CFC, June 20, 2003).

(1994) (see R's Ex. G which contains pages 19 - 33). The point is similar to the dose-response point in the prior exhibit: "causality is strengthened by evidence that the risk of occurrence of an outcome increases with higher doses or frequencies of exposure."

Petitioner's fourth exhibit is a brief report, "Hair Loss After Routine Immunizations," by R.P. Wise, et al., 278 *JAMA* 1176-78 (1997). Out of 60 cases examined since 1984, there were 16 cases of alopecia with positive rechallenge (they suffered hair loss after vaccination more than once) of which 4 cases were definite and 12 were possible or probable. Of these 60 cases, 46 had received hepatitis B vaccines.

Petitioner's fifth exhibit is a summary of his fourth exhibit.

Petitioner's sixth exhibit is a summary of "Postlicensure Safety Surveillance for Varicella Vaccine," by R.P. Wise, et al., 284 *JAMA* 1271-79 (2000), describing reviews of VAERS reports of reactions, including a few positive rechallenge reports.

Petitioner's seventh exhibit is the CDC's Vaccine Safety Post-marketing Surveillance: The Vaccine Adverse Event Reporting System, by J.K. Iskander, et al., a continuing education course. On page 3, the authors state that an adverse event can be causally attributed to a vaccine more readily if, inter alia, the event recurs on re-administration of the vaccine ("positive rechallenge").

Petitioner's eighth exhibit is a "Statement on Anthrax Vaccine" by Susan S. Ellenberg, Ph.D. before the Committee on Government Reform, July 21, 1999. On page 4, Dr. Ellenberg repeats the VAERS criterion that causation of an adverse event may be attributed to a vaccine if the event recurs on re-administration of the vaccine ("positive rechallenge"). An example of this is the occurrence of hair loss following hepatitis B vaccination.

Petitioner's ninth exhibit is another statement from Dr. Ellenberg, this one dated May 18, 1999. On page 4, she repoints the point about positive rechallenge.

Respondent submitted the expert report from Dr. M. William Schwartz, a pediatric nephrologist, dated September 23, 1003 (R's Ex. C), in which Dr. Schwartz states, at page 4, Matthew "had sub-clinical disease that was unbalanced by the normal tissue reaction following the [second hepatitis B] immunization and ... the immunization did not cause the focal glomerulosclerosis."

Respondent submitted (Ex. A) a discussion of glomerular diseases from the National Kidney and Urologic Diseases Information Clearinghouse. At page 3 of the exhibit is the section entitled "What causes glomerular disease?" The authors state:

> A number of different diseases can result in glomerular disease. It may be the direct result of an infection or a drug toxic to the kidneys....

On page 5 of Ex. A is a discussion of glomerulosclerosis which is scarring (sclerosis) of the glomeruli. On page 6 of Ex. A is a discussion of focal segmental glomerulosclerosis (FSGS) which is scarring in scattered regions of the kidney, typically limited to one part of the glomerulus and to a minority of glomeruli in the affected region. One of the causes the authors mention is an immune response to infection.

Respondent submitted (Ex. B) another discussion of FSGS from Medline plus, which states, on page 2, that the disorder seems to be immune-system related.

In a supplemental report dated November 24, 2003, Dr. Schwartz states, on page 2, that the cold Matthew had in February 1997 precipitated his edema, but did not cause it or make it worse. R's Ex. E. He explains that "trigger" means making a subclinical disease become evident. Id.

In a second supplemental report (R's Ex. I) dated April 3, 2004 (after the hearing in this case), Dr. Schwartz commented on various exhibits Matthew filed previously: Exhibit 20 deals with acute glomerulonephritis, not focal sclerosis, which is a different kidney condition. This case does not involve acute glomerulosclerosis but focal glomerulosclerosis; Exhibit 21 deals with two atopic (allergic) children who had nephrotic syndrome after receiving MMR vaccine but does not discuss biopsy or specialized tests; it is a mere observation, published as correspondence, not subject to peer review; the second article also concerns measles vaccine and nephrotic syndrome and is another observation rather than proof of causation; Exhibit 22 discusses causes of nephrotic syndrome, including immunizations, but does not explain or provide details; horse serum which was used to treat tetanus caused systemic reactions including kidney disease, but this would not support a claim that hepatitis B vaccine causes focal sclerosis; and Exhibit 23 shows that Matthew's immunofluorescent stain should have been positive but was normal, indicating that he did not have involvement of the immunoglobulins IgA, IgD, IgG, and IgM in his disease. Dr. Schwartz had no comment on P's Ex. 19.

TESTIMONY

Matthew Larive testified first. He received the first hepatitis B vaccination on June 12, 1996 and did not have any reaction to it. Tr. at 19. On July 10, 1996, he received the second hepatitis B vaccination. One month later, he had edema in his feet lasting one week, and intermittent loss of appetite, fatigue, sporadic headaches, and nausea. Tr. at 19-20. On December 10, 1996, Matthew received the third hepatitis B vaccination. One week later, he had vomiting without fever, and associated nausea. One to two weeks later, he had the same constellation of symptoms with edema. Tr. at 22.

In February 1997, he had a cold, followed one to three weeks later by edema without fever. Tr. at 25. He saw Dr. Siddique on March 4, 1997, but did not mention the cold. When he saw Dr. Bashir, he did mention the cold because Dr. Bashir prodded him more than Dr. Siddique did. Tr. at 27. Matthew used Prednisone and diuretics, and, in three months (by May 1997), his edema disappeared. The doctor wanted to taper him off Prednisone in December 1997, but slowly his symptoms of nausea, loss of appetite, and fatigue started again and he began to retain fluid. The doctor put him back on Prednisone. Tr. at 28.

Because Matthew needed MMR vaccine for work, he received it July 30, 1998. One month later, he had severe edema and was hospitalized. He also had headaches, nausea, and fatigue. Tr. at 29.

Dr. Joseph A. Bellanti, an immunologist, testified next for petitioner. He stated that Matthew has focal segmental glomerulosclerosis (FSGS) which does not have the same degree of inflammation as nephritis (which is related to immune complexes in the glomerulis). Tr. at 85, 86. No one knows the cause of this disease. Tr. at 87. However, its cause fits with T-cell lymphocytes and delayed hypersensitivity (what are called type IV reactions). Id. Nephrotic syndrome can follow bee stings, drugs, diabetes, lupus, infections such as hepatitis B, malaria, and measles, and immunizations such as tetanus and hepatitis B. Tr. at 87-88. Dr. Bellanti suspects a genetic susceptibility is involved. Tr. at 88. T cells are involved in nephrotic syndrome and MMR disrupts the T-cell lymphocyte population. Tr. at 89-90.

Dr. Bellanti's opinion is that Matthew's second hepatitis B vaccination caused his nephrotic syndrome. His basis is that the reaction took one month, which is the period of latency for causation. The edema in his feet lasted one week, and nausea and headache were intermittent. Tr. at 91.

Matthew's third hepatitis B vaccination was followed by nausea and headache with the new symptom of vomiting (showing a progression in sensitization). Tr. at 91-92. Matthew's cold in February 1997 could have upset his T-cell regulation and acted as another trigger for his disease. Tr. at 93.

Perhaps Matthews's first hepatitis B vaccination sensitized his lymphocytes so that the second hepatitis B vaccination was a rechallenge, the third hepatitis B vaccination was another rechallenge (because of immunological memory), the cold was a trigger, and the MMR another trigger. Tr. at 94, 95-96, 97, 103. Nephrotic syndrome is so rare (and FSGS is even rarer) than it is unlikely that an epidemiologic study could be done. Tr. at 102.

Hepatitis B vaccine is a recombinant vaccine, and most of the medical literature deals with the virus hepatitis B. Dr. Bellanti does not know why hepatitis B vaccine can do the same as the virus, since the vaccine is a killed antigen. Tr. at 105. However, Matthew's periods of latency are consistent with his immunologic theory. Tr. at 107.

Glomerulosclerosis and glomerulonephritis are different diseases, with the latter involving antigen-antibody complexes and inflammation. Tr. at 108. We do not understand nephrotic syndrome except that T cells play a role. Tr. at 109. There has to be an outside trigger plus genetic susceptibility. Tr. at 110. For most autoimmune diseases, we do not know the outside cause, but we think they are viruses or chemicals. Id.

FSGS is a type of autoimmune disease and steroids are effective treatment, but not completely. Tr. at 109, 110. Electron microscopy done on tissue from Matthew's kidney showed no inflammatory cellular infiltrates. Tr. at 118. Since he had negative IgG, IgA, and IgM, he did not have glomerulonephritis, but did have glomerulosclerosis. Tr. at 123. Nephrotic syndrome is as

close to the type IV of the phases of the immune system as possible. Tr. at 125. FSGS does not have to be an autoimmune disease as the basis for his opinion. Tr. at 126. Someone can have FSGS without showing symptoms immediately. Tr. at 128. Medical texts list vaccines as the cause of nephrotic syndrome. Tr. at 137.

A period of latency of one month between the second hepatitis B vaccination and the edema of Matthew's feet is consistent with causation. Tr. at 138. The pathogenesis of Matthew's disease is dysregulation of his T cells following immunologic challenges. Tr. at 141. Every viral vaccine changes the distribution of T-helper and -suppressor cells. Id. The increasing severity of Matthew's symptoms shows that the loss of protein was increasing after each vaccination. Tr. at 142. What is important is that the severity of Matthew's swelling increased. By the time he received his MMR, the swelling had gone from his feet to his legs and scrotum to his abdomen. Id. The latency period can vary. Tr. at 144. FSGS is 5 to 10 percent of nephrotic syndrome, which is a rare disease. Tr. at 150. Because it is so rare, it does not bother Dr. Bellanti that the medical literature does not discuss FSGS following hepatitis B vaccine. Tr. at 150. FSGS fits the immunologically-mediated basis for injury discussed in the medical literature. Id.

Dr. M. William Schwartz, a pediatric nephrologist, testified for respondent. He has seen hundreds of cases of FSGS, which is ill-defined. It is a nephrotic syndrome which usually does not respond to steroids. Matthew's case is typical. FSGS is not an autoimmune disease because we do not know its cause. Dr. Schwartz admitted that Matthew could have had FSGS in the six months before he was diagnosed in March 1997. Tr. at 167, 168.

The classic symptoms of FSGS are edema; protein loss in the urine; low protein in the blood; and high cholesterol. Other symptoms are hypertension, blood in the urine, and poor renal function

(headaches, vomiting, poor vision, sleepiness). Tr. at 169. There are no case reports linking hepatitis B vaccine with FSGS. Tr. at 174.

Someone can have FSGS without having symptoms. Tr. at 175. Then something will tip the scales and the person will develop symptoms. Id. There must be a genetic susceptibility for FSGS. Id. The MMR triggered a loss of protein in Matthew and that produced edema. Tr. at 165, 167. The diagnostic entity is not FSGS but the FSGS form of nephrotic syndrome. Tr. at 166.

When Dr. Schwartz wrote in his initial report that Matthew had subclinical disease which was unbalanced by the normal tissue reaction following the immunization, that could be significant aggravation of his underlying disease. Tr. at 176. He meant that the immunization made the protein loss worse. Tr. at 177. He does not know what the immunization does to the underlying disease. Id. The following question and answer followed:

> THE COURT: ... You do think that there was significant aggravation of the edema after the hepatitis B?
> THE WITNESS: Yes.

Tr. at 178.

After the second hepatitis B vaccination, Dr. Schwartz testified that "it's conceivable that the reaction to the immunization caused his edema to get worse." Tr. at 180. The undersigned inquired how the second hepatitis B vaccination could have made Matthew's edema worse since Matthew never had edema before the second hepatitis B vaccination, and Dr. Schwartz responded that he meant "the protein loss could get worse, causing the edema." Id.

Dr. Schwartz agreed that Matthew's cold in February 1997 probably caused his worsening of edema within two weeks. Tr. at 191. This is because his body had an immunologic reaction. Tr.

at 193. The typical time frame for a tissue reaction is two weeks, but there is a lot of give in that. Tr. at 193. Four weeks is also typical for a tissue reaction to an immunologic challenge. Tr. at 194.

Someone could have a virus infection that could damage his kidneys. Tr. at 195. But Matthew's electron microscopy did not show any immune complexes. Tr. at 196. One plus mesangeal is not specific. Tr. at 195. Dr. Bellanti interjected that nephrotic syndrome probably has a different mechanism, probably mediated by T cells in the type IV reaction. One would not expect IgG, IgA, IgM, or complement. Tr. at 196. This is not an immune complex injury but some other mechanism. Tr. at 197, 199-200. In a text for which Dr. Schwartz was general editor is a chapter on nephrosis written by Dr. Thomas Kennedy in which he lists one of the causes of nephrotic syndrome as vaccines. Tr. at 201.

Dr. Schwartz then denied that hepatitis B vaccine caused or significantly aggravated Matthew's condition. Tr. at 202. On cross-examination, Dr. Schwartz admitted that vaccinations can be included in the list of factors associated with relapses of FSGS. Tr. at 203-04. He admitted again that the second hepatitis B vaccination had some relationship to Matthew's edema in his feet. Tr. at 205. Some immunizations are associated with nephrotic syndrome. Tr. at 206. Even though he views FSGS as not an immune-mediated disease, using Prednisone and other drugs to suppress the immune system is standard treatment. Tr. at 208. They work even though doctors do not know why. Id.

DISCUSSION

Petitioner is proceeding on a theory of causation in fact. To satisfy his 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 he 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.
>
> 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, 141, 151 (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 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 nephrology, 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 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

[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."

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. See the lengthy discussion of this point in the Honorable Francis M Allegra's recent decision in Hart v. Secretary of HHS, No. 01-357 (CFC May 3, 2004) (vacating a decision dismissing the allegation that MMR caused vaccinee's death and remanding for further proceedings).

Petitioner's case may be summed up as immunological challenge, rechallenge, trigger, and trigger, as follows:

Immunologic Event	Date	Onset	Symptoms
Hepatitis B # 2	6/12/96	1 month	edema in feet lasting one week, intermittent loss of appetite, fatigue, sporadic headaches, nausea
Hepatitis B #3	12/10/96	1 week	vomiting, nausea, edema
URI	2/97	1-3 weeks	edema in ankles and in scrotum
MMR	7/30/98	1 month	severe edema

Petitioner's theory of causation is that the second hepatitis B vaccination was the challenge to petitioner's immunologic system, causing edema in his feet lasting one week with other intermittent symptoms. Petitioner then asserts that the third hepatitis B vaccination was a rechallenge to petitioner's immunologic system, causing vomiting, nausea, and edema. This was followed by the trigger of an upper respiratory infection (URI), causing a relapse (worsened edema).

The next trigger was MMR vaccination, causing such severe edema that Matthew needed to be hospitalized to receive an intravenous diuretic. Petitioner's theory is that all these events show petitioner's immunologic susceptibility to exogenous factors, first manifested after the second hepatitis B vaccination, resulting in his FSGS form of nephrotic syndrome.

Respondent's most salient objection to petitioner's theory is that electron microscopy shows that Matthew does not have an inflammatory disease. Can someone with a non-inflammatory disease claim that a vaccine caused it? Although Dr. Bellanti, petitioner's expert immunologist, initially spoke of Matthew's first hepatitis B vaccination being the initial sensitization without clinical signs, followed by four rechallenges (the second and third hepatitis B vaccinations, the cold, and the MMR), the more sensible analysis is that of respondent's expert pediatric nephrologist, Dr. Schwartz: the second hepatitis B vaccination triggered clinical signs of a subclinical FSGS (as Dr. Schwartz stated in his report), and the third hepatitis B vaccination, cold, and MMR similarly triggered relapses.

To the undersigned, this case is more appropriately analyzed as significant aggravation, relying on respondent's expert Dr. Schwartz's view that hepatitis B unmasked Matthew's underlying FSGS. (As Dr. Schwartz clarified his opinion, which he waffled on considerably, the vaccine triggered the worsening of his protein loss, resulting in a worsening of Matthew's edema). Once the FSGS was significantly worsened, by the triggering of symptomats, it subsequently went through two more aggravations due to vaccinations (the third hepatitis B vaccination and the MMR vaccination). Matthew's immunologic susceptibility is quite apparent because, every time his body is challenged (the second and third hepatitis B vaccinations, the cold, the MMR vaccination), his symptoms either

appear for the first time (the second hepatitis B vaccination) or significantly worsen (the third hepatitis B vaccination, the cold, the MMR vaccination).

The medical literature mentions, even in the chapter of the text for which Dr. Schwartz is one of the general editors, that immunizations have been causally linked to nephrotic syndrome. FSGS is a form of nephrotic syndrome. The Institute of Medicine repeatedly includes positive rechallenge among its criteria for proving causation. Although medical understanding of the FSGS form of nephrotic syndrome is not currently at a satisfactory stage, both doctors testified that it probably has a genetic basis. Dr. Bellanti testified credibly that an exogenous factor, such as a vaccination, may provoke the clinical form of the disease and did so in this case. The undersigned accepts his testimony as dispositive in this case. Dr. Schwartz danced back and forth over the question of causation, admitting on the one hand the trigger or unmasking effect of the vaccination, but denying on the other hand that this showed causation since Matthew probably had the underlying disease (the FSGS form of nephrotic syndrome) before his second hepatitis B vaccination. Both doctors agreed that the timing of Matthew's symptoms after the vaccinations was consistent with their understanding of an appropriate time interval after a triggering factor that provokes symptoms.

The undersigned accepts that hepatitis B vaccine significantly aggravated Matthew's preexisting FSGS form of nephrotic syndrome. Congress defined "significant aggravation" as "any change for the worse in a preexisting condition which results in markedly greater disability, pain, or illness accompanied by substantial deterioration of health." 42 U.S.C. § 300aa-33(4). The second hepatitis B vaccination significantly aggravated Matthew's preexisting, but subclinical, FSGS form of nephrotic syndrome. The third hepatitis B vaccination worsened it again, causing a relapse. His MMR vaccination worsened it further, sending him to the hospital for an intravenous diuretic.

Petitioner has proved a prima facie case of causation in fact that hepatitis B vaccine was a substantial factor in significantly aggravating his pre-existing FSGS form of nephrotic syndrome, and that, but for his vaccination, he would not have had the clinical manifestation of his FSGS at the time he had it. Whether it would have manifested clinically in the future, e.g., after a cold, is speculative at this point. His subsequent URI which triggered a relapse was down the road from the prior symptoms he experienced after his second and third hepatitis B vaccinations. And his MMR vaccination, which he received after the URI, worsened his FSGS even more.

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