OFFICE OF SPECIAL MASTERS

June 27, 2002

JAMES TODD ROBINSON SMITH NASH, a minor, by and through his Guardian and Next Friend, PATRICIA NASH,	*	
Petitioner,	*	No. 00-149V
v.	*	PUBLISHED
SECRETARY OF HEALTH AND HUMAN SERVICES,	*	
Respondent.	*	

John C. Wunsch, Chicago, IL, for petitioner.
Gregory W. Fortsch, Washington, DC, for respondent.

DECISION

MILLMAN, Special Master

On March 24, 2000, petitioner filed a petition on behalf of her son, James Todd Robinson Smith Nash (hereinafter, "James"), 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) she

[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.

has not previously collected an award or settlement of a civil action for damages arising from the alleged vaccine injury; and (2) DPT vaccine was administered to James in the United States.

Petitioner initially alleged that DPT caused James' seizure disorder and, in the alternative, that he suffered the Table injury of residual seizure disorder (RSD). However, RSD is no longer a Table injury.[2] In addition, petitioner initially alleged that DPT significantly aggravated James' latent meningitis, resulting in his seizure disorder, developmental delay, and deafness.

At a telephonic status conference on February 21, 2002, the parties agreed that James had a Table encephalopathy after his DPT vaccination, and also that meningitis, a known factor unrelated to the vaccine,[3] was a substantial factor in causing James' current condition. The only issue remaining for the court to decide was whether or not DPT was also a substantial factor in causing his current condition.

The court held a hearing in this case on March 1, 2002. Testifying for petitioner was Dr. Kevin C. Geraghty. Testifying for respondent was Dr. W. Paul Glezen.

FACTS

James was born on October 17, 1996. Dr. Joon Pai was his pediatrician. James received his first DPT vaccination on Wednesday, April 2, 1997, at the age of five months and two weeks when he had a low grade fever of 100.1° and a stuffy nose. Med. recs. at Ex. 2, p. 3.

On Friday, April 4, 1997, James returned to Dr. Pai. In the prior two days, James had had fever and had been vomiting. Med. recs. at Ex. 2, p. 5. Dr. Pai examined James and found his

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[2] Effective March 10, 1995, the Vaccine Injury Table includes only anaphylaxis and encephalopathy as Table injuries after DPT. 42 C.F.R. 100.3(a). 60 Fed. Reg. 7694 (Feb. 8, 1995).

[3] 42 U.S.C. 13(a).

neck to be supple and his fontanel soft. James had a negative Kernig sign.[4] Med. recs. at Ex. 2, p. 5. The diagnosis Dr. Pai made was "reaction to DPT (?)." Med. recs. at Ex. 2, p. 6. Dr. Pai sent James to South Suburban Hospital for a complete blood count and other testing. Id.

On April 4, 1997, he was taken to South Suburban ER because of fever, lethargy, and bulging fontanels. The history given was that he was seen two days prior when he had a low grade fever, was given DPT, and became more febrile and lethargic. He had one episode of vomiting, three or more episodes of diarrhea, decreased fluid intake, and an umbilical hernia. On physical examination, his fontanels were mildly bulging. He was prescribed antibiotics. Med. recs. at Ex. 19, p. 9.

A gram stain of James' cerebrospinal fluid (CSF) showed many gram positive cocci. His protein count in his CSF was 315. He was diagnosed with acute meningitis, most likely bacterial. Med. recs. at Ex. 19, p. 10.

James was transferred from South Suburban to Christ Hospital on April 5, 1997. The Transport Patient Record states he vomited and had loose stools, and was lethargic. Med. recs at Ex. 4, p. 391. He had a weak cry. Med. recs. at Ex. 4, p. 392.

A head CT scan on April 6, 1997 showed multifocal lesions in the frontal, right temporal, and parietal lobes consistent with cerebritis and probably multiple areas of infarction. The findings were presumed secondary to meningitis. Med. recs. at Ex. 3, p. 367. There was no significant change in a CT scan done April 8, 1997. Med. recs. at Ex. 3, p. 362. A CT scan done

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[4] Kernig sign is "when a subject is supine and the thigh is flexed to a right angle with the axis of the trunk, complete extension of the leg on the thigh is impossible; present in various forms of meningitis." A positive Kernig sign would indicate meningitis. Stedman's Medical Dictionary, 27th ed. (2000), at 1638.

on April 17, 1997 showed evolving cerebritis and/or subacute infarcts in the frontal regions bilaterally. There was also moderate atrophy in that the lateral ventricles appeared larger. Med. recs. at Ex. 3, pp. 355-56. A CT scan done April 22, 1997 showed an increased volume of the lateral ventricles and third ventricle. The cortical sulci were visible and slightly prominent. The most significant findings was increased ventricular volume consistent with communicating hydrocephalus. Med. recs. at Ex. 3, p. 354.

A letter dated June 26, 1997 from Dr. Robert T. Egel, a pediatric neurologist, stated that James had made a remarkable recovery and left the hospital with minimal neurological deficit, i.e., fluctuating increased tone in the lower extremities, truncal ataxia, and deafness. Med. recs. at Ex. 5, p. 21. While he did not sit, he was able to roll. Id. He has a profound sensorineural hearing loss. Med. recs. at Ex. 5, p. 22.

A July 10, 1997 EEG showed sharp waves and spikes in a pseudoperiodic pattern over the right frontal region. Med. recs. at Ex. 6, p. 13.

Other Submissions

Joyce Hodges, James' foster mother, submitted an affidavit dated September 1, 2000, stating that, on April 2, 1997, she took James to Dr. Joon Pai for a routine examination and vaccinations. He had a slight temperature. After the DPT vaccination, James's physical condition changed. He became more febrile and lethargic. He did not want to drink his milk or eat. Whereas he was previously an active baby, after the vaccination he just lay in bed and did not move even when she attempted to play with him. Later on April 2nd, James vomited three or four times. He also had diarrhea on April 2nd three or four times. These symptoms continued. On April 4, 1997, she took James back to Dr. Pai who examined James and told her to take him to

South Suburban Hospital immediately, which she did. When he was transferred to Christ Hospital, he had seizures. Med. recs. at Ex. 17, pp. 1-2.

On June 21, 2000, respondent submitted Ex. 1, an excerpt entitled "Acute Bacterial Meningitis Beyond the Neonatal Period," ch. 12.15 from Nelson Textbook of Pediatrics, 14th ed. (1992), pp. 683-90. The authors state:

> The incidence of bacterial meningitis is sufficiently high that it should be suspected in all febrile infants who demonstrate altered mental status, irritability, and poor peripheral perfusion.

Id. at 683.

> *Increased intracranial pressure* is due to cell death (cytotoxic cerebral edema), cytokine-induced increased capillary vascular permeability (vasogenic cerebral edema), and, possibly, increased hydrostatic pressure (interstitial cerebral edema) following obstructed reabsorption of cerebrospinal fluid in the arachnoid villus or obstruction of the flow of fluid within or exiting from the ventricles.
>
> *Hydrocephalus* is an uncommon acute complication of meningitis occurring after the neonatal period. Most often it takes the form of a communicating hydrocephalus due to adhesive thickening of the arachnoid villi around the cisterns at the base of the brain.
>
> Raised CSF protein levels are due in part to increased vascular permeability of the blood-brain barrier and the loss of albumin-rich fluid from the capillaries and veins traversing the subdural space. Continued transudation may result in subdural effusions, noted in the later phase of acute bacterial meningitis. Hypoglycorrhachia (reduced CSF glucose levels) is due to decreased glucose transport by the inflamed meninges and increased glucose utilization by the cerebral tissue. The latter may produce a local lactic acidosis.
>
> Damage to the cerebral cortex may be due to the focal or diffuse effects of vascular occlusion (infarction, necrosis), hypoxia, bacterial invasion (cerebritis), toxic encephalopathy (lactic acidosis), raised intracranial pressure, ventriculitis, and transudation (subdural effusions). The resultant manifestations of impaired consciousness, seizures, hydrocephalus, cranial nerve deficits, motor and sensory deficits, and later psychomotor retardation can be explained by one or more of the pathologic factors described earlier.

Id. at 684.

> **CLINICAL MANIFESTATIONS.** The mode of onset of acute meningitis has two predominant presentations. *Sudden onset*, with rapidly progressive manifestations of shock, purpura, disseminated intravascular coagulation, and reduced levels of consciousness, is a dramatic and often fatal presentation of meningococcal sepsis with meningitis; it may evolve to death within 24 hr. *H. influenza* type b and pneumococcal meningitis less frequently presents as a rapidly progressive infection. More often, meningitis due to *H. influenza* type b and pneumococcus (and some cases of meningococcal meningitis) is preceded by several days of upper respiratory tract or gastrointestinal symptoms.
>
> The signs and symptoms of meningitis are related to the nonspecific findings associated with a systemic infection or bacteremia[5] and to the specific manifestations of meningeal irritations with central nervous system inflammation. The former include fever (present in 90-95%), anorexia and poor feeding, upper respiratory tract infection, myalgias, arthralgias, tachycardia, hypotension, and various cutaneous signs such as petechiae (present in 10%), purpura, or an erythematous macular rash. Meningeal irritation is manifest as nuchal rigidity, back pain, **Kernig sign** (flexion of the hip 90 degrees with subsequent pain on extension of the leg),... Increased intracranial pressure is suggested by headache, emesis, bulging fontanel or diastasis (widening) of the sutures....
>
> Alterations of mental status and reduced level of consciousness are common among patients with meningitis and may be due to increased intracranial pressure, cerebritis, or hypotension; manifestations include irritability, lethargy, stupor, obtundation, and coma.

Id. at 685.

Respondent submitted on November 30, 2001, Exhibits 6 through 10, consisting of various articles: "The Altered Reactivity of Mice After Immunization with *Hemophilus Pertussis* Vaccine," by L.S. Kind, 70 *J. Immunol.* 411-20 (1953) (Ex. 6); "Reversible Changes in the Susceptibility of Mice to Bacterial Infections. I. Changes Brought About by Injection of Pertussis Vaccine or of Bacterial Endotoxins," by R.J. Dubos, et al., 104 *J. Exp. Med.* 53-65 (1956) (Ex. 7); *Bordetella pertussis*: Immunological and Other Biological Activities, by J.J. Munoz, et al. (Marcel Dekker, Inc., 1977) 118-21, 126-35, 138-39, 164-75, 180-83 (Ex. 8); "Effect of

[5] Bacteremia is "[t]he presence of viable bacteria in the circulating blood...;may be persistent ... as a result of infection." Stedman's Medical Dictionary, 27th ed. (2000) at 182

Pertussis Toxin on Susceptibility of Infant Rats to *Hemophilus influenzae* Type b," by M.H. Samore, et al., 165 *J. Infect. Dis.* 945-48 (1992) (Ex. 9); and "Safety and Immunogenicity of a New *Hemophilus Influenzae* Type b Vaccine in Infants Under One Year of Age," by S.D. King, et al., 2 *Lancet* 705-09 (1981) (Ex. 10).

In the Kind article (Ex. 6), the author discusses the sensitization to histamine produced in certain mice inoculated with H. pertussis vaccine. Previous injection of mice with H. pertussis vaccine increased the sensitivity of these mice to the lethal effects of E. coli vaccine, but previous injection of mice with E. coli vaccine did not make them more sensitive to a subsequent dose of H. pertussis vaccine. 70 *J. Immunol.* at 417. The author states:

> A significant feature of the increased susceptibility of pertussis-inoculated mice to various gram negative vaccines is the concurrent sensitivity of these animals to histamine, a substance which has been implicated in anaphylaxis and human allergy. ... The foregoing experiments have demonstrated that mice inoculated with *H. pertussis* vaccine become susceptible to *H. pertussis, E. coli*, and *Sh. dysenteriae* vaccines, to passive anaphylaxis, and to histamine.

Id. at 419.

In the Dubos article (Ex. 7), the authors found that injecting mice with pertussis vaccine one hour before injecting them with staphylococcus aureus resulted in 10 deaths after 12 days, but injecting mice with pertussis vaccine 8 days before injecting them with staphylococcus aureus resulted in 5 deaths after 12 days. Seven mice who had not been injected with pertussis vaccine but received staphylococci died after 12 days. 104 *J. Exp. Med.* at 55. Mice infected with staphylococci just hours after receiving pertussis vaccine died more rapidly than mice infected 1 or 8 days later or than mice who did not receive vaccine. Id. at 55-56. The authors note:

> Whereas the protective effect was not apparent during the first few hours after treatment, it was very marked in animals infected 24 days later.

Id. at 62.

The authors conclude:

> It was found that mice receiving the infective dose of virulent culture a few hours after treatment with the endotoxin material were usually more susceptible to infection than were untreated animals. In contrast, mice infected at a later period proved far more resistant to infection than did untreated animals.

Id. at 64.

In the Munoz book (Ex. 8), the authors state:

> Pertussis vaccine given to mice renders them more susceptible to infections with Gram-negative bacteria that normally are nonpathogenic or only weakly so. Parfentjev and Arch [citations], for example, found that pertussis vaccine-treated mice could be fatally infected with *Proteus vulgaris, Pasteurella multocida,* and *Pseudomonas fluorescens*, and Kind [citation] produced fatal infections with *E. coli*. ... Dubos and Schaedler [citation] observed an increased susceptibility of mice to staphylococcus infection when treated a few hours before with *B. pertussis* vaccine, while, if the infection was given a few days later, an increased resistance was observed.

Bordetella pertussis: Immunological and Other Biological Activities, at 165-66.

In the Samore article (Ex. 9), the authors describe pertussis toxin (PT) as having systemic effects, including

> enhanced susceptibility to histamine in mice and lymphocytosis and hypoglycemia secondary to increased insulin secretion. The lymphocytosis is caused by an inhibition of lymphocyte migration. ... These inhibitory effects of PT may impair mucosal immune responses.... The immunologic effects of PT may also contribute to the toxicity of pertussis vaccines. For example, there is concern that pertussis vaccines containing active PT may enhance susceptibility to bacterial infections. [citations excluded].

165 *J. Infect. Dis.* 945.

The authors examined the hypothesis that PT enhances susceptibility to bacterial infections by testing Hib (*Haemophilus influenzae* type b) in infant rats. On day 4 of life, the pups were

administered PT. On day 8 of life, they were inoculated with Hib. The control animals received saline instead of Hib. All blood cultures in the Hib-challenged rats were positive for Hib. The concentration of bacteremia was 10-fold greater in the PT groups than in the control group on day 1 after Hib challenge. This same higher incidence of bacteremia pertained on day 3. The PT groups showed significantly higher endotoxin levels than the control group. The 10- to 13-fold relative increase in endotoxin concentration in the PT groups mirrored the increase in concentration in bacteremia. Mortality in the PT groups was higher than in the control group: 34% in the PT group, 10% in the control group. Id. at 946.

The authors state:

> Infant rats were chosen as animal subjects because many features of this model mimic human disease, including their age-dependent susceptibility to Hib infection and the development of bacteremia and meningitis. PT was administered 4 days before Hib challenge because other biologic effects of PT, such as lymphocytosis, are maximal at that time.
>
> Administration of PT 4 days before challenge with Hib resulted in increased concentration of bacteremia, higher serum endotoxin levels, and enhanced mortality. Enhanced susceptibility to Hib occurred with a dose of PT less than the threshold dose required for inducing leukocytosis.
>
> It is plausible that PT inhibits clearance of bacteria from the peritoneum and from the bloodstream by inhibiting phagocytosis and killing of bacteria by the reticuloendothelial system.
>
> The higher concentration of bacteremia and endotoxemia in PT-treated animals presumably contributed to their enhanced mortality. Previous studies of this model of Hib infection have shown that meningitis and death correlate with concentration of bacteremia. [citations excluded.]

Id. at 946.

The authors continue:

> Since enhanced bacterial replication was observed in our experiments and since PT is known to affect phagocytic defense mechanisms, an effect of PT on host defense remains the most likely mechanism to explain enhanced mortality after Hib

> challenge. ...Our study suggests that small doses of active toxin (10 ng) increase the susceptibility of infant rats. [citations excluded.]

Id. at 947.

In the King article (Ex. 10), vaccines against *H. influenzae* type b disease were augmented in effect with a quarter dose of *B. pertussis* in children under one year of age who would normally not develop protection against Hib with that particular vaccine. The studies were done in 1979 and 1980.

Respondent submitted Exhibits 11 and 12 on February 22, 2002. Exhibit 11 is "Three-Year Multicenter Surveillance of Pneumococcal Meningitis in Children: Clinical Characteristics, and Outcome Related to Penicillin Susceptibility and Dexamethasone Use," by M. Arditi, et al., 102 *Ped.* 1087-97 (1998), which describes the outcomes of meningitis caused by *Streptococcus pneumoniae*. Males outnumbered females, and whites outnumbered blacks. 102 *Ped.* at 1089. Twenty-five percent of children on discharge from the hospital had neurologic sequelae: hemiparesis, quadriplegia, spasticity, ataxia, cranial nerve dysfunction, cortical blindness, vegetative state, and obstructive hydrocephalus. Thirty-two percent had unilateral or bilateral deafness. Id. at 1091. The authors note that since the introduction of Hib vaccines in 1989 and the dramatic decline in the incidence of Hib meningitis, *S. pneumoniae* has become the most common cause of bacterial meningitis in children under two year of age in this country. Id. at 1093.

Exhibit 12 is "Addressing Parents' Concerns: Do Multiple Vaccines Overwhelm or Weaken the Infant's Immune System?" by P.A. Offit, et al., 109 *Ped.* 124-29 (2002). The authors state, "Data on the capacity of vaccines to induce protective immune responses in children with

severe infections (such as those with bacterial pneumonia or meningitis) are lacking." 109 *Ped*. at 126.

On February 26, 2002, petitioner filed Exhibits 23-35: "Unsuspected Bacteremia in Young Children: A Common and Important Problem," by D. Teele, et al., 26 *Ped. Clinics of N. America* 773-84 (1979) (Ex. 23); "No Increased Risk For Invasive Bacterial Infection Found Following Diphtheria-Tetanus-Pertussis Immunization," by M.R. Griffin, et al., 89 *Ped.* 640-42 (1992) (Ex. 24); "Development of Acute Autoimmune Encephalomyelitis in Mice: Factors Regulating the Effector Phase of the Disease," by D.S. Linthicum, 162 *Immunobiol.* 211-20 (1982) (Ex. 25); "Three-Year Multicenter Surveillance of Pneumococcal Meningitis in Children: Clinical Characteristics, and Outcome Related to Penicillin Susceptibility and Dexamethasone Use," by M. Arditi, et al., 102 *Ped.* 1087-97 (1998) (Ex. 26); "Nature and Rates of Adverse Reactions Associated with DTP and DT Immunizations in Infants and Children," by C.L. Cody, et al., 68 *Ped.* 650-60 (1981) (Ex. 27); "The Febrile Child and Occult Bacteremia," by J.O. Klein, 312 *New Eng. J. Med.* (editorial) 1219-20 (1987) (Ex. 28); "Bacteremia in Febrile Children Seen in a 'Walk-In' Pediatric Clinic," by J.E. McGowan, Jr., et al., 288 *New Eng. J. Med.* 1307-12 (1973) (Ex. 29); "Seizures and Other Neurologic Sequelae of Bacterial Meningitis in Children," by S.L. Pomeroy, et al., 323 *New Eng. J. Med.* 1651-57 (1990) (Ex. 30); "Bacteremia in Ambulatory Children," by J.O. Klein, *Ped. Infect. Dis.* S5-S8 (1984) (Ex. 31); "Acute Experimental Autoimmune Encephalomyelitis in Mice. I. Adjuvant Action of *Bordetella pertussis* is Due to Vasoactive Amine Sensitization and Increased Vascular Permeability of the Central Nervous System," by D.S. Linthicum, et al., 73 *Cellular Immunology* 299-310 (1982) (Ex. 32); "Constancy of Distribution of Serogroups of Invasive Pneumococcal Isolates Among Children:

Experience during 4 Decades," by F.E. Babl, et al., 32 *Clinical Infect. Dis.* 1155-61 (2001) (Ex. 33); "Apparent Decreased Risk of Invasive Bacterial Disease After Heterologous Childhood Immunization," by S.B. Black, et al., 145 *AJDC* 746-49 (1991) (Ex. 34); "Outcome of unsuspected pneumococcemia in children not initially admitted to the hospital," by L. Bratton, et al., 90 *Ped.* 703-06 (1977) (Ex. 35).

In the Teele article (Ex. 23), the authors state that *Streptococcus pneumoniae* causes the majority (65%) of bacteraemia in children, and the risk of bacteremia rises with increasing temperature. 26 *Ped. Clinics of N. America* at 775.

In the Griffin article (Ex. 24), the authors found no increased risk of serious bacterial infections after administration of DPT vaccine. Their conclusion contrasts with earlier studies showing that certain vaccines could convert latent infections into clinically apparent disease. 89 *Ped.* at 640.

In the Linthicum article (Ex. 25), the author used *Bordetella pertussis* vaccine to induce or accentuate acute experimental autoimmune encephalomyelitis (EAE) in mice. The reason the pertussis worked is that it increased the vascular permeability of the mice's central nervous system. 162 *Immunobiol*. at 211. The author states:

> *B. pertussis* has been used as an immunoadjuvant, shock-enhancing agent, and lymphocytosis-promoting agent for a number of studies. [citation excluded.]

Id. at 218.

In the Arditi article (Ex. 26), of 166 children with pneumococcal meningitis studied, 25% developed neurologic sequelae, and 32% of 151 children had unilateral or bilateral hearing loss.

102 *Ped.* at 1087. The authors state that *S. pneumoniae* has become the most common cause of bacterial meningitis in children under two years of age in the United States. Id. at 1093.

In the Cody article (Ex. 27), the authors review the reactions to DPT in children up to six years of age. The reactions included fever, drowsiness, fretfulness, vomiting, and, in some, convulsions and hypotonic-hyporesponsive episodes. Fever was most likely to occur at three and six hours post-vaccination. 68 *Ped.* at 652. Only children from 2 to 18 months of age who had received their first DPT were shocky. Id. at 654. The authors state:

> The vaccine is known to contain potentially reactogenic components including adenylate cyclase, endotoxin, and a factor capable of producing lymphocytosis, sensitization to histamine, and changes in glucose-insulin homeostasis. One or more of these may be responsible for the more serious reactions.

Id. at 657.

In the Klein editorial (Ex. 28), the author discusses diagnosis and treatment of bacteremia.

In the McGowan article (Ex. 29), the authors recommend blood cultures for children with fever.

In the Pomeroy article (Ex. 30), the authors studied children who had meningitis and found that only those with permanent neurologic deficits were at risk for epilepsy.

In the Klein article (Ex. 31), some children with bacteremia cleared the disease without treatment, but most did not.

In the Linthicum article (Ex. 32), intravenous administration of *B. pertussis* caused increased vascular permeability in brain tissue of mice and increased vascular sensitivity to vasoactive amines, inducing EAE.

In the Babl article (Ex. 33), the authors state that the "polysaccharide capsule of *S. pneumoniae* is the major virulence factor...." 32 *Clinical Infect. Dis.* at 1157.

In the Black article (Ex. 34), the authors discovered that DPT, MMR, and OPV had protective effects in vaccinees against invasive bacterial disease. However, when they adjusted for the effect of frequency of well-care visits and day-care attendance, no significant relationship was seen between receipt of routine childhood vaccinations and the risk of bacterial infection for an individual vaccinee. The authors commented:

> It is possible that the apparent difference in disease risk between cases and controls is the result of selection bias. That is, children who were ill at the time of their well-care visits were less likely to be immunized than children who were well.

Id. at 748. The authors concluded that

> receipt of routine well-child pediatric care is associated with a decreased risk of invasive bacterial disease that appears to be unrelated to the receipt of childhood vaccinations and may relate to other factors such as nutrition counseling, other preventive health care measure, or an increased level of health consciousness and hygiene among parents bringing their children in for well-care visits.

Id. at 749.

In the Bratton article (Ex. 35), the authors compared children with pneumococcal bacteremia who were administered antimicrobial agents at their first visit with those who did not receive treatment. The first group did significantly better. The authors stated:

> However, the treated and untreated groups were not comparable, in that the former did have a recognizable focus of infection when first seen. Moreover, two children in the "treated" group did develop meningitis. Thus our data do not permit us to make recommendations for or against expectant antimicrobial therapy for the febrile child with no focus of infection....

90 *Ped.* at 705.

The authors continued:

> Is it possible to predict which children will have persistent bacteremia or will develop meningitis or other significant foci of infection? Our analysis of clinical and laboratory features ... did not reveal any statistically significant features on which to base such a prediction.

Id. at 706.

Petitioner filed on February 28, 2002 an article (Exhibit 36) entitled "Pertussis Vaccine Project: Rates, Nature & Etiology of Adverse Reactions Associated With DTP Vaccine," by L.J. Baraff, et al., Bureau of Biologics, March 18, 1980 (US Dep't of Commerce). In a population of 16,536 children aged 0-6 years who received DTP (15,752) or DT (784), DPT recipients had a higher rate of reaction, including fever, vomiting, seizures, and hypotensive-hyporesponsive episodes.

On March 27, 2002, respondent filed Exhibits 13-17: "Severe Reactions Associated with Diphtheria-Tetanus-Pertussis Vaccine: Detailed Study of Children With Seizures, Hypotonic-Hyporesponsive Episodes, High Fevers, and Persistent Crying," by D.A. Blumberg, et al., 91 *Ped.* 1158-65 (1993) (Ex. 13); "Risk Factors in Bacterial Meningitis: Charleston County, South Carolina," by D.W. Fraser, et al., 127 *J. Infect. Dis.* 271-77 (1973) (Ex. 14); "Pneumococcal Bacteremia in Charleston County, South Carolina: A Decade Later," by R.F. Breiman, et al., 150 *Arch. Intern. Med.* 1401-05 (1990) (Ex. 15); Letter from Loretta Hill, Wyeth-Ayerst Pharmaceuticals, to Dr. Vito Caserta, National Vaccine Injury Compensation Program, of Feb. 25, 2002, describing batch and lot administered (Ex. 16); and "Drug Information for the Health Care Professional," 20th ed. (2000), at 1282 (Ex. 17).

In the Blumberg article (Ex. 13), the authors pinpoint DPT endotoxin, but not pertussis toxin, as the cause of febrile DPT reactions. They studied 76 children and included 60 in the final

analysis. Of these, 32 had seizures, 14 had hypotonic-hyporesponsive episodes, 2 had only high fever, and 6 had seizures with high fevers. None had encephalopathy. 91 *Ped.* at 1160. Subjects younger than one year of age had a trend toward higher insulin values acutely and this was noted with the insulin-glucose ratio. Id. at 1161. The authors stated:

> An intriguing finding was the trend toward higher insulin values (and higher insulin-glucose ratios) in subjects younger than 1 year of age with severe DTP vaccine reactions. Although this may indicate an unusual susceptibility to alterations in insulin metabolism in this age group, this finding is consistent with previous studies. [citations excluded.]

Id. at 1163.

Vaccine endotoxin content correlated with febrile reactions. Id. at 1164.

In the Fraser article (Ex. 14), blacks in the poorest areas of a South Carolina county had a greater rate of pneumococcal meningitis. There were 106 cases of bacterial meningitis due to *Hemophilus influenzae*, but only 9 cases due to *Streptococcus sp.* 127 *J. Infect. Dis.* at 273.

In the Breiman article (Ex. 15), the authors noted the increase in the rate of pneumococcal bacteremia and the need to promote use of the pneumococcal vaccine.

On April 8, 2002, petitioner submitted Exhibit 37, "Metabolic and Hematologic Effects and Immune Complex Formation Related to Pertussis Immunization," by C.M. Mink, et al., 27 *Ped. Res.* 353-57 (1990), and Exhibit 38, "Changes in Plasma Insulin Concentration and Temperature of Infants After Pertussis Vaccination," by C.A. Hannik, et al., Third International Symposium on Pertussis, US Department of Health, Education & Welfare (1978) 297-99.

In the Mink article (Ex. 37), the authors evaluated three- to six-month-old babies (as well as older children) who received DPT. Infants (but not the older children) experienced an increase in their mean plasma insulin concentration, but no change in glucose concentration one day after

vaccination. Neutrophilia (increase in white blood cells) in vaccinees was probably due to endotoxin, and some reactions might be due to circulating immune complexes. 27 *Ped. Res.* at 355. The authors concluded:

> The etiology of adverse reactions after DTP immunization is multifactorial. Some reactions are due to circulating immune complexes that may involve either toxoid or bacterial antigens. The degree of fever in vaccinees correlates directly with the endotoxin content of the vaccine administered. [citations excluded.]

Id. at 356.

In the Hannik abstract (Ex. 38), the authors explored the reasons for serious reactions in infants to DPT. Recognizing that pertussis vaccine markedly elevates the level of circulatory immunoreactive insulin and induces hypoglycemia in mice, the authors theorized that the same process could occur in infants experiencing serious reactions:

> A low blood sugar level and an extremely low CSF-glucose concentration have been reported in children who developed convulsions 3 and 36 hours after receiving pertussis vaccine.

Third International Symposium on Pertussis, US Department of Health, Education & Welfare at 297.

Fifty-four children were tested at ages three and four months. Their glucose levels did not change over eight hours post-vaccination, but their plasma insulin concentration significantly changed. The children receiving a pertussis component in their vaccinations had a significantly elevated mean temperature. Id. at 298.

TESTIMONY

Dr. Kevin C. Geraghty testified for petitioner. Tr. at 12. Dr. Geraghty is board-certified in pediatrics, allergy, and immunology. Tr. at 15. His practice includes both adults and children.

Id. His opinion is that DPT was a substantial factor in causing James' encephalopathy and current condition. Tr. at 54.

On April 2, 1997, James had a stuffy nose, and a low grade fever of 100.1°. Tr. at 22. He received DPT, HiB, and OPV. Id. After the injections, he was feverish and vomited for two days. Tr. at 24. He was brought in for an examination which was normal neurologically. Id. His neck was supple, the Kernig sign was negative, and his fontanels were soft. Id. There was no sign of meningitis, but concern because of his symptoms. Id. James looked all right, but he was sent to South Suburban ER. Tr. at 25. Dr. Geraghty stated he was impressed by the rapidity of James' decompensation. Tr. at 25-26. Dr. Pai, his physician, questioned whether James was reacting to DPT. Tr. at 26. There was a crescendo in the first phase. Id. From runny nose and low temperature, James decompensated to vomiting and fever. Id. By Friday, he had completed phase 1. Id.

Phase 2 was in Dr. Pai's office where James had a temperature of 97.3°. Id. Dr. Geraghty questioned whether this was a mistake or whether James was going into shock due to hypoperfusion or perhaps it was due to the Tylenol given at 2:00 p.m. Tr. at 30. The rate of deterioration in James' condition is startling. Tr. at 26. At South Suburban, James had lethargy which reflected early involvement of the neurological system. Tr. at 27. His mother gave him Tylenol, but James' temperature rose to 101.9° rectally. Id. This is the magic number for blood-borne pathogens. Tr. at 28.

In South Suburban, at 7:20 p.m., on April 4, 1997, James' temperature was 101.9° rectally or 100.9° orally. Id. His mother said he was lethargic. Tr. at 31. James was poorly responsive and comatose in hours. Id. His fontanels were full. Id. Routine blood work showed severe

bacterial infection with immature pus cells. Tr. at 31. His white blood count was 9500, which is the upper limits of normal, but the percentage of pus cells was higher. Tr. at 34. Very toxic infections kill off white cells. Tr. at 35. James' cerebrospinal fluid (CSF) was cloudy and filled with pus. Tr. at 36. The strep was in James' CSF and also his brain in Dr. Pai's office. Tr. at 40.

James had decreased sodium due to vomiting and no fluids. Tr. at 40-41. An infection in the brain affects the level of sodium. Id. James' CSF glucose was zero, which is devastating. Tr. at 42. It means the infection was massive or had been there a while. Id. The CSF protein of 315 was a high level, which means the blood-brain barrier had been breached. Tr. at 43. Pertussis augments breach of the blood-brain barrier. Tr. at 42. Dr. Geraghty found a lab error in the multiplication of pus cells. Tr. at 43. The 26 white blood cell count would not produce a cloudy CSF. Id.

James was transferred to Christ Hospital on April 5, 1997. Tr. at 48. Bulging fontanel is not in Dr. Pai's records. Tr. at 46. As an inpatient, James was most unusual in going from a flat to a bulging fontanel, and from lethargy to a coma to seizures. Tr. at 47. James is quite different because of the extraordinary rapidity and seriousness of his symptoms in four to six hours. Id. (He had been at South Suburban Hospital ER for approximately 3½ hours, where he had received intravenous antibiotic. Tr. at 49.) James received additional antibiotic at Christ Hospital. Tr. at 51.

Dr. Geraghty disagrees with Dr. Egel, a treating pediatric neurologist, about the extent of James' recovery. Tr. at 51-52. James has sensory processing and attention problems, and bites others. Tr. at 52.

The basis for Dr. Geraghty's opinion that DPT was a substantial factor in causing James' encephalopathy is the unusual course of his illness, as well as components in the pertussis part of DPT which affect multiple aspects of the vaccinee's immune response. Tr. at 54. The blood-brain barrier protects the brain against infection. Id. Streptococcus pneumoniae in one out of 25 children (or 4-6 percent) has the ability to get in the brain where it causes vasculitis which allows death of tissue. Tr. at 55. In James' case, pertussis toxin modulated and worsened that process, which explains the rapidity and seriousness of his illness. Id.

Ordinarily, one would expect 15,000 to 25,000 white blood cells as the probable effect of pertussis toxin. Tr. at 56. Dr. James Cherry has written in the medical literature that pertussis affects the white count in healthy children. Id. But James was not healthy when he received DPT. Id. Pertussis vaccine decreases glucose by increasing insulin. Tr. at 57-58. (The islet cells of the pancreas make insulin.) Dr. Cherry has written that pertussis raises insulin, but not sugar. Tr. at 59. The islet-activating protein (IAP) of pertussis vaccine elevated the mean plasma insulin concentration in James' blood. Tr. at 60. Pertussis toxin goes to the pancreas that stimulates IAP which produces insulin. Id. Pertussis toxin is a protein in the vaccine, an islet-activating protein. Tr. at 64. It is a modulator and a stimulator. Tr. at 65. IAP induces immunity as well as stimulates production of insulin. Id. If one puts an infant under stress, this is not good. Tr. at 66.

An increase in insulin after receipt of DPT vaccine will not permit a rise in glucose if the vaccinee is already stressed by an infection and needs a rise in glucose. Tr. at 68. Dr. Geraghty radically disagrees that DPT protects the vaccinee from infection. Tr. at 70. It puts the immune system on a state of alert. Id. There is a high percentage of children carrying pneumococci on the outside of their bodies, i.e., it has not breached their blood-brain barrier to enter the blood stream.

Id. Cytomegalovirus can breach the blood stream. Id. James' pneumococcus went from his nose and entered his blood stream. Tr. at 70-71. Dr. Geraghty thinks DPT moved the pneumococcus from his nose to his blood stream, although he does not know. Tr. at 71. Even if pneumococcus enters the blood stream, a sizable percentage of children cure themselves. Tr. at 74. A bacterial infection takes longer that a viral infection to develop. Tr. at 75.

DPT has other effects besides raising insulin. Tr. at 77. DPT has a permeability factor which makes blood vessels leak. Id. Pertussis toxin has histamine-sensitizing factor. Tr.at 79. Increasing permeability of the blood vessels leads to a shock-like state. Tr. at 81. Pneumococcus breached the blood-brain barrier to cause meningitis, but one needs an additional factor to allow it to do so. Tr.at 82. James did not develop a high fever. Tr at 84. He was also on Tylenol. Tr. at 85. James' inability to mount a brisk stress reaction (indicated by his low white blood cell count) also muted his temperature response. Id.

His condition was complicated by his hydration state. Tr. at 87. He had a history of vomiting and low oral intake, leading to hypoperfusion (low blood sodium). Id. James had extraordinarily concentrated urine. Id. He shunted blood to the interior of his body to perfuse his interior organs. Id.

James did not have fulminant meningitis when he received his DPT. Tr. at 92. If he had had fulminant meningitis at that time, he would have been obtunded and lethargic. Id. Streptococci was probably in his blood stream before he received DPT because he had fever, but on physical examination from April 2, 1997 to April 4, 1997, James did not have meningitis. Tr. at 98. It is normal for a blood borne infection to linger for a couple of days. Tr. at 100. DPT

does not protect the vaccinee from infection. Tr. at 103. It increases vascular permeability in the brain and spinal cord. Id.

Dr. William Paul Glezen, a board-certified pediatrician and epidemiologist, testified for respondent. Tr. at 157. He specializes in pediatric infectious diseases, although he is not board-certified in that specialty. Id. He has treated many children with meningitis. Tr. at 158. His opinion is that James had fulminant meningitis when he received his DPT vaccination on April 2, 1997. Tr. at 159. The CSF results on April 4, 1997 of a protein of 315 and a glucose of zero would not have occurred if this were "fresh" meningitis. Id. To Dr. Glezen, everything that James experienced is explained by the bacterial meningitis. Tr. at 160.

Meningitis is inflammation of the meninges. Tr. at 161. The infection is not in the brain, but on the surface between the pia mater and the dura mater in the subarachnoid space. Id. Dr. Glezen participated in studies that monitored bacteria in the nose. Tr. at 162. Children acquire it regularly, particularly in low income areas. Id. Forty percent carry pneumococcus in the nose up to five months of age. Tr. at 162-163. If it is in the CSF, the person cannot clear it and it sets up a response. Tr. at 163-164. Cytokines and chemokines increase diffusion in the subarachnoid space. Tr. at 164. It has nothing to do with the blood-brain barrier. Id. Untreated meningitis is always fatal and pneumococcus is the hardest to treat. Id. Even if treated, eight percent of patients die. Tr. at 165.

James' course of meningitis was well within the spectrum that doctors see. Id. Medical literature confirms that DPT does not enhance the possibility of bacterial infection. Tr. at 167. James did not have regular well-baby care, and he was exposed to a lot of germs which increased his risk for developing serious complications. Tr. at 169-170. He went into respiratory distress,

necessitating a ventilator. Tr. at 170. Dr. Glezen testified that DPT acts as an adjuvant, enhancing antibody response. Id. No literature supports the idea that DPT aggravates infection and leads to meningitis. Tr. at 172. Animal studies, where massive doses of whole cell pertussis are employed, have no relevance to toxicity in humans. Tr. at 173. Pertussis toxin is an exotoxin. Tr. at 174. There is no evidence that pertussis toxin is active in a severe reaction. Tr. at 175. It is endotoxin that is active. Id. Endotoxin is like a polysaccharide in the cell wall of bacteria. Id. It excites an inflammatory response. Id. In large doses, endotoxin can induce shock. Id.

What was abnormal about James' blood count was the percentage of immature white cells. Tr. at 178. One generally expects to see a much higher count. Id. James was not responding very well to his infection, although he was not immune-compromised. Id. Asked why a doctor should not inoculate someone with a fever, Dr. Glezen responded that one might attribute the fever to the vaccine, instead of something else. Tr. at 179. DPT does not facilitate or amplify the process of disease. Tr. at 184.

Dr. Glezen is not board-certified in allergy and immunology. Tr. at 187. He opined that James had fulminant pneumococcal meningitis when he got the DPT and that bacteria entered his subarachnoid space. Tr. at 188. The fever, vomiting, and CSF findings on April 4, 1997 show he almost did not survive. Tr. at 191. Meningitis can be fairly subtle in infants; hence, James' normal examination with Dr. Pai on April 4, 1997. Tr. at 192. Infants' skulls can expand, allowing an inflammatory response. Id.

Dr. Glezen thought it unclear when James had full fontanel. Id. On April 4, 1997, the notes state the fontanel were soft, but referred to bulging fontanel. Tr. at 193. Dr. Glezen would defer administering DPT to a sick child until a fever resolves in order to avoid a reaction to the

vaccine on top of the underlying illness. Tr. at 195. Vaccine is an inert substance, but one can have an inflammatory response to the vaccine. Tr. at 196. With an infection, the agent is multiplying and increasing. Id. In order to respond to the vaccine, the recipient has to process antigen, but he needs a parallel response to the infection. Tr. at 197. We do not know when James had the onset of his meningitis, but it was probably at the time of his DPT and the DPT is coincidental. Id. James is black, and blacks and males are at a higher risk of bacterial meningitis. Tr. at 201. They are 36 times more likely than Caucasians to have meningitis. Id. In addition, he had no well baby care and there were older siblings in the household. Id.

James had a bad disease fast. His blood count of white cells showed he was having trouble responding to the infection. Tr at. 219. The average white blood count is 3,000; James' white blood count was 26. Id. DPT increases insulin levels but does not decrease glucose levels. Tr. at 203. The body has compensatory mechanisms. Id. DPT does not cause important hypoglycemia. Id. This is true for shock as well. Id. DPT minimally increases insulin. Id. DPT does not affect vascular permeability in people. Tr. at 204. In animals given a massive dose of histamine-sensitizing factor, it happens. Id. There are no studies of humans concerning vascular permeability. Id. Dehydration usually raises the temperature. Tr. at 205. James had shunting, and was shocky with poor color. Tr. at 206. Shunting is delayed capillary feeling in the skin and the skin temperature is cold. Id. Most of the time, someone with meningitis has 103° or higher temperature. Tr. at 207. DPT would stimulate the immune system. Tr. at 210. It should have stimulated James' immune system, but it is hard to conclude that. Tr. at 212. Fever and insulin changes are well documented after receipt of DPT. Id. We do not know if James was immune-compromised. Id.

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 DPT, James 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 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.

> 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.[6] 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

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[6] RCFC Rules, Appendix B, Vaccine Rule 8(c) 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."

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 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. Geraghty, an expert in allergy and immunology, opined that James' streptococcus pneumoniae was just beginning when he went to Dr. Pai for his first well-baby visit at the age of six months. He had never received DPT before. He had a low-grade fever and a stuffy nose. After his receipt of DPT vaccine, his fever became greater, and he started vomiting, stopped eating, had diarrhea, and became lethargic. When Dr. Pai saw James two days later, he specifically looked for meningeal signs, i.e., nuchal rigidity (stiff neck), bulging fontanels, and the Kernig's sign, and found none. But he was suspicious and sent James to the South Suburban ER where blood tests and a spinal tap showed he had streptococcal pneumoniae. He had elevated protein and zero glucose in his spinal fluid. His symptoms dramatically worsened rapidly: bulging fontanelles, cerebritis, left-side twitching and weakness, cortical infarctions, ataxia, and deafness.

The parties agree that meningitis due to the streptococcal pneumoniae was a substantial factor in James' illness and current condition. They do not agree whether the DPT was another substantial factor in his illness and sequelae.

Dr. Glezen, respondent's expert in pediatric infectious diseases, opined that when James first saw Dr. Pai on April 2nd, his pneumococcal meningitis was fulminant. And it was still fulminant two days later, on April 4th, when Dr. Pai saw James again before sending him to the ER. Therefore, DPT had no effect on James. Moreover, Dr. Glezen testified, DPT would have

had a protective effect on James, rather than made him more susceptible to the infection, relying on medical literature. Dr. Glezen does admit that James was not fighting the infection well. His white blood count was lower than it should have been.

Dr. Geraghty, on the other hand, stated that on April 2nd, James' pneumococcal meningitis was not fulminant. He had a stuffy nose and a low grade temperature from the streptococcal pneumoniae, but no clinically observable signs of fulminant meningitis, such as a stiff neck, bulging fontanels, and the Kernig sign. Over the next two days, James' symptoms worsened. His fever increased. He was vomiting and had diarrhea. He stopped taking his feeds. He became lethargic. But, Dr. Geraghty stated, when James saw Dr. Pai on April 4th, he still did not have signs of fulminant pneumococcal meningitis, i.e., no neurological signs. His neck was still supple, his fontanels were soft, and he had a negative Kernig sign. Dr. Pai questioned, in light of the increased fever, vomiting, diarrhea, anorexia, and lethargy, whether James was a having a reaction to DPT.

These factors plus James' rapid decompensation afterward form the basis for Dr. Geraghty's opinion that James' pneumococcal meningitis was not fulminant until after he saw Dr. Pai on April 4th and that, therefore, DPT was a substantial factor in James' illness and sequelae since the vaccine made it more difficult for him to fight the underlying streptococcal pneumoniae. Dr. Geraghty testified that medical literature supports the view that DPT, instead of having a protective effect, makes the vaccinee more susceptible to infection, which is why it is standard practice not to inoculate an ill child.

The experts do agree upon a few items. They agree that James mounted a poor response to the streptococcal pneumoniae. He had a very low white blood cell count and his glucose was

zero. Dr. Glezen could not give a reason for James' poor response and wondered if James is immune-compromised. Dr. Geraghty, on the other hand, opined that DPT modulated James' immune system so it could not produce the appropriate white cell response to the streptococcal pneumoniae. The zero glucose showed his defenses were devastated.

As for the medical literature, voluminous as it is, it shows one thing for certain: one can prove anything with it. The medical literature supports both experts. However, one must be cognizant of the fact that children in the studies who were inoculated and did not have an increase in their rate of infections post-vaccination were also not inoculated if they were already sick. (James was already sick when he received his vaccination.) Moreover, children who regularly receive well-baby care (which James, as a foster child, did not) generally have fewer infections.

As for the animal studies, it is well-established that pertussis is used as an adjuvant to increase vascular permeability in laboratory animals, inducing EAE, among other diseases. Moreover, in animals, such as mice and rats, the administration of pertussis, followed closely by injection with bacteria, induces an increased susceptibility to infection compared to control animals. On the other hand, administration of pertussis, followed 8 days later by injection with bacteria, shows a protective effect from the pertussis so that the animal is not ill.

The undersigned does not find credible the view, expressed by Dr. Glezen and some of the medical literature, that standard medical practice is to avoid inoculating already-ill children so that if they become sicker, one avoids blaming the illness on (or confusing the cause with) the vaccine. Doctors proceed because they want their patients to be healthy. It makes a lot of sense not to inoculate someone whose immune system is already busy fighting a disease rather than to stress it

further with the necessity of making antibodies for a new antigen or, in James' case, five new antigens since he received DPT, HiB, and OPV on April 2, 1997.

The undersigned is more impressed with Dr. Geraghty's testimony than with Dr. Glezen's. Clearly, on April 2nd, James' meningitis was not fulminant. There were no neurologic signs. Also, it is well-accepted (see the Cody article, e.g.), that DPT causes the very symptoms that James experienced after April 2nd: an increase in temperature, vomiting, anorexia, and lethargy. When James' foster mother brought him back to Dr. Pai on April 4th, James still had no neurologic signs. His neck was still supple. He had a negative Kernig's sign. His fontanels were soft. Dr. Pai entertained the possibility of James' having a reaction to his DPT, but he sent him to the South Suburban ER for a complete blood count and a spinal tap. By the time James arrived at the ER, his fontanels were slightly bulging. And his course proceeded downward from there. It is a wonder that he survived.

Dr. Geraghty's testimony illustrates a logical sequence of cause and effect. James' streptococcal pneumoniae was not in the fulminant stage, i.e., he did not have meningitis, when he received his DPT vaccination. The immediate effect of the vaccine was to increase his fever and bring on other signs of illness: lethargy, anorexia, vomiting, a weak cry, dehydration. Dr. Pai, although not seeing fulminant meningitis when he examined James two days later, was cautious enough to send James to the ER. Only then, did his clinical signs of meningitis become manifest: bulging fontanels, cerebritis, seizures, ataxia, and ultimately deafness.

This case is quite similar to Shyface, supra. Cheyenne Shyface received DPT at the age of two months on April 1, 1993. On the next day, he was less responsive and would not cry. On April 3rd, he did not respond to his caregivers or his environment. Cheyenne would not move his

head, grasp, vocalize, smile, or cuddle as he did before. He would not eat and lay with glazed and staring eyes. When his diaper was changed, the leg where the vaccine was injected jerked uncontrollably. He developed a fever on April 4th. On April 5th, he was brought to the emergency room at 5:23 a.m. with a temperature of 109° F. He went into respiratory arrest and died an hour later. The cause of death was listed as respiratory arrest due to 110° fever with dehydration and infection. An autopsy showed that James had a modest growth of E.coli bacteria. 165 F.3d at 1345.

Petitioners in Shyface alleged a Table encephalopathy and, in the alternative, causation in fact encephalopathy. Respondent defended on the basis that the E.coli infection (sepsis) was the principal cause of Cheyenne's death and was a known factor unrelated to the DPT. Testimony showed that the high fever, resulting from a combination of the DPT and E.coli infection, caused Cheyenne's death. The expert witness for petitioners testified that both were instrumental in causing the death. The expert witness for respondent testified that pneumonia existed in Cheyenne's cell linings, although not in his air passages. She said his temperature was very unusual and, generally, infants with bacterial infections do not have 110°. But when one sees either mild or moderate sepsis, one need look no further for a cause of death. Respondent's other expert testified that E.coli pneumonia caused Cheyenne's death. Id. at 1345-46.

The special master found that Cheyenne sustained an encephalopathy and that, contrary to respondent's position, Cheyenne did not have an overwhelming or fulminating sepsis, since the levels of E.coli at autopsy were modest in the lung and bladder. Id. at 1346. However, on remand from the United States Court of Federal Claims, the special master found that the E.coli

infection and the DPT were in equipoise and, therefore, petitioners could not prevail. Id. at 1347. The dismissal was affirmed by the U.S. Court of Federal Claims.

The Federal Circuit reversed and awarded petitioners the death benefit of $250,000.00, saying that petitioners had proven that but for the vaccine, Cheyenne would not have died, and also that the vaccine was a substantial factor in his death. Id. at 1348. The Federal Circuit held "that an action is the 'legal cause' of harm if that action is a 'substantial factor' in bringing about the harm, and that the harm would not have occurred but for the action." Id. at 1352. Even though the Shyfaces did not prove that DPT was the only or predominant cause of Cheyenne's death, they satisfied the requirements of the Vaccine Act that DPT was a substantial factor. Id. at 1353.

In the instant case, Dr. Geraghty testified that DPT worsened James' condition, stressing his immunologic system beyond what he could handle, so that his meningitis, once it developed, was extraordinary in its rapid and devastating symptoms. He testified that, had it not been for the vaccine, James would have had a chance to clear the infection from his system. Medical literature shows that those with less severe meningitis can clear the infection from their systems. But James' increased fever, vomiting, and anorexia led to dehydration (his urine was highly concentrated), lethargy, and a weak cry, and this was all before his meningitis became fulminant and neurologically manifest. It is logical and credible that the effect of DPT on James' immune system imposed a burden he could not meet, hence his failure to produce a high enough white cell count to fight the infection, and the zero reading of glucose. If DPT had not made him so ill, he would have fought the streptococcal pneumoniae better, and not have suffered the rapid

decompensation he experienced with the sequelae he has today. This satisfies the "but for" prong of the Shyface decision.

See also Herkert v. Secretary, HHS, No. 97-518V, 2000 WL 141263 (Fed. Cl. Spec. Mstr. Jan. 19, 2000), in which the undersigned held that an acellular DPT was a substantial factor (as was cytomegalovirus or CMG) in causing John Herkert's transverse myelitis (TM). The little boy had been fighting CMG when he received his DPT. He became feverish and cranky the night of vaccination (a reaction to DPT) and, the next morning, he was almost comatose from transverse myelitis (TM). The undersigned held that DPT modulated John Herkert's immune system so that he could no longer fight the underlying infection, which opportunistically caused his TM.

Petitioner prevails on the theory that but for the DPT vaccine, James would not have had the injury, but also that the vaccine was a substantial factor in bringing about his injury and its sequelae.

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. 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