



(TS) in the form of a residual seizure disorder (RSD) and/or encephalopathy within the Table time limits of the Act. 42 U.S.C. § 300aa-14(a)(I)(B),(D), and (E). Respondent defends with the assertion that a factor unrelated to MR vaccine, i.e., an intercurrent infection, caused her fever which caused her initial seizure, which was within Table time of her vaccination. In any event, respondent asserts that Tammy's on-Table seizure does not constitute a significant aggravation of her TS.

The hearing was held on October 21, 1991 (at the Mayo Clinic as part of all the TS cases), May 3, 1995, October 28, 1996, and April 11, 1997 (in Washington, DC). Testifying for petitioners were Dr. Manuel Gomez at the Mayo Clinic, and Dr. G.L. Smith and Dr. Marcel Kinsbourne in Washington, DC. Testifying for respondent were Dr. W. Paul Glezen, Dr. Phillip S. Lesser, Dr. James C. Parke, Jr., and Dr. Michael Pollack.

## **FACTS**

Tammy was born on May 23, 1971. Med. recs. at 3. She received a MR vaccination on June 12, 1972. On June 21, 1972, she began to have a cough and fever. Med. recs. at 60. She began pulling at her ears and also vomited. On June 22, 1972, at 3:00 a.m., Mrs. Evans was awakened by a strange noise and saw Tammy have a generalized tonic-clonic seizure with greater activity on the left. This seizure lasted an hour before Tammy was brought to the Emergency Room of Charlotte Memorial Hospital, where she was medicated and her seizures controlled. She had a temperature of 104 degrees and was in a postictal state with decreased movement on her left side. Tammy also seized in the hospital. Her four and a half year old brother had petit mal seizures. Med. recs. at 68-71.

Dr. Richard Taylor, a pediatric resident at Charlotte Memorial, examined Tammy on June 22, 1972. He recorded that she had a three- to four-day history of isolated cough progressing to vomiting with the cough. She had had a classic grand mal seizure. She was low normal in development, but with no abnormal neurological findings. She had a rash on her trunk which was becoming more prominent. Med. recs. at 75-76. A spinal tap performed on June 22, 1972 showed elevated protein of 193 and elevated glucose of 105. Med. recs. at 87. Her discharge summary states Tammy had a papular rash on her neck and groin region and many small white maculae on her trunk and extremities. Her right tympanic membrane appeared to be red and bulging. Her throat was not injected and her nose was within normal limits. Med. recs. at 70-71. On June 24, 1992, Tammy was doing well and moving the left side of her body well. Med. recs. at 76. She was to be maintained on Phenobarbital. Med. recs. at 71. An EEG performed on July 20, 1972 showed an abnormal focus. Med. recs. at 112.

Tammy visited the Outpatient Department of Charlotte Memorial Hospital on December 6, 1972. The pediatric neurologist wrote that when she was hospitalized in June, she had right otitis media at the time. She had left-sided paralysis for one day which cleared afterward without deficit. Her skull films and last lumbar puncture were normal. Her neurological exam was grossly within normal limits. She was on Phenobarbital. Med. recs. at 130.

On June 6, 1973, the doctor noted that Tammy was slower than her siblings were at her age since her last visit six months earlier, and that she had spells of staring and shaking which she had not had before the last six months. Her Phenobarbital was increased. Med. recs. at 131-32.

A notation for August 1, 1973 states that Tammy had frequent minimal seizures consisting of stiffening and shaking of her extremities, and staring, lasting about ten seconds. Med. recs. at 132.

Her next visit to the doctor was on November 7, 1973. Tammy had had an increase in the frequency of her seizures, two to four per week. The seizures consisted of staring and chewing movements of her mouth, which lasted one to three minutes. She was more active than her siblings were at her age. She

walked at ten to eleven months, but now had only about a twelve-word vocabulary and did not use sentences. Med. recs. at 133.

Tammy had a skull x-ray on April 3, 1974 which did not detect the classic intracranial calcifications of TS; the skull was within normal limits although Tammy had a history of TS. Med. recs. at 129.

Tammy was evaluated on December 4, 1974. She had not had seizures for a year. Med. recs. at 139. An EEG performed on November 18, 1977 showed Tammy's brain to be diffusely abnormal and very poorly organized. Med. recs. at 113. An EEG performed on May 19, 1980 was markedly abnormal. Med. recs. at 114.

A CT scan performed on August 1, 1980 showed normal subependymal calcifications consistent with TS. Med. recs. at 122. An EEG performed on September 12, 1980 was diffusely abnormal, suggestive of a primary cerebral dysrhythmia. Med. recs. at 115. Further EEGs on November 24, 1981, October 6, 1982, and December 20, 1983 were all abnormal. Med. recs. at 116-19.

## TESTIMONY

Dr. Manuel Gomez, the world's expert in TS, testified on October 21, 1991 as part of all TS cases. Dr. Gomez's testimony on TS was taken at the Mayo Clinic and is described in *Costa v. Secretary HHS*, No. 90-1476V, 1992 WL 47334, \*5-\*8 (Cl. Ct. Spec. Mstr.), *remanded*, 26 Cl. Ct. 866, *on remand*, 1992 WL 365421 (Fed. Cl. 1992). Dr. Gomez's textbook on TS<sup>(2)</sup> and other material<sup>(3)</sup> are described in the first opinion in *Costa*.

Dr. Gomez testified that TS is not an encephalopathy. Gomez tr. at 99. Rather, TS is a genetic disorder which is either inherited or results from a mutation. Gomez tr. at 96. Brain growth controls tuber growth. Tubers exist at birth and do not multiply. Gomez tr. at 97. The most common presenting symptom of TS is seizures. Gomez tr. at 100. There is a demonstrable correlation between the presence of many low attenuated lesions and the frequency and severity of seizures and mental retardation in an infant less than one year old. Gomez tr. at 101.

The most common age for an onset of seizures in TS children is the first year of life. The most common symptom of presentation is infantile spasms. Infantile spasms are age-dependent seizures occurring between the ages of three and eight months, regardless of the cause. Gomez tr. at 103.

In the first part of the hearing in this case held in Washington, DC in May 1995, Dr. W. Paul Glezen testified for respondent. Tr. at 7. (Since petitioners benefited from the statutory presumption of causation of Tammy's on-Table seizure, the court directed respondent to put its evidence on first.) Dr. Glezen is an expert in pediatrics and the epidemiology of infectious diseases. Tr. at 8-9. He studies acute respiratory illnesses of children and viral etiologies. Tr. at 8. He has over one hundred publications directed toward these problems. Tr. at 9.

Dr. Glezen's opinion is that an intercurrent viral infection, not the MR vaccination, caused Tammy to have a fever which caused her seizure. Tr. at 15-16. TS made Tammy more vulnerable to seize with fever. Tr. at 16. By "intercurrent," Dr. Glezen means that the viral infection occurred in the time period during which we are looking for a reaction to the vaccine. Tr. at 17.

Tammy had four older siblings, putting her at high risk for a viral illness. Tr. at 18. She was coughing severely enough to vomit mucous. *Id.* She was put on Phenergan suppository to stop her vomiting. *Id.*

Her fever continued for two days in the hospital. Tr. at 19. If she had been reacting to MR vaccine, Tammy's fever would have been transient. *Id.*

Tammy's rash is non-specific and could be associated with many different viral infections. *Id.* Enteroviruses are common in June. Tr. at 19-20. Her cough, vomiting, and pulling at her ears are more likely related to a viral illness. Tr. at 22.

In control trials of MR vaccine, there were no excess symptoms of respiratory illness in vaccinees. *Id.* Only low grade fever occurred more in vaccinees than non-vaccinees. *Id.* High grade fever did not occur in excess. Tr. at 22-23. Tammy had a high grade fever. Tr. at 27. The vaccinees and non-vaccinees were observed for ten days. Tr. at 23. Dr. Glezen referred to R. Ex. CC, Ramos-Alvarez, M., et al., *Immunization of Children with Attenuated Measles-Rubella Bivalent Vaccine*, 29 Am. J. Dis. Child 474, 475-76 (1975). Tr. at 26.

In the April 1997 part of the hearing, Dr. Glezen testified that he has spent forty years in infectious diseases. Tr. at 447. Tammy received the Schwartz strain of MR vaccine, which is further attenuated than the earlier Edmondston strain. <sup>(4)</sup> Tr. at 449. Package inserts report everything that has been associated with the vaccine, not what the vaccine causes. Tr. at 455. Attenuated vaccine is administered intramuscularly, not in the respiratory tract. *Id.* It does not get into the respiratory tract. *Id.*

It is possible to have both a cold and a vaccine reaction. Tr. at 460. Dr. Glezen found Tammy's rash problematic. Tr. at 461. Tammy's throat was not injected. Tr. at 467.

In the April 11, 1997 part of the hearing, Dr. Phillip S. Lesser testified for respondent. Tr. at 305. This was his first vaccine case testimony. *Id.* He is a pediatric neurologist, board-certified in both pediatrics and neurology with a specialty in children. Tr. at 306. He belongs to the epilepsy team at the Carolina Medical Center and is on the faculty of the University of North Carolina. *Id.* He has been practicing pediatric neurology for twenty years. *Id.* He has seen twenty-five to fifty patients with TS in his career. Tr. at 309.

When he was a pediatrician from 1971-74, he had experience with measles vaccine and routinely immunized his patients with MMR and less so with MR (bivalent) vaccine. *Id.* It was an excellent vaccine with few side effects. Tr. at 310. There was no large percentage of rashes or upper respiratory infections among vaccinees. Tr. at 310-11. When a child did have symptoms following MR or MMR, an intercurrent illness, upper respiratory infection, fever or some other easily identified illness was occurring at the same time. Tr. at 311.

Tammy was his patient. Tr. at 316. Dr. Lesser knows Dr. Parke who was Chairman of Pediatrics when Dr. Lesser came to Charlotte, NC. Tr. at 313. He also knows of the work of Dr. Glezen and has met Dr. Kinsbourne. Tr. at 314.

Dr. Lesser's opinion of Dr. Parke is that he is a superb pediatrician with unusual experience in infectious disease, neonatology, and genetics. Tr. at 315-16. The first year Dr. Lesser came to Charlotte in 1977, he saw Tammy when she was about six years old and continued to follow her until about two years ago. Tr. at 316-17, 331. He managed her seizures for years. Tr. at 317. Two years ago, an epileptologist, Dr. Wilner, joined the group and Tammy became his patient. *Id.*

In 1991, Dr. Lesser sent a letter to Tammy's mother (R. Ex. FF) because she asked him on a number of occasions if Tammy's seizures and developmental delay were related to her MR vaccine. Tr. at 317-18. He was surprised at the question. Tr. at 318. He was never aware that MR was an issue. *Id.* He reviewed

Tammy's hospital records from 1972 at Mrs. Evans' request. *Id.* He found Tammy's condition consistent with the diagnosis of TS, and there was no relationship to her MR vaccine. Tr. at 318-19. She had symptoms of an upper respiratory infection and fever, possibly otitis media. Tr. at 319. She recovered quickly from status epilepticus and was discharged from the hospital two days later. *Id.* Her condition was unchanged from baseline. Tr. at 319-20. Dr. Lesser stated Tammy could not have had a serious vaccine reaction and recover two days later. Tr. at 320.

Dr. Lesser thought the fever was significant and part of her upper respiratory infection, not due to her MR. Tr. at 320. The symptoms of upper respiratory infection that she had were cough, pulling at her ears, gagging, vomiting and fever. *Id.* This occurred ten days after her MR vaccination. *Id.* Dr. Lesser admitted that since measles virus causes inflammation of the respiratory system, it makes sense that measles vaccine can also inflame the respiratory system. Tr. at 339-41. Measles vaccine could possibly lead to vomiting. Tr. at 341. The package insert for measles vaccine warns of vomiting, sore throat, cough, rash, and fever. Tr. at 341-42. Tammy had all these symptoms, but Dr. Lesser believes she had a virus (and not a measles virus) because a vaccine reaction is rare. Tr. at 342-43. Tammy's nose, throat, and chest were normal on discharge. Tr. at 348. The average respiratory infection clears in five to seven days. *Id.*

Tammy did not have measles encephalitis because her cerebrospinal fluid was normal, her seizure was easily managed and stopped, she had a quick recovery from her seizure, and her fever went down. Tr. at 321. The fever triggered the seizure. Tr. at 322. Tammy's signs of TS were already there (she had hypopigmented macules). *Id.* Her brother had had seizures. *Id.*

Tammy's seizure was prolonged because of her TS. *Id.* She was at high risk for developing a seizure disorder. *Id.* Tammy had a seizure with paralysis on the left, which means there was a focal emphasis on the right hemisphere of her brain. Tr. at 338. This cleared the following afternoon. Tr. at 337-38. Fever can cause status epilepticus and be the only cause. Tr. at 325. Dr. Lesser doubted that Tammy suffered ill effects from the seizure because she was back to baseline at discharge. Tr. at 329. Her seizures recurred later when she was followed in the clinic, but she was not in bad condition in between. Tr. at 329-30.

Tammy has mild to moderate mental retardation today. Tr. at 330. Her seizures are well-controlled; she has one to two a year. *Id.* She does not have any other complications of TS. *Id.*

Dr. James C. Parke, Jr., testified next for respondent. Tr. at 355. He is a pediatrician who was chairman of the Department of Pediatrics at the Carolinas Medical Center from 1968-91. Tr. at 356. From 1969-70, he performed clinical evaluation of vaccines against bacterial disorders. *Id.* He has seen twenty TS patients in his career. Tr. at 359. He has administered MR vaccine. Tr. at 360. Reactions to measles vaccine can include fever, rash, and respiratory symptoms. Tr. at 362-63. He knows Dr. Lesser, Dr. Glezen, and Dr. Kinsbourne. Tr. at 364. He does not remember Tammy independently from her 1972 hospital admission, but he remembers her from visits to the clinic. Tr. at 366.

Tammy received MR vaccine on June 12, 1972. Tr. at 367. On June 21, 1972, she had fever in the morning, followed by coughing in the afternoon and at night that led to regurgitation of mucous; she pulled at her ears and had a temperature of 102 degrees. *Id.* On June 22, 1972, at 3:00 a.m., Tammy had a major motor seizure, slightly more active on the left. which continued for one or more hours. *Id.* He attributes her seizure to the fever which, in the emergency room, was 104 degrees. *Id.*

Her physical examination in the ER and in the hospital showed a normal head circumference, a small area of abnormality of skin on the right side of her face, and numerous small areas of macular

pigmentation. Tr. at 368. The respiratory tract was the primary site of Tammy's infection. Tr. at 369. He thinks the most likely virus to be the cause is enterovirus (echovirus or Coxsackie). *Id.* An enterovirus is much more likely to produce a high fever than a reaction to MR vaccine. Tr. at 371. Moreover, the short duration of her illness and the occurrence of a fleeting, macular, reddish rash points to an enterovirus. *Id.*

When MR was experimentally administered, two percent who received placebo had a rash in the next seven days and three percent who received MR had a rash in the next seven days. *Id.* One is not so likely to see a rash occur after a MR vaccination. Tr. at 372.

The degree of fever suggests if it were secondary to MR, one would expect the duration of the illness to last longer. Tr. at 373. As for having mucous and a cough, there was no difference in occurrence between non-vaccinees with placebo or vaccinees with MR or measles vaccine. Tr. at 372.

Tammy did not have measles encephalitis. Tr. at 374. If she did have it, her symptoms should have persisted, but she recovered quickly. *Id.* Her cerebrospinal fluid also did not show encephalitis. *Id.* She had a few red blood cells in her spinal fluid, denoting a bloody tap which caused the mild elevation of her protein. Tr. at 374-75. Her next spinal tap showed normal levels. Tr. at 375.

Dr. Parke's conclusion is that it is much likelier that Tammy had an intercurrent enterovirus than a vaccine reaction. Tr. at 376. Her seizure disorder is unrelated to her June 22, 1972 seizure. Tr. at 376-77. Her seizure disorder is related to the natural history of her TS. *Id.* Because an attenuated virus is in the vaccine, there is less likelihood of having a reaction and the reaction, if it occurred, would be less severe. Tr. at 380. MR vaccine occasionally causes high fever. *Id.* If Tammy had had a high fever from measles vaccine and other symptoms of measles itself, he would have expected the symptoms to last longer than Tammy's illness. Tr. at 390-91. The majority of reactions to MR vaccine are shorter and have a low temperature. Tr. at 394. A cough can be a reaction to a vaccine. Tr. at 397. A rash is compatible with enterovirus. Tr. at 405.

Dr. Michael Pollack testified next for respondent. Tr. at 406. He is a pediatric neurologist certified in both pediatrics and neurology with a specialty in children. Tr. at 407. He is also a board-certified clinical neurophysiologist. *Id.* The overwhelming majority of his patients have seizures. Tr. at 408. He has two years of general pediatric practice. Tr. at 411. In his career, he has seen more than fifty patients with TS. *Id.* Currently, he is seeing twenty TS patients. *Id.*

His opinion is that Tammy's initial seizure was caused by TS and precipitated by fever. Tr. at 412. With reference to the residual effect of Tammy's first seizure, Dr. Pollack stated it did not alter the course of her TS or seizure disorder. Tr. at 412-13. The cause of Tammy's current condition is TS. Tr. at 413.

The seizure began in the right cerebral hemisphere, causing left Todd's paralysis. *Id.* Her EEG showed slow wave focus in the parietal and temporal areas on the right. *Id.* Tammy has a tuber in her right parietal-temporal lobe and three tubers in the right hemisphere. Tr. at 414.

Fever definitely makes seizures more likely in those predisposed to seize. *Id.* A transient infectious process, probably viral, caused Tammy's fever. *Id.* Tammy had a rash at the site of her intravenous line which resulted from irritation from the cleaning solution and tape. Tr. at 415. She had a papular rash of her neck and inguinal region which were due to sweating from the fever. *Id.*

Tammy did not have prolonged alteration of her neurological status. Tr. at 416. There was an interlude of time between the June 22, 1972 seizure and the onset of her seizure disorder. Tr. at 417. Staring and shaking were noted on June 6, 1973 as occurring in the last six months. Tr. at 418. Afebrile seizures

began before June 1973. Tr. at 417. There is no causal relationship between her June 22, 1972 febrile status epilepticus of focal onset and her January 1973 staring and shaking. Tr. at 420. There is no medical evidence to support that MR significantly aggravated her TS by her first seizure. Tr. at 420-21. Tammy did not have sequelae to her June 22, 1972 seizure. Tr. at 421. She recovered neurologically by the time she was discharged. *Id.* Tammy was thirteen months old at the time of her first seizure. Tr. at 426-27. Seizures can start in the second year in TS. Tr. at 427. Her subsequent history would have been the same. Tr. at 428. Status epilepticus is more common among TS patients than in the general population. Tr. at 429.

It is helpful to know that Tammy has a lesion on the side of the brain where her seizure occurred. Tr. at 433. There is an anatomic basis to associate TS with her seizure. *Id.* One month after her hospitalization, on July 20, 1972, Tammy had an abnormal EEG. Tr. at 435. The persistence of EEG abnormalities shows that there is an anatomic correlative to her seizure. *Id.* Her EEG might have looked like that before her first seizure. Tr. at 438. The EEG from 1972 could not be interpreted to show brain damage from her status epilepticus in June 1972. Tr. at 439. She recovered neurologically to her premorbid state after discharge, even though her EEG was abnormal. Tr. at 440.

Dr. G.L. Smith testified for petitioners at the May 3, 1995 part of the hearing. Tr. at 94. 1995. He would not offer an opinion as to whether or not Tammy had an intercurrent viral infection. Tr. at 111. His expertise devolved to the question of whether or not Tammy had otitis media. Tr. at 95. His opinion is that she did not. *Id.* She did not have an elevated white count, which she would have had if she had had otitis media. Tr. at 98. He recognized that something was going on in her respiratory tract because she was coughing and vomiting mucous. Tr. at 99-100. On discharge, she was not prescribed any more antibiotics, showing that there was not a significant infectious process. Tr. at 100.

Dr. Smith thought a diagnosis of viral infection conjectural. Tr. at 111. The only evidence of it was her cough, rales, and temperature elevation. Tr. at 111-12. He offered no opinion as to whether her MR vaccination caused her cough and vomiting. Tr. at 112. Respiratory viruses are most common for Tammy's age. *Id.* They can cause vomiting. *Id.* In fact, the most common cause for the combined symptoms of vomiting, coughing, pulling at the ears, and temperature is viral infection. *Id.*

In the October 28, 1996 part of the hearing, Dr. Marcel Kinsbourne testified for petitioners. Tr. at 127. He is board-certified in pediatrics and has British credentials in neurology. Tr. at 128. Tammy's rash was on part of her trunk. Tr. at 133. It began as macular (spots which were not raised) and became macular-papular (center of blotches which are raised). *Id.* This is very typical of a measles rash, but also happens in a virus. Tr. at 136-37.

Tammy's nose was slightly congested and she coughed up mucous. Tr. at 138. A congested mucous membrane is a component of measles. *Id.* Tammy's throat was not injected and her nose was within normal limits. Tr. at 141. Her ears did not have an acute process noted. Tr. at 142. No treating doctor diagnosed Tammy with a respiratory infection when she was hospitalized. *Id.* Her protein level in the spinal fluid was elevated at 193 because it was a bloody tap. Tr. at 144. However, protein sometimes goes up when there is status epilepticus as well as a bloody tap. Tr. at 145. In her second tap, the protein was 21, which is normal. *Id.* This was two days after the first spinal tap. *Id.* Her white blood cell count of 7800 was moderately elevated, which is consistent with a virus, but it does not tell one which virus: the measles, respiratory or gastrointestinal. Tr. at 148.

Any foreign protein can elicit a temperature elevation. Tr. at 149. The package insert to MR vaccine says that a moderate fever (101-102.9 degrees) occurs occasionally and a high fever (above 103 degrees) occurs less commonly. Tr. at 150. Tammy's fever is consistent with a measles reaction. Tr. at 150. It is also consistent with a viral infection; however, if Tammy had a respiratory infection, it was a mild one.

*Id.* She was discharged two days later and everything had cleared up. Tr. at 151.

Tammy's seizure was more marked on the left than on the right. Tr. at 153. It could not be a simple febrile seizure. Tr. at 153-54. Children with TS have a propensity to seize, but usually it is not status epilepticus. Tr. at 155.

In Dr. Kinsbourne's opinion, a mitigated measles virus attacked Tammy's brain. Tr. at 156. Tammy did not have the full picture of measles encephalitis, but she had a severe seizure. Tr. at 157. Prior to her measles vaccination, Tammy had had fevers. *Id.* Both DPT and measles vaccines contain agents causing comas and encephalopathy. Tr. at 158-59.

Tammy was discharged two days after admission. Tr. at 159. She made a rapid recovery. *Id.* Her other symptoms were slight. *Id.* Her rash was more prominent. Tr. at 159-60. She was not developmentally different after her discharge. Tr. at 160. There was possible damage to parts of her brain that were not known until later. *Id.*

Tammy has borderline mental retardation which is found only in a TS child with seizures. Tr. at 161. Dr. Kinsbourne thinks the beginning of Tammy's seizure disorder was June 22, 1972, the date of her first seizure. Tr. at 162. It could be that the measles vaccine or her status epilepticus caused the damage to Tammy's right hemisphere that was reflected in the EEG of July 20, 1972. Tr. at 164. Measles vaccine caused the status epilepticus. Tr. at 165-66. Some of the time, status epilepticus damages the brain. Tr. at 167.

Because Tammy has TS, her first seizure initiated mental deterioration and subsequent seizures. Tr. at 168. Dr. Kinsbourne stated that if Tammy had not received MR vaccine, she would not have seized when she did because she had reached thirteen months of age without seizing. Tr. at 168-69. TS predisposed Tammy to seizures, but not to status epilepticus. Tr. at 169.

The records do not show that Tammy's four older siblings had a viral illness at the time Tammy became sick. Tr. at 172-73. She was given six and one-half mg. of Valium, which is a substantial amount for a thirteen-month old. Tr. at 176. Under the growth and development portion of the hospital records is noted that Tammy said only "da da." Tr. at 177. This seems to show low normal development. *Id.* No neurologist was consulted, which is perplexing. Tr. at 180. Yet, Tammy walked at ten months, which is early. *Id.*

Dr. Kinsbourne does not claim expertise in infectious diseases. Tr. at 186. Fever per se does not cause status epilepticus. Tr. at 197. About three-quarters of TS children have seizures. Tr. at 194. The most common cause of status epilepticus in a child under three is fever. Tr. at 198. It is not often that status epilepticus is the first sign of epilepsy. Tr. at 201. It usually begins with individual seizures -- little jerks and infantile spasms. Tr. at 202. The significance is that something else severe was going on if status epilepticus was Tammy's first sign of epilepsy. *Id.* Status can happen without subsequent epilepsy. Tr. at 205. He does not think that fever by itself is a reasonable cause of status epilepticus. Tr. at 207. To Dr. Kinsbourne, once a TS child has a seizure, he has a seizure disorder. Tr. at 242. Intercurrent infections can cause the onset of seizures in a TS child. Tr. at 249. Dr. Kinsbourne's opinion is that fever and the effects of the measles vaccine on Tammy's brain caused her status epilepticus. Tr. at 255.

No specific literature links measles vaccine to the onset of seizures in TS patients. Tr. at 258-59. But measles vaccine can trigger the onset of seizures in normal children. Tr. at 259. There is no literature showing an increase of respiratory symptoms following MR vaccine. Tr. at 264. Tammy had morbilliform rash (which is mild) on parts of her trunk. Tr. at 282. There is literature that conjunctivitis,

rhinitis and cough were significantly less frequent in bivalent vaccines than in measles monovalent vaccines (R. Exc CC). Tr. at 283. Whatever caused Tammy's status epilepticus caused her propensity to generate discharges showing irritable dysfunction of that part of her cortex. Tr. at 287. A seizure simply caused by a fever does not result in a temporal focus. *Id.* Dr. Kinsbourne does not see sufficient evidence for a viral infection. Tr. at 292. To him, the strikingly abnormal EEG one month later shows a significant aggravation of her TS. Tr. at 294. This was her first EEG. *Id.*

## **DISCUSSION**

### Significant Aggravation

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** [emphasis added]." 42 U.S.C. § 300aa-33(4). In order for this court to hold that MR vaccine significantly aggravated Tammy's TS, it must find that Tammy experienced greater disability, pain, or illness accompanied by a substantial deterioration of health within Table time of the vaccination.

Legislative history provides insight into Congress' interpretation of "significant aggravation:"

The committee has included significant aggravation in the Table in order not to exclude serious cases of illness because of possible minor events in the person's past medical history. This provision does not include compensation for conditions which might legitimately be described as pre-existing (e.g., a child with monthly seizures who, after vaccination, has seizures every three and a half weeks), but is meant to encompass serious deterioration (e.g., a child with monthly seizures who, after vaccination, has seizures on a daily basis).

H.R. Rep. 98, 99th Cong., 2d Sess. 15-16, reprinted in U.S.C.C.A.N. 6344, 6356-57.

The language of the statute indicates that onset of an on-Table significant aggravation must occur within fifteen days of a MR vaccination. "Time period for first symptoms or manifestation of onset or of significant aggravation after vaccine administration: ...15 days...." 42 U.S.C. § 300aa-14(a)(II)(B) and (C). The records clearly establish that Tammy had a seizure within ten days of her MR vaccination. Therefore, the statutory presumption is that the MR vaccine caused Tammy's seizure.

The presumption, however, does not extend to the seizure constituting a significant aggravation of her pre-existing TS. That determination is left to the court, based on the case law already before it in *Whitcotton v. Secretary, HHS*, 81 F.3d 1099 (Fed. Cir. 1996); *Suel v. Secretary, HHS*, 31 Fed. Cl. 1, 12 (1993); and *Costa v. Secretary, HHS*, 26 Cl. Ct. 866, 870 (1992) (dictum), as well as the evidence in this case.

However, the court does not need to proceed to an evaluation of whether or not Tammy's seizure on June 22, 1972 significantly aggravated her TS if respondent rebuts the presumption that the MR vaccine caused her seizure. Section 13(a)(1)(B) and (2)(B). There is no dispute that the fever caused her seizure.

Respondent's position is that an intercurrent viral infection, not the MR vaccine, caused Tammy's fever which caused her seizure. If the infection caused the fever, then the MR vaccine could not have significantly aggravated Tammy's pre-existing TS. As a secondary position, respondent defends that Tammy's first seizure is unrelated to her subsequent seizures.

This case is different from the other TS cases pending before this court (and those already concluded) in that it deals with MR vaccine, not DPT vaccine, and the child at issue is not within the first year of life.

In addition, respondent has provided epidemiological evidence that a TS child with eight or more tubers is more likely than not to experience seizures.<sup>(5)</sup> However, Tammy had seven tubers, according to the MRI interpreted by respondent's Dr. Robert A. Zimmerman. R. Ex. MM. (Dr. Zimmerman found the MRI report acceptable, though not ideal.) Even assuming the court accepted respondent's epidemiological tuber count defense, it would not be sufficient in this case because Tammy, by current count, has less than the number of tubers that make it probable she would have seized anyway, according to this defense.

As Dr. Gomez, the world's expert in TS, testified, TS leads to infantile spasms. These spasms generally occur in a child between the ages of three and eight months. But, Tammy did not have infantile spasms. She was beyond the age when those seizures occur when she received her MR vaccine at thirteen months of age. She had a classic grand mal seizure which put her in status epilepticus because it lasted more than an hour.

Dr. Parke, Tammy's attending physician, with impeccable credentials in the areas of pediatrics, infectious disease, and vaccines, expressed his opinion that Tammy was hospitalized June 22, 1972 because of a viral infection. He stated this was probably an enterovirus because she had vomited and had a rash on her face and torso. He attributed the fever to this virus and the seizure to the fever. He expressly rejected the MR vaccination as the cause of her fever because respiratory symptoms, e.g., a three- to four-day cough, do not occur more frequently in children who received a measles vaccination than in non-vaccinated children. He attributed her cough and vomiting to the acute viral infection. That her fever disappeared rapidly was further proof to him of the enterovirus infection.

The court finds the statements of a treating physician, particularly one of the caliber of Dr. Parke, to be particularly impressive. Moreover, the court doubts that Tammy had a measles virus encephalitis. But that does not mean she did not have a mild reaction to her measles vaccination, which entailed fever. All the doctors concluded that the fever led to her seizure. Even though Tammy had had fevers previously without seizing, she began to seize after this particular fever. Her seizure was more than a simple febrile seizure because, as respondent's Dr. Pollack and petitioners' Dr. Kinsbourne stated, her TS, particularly the tubers on the right side of her parietal-temporal lobe, made her susceptible to a prolonged seizure.<sup>(6)</sup>

Coughing, vomiting, and nasal congestion can be symptoms equally of a measles vaccine reaction as well as of a respiratory infection. Although Dr. Parke and the extremely well-experienced Dr. Glezen now diagnose Tammy as having had a respiratory infection, no one during the June 1972 hospitalization (including Dr. Parke) so diagnosed her.

It seems more likely to the court that, at the perfect interval of ten days after her MR vaccination,<sup>(7)</sup> Tammy developed a mild measles reaction, including fever and a rash. It was Tammy's TS that turned the fever into a serious neurological event. The court notes with interest that Dr. Glezen found the rash to be problematic. To the court, this means Dr. Glezen had doubts linking the rash to an infection, rather than to the MR vaccine. Although Dr. Pollack explained it away (due to sweating, or tape), the court is cognizant that a rash is the appropriate symptom for a mild measles vaccine reaction. The rapidity of Tammy's recovery is consistent with that explanation. This seems more tenable than her having recovered from an upper respiratory illness of such short duration.

Even assuming, arguendo, that Tammy had an intercurrent infection while she had a reaction to MR vaccine, she would not be precluded from recovering compensation. In *Knudsen v. Secretary, HHS*, 35 F.3d 543 (Fed. Cir. 1994), the Federal Circuit reversed and remanded the lower courts' dismissal of the petition of a child with an alleged DPT-encephalopathy who also had symptoms of an unspecified viral infection. The Federal Circuit held, with particular relevance here: (1) the vaccinee could recover

damages even with symptoms of a virus if the vaccine caused a reaction; (2) the "unity theory" (that all symptoms must be explained by a single cause) is rejected; and (3) evidence that more encephalopathies occur due to viral infections than to DPT is irrelevant. 35 F.3d at 549-50.

Thus, even if the evidence of cough, pulling at the ears, and vomiting of mucous was more likely due to an infection than to a MR reaction, the Federal Circuit has established that this alone would not defeat the parallel holding that Tammy's fever and rash were due to her MR vaccination. But the court is content with its conclusion, based on Dr. Parke's and others' testimony, that respiratory symptoms are recognized adverse reactions to MR vaccine.<sup>(8)</sup>

Having decided that Tammy's MR caused her fever, and that the fever caused her seizure for which her pre-existing TS made her more susceptible, the remaining question is whether or not there were sequelae to her seizure, i.e., is her current condition causally related to her first seizure? If so, petitioners will have met the requisite prongs of *Whitecotton v. Secretary, HHS*, 81 F.3d 1099 (Fed. Cir. 1966) to show significant aggravation of Tammy's TS. Those prongs distill basically into two questions: (1) is the child's current condition significantly worse than her prevaccination condition, and (2) is the beginning of that substantial deterioration within Table time?<sup>(9)</sup>

There is no question that Tammy's current condition, with mental retardation and developmental delay, is substantially worse than her prevaccination condition. Was the seizure on June 22, 1972 the onset of that substantial deterioration?

Respondent's witnesses deny that there is any link between Tammy's seizure on June 22, 1972, and her subsequent staring and shaking noted in January 1973 and her afebrile seizures detected in June 1973. But Tammy was put on Phenobarbital, an anti-convulsant, after her June 22, 1972 seizure. It would be unfair to attribute the lack of her seizures until January 1973 solely to the benignity of her status epilepticus rather than to the effect of her anti-convulsants. Thus the argument could be made that she would have had more seizures (to reflect the beginning of her seizure disorder) but for the anti-convulsant. Of course, the correlative question is, why, despite being on an anti-convulsant, did she manifest staring and shaking in January 1973, or, though still on anti-convulsants, afebrile seizures by June 1973? The court is well aware that the course of TS is perilously unpredictable, else no TS child would experience breakthrough seizures and all anti-convulsant therapies would be successful.

Tammy's EEG in July 1972 was markedly abnormal. Petitioners point to that as proof that her status epilepticus June 22, 1972 caused damage to her brain, but respondent defends that we do not know if her EEG would have been abnormal before her MR vaccination if one had been performed. We do know that Tammy did not seize before her MR vaccination and was not on anti-convulsants before her MR vaccination.

Evidence from both parties' doctors establishes what the court has heard in all TS cases: a child with TS is susceptible to seizures. All TS children with mental retardation have seizure disorders.

Tammy was fortunate enough to have lived beyond her first year when the threat to TS children of seizing in the form of infantile spasms exists and yet she remained seizure-free (perhaps because she did not have numerous tubers). The longer her brain remained seizure-free, the more likely that she would be developmentally and mentally normal. The obverse is also true: the sooner she seized, the worse off she would be since TS children are notorious for developing seizure disorders and consequent mental retardation and developmental delay.

The court knows that Tammy did not seize before June 22, 1972. There is no credible proof before the

court as to when, if ever, Tammy would have seized absent the MR vaccination. Respondent's defense of eight or more tubers being a biomarker to neurological severity in TS cases is not applicable here because Tammy had seven tubers, putting her below respondent's level for seizing more probably than not due to the TS alone.

The court believes that a TS child, not only because of the number of tubers, but also because of tuber location and size,<sup>(10)</sup> is so liable to develop a seizure disorder that anything that initiates a seizure, such as fever in this case, can hardly be of innocent effect. The cortical lesions are there, waiting to fire off electrical impulses. When Tammy experienced her first seizure, beyond the age when TS children are most vulnerable to brain damage (in their first year), she was unlikely to maintain her clinical normalcy for very long. Even though her developmental delay did not begin immediately, over time, the damage was done. The symptoms of Tammy's TS obviously progressed in the form of staring, shaking, and afebrile seizures, all while Tammy was taking anti-convulsants.

Petitioners have satisfied their burden of proving that Tammy's MR significantly aggravated her TS. The onset of the substantial deterioration, which was the beginning of her seizure disorder, occurred within Table time of her vaccination and her current condition is significantly worse than her pre-vaccination condition. The court finds MR vaccine more likely the cause of Tammy's fever which caused her seizure than respondent's theory of an intercurrent viral infection. Moreover, respondent has failed to satisfy its burden<sup>(11)</sup> that TS caused in fact Tammy current condition so as to defeat petitioners' prima facie case of significant aggravation.

### CONCLUSION

Petitioners are entitled to a Program award. The court encourages the parties to engage in settlement of the damages portion of this case and will set a status conference to schedule the filing of life care plans.

### IT IS SO ORDERED.

DATED: \_\_\_\_\_ Laura D. Millman

Special Master

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.
2. Manuel Rodriguez Gomez, *Tuberous Sclerosis* (2d ed. 1988).
3. Gomez M.R., Kuntz, N.L., & Westmoreland, B.F., *Tuberous sclerosis, early onset of seizures, and mental subnormality: Study of discordant [mono]zygous twins*, 32(6) *Neurology* 604-11 (1982).
4. *See* R. Exs. JJ and KK as further proof of the use of more attenuated measles virus vaccine at the time of Tammy's vaccination.
5. Goodman, M., Lamm, S.H., Engel, A., Shepherd, C.W., Houser, O.W., & Gomez, M.R., *Cortical Tuber Count: A Biomarker Indicating Neurological Severity of Tuberous Sclerosis Complex*, 12(2) *Journal of Child Neurology* 85 (1997). R. Ex. SSS.

6. The court does not find credible Dr. Kinsbourne's opinion that measles virus from the vaccine invaded Tammy's brain since he does not give support to this opinion.

7. "About 5% to 15% of susceptible vaccinees develop a fever of ... (103°F) or higher, usually beginning 7 to 12 days after vaccination; the fever generally lasts 1 to 2 days.... Transient rashes have been reported in approximately 5% of vaccinees." From the Report of the Committee on Infectious Disease, American Academy of Pediatrics ("The Red Book"), p. 317 (1974). R. Ex. VVV.

8. "The adverse clinical reactions associated with [MR vaccine] are ... malaise, sore throat, cough, rhinitis, headache, fever, rash, nausea, vomiting or diarrhea...." Physician's Desk Reference 1733 (49th ed. 1994). R. Ex. WWW.

9. There is always the possibility of proving an off-Table significant aggravation case, but the Federal Circuit in *Whitecotton* was not addressing itself to that situation in its delineation of the requisite proof for petitioners to make out a prima facie case.

10. Shepherd, C.W., Houser, O.W. & Gomez, M.R., *MR Findings in Tuberos Sclerosis Complex and Correlation with Seizure Development and Mental Impairment*, 16 A.J.N.R. 149-55 (Jan. 1995) (R. Ex. S); Roach, E.S., *Tuberous Sclerosis: Function Follows Form*, 12(2) *Journal of Child Neurology*, 75 (1997) (accompanying editorial) (R. Ex. SSS).

11. *Whitecotton v. Secretary, HHS*, 81 F.3d 1099, 1107 (Fed. Cir. 1996).