

OFFICE OF SPECIAL MASTERS

July 22, 2002

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EDWARD J. ANTHONY, \*

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Petitioner, \*

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v. \*

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SECRETARY OF THE DEPARTMENT OF \*

HEALTH AND HUMAN SERVICES, \*

\*

Respondent. \*

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No. 01-0594V  
TO BE PUBLISHED

John P. Konecky, Rock Island, IL, for petitioner.  
Catherine E. Reeves, Washington, DC, for respondent.

**DECISION**

**MILLMAN, Special Master**

On October 12, 2001, petitioner filed a petition on his own behalf under the National Childhood Vaccine Injury Act of 1986<sup>1</sup> (hereinafter the "Vaccine Act" or the "Act"). Petitioner has satisfied the requirements for a prima facie case pursuant to 42 U.S.C. § 300aa-11(c) by showing that: (1) he has not previously collected an award or settlement of a civil action for damages arising

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<sup>1</sup> 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.

from the alleged vaccine injury; and (2) tetanus vaccine was administered to him in the United States.<sup>2</sup>

Petitioner alleges that tetanus toxoid caused his persistent ataxia and ocular visual disturbance with transient meningeal clonal lymphocytosis. Respondent denies causation from the tetanus vaccine.

The court held a hearing in this case on May 30, 2002. Testifying for petitioner were James Edward Anthony, Mary Anthony, and Dr. Lawrence W. Allen. Testifying for respondent was Dr. Douglas Kerr.

### **FACTS**

Mr. Anthony was born on November 7, 1949. He had a physical examination with Dr. Deepak Ahuja on September 8, 1999, and told Dr. Ahuja that he had had a cough at night from January to May 1999, but, since then, the cough was occasional. He also complained of heartburn. At this time, Dr. Ahuja administered tetanus vaccine to him. P. filing of June 14, 2002.

On October 12, 1999, Mr. Anthony saw Dr. Vardges Vandian at Trinity Medical Center and complained of having numbness and tingling in his legs for the prior three weeks (which would be approximately 13 days after his vaccination), and difficulty walking. Initially, three weeks previously, he noticed that his walking was not well-balanced. His appetite decreased and he lost five pounds in three weeks. He had occasional slurred speech. For the prior nine months, he had occasional nausea with vomiting and persistent cough. Med. recs. at 269.

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<sup>2</sup> Although petitioner did not file an actual vaccination record, respondent does not contest that he received tetanus toxoid on September 8, 1999. See transcript of hearing at 35.

Mr. Anthony also saw Dr. Randall G. Bay at Trinity Medical Center on October 12, 1999. He complained that he had vertigo while lying flat and has had nausea and two to three episodes of vomiting per day for the prior year or so. Med. recs. at 266.

An MRI was done on October 13, 1999 which showed no acute abnormality or convincing evidence of a demyelinating process or a tumor. A previous MRI had been done on November 27, 1996. Med. recs. at 268.

Another MRI was done on October 18, 1999 of the cervical and thoracic spine. It was normal. Med. recs. at 258.

A further MRI was done of the brain and brain stem on October 27, 1999. It showed multiple minute foci of enhancement along the pons, cerebellum, and temporal lobes. There was abnormal enhancement of the leptomeninges and perivascular spaces. The findings were consistent with an inflammatory process of the cerebrospinal fluid (CSF). Med. recs. at 242.

On November 1, 1999, Mr. Anthony returned to Trinity Medical Center and saw Dr. Anthony H. Kwan, who took a history of Mr. Anthony's problems and thought they were secondary to a postvaccinal cerebellar syndrome. Mr. Anthony had received a tetanus vaccination on September 8, 1999 and, a couple of weeks later, had difficulty walking, numbness and tingling in his legs, decreased appetite, some slurred speech, and severe processing delay cognitively. Three years previously, he had a head injury which led to testosterone insufficiency. Med. recs. at 13.

On November 17, 1999, Dr. Kwan discharged Mr. Anthony with a diagnosis of postvaccinal cerebellar syndrome, and deficit in fine motor coordination, balance, and cognition. Med. recs. at 19.

On January 13, 2000, Mr. Anthony saw Dr. Thomas Carlisle at the University of Iowa Health Care Center. Dr. Carlisle described him as being in the very early stage of chronic lymphocytic leukemia (CLL). Mr. Anthony had evidence of what appeared to be CLL cells in his CSF as well as in his peripheral blood by immunotyping. However, he did not have other findings which meet the standard criteria for CLL. Med. recs. at 21-22.

On February 7, 2000, Mr. Anthony saw Dr. Lawrence W. Allen, a hematologist-oncologist, who recorded a history that Mr. Anthony did well with the tetanus injection until one week afterwards when he had weakness in his lower extremities and then in his upper extremities. He had severe ataxia, truncal ataxia, ataxia of speech with dysarthria, and a 20-pound weight loss. Mr. Anthony fell several times. He had an abnormal CSF with elevated lymphocyte counts of 64 and 58. His cells showed monoclonal B-cell typing. He had abnormal head CT and brain MRI scans, suggesting leptomeningeal infiltrate (abnormal meninges). Biopsies were done of Mr. Anthony's cerebellum, right cerebral cortex, and white matter. Peripheral blood B-lymphocytes were found. He did not have lymphadenopathy but was treated as if he had CLL. Med. recs. at 10.

On June 12, 2000, Dr. Allen noted that Mr. Anthony's diagnosis remained a mystery despite clear-cut ataxia and neurologic dysfunction. Mr. Anthony had some difficulty seeing, especially with his left eye. On spinal tap, his CSF findings did not support a diagnosis of progressive lymphoproliferative malignancy. His last CSF showed an essentially normal lymphocyte count. Med. recs. at 23.

On March 6, 2001, Dr. Allen recorded that Mr. Anthony's persistent ataxia and left ocular visual disturbance associated with transient meningeal clonal lymphocytosis "most likely represents a reactive phenomenon very probably related to the tetanus vaccination." Med. recs. at 5. He could

not have had such a stable course if he in fact had a monoclonal lymphocytic malignancy in his central nervous system. Id.

### **Other Submissions**

Petitioner filed an affidavit from Dr. Anthony H. Kwan, dated May 14, 2001, stating that Mr. Anthony had an ongoing neurologic impairment related to cerebellar dysfunction. He had ataxia, balance, and ambulation problems as well as cognitive impairment. He needed help with memory, sequencing, calculation, and processing. Tetanus vaccine was the cause of his problems. Dr. Kwan treated Mr. Anthony from November 1, 1999 to April 6, 2000. Med. recs. at 29. Dr. Kwan is a staff psychiatrist for Trinity Medical Center and has lectured for Merck & Co. from 1987 to 1990. Med. recs. at 16.

On May 21, 2002, petitioner filed an article entitled, “Two Episodes of Leukoencephalitis Associated with Recombinant Hepatitis B Vaccination in a Single Patient (Brief Report),” by D. Konstantinou, et al., 33 *Clin. Infect. Dis.* 1772073 (2001), describing the case of a woman who received hepatitis B vaccination twice (her second and third doses), each time followed by leukoencephalitis. The occurrence of the same illness following vaccination and revaccination (rechallenge) led the authors to conclude there was causation from the vaccine.

Specifically, four weeks after her second dose of hepatitis B vaccine, the woman developed complete right homonymous hemianopia (loss of vision) and severe dyslexia. Brain MRI showed a large lesion occupying most of her left occipital lobe, extending into the splenium of the corpus callosum. A craniotomy and biopsy of the lesion were performed. She received her third dose of hepatitis B vaccination three months after her operation for leukoencephalitis. Eleven days post-vaccination (a shorter time period than after her second dose), she developed left hemiparesis and

acute progressive deterioration of vision. She had neither fever nor any other reaction after either vaccination. She had no preexisting neuropathy. Brain MRI revealed a new, large lesion in the right parieto-occipital region with the same characteristics associated with the previous lesion. She was treated with dexamethasone and improved markedly.

The authors conclude that a direct causal link between the hepatitis B vaccinations and the leukoencephalitic episodes is strongly suggested by the absence of previous disseminated neurologic disease, the presence of large single lesions with gray-matter involvement as shown by MRI, the resolution of the lesions, histopathologic findings, the absence of new neurologic deficits, the lack of detection of new lesions during follow-up, and the occurrence of two similar but separate clinical and radiological neurologic events soon after administration of the second and third doses of vaccine.

### **TESTIMONY**

James Edward Anthony testified first. Before September 8, 1999 when he received a tetanus booster from Dr. Ahuja, he was active and without health problems. He had just retired after 30 years of work and was employed part-time as a security guard. He drove vehicles, walked floors, and checked boxes. Tr. at 5.

Within five days of receiving the tetanus vaccine, he had bad balance which got worse. His legs got colder and he put on blankets when he sat. Tr. at 7. A week after he received the tetanus vaccine, he told his employer he could not work for eight hours, and on Sunday, September 19, 1999, he could not complete work. Tr. at 9.

Mr. Anthony's first visit to a doctor after the tetanus vaccination was on October 12, 1999 at Trinity Medical Center. Tr. at 10. He was getting weaker and had lost his sense of taste. He lost

44 pounds. Tr. at 14. Mr. Anthony does not remember telling Dr. Vandian on October 12, 1999 that he had occasional nausea with vomiting and a persistent cough for the prior nine months. Tr. at 11, 41. He had a head injury in 1996 from hitting a metal plate which affected his pituitary gland. Tr. at 26. On January 20, 2000, he admitted to a doctor that he had a problem with his golf swing a couple of months prior to admission. Tr. at 43. He denied having any numbness in his feet at the time. Tr. at 44.

Mr. Anthony stated he is stable today but has visual problems in one eye. He drives and walks, but his feet feel as if he is on pin cushions. Tr. at 39.

Mary Anthony testified next for petitioner. Tr. at 46. She has been married to Mr. Anthony for 32 years. Tr. at 47. Before September 8, 1999, she did not observe any physical disability or ailment in her husband. Tr. at 48. On September 8, 1999, Dr. Ahuja gave Mr. Anthony a physical examination and a tetanus vaccination. A week later, Mr. Anthony said he felt he was bouncing off the wall and did not feel right. Id. He walked with a wider gait to keep his balance. Tr. at 48-49. On Sunday, September 19, 1999, he came home early from work because he did not feel right. Tr. at 49.

She had Mr. Anthony's father come to stay with him while she worked as an assembler, and her husband would just sit. Id. He lacked energy and lost his appetite. By October 12, 1999, he would not walk. He saw Dr. Spaude because Dr. Ahuja was too busy and Dr. Spaude referred them to Dr. Vandian. Tr. at 50-51. She stated that Mr. Anthony's cognitive ability suffered after the vaccination and continues today. Tr. at 52. Before September 8, 1999, Mr. Anthony had some coughing, vomiting, and nausea whenever he ate ice cream or milk, but she does not remember his being dizzy. Tr. at 54.

Dr. Lawrence W. Allen testified next for petitioner. Tr. at 56. He first saw Mr. Anthony on February 7, 2000 on referral from Dr. Carlisle and Dr. Stoffel. Tr. at 57. Mr. Anthony said he was weak and staggering. The problem started with his legs and then went to his balance. He had trouble holding his trunk straight. He also lost his appetite and had fallen several times. Tr. at 58-59. Mr. Anthony had received a tetanus shot and was diagnosed with leukemia. Tr. at 59. He was referred to Dr. Allen so that he could treat Mr. Anthony with intraspinal injections of chemotherapy. Id.

An analysis of his blood cells showed evidence suggestive of leukemia: a clonal population (clonal means “single parent”) of abnormal lymphocytes. Id. Mr. Anthony’s CSF was abnormal because all the white cells were the same, which is typical of leukemia. Most patients with neurological illness may have an increase in their white blood cells, but they are polyclonal, not clonal, lymphocytes. Tr. at 63-64. Different bacteria and viruses produce different white blood cells in response. Tr. at 64. Malignancy leads to exactly alike white blood cells. Id. Dr. Allen had never seen this type of patient before with a neurological problem but no increase in clinical lymphocytes. Tr. at 60. He did not have any significant lymphocytosis as most patients who have leukemia do. Most patients with lymphocytic leukemia will have a high percentage of abnormal lymphocytes in the peripheral blood: 60, 70, or 80 percent or more. Mr. Anthony had virtually a normal percentage of lymphocytes. Tr. at 62.

Dr. Allen was aware of the possible association of tetanus vaccine with brachial neuritis and Gullain-Barre syndrome (GBS), and did not want to administer anti-leukemia chemotherapy to Mr. Anthony without investigating the possibility of tetanus vaccine being the cause of his problem. Tr. at 61. He tried to obtain any original samples of Mr. Anthony’s bone marrow cells or blood cells



or spinal fluid to analyze them for a possible tetanus toxoid reaction, but no samples had been saved. Tr. at 61-62.

Tetanus toxoid is the juice of the protein that comes from the bacteria, inactivated by formaldehyde. Tr. at 65. Dr. Allen thinks that when Mr. Anthony received the tetanus toxoid, he probably had some preformed antibodies from previous vaccinations which then reacted with the antigen. Then, Mr. Anthony had a cascade of immune reactions in which his body enlisted some of his B and T cells to start reproducing and make more antibody or antitoxin. The situation got out of hand and his body overreacted. Not only did Mr. Anthony have neurological damage, but also he overproduced lymphocytes which caused some of the reaction he had. They were present in his brain, spinal cord, and throughout his body. Eventually they went away. Tr. at 66.

Dr. Allen believes there are descriptions of antigen-antibody complex disease causing neurological illness which is the basis of the acceptance that tetanus toxoid causes an immune complex disease formation leading to brachial neuritis. That process is what he thinks happened to Mr. Anthony. Tr. at 67.

He cited two papers. The first, by Yachie, showed that tetanus toxoid stimulates interleukin, which indicates there is a lot going on in the immune and nervous systems.<sup>3</sup> Tr. at 68. The second, by Konstantinou, showed that a hepatitis B challenge and rechallenge resulted in leukoencephalitis which affects the white matter of the brain. Dr. Allen stated the illness and vaccine were causally related and not just an accident. Tr. at 68-70. Mr. Anthony did not have leukoencephalitis, but he had other changes: small, bright spots consistent with collections of damaged cells or lymphocytes.

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<sup>3</sup> Yachie, A., et al., "Sequential Expression of T Cell Activation (Tac) Antigen and Ia Determinants on Circulating Human T Cells After Immunization With Tetanus Toxoid," 131 *J. Immunol.* 731-35 (1983).

There were changes in his MRI even though the biopsy did not show anything abnormal. Tr. at 70.

Dr. Allen stated that rare neurological events can be associated with vaccines, such as a series of Guillain-Barre patients who had previously received tetanus toxoid. Id. In one case, the individual had three recurrences of his neurological syndrome after each tetanus vaccination. Tr. at 70-71.

He thinks Mr. Anthony's neurological disease is very unusual and he has never come across this particular type of illness connected with tetanus toxoid. Tr. at 71. Tetanus can affect the nervous system. Mr. Anthony clearly does not have a malignancy, but he does have a neurological disease which Dr. Allen believes is connected to the tetanus toxoid. Id.

A lymphocyte is a type of white blood cell that is related to the immune system. It makes antibodies and recognizes antigens. Tr. at 72. Mr. Anthony's blood, bone marrow, and spinal fluid had a high number of abnormal cells. Mr. Anthony's spinal fluid contained 60 or 70 cells, virtually all of them lymphocytes, whereas he should not have had more than five or six. Thus, Mr. Anthony had ten times the normal number of lymphocytes plus high protein. He had all the signs of a neurological illness which then got better. Tr. at 72-73. That would not have occurred with a malignancy like leukemia. Tr. at 73.

Dr. Allen agrees with Dr. Kwan that Mr. Anthony had an unspecified cerebellar syndrome as part of his entire neurological illness, which also included cognitive, cerebral, peripheral, balance, and vision problems. Id. Dr. Allen's diagnosis is that Mr. Anthony had a slowly evolving cerebellar ataxia associated with peripheral neuritis and mild transient cerebral symptoms. Id. He had transient monoclonal lymphocytosis in his spinal fluid, blood, and bone marrow. Tr. at 73-74. When asked

why the number of lymphocytes in his blood was normal but the number in his spinal fluid was ten times normal, Dr. Allen replied that the main thrust of his illness was in his nervous system even though there was a systemic reaction through his whole body evidenced by the blood and bone marrow findings. Since most of the illness was in his nervous system, that is where most of the abnormal lymphocytes were—in the brain and spinal fluid. Tr. at 74.

Dr. Allen thought it would be significant if Mr. Anthony had vertigo, nausea, and vomiting prior to September 8, 1999, if it occurred at times other than when he ate ice cream. Tr. at 75. It would also be of concern if Mr. Anthony had had viral illnesses, but Dr. Allen did not receive any history to that effect. Id. The injury to Mr. Anthony's head in 1996 which created a pituitary problem does not have any significance to Dr. Allen. Id.

Dr. Allen's opinion is that tetanus vaccine more likely than not caused Mr. Anthony's illness because of: (1) the temporal association, (2) he was well before vaccination, (3) his awareness of the potential for a neurological event following tetanus toxoid vaccination in other people who had a reaction similar to Mr. Anthony's with peripheral neuritis and brachial neuritis, and (4) no malignancy caused his problems. Tr. at 77. Mr. Anthony has the remnants of a neurological disease today. Id. He should not receive more tetanus toxoid. Tr. at 79-80.

Dr. Allen has never seen a patient like Mr. Anthony and is thinking of writing him up in an anecdotal report. Tr. at 77-78. Mr. Anthony was referred to Dr. Allen as a patient because of the diagnosis of lymphocytic leukemia. But Dr. Allen noted the unusual distinct onset of neurological atactic symptoms which he had never personally seen or been aware of. Tr. at 80. He was so struck by the possibility of a neurological reaction due to a different stimulus such as a toxoid vaccination

that he could not accept the diagnosis of leukemia 100 percent and go ahead with the recommended treatment. Tr. at 81.

He consulted with Dr. Carlisle who admitted he too was not sure of the diagnosis, and could see no other course of action than to recommend treatment, but agreed to watch Mr. Anthony as Dr. Allen was doing rather than begin treatment. Tr. at 81-82. Dr. Allen realized that if the diagnosis of leukemia were wrong, treatment for it (brain radiation and spinal fluid chemotherapy) might make Mr. Anthony much worse. Tr. at 84.

Part of the reason Dr. Allen came to regard tetanus toxoid as the cause of Mr. Anthony's illness was the spontaneous remission of his symptoms. Id. Although spontaneous remissions occur in leukemia as well, they do not last for years as Mr. Anthony's has, but rather for weeks or a few months when the lymphocytes are present in the central nervous system. Tr. at 85. It is difficult to prove a relationship between tetanus vaccine and Mr. Anthony's condition, but Dr. Kwan and Dr. Vandian (in a personal conversation with Dr. Allen) both thought tetanus vaccine caused it. Tr. at 88. The Konstantinou article strongly suggests causation. Tr. at 89.

Dr. Allen stated that Mr. Anthony did not have a spontaneous remission of cancer. Tr. at 95. Dr. Allen never heard or read about another patient with this extensive an involvement of abnormal lymph cells including this much neurological disease whose condition went away. Tr. at 95. Mr. Anthony started improving shortly after he saw him. He has no signs of leukemia. Tr. at 96.

Dr. Douglas Kerr, assistant professor of neurology at Johns Hopkins Hospital, testified for respondent. Tr. at 97. He is a board-certified neurologist with a doctorate in neuroimmunology and neurovirology in the central nervous system. Id. Sixty-five percent of his time is spent on researching how the immune system affects the central nervous system. Tr. at 97-98. His specialty

is transverse myelitis. Tr. at 98. Clinically, he sees patient with transverse myelitis and multiple sclerosis, and carries out research in those areas as well. Id.

He saw a case like Mr. Anthony's in early December 2001 when he was the attending physician on the Neurology Service. The case concerned a 71-year-old woman with an elevated level of monoclonal lymphocytes in her spinal fluid, and monoclonal cells in her bone marrow and peripheral blood, although not as high. Tr. at 100. It caused active, inflamed lesions up and down her brain and spinal cord. Tr. at 100-01. She had a biopsy performed on her brain and the covering of her spinal cord, leading to a diagnosis of chronic lymphocytic leukemia or CLL with central nervous system involvement, based on the monoclonal proliferation of cells. Tr. at 101.

Dr. Kerr transferred her to oncology for chemo and radiation therapy treatment but she declined it. She had neurological symptoms: she could not walk or focus, and she was unsteady. He thought she was going to die, but her CLL is gone. She is still a bit unsteady. Her case is in remission and the oncologist said it would come back. She had not received vaccinations. Tr. at 102.

When asked if Dr. Kerr thinks that the 71-year-old woman did indeed have CLL, he deferred to Dr. Allen as the expert on whether or not this was CLL. He said that Dr. Allen has the expertise to determine that Mr. Anthony did not have CLL. Dr. Kerr said he does not have the expertise in that area. Dr. Kerr has had multiple conferences with the oncologists in his hospital about the CLL diagnosis of the woman, and he defers to them. Tr. at 104.

He knows that the woman had not received any vaccinations previous to the onset of her problem because he asked her. Tr. at 105. Her symptoms began many months prior to December 2001. She started to dwindle in May and was not feeling as active or steady. Tr. at 106. By asking

her to what she had been exposed, he discovered that the oil burner in her basement had burst. Tr. at 106. There was a very prominent smell to which she and her husband had become accustomed but which her daughter noticed when she visited them. The woman and her husband attributed her illness to this toxic exposure. Id.

The woman had been exposed to a lot of organic solvents that were aerosolized. Any of them could potentially have an effect on the immune system and plausibly could be associated with her illness, although there are no reports in the medical literature or biological data in tissue culture to support that conclusion. Tr. at 107. Although deferring to Dr. Allen as the expert on this, Dr. Kerr stated that we do not know the clear-cut triggers for the vast majority of leukemias and lymphomas. Tr. at 108.

In most processes that involve the central nervous system, the lymphocytes that you find are reactive and not primary. In other words, they are not all of the same clone, not identical to each other. There are many different types of T and B lymphocytes or a mixture of the two and, therefore, it is called a reactive process, such as in multiple sclerosis and transverse myelitis. Doctors see this with most viral infections of the central nervous system. They are not clonal or monoclonal. The onset can be minutes to days following a trigger. Dr. Kerr thinks that a monoclonal process, a lymphoma or leukemia, is often due to a genetic mutation stimulated by an environmental trigger. Tr. at 109. The monoclonal process may confer a survival advantage to a particular cell. Tr. at 110. Primary lymphocytes are reactive to an environmental trigger. Tr. at 111-12.

Dr. Kerr would not testify about whether Mr. Anthony had leukemia at any time because that is not his expertise. He thinks Dr. Allen is the best one to comment on that. He does not know if the woman patient whom he described has leukemia in remission. Tr. at 112.

Dr. Kerr testified that it is unlikely that tetanus toxoid caused Mr. Anthony's unfortunate and very strange condition. The basis for Dr. Kerr's opinion is the existing medical literature. Most of the studies on Guillain-Barre, brachial neuritis, and multiple sclerosis say there is no relationship with vaccinations. Tr. at 113-14. Occasionally, one sees a case report but case reports of a single presentation really are meaningless in establishing causation. Tr. at 114. He needs epidemiologic data with a whole series of patients to show an increased risk following vaccination and, if there is a risk, it is very very slight. Id. Data concerning other neurologic diseases leads him to think that causation is plausible but not likely. He is actively looking at that question in some of his studies, but unless he has stronger evidence to support such an association, it remains an unlikely possibility. Id.

As for the histories of nausea, vertigo, vomiting, and coughing, Dr. Kerr said it was a struggle to link them with Mr. Anthony's problem. Mr. Anthony did not report any clear-cut symptomatology that makes Dr. Kerr link these symptoms to his condition. Tr. at 115.

Dr. Kerr thinks Dr. Allen's description makes sense, i.e., that tetanus toxoid antigen itself interacted with Mr. Anthony's preformed antibodies that he had due to prior tetanus vaccination and that started a cascade of immune derangements, contributing to his disease. Tr. at 115-16. He thinks this is biologically plausible. The major central nervous system problem Mr. Anthony had was not antibody itself. It was really the cells, a different arm of the immune system. Dr. Kerr stated that Mr. Anthony had a clonal proliferation of lymphocytes, and the process may not have been so much antibody-antigen complex formation as cellular proliferation. Tr. at 116.

Dr. Kerr divided autoimmunity into two parts: (1) B lymphocytes leading to antibodies, which may produce too many antibodies or bad antibodies, as in myasthenia gravis (humoral

immunity); and (2) lymphocytes becoming deranged, often as T lymphocytes with abnormal proliferation or activation, as in multiple sclerosis (cellular immunity). Tr. at 117. Killer lymphocytes are T lymphocytes that primarily express a surface marker called CD-8 and they are the “hit men” who will attack bacteria or rogue cells. Id.

When one injects tetanus toxoid, one hopes for both a cellular and humoral response against the toxoid. Tr. at 119. The protection from the vaccine is greater if one obtains both responses, although one can get a good vaccine that induces protection of only a humoral or cellular response. Id. In tetanus, the toxin itself is released into the blood and is lethal if not immediately neutralized. The T lymphocytes do not have the capacity to neutralize it instantaneously, but preformed circulating antibodies do. Tr. at 120-21.

When one receives a tetanus booster, as Mr. Anthony did, memory B lymphocytes remember the prior vaccine and readily awaken, stimulating their offspring to produce antibodies which they do very rapidly, much more quickly than if this were the first tetanus vaccination one had received. Tr. at 121. There are memory T lymphocytes as well, and they also do the same. Tr. at 121-22. It is plausible that if someone were going to have an aberrant response to a vaccine, he would be more likely to have it to a booster because he has a more prompt stimulus there. Tr. at 122.

There is mostly no association between vaccines and brachial neuritis, multiple sclerosis, and GBS, but brachial neuritis was long held to be associated to vaccines without strong evidence. However, Dr. Kerr conceded that it is plausible that brachial neuritis would follow vaccination and it is a Table injury under the Vaccine Program. Tr. at 123-24. The Table events were created by the Institute of Medicine which went through the entire medical literature and suggested causation of brachial neuritis. Tr. at 124. If Mr. Anthony had had brachial neuritis as the issue in this case, and



it were not listed as a Table injury, Dr. Kerr would probably testify that it was not related to the vaccine. Id. If it is not on the Table, one needs to show not only biologic plausibility but biochemical or molecular proof of a relationship. Id.

Dr. Kerr believes there may be a relationship between transverse myelitis and vaccines, although a very rare event. Tr. at 124-25. There are two reports in the medical literature linking two patients with transverse myelitis to preceding vaccinations, but they showed production of antibody to vaccine in the central nervous system.<sup>4</sup> Tr. at 125. Dr. Kerr was very impressed with the biological evidence of antibody production in the central nervous system to Hepatitis B vaccine in the particular case. It made him a believer in causation. Id. He knows that Dr. Allen thought of obtaining this biological evidence in Mr. Anthony's case and it is hard to do. It is not easy to get someone to run a clonal analysis of lymphocytes to see to what they react. Id.

Referring to the 71-year-old woman for whom he had been responsible in December 2001, he asked her if she had received a prior vaccination because he believes that, in a rare case, there may be an association. He asks everyone for his or her vaccine history. He was particularly interested in the woman's history because he had already seen parallels to Mr. Anthony. He went back to her several times to inquire about her vaccine history. Tr. at 127.

Dr. Kerr thinks that Dr. Allen's logic is right. Dr. Kerr has an enhanced suspicion that vaccines cause neurological injury. He has current prospective case control studies to determine the incidence of vaccines preceding transverse myelitis compared to a series of other neurologic

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<sup>4</sup> Sindern, N., et al., "Inflammatory Polyradiculoneuropathy with Spinal Cord Involvement and Lethal Outcome After Hepatitis B Vaccination," 186 *J. Neurol. Sci.* 81-85 (2001), and Matsui, M., et al., "Recurrent Demyelinating Transverse Myelitis in a High Titer HBS Antigen Carrier," 139 *J. Neurol. Sci.* 235-37 (1996).

conditions. He wants to determine if there is a higher incidence of vaccination in the 30 days preceding the onset of transverse myelitis than there is with ischemic stroke, spinal cord stroke (his control population). Tr. at 128. No one would propose that a vaccine causes spinal cord stroke. If he finds that the control population has three percent of patients having received a vaccination within the prior 30 days, but 20 percent of the transverse myelitis population received vaccine in the preceding 30 days, that would suggest a causal link. Tr. at 128-29. The study will be concluded three years from now. Tr. at 129. They are also looking at brachial neuritis. Tr. at 130. There is a further study of local reactions, i.e., swelling, urticaria, and pain at the injection site. Id. They are looking at any vaccines, including tetanus. Tr. at 130-31.

He would advise Mr. Anthony to be cautious about getting another tetanus toxoid even if there were a five percent chance of a reaction. Tr. at 131-32. He thinks it is probably right that there is a five percent chance that tetanus vaccine caused Mr. Anthony's condition, although he cannot say for sure. One thing one would certainly do is check Mr. Anthony's circulating tetanus antibodies. If he is above a certain threshold, he does not need more vaccine. Tr. at 132.

When asked how he arrived at the five percent, Dr. Kerr said he just made it up although he has clinical experience and is familiar with the medical literature. Id.

Dr. Kerr is interested in the Konstantinou article. It describes a different vaccine and different neurologic disease than the case before us, but he is frustrated because the doctors did a biopsy and thus had the opportunity to find biologic evidence to support causation, but did not pursue it. Tr. at 133. They could have looked at her lymphocytes and analyzed them to see to what they were reacting, e.g., were they reacting against the vaccine. One would put the lymphocytes in a dish, sprinkle some of the vaccine over them, and measure the cells to see if they become activated.

Pollard and Selby did that in the 1970's and showed that some of those lymphocytes could be activated.<sup>5</sup> Id. [Dr. Allen had referred earlier in his testimony to the Pollard and Selby article.] Dr. Kerr does not think that Konstantinou and his co-authors showed a causal link between Hepatitis B vaccine and the woman's two episodes of leukoencephalitis. Tr. at 134. However, Dr. Kerry thinks it is interesting that the time period between the vaccine and the neurologic injury was less for the second attack of leukoencephalitis than for the first attack in the Konstantinou article. Tr. at 134-35. He thinks that shortening of time for the neurologic injury after the second vaccination was appropriate. If one is attempting to link the vaccine and the neurologic injury, one would want to see a quicker response on rechallenge.

Even though the shortening is interesting to Dr. Kerr, he believes it is not causal. Tr. at 135. Any single case report can never prove causality. The only way to prove causality is through theories plus biological evidence or epidemiologic studies. Id. He mentioned three ways to prove causality: (1) a retrospective huge population study; (2) a prospective case control study, and (3) biological assays for lymphocyte activation or antibodies in the particular compartment. Tr. at 136. The study

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<sup>5</sup> Pollard, J.D., and Selby, G., "Relapsing neuropathy due to tetanus toxoid: report of a case," 37 *J. Neurol. Sci.* 113-25 (1978). The Institute of Medicine describes the article: "One particular case reported by Pollard and Selby (1978) is particularly relevant for a possible causal relation between tetanus toxoid and GBS for that case. A 42-year-old male laborer received tetanus toxoid on three separate occasions over a period of 13 years, and following each vaccination a self-limited episode of clear-cut, well-documented polyneuropathy of the GBS variety ensued. The latencies for each episode were 21, 14, and 10 days, respectively. He had minimal residual neurologic signs following the second episode, and made a full functional recovery following the third episode.... A well-studied sural nerve biopsy during the third episode showed demyelination, onion bulb formation, and incipient hypertrophic neuropathy. The patient's lymphocytes could be induced to proliferate upon exposure to tetanus toxoid and to elaborate the lymphokine macrophage inhibition factor upon exposure to peripheral nerve homogenate, although these responses can be seen in vaccinees without GBS." Because of the Pollard and Selby case, the IOM concluded that tetanus toxoid can cause GBS. Adverse Events Associated With Childhood Vaccines. Evidence Bearing on Causality, IOM (1994), 87-88, 89.

with which he is involved is prospective and case-controlled. They will bank serum, spinal fluid, and lymphocytes for biologic study. Id.

Dr. Kerr would say there is no causal link between brachial neuritis and vaccination even though the Vaccine Injury Table lists it as a Table injury for tetanus due to the conclusion of the Institute of Medicine (IOM)<sup>6</sup>. He said that the IOM did not need conclusive proof, but, when asked if he had a higher standard of proof than the IOM before recognizing causality, he answered that may be true but may not be true. Tr. at 137. Dr. Kerr said he is looking for more likely than not in his work because it is too hard to get conclusive proof. Tr. at 138.

## DISCUSSION

Petitioner is proceeding on a theory of causation in fact. To satisfy his burden of proving causation in fact, petitioner must offer "proof of a logical sequence of cause and effect showing that the vaccination was the reason for the injury. A reputable medical or scientific explanation must support this logical sequence of cause and effect." Grant v. Secretary, HHS, 956 F.2d 1144, 1148 (Fed. Cir. 1992). Agarwal 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.

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<sup>6</sup> The Vaccine Injury Table lists brachial neuritis as a Table injury for tetanus toxoid if it occurs within two to 28 days of vaccination. 42 C.F.R. 100.3(a)(I)(B). Causation is presumed if a petitioner proves a Table injury.

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

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

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 aids 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.<sup>7</sup> 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).

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<sup>7</sup> 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.”

As the Federal Circuit stated in Knudsen, supra, 35 F.3d at 548, “Causation in fact under the Vaccine Act is thus based on the circumstances of the particular case, having no hard and fast *per se* scientific or medical rules.” Thus, the task before the undersigned is not to delineate how petitioner’s evidence does or does not satisfy the Daubert litany of support in peer-reviewed medical literature, concurrence among a majority of physicians in the field of oncology and 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.

In this case, the undersigned was privileged to hear the testimony of two excellent physicians. Dr. Allen, petitioner’s treating oncologist/hematologist, was appropriately inquisitive in treating Mr. Anthony. His thinking processes and conclusions were heroic in that he recognized that Mr. Anthony’s condition did not satisfy the criteria of CLL and, once he learned of the preceding tetanus vaccination, he seriously entertained that Mr. Anthony had been misdiagnosed, thus avoiding treating him for a disease he did not have, which would have made him much worse. Although Dr. Allen attempted to find biological proof that tetanus vaccine caused Mr. Anthony’s illness, he could not obtain it.

Dr. Kerr, respondent’s expert neurologist, is the quintessential scientist. He knows what he wants to see proved before he is willing to draw conclusions. In essence, Dr. Allen and Dr. Kerr negotiate different worlds with some overlap. Dr. Allen’s role was to treat Mr. Anthony and, at the very least, not to make his condition worse. He succeeded by not treating Mr. Anthony, who began to improve almost immediately after seeing Dr. Allen. Dr. Kerr’s role is, for the most part, to conduct appropriate research to determine causality and he is engaged at the present time in determining whether or not vaccines cause transverse myelitis. He suspects that they do. Although

he has clinical experience, and recounted the case of the 71-year-old woman who manifested what the oncologists at the hospital diagnosed as chronic lymphocytic leukemia, about which he proffered no opinion, his main emphasis is on research. Dr. Kerr deferred to Dr. Allen's expertise in diagnosing Mr. Anthony and concluding that he did not have CLL.

Dr. Allen testified that tetanus toxoid caused Mr. Anthony's condition because the timing was right, he had been well beforehand, Dr. Kerr was aware of the potential for a neurological event following tetanus toxoid vaccination in other people who had a similar reaction to Mr. Anthony with peripheral neuritis and brachial neuritis, and no malignancy caused his problems. Moreover, the Konstantinou article which describes a neurologic injury after hepatitis B vaccine and hepatitis B rechallenge supported of his opinion.

Mr. Anthony's purported history of vomiting, vertigo, nausea, persistent cough, and a bad golf swing are difficult to assess. Dr. Allen did not include it in his evaluation of his case and Dr. Kerr said it was a struggle to link them to his problem. The only medical record prior to Mr. Anthony's illness was his visit to Dr. Ahuja on September 8, 1999, during which he complained of a persistent cough and heartburn, but not vomiting, vertigo, or nausea. It is significant that when he saw Dr. Ahuja, Mr. Anthony had his full cognitive faculties. Moreover, the serial MRIs show the progression of his disease post-vaccination. The MRI done on October 13, 1999 showed no acute abnormality or convincing evidence of a demyelinating process or tumor. A further MRI of the brain and brain stem two weeks later, on October 27, 1999, showed multiple minute foci of enhancement along the pons, cerebellum, and temporal lobes with abnormal enhancement of the leptomeninges and perivascular spaces, consistent with an inflammatory process of the cerebrospinal fluid. The undersigned considers the later histories of vomiting, vertical, and nausea to be suspect.

Dr. Kerr testified that tetanus toxoid did not cause Mr. Anthony's condition because no retrospective study of huge populations had been done, no prospective case-controlled studies had been done, and no biological testing of his lymphocytes with tetanus vaccine had been done. In other words, Dr. Kerr would not accept a causal link to vaccination without epidemiological or biochemical evidence. This is a stalwart scientific view, but it is not what the law requires, according to the Federal Circuit.

In Knudsen, *supra*, the Federal Circuit evaluated inter alia the decision that a child's encephalopathy had to be caused by a virus rather than DTP vaccine because evidence showed that encephalopathies occur more often after viral infections than after vaccinations. The Federal Circuit rejected the prior holding, stating:

The bare statistical fact that there are more reported cases of viral encephalopathies than there are reported cases of DTP encephalopathies is not evidence that in a particular case an encephalopathy following a DTP vaccination was in fact caused by a viral infection present in the child and not caused by the DTP vaccine.

35 F.3d at 550.

Therefore, even if epidemiologic evidence exists to the contrary of proof that a vaccine caused petitioner's illness, the Federal Circuit was not swayed that, in the particular case before it, petitioner could not prevail.

As for the necessity of petitioner's proving a biological mechanism in order to prevail, the Federal Circuit similarly rejected that as a requirement, stating 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.

This research is for scientists, engineers, and doctors working in hospitals, laboratories, medical institutes, pharmaceutical companies, and government agencies.

35 F.3d at 549.

Thus the Federal Circuit did not envision the undersigned in evaluating vaccine injury cases engaging in the type of scientific endeavor which occupies Dr. Kerr. In a similar case, Johnson v. Secretary, HHS, No. 99-0219V, 2000 WL 1141582 (Fed. Cl. Spec. Mstr. July 27, 2000), the undersigned held that tetanus vaccine caused Hillary Johnson’s acute disseminated encephalopathy (ADEM). Onset was approximately 13 days after vaccination. Petitioner submitted considerable medical literature, including the Pollard and Selby article. In Johnson as in the instant action, petitioner’s treating physician testified for her. (It is worth noting here that two additional treating physicians of Mr. Anthony, Dr. Kwan and Dr. Vandian, agreed with Dr. Allen that tetanus vaccine caused his illness.)

Dr. Kerr is not satisfied with biologic plausibility, but he does agree with Dr. Allen’s logic in describing how the cascade of lymphocytes in an aberrant reaction to the tetanus toxoid led to Mr. Anthony’s condition. “Logic” is the key word here because the Federal Circuit in Grant states that all petitioner need show in order to prevail is a logical sequence of cause and effect, supported by a reputable medical or scientific explanation.

Dr. Kerr admits that providing biological evidence is difficult (Dr. Allen’s attempt was unsuccessful). Epidemiological evidence is absent here and he is unsatisfied with case reports,

although he finds one intriguing.<sup>8</sup> He wants retrospective or prospective epidemiologic studies. Yet, two case reports on vaccinations followed by transverse myelitis (his specialty) have led him to believe that these vaccinations caused this neurological disease because biological evidence was there. It seems that case reports, then, can persuade Dr. Kerr of causation, even in the absence of epidemiological studies (retrospective or prospective).<sup>9</sup>

The Federal Circuit does not interpret the Vaccine Act as imposing difficult if not daunting steps for petitioner to take in order to prevail. Dr. Allen has testified to a logical sequence of cause and effect to show that tetanus vaccine caused Mr. Anthony's condition. He based his logic on a reputable medical explanation with which Dr. Kerr agreed. Although Dr. Kerr agrees with the logical sequence of cause and effect, he does not reaching the same conclusion because he wants proof that would satisfy scientific researchers. This is expressly what the Federal Circuit stated in Knudsen is not required. 35 F.3d at 549.

Undoubtedly, this legal opinion will not be published in a scientific journal. But that is appropriate because it is a legal holding, not a scientific conclusion. Petitioner has provided credible evidence, with Dr. Allen's testimony, Dr. Kwan's opinion, the medical records, and the medical literature, to prove his case.

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<sup>8</sup> Dr. Kerr was intrigued with the Konstantinou article because, although its standards did not satisfy his for proving causation, he thought the shortened onset period for leukoencephalitis in the vaccinee after her subsequent exposure to the vaccine was appropriate for a vaccine reaction. Dr. Kerr still would have preferred that the authors do an analysis of the vaccinee's cells to determine whether or not they were sensitized to the vaccine in order to prove causation.

<sup>9</sup> The undersigned has held that a vaccine caused transverse myelitis: Herkert v. Secretary, HHS, No. 97-518V, 2000 WL 141263 (Fed. Cl. Spec. Mstr. Jan. 19, 2000) (acellular DPT caused transverse myelitis by modulating child's immune system so that he could not longer fight cytomegalovirus, which was also a substantial factor in causation).

Petitioner prevails on the allegation that but for the tetanus vaccine, he would not have had the injury, and also that the tetanus 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.**

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DATE

\_\_\_\_\_  
Laura D. Millman  
Special Master