IN THE UNITED STATES COURT OF FEDERAL CLAIMS
OFFICE OF SPECIAL MASTERS

* *		
W.C.,	*	No. 07-456V
	*	Special Master Christian J. Moran
Petitioner,	*	
	*	Filed: February 22, 2011
v.	*	Released: September 26, 2011
	*	
SECRETARY OF HEALTH	*	
AND HUMAN SERVICES,	*	Entitlement, influenza vaccine,
	*	multiple sclerosis, significant
Respondent.	*	aggravation
	*	
* *		

Ronald C. Homer, Conway, Homer & Chin-Caplan, P.C., Boston, MA., for petitioner;
Debra A. Filteau Begley, United States Dep't of Justice, Washington, D.C. for respondent.

DECISION DENYING ENTITLEMENT[*]

[*] When the decision was originally issued, the parties were informed that it would be posted on the United States Court of Federal Claims's website, in accordance with the E-Government Act of 2002, Pub. L. No. 107-347, 116 Stat. 2899, 2913 (Dec. 17, 2002). The parties were also informed that they may seek to prevent disclosure of some information by filing a motion within 14 days. 42 U.S.C. § 300aa–12(d)(4); Vaccine Rule 18(b).

The petitioner filed a timely motion for redaction, which was denied in a ruling issued on March 16, 2011. The public release of this decision was delayed to allow the petitioner to seek further review. The Court of Federal Claims ordered redaction of the petitioner's name to initials and permitted petitioner to seek additional redactions. W.C. v. Sec'y of Health & Human Servs., No. 07-456V, 2011 WL 3439131 (Fed. Cl. July 22, 2011).

Petitioner's proposed additional redactions were found not in accord with the Court's order. Thus, the February 22, 2011 decision is being made available to the public without petitioner's name. In addition, one spelling mistake is corrected.

W.C. received the flu vaccine in December 2004, and later was diagnosed with multiple sclerosis. He seeks compensation pursuant to the National Vaccine Injury Compensation Program, 42 U.S.C. § 300aa—10 et seq. (2006). W.C. presents two different theories that assume different dates of onset for his multiple sclerosis. Primarily, W.C. maintains that his multiple sclerosis developed after the flu vaccine and that the flu vaccine caused his multiple sclerosis. Alternatively, W.C. argues that if he had multiple sclerosis before he received the flu vaccine, then the flu vaccine significantly aggravated his condition.

To support these two theories, W.C. presented the opinion of Dr. Carlo Tornatore, a well-credentialed neurologist. Respondent disagrees with W.C.'s position and relies upon testimony provided by Dr. Arun Venkatesan, another well-qualified neurologist. Dr. Venkatesan opined that the two theories offered by Dr. Tornatore were not persuasive.

W.C.'s first theory fails because a preponderance of evidence establishes that he had developed lesions in his brain, which can be signs of multiple sclerosis, before he received the flu vaccine. Thus, the flu vaccine could not have caused the initial sub-clinical development of multiple sclerosis. W.C.'s second theory also fails. He has not established, by a preponderance of the evidence, that the flu vaccine significantly aggravates multiple sclerosis. The reasons for these conclusions follow.

I. Facts

The parties do not challenge the accuracy of W.C.'s medical records. These records reveal the following.

At age 34, W.C. received the flu vaccination on December 13, 2004. At this time, W.C. was working for the federal government and described himself as healthy. See exhibit 9 (W.C.'s affidavit, dated June 26, 2007) ¶ 13. Before December 13, 2004, W.C. was not displaying any clinical symptoms of a neurological problem. Id.; exhibit 3 at 44 (notes from visit on December 13, 2004); see also tr. 233 (testimony of Dr. Venkatesan); tr. 316 (testimony of Dr. Venkatesan). Whether W.C. actually had a sub-clinical neurological problem on December 13, 2004, is a critical issue in this case.

On December 24, 2004, W.C. noticed that his left arm and hand were numb. He also had numbness on the left side of his head and face. Exhibit 1 at 8; exhibit 9 ¶ 17. Dr. Tornatore and Dr. Venkatesan accept W.C.'s report of numbness as

the first expression of his neurological problem. See tr. 15; tr. 316 tr. 356; tr. 377; tr. 390-391.

On December 29, 2004, W.C. saw his family doctor, Deborah Darrington. Dr. Darrington recommended, among other tests, an MRI. Exhibit 1 at 8-9.

The MRI was performed on December 30, 2004, and it is one of the critical pieces of evidence about the onset of W.C.'s condition. The MRI was performed with and without contrast. The interpreting physician, Jason Arthur, reported "[s]cattered nonspecific T2 high signal lesions are noted in the deep white matter. Findings on MRI in conjunction with the patient's clinical history suggest multiple sclerosis as a possible etiology. There is focal high T2 signal intensity lesion within the anterior aspect of the corpus callosum on the right and within the posterior body of the corpus callosum within the midline. There are no focal contrast enhancing lesions." Exhibit 1 at 27. Dr. Darrington reported these findings to W.C., who recounted that this was "one of the worst and most frightening days" of his life. Exhibit 9 ¶ 21.

On January 8, 2005, W.C. went deer hunting. That night, his symptoms, which had previously abated, returned. He lost most motor functions in his left hand and arm. Exhibit 1 at 33; exhibit 9 ¶ 22.

On January 10, 2005, W.C. saw John Hannam, a neurologist. Dr. Hannam obtained a history that is consistent with that recounted above. Dr. Hannam commented that "the MRI findings . . . conceivably could be explained by multiple sclerosis and it is possible that the recent onset of his left sided tingling and numbness represents the first clinical attack." Dr. Hannam requested an analysis of W.C.'s spinal fluid. Exhibit 1 at 33-34.

The cerebral spinal fluid was negative for oligoclonal bands. Exhibit 1 at 19. Dr. Hannam told W.C. that "it remains unclear whether he does or does not have MS at the present time." Exhibit 1 at 50 (note from January 19, 2005).

Less than one week later, W.C. called Dr. Hannam. W.C. reported that eleven days before his symptoms began, he had gotten the flu shot. W.C. also inquired as to whether he might have Guillain-Barré syndrome, but Dr. Hannam said that he did not have the clinical findings to support this diagnosis. W.C. also reported that his symptoms were improving. Id. (note from January 24, 2005).

At the next office visit with Dr. Hannam, W.C. reported feeling better, except for some tingling in the tips of the fingers of his left hand. W.C. "remain[ed] suspicious that there is a causal connection between his symptoms and receiving the flu shot about 11 days earlier." Dr. Hannam told W.C. that no evidence shows that he had Guillain-Barré syndrome, but that he might have multiple sclerosis. Dr. Hannam added that "if he had MS, I [Dr. Hannam] can't blame it on the flu shot." Dr. Hannam recommended a second opinion from Dr. Bashir, who specializes in multiple sclerosis. Id. Dr. Darrington also suggested a second opinion from Dr. Bashir. Exhibit 1 at 6 (note dated March 2, 2005).

On March 22, 2005, W.C. saw Dr. Rifaat Bashir from the Department of Neurology of the Creighton University Medical Center. Dr. Bashir recorded a history from W.C. and noted that he reviewed the MRI with a neuroradiologist. W.C. said that his "main symptoms are sensory and come on with exercise." Dr. Bashir conducted a neurologic examination. Dr. Bashir's impression was that W.C. had a "clinically isolated syndrome in December that gave him sensory changes in his left upper extremity and neck. His head MRI is certainly consistent with a demyelinating disease. He could have had a single isolated event possibly related to his vaccination which he did receive two weeks before the event." Regarding W.C.'s diagnosis and prognosis, Dr. Bashir was not sure whether W.C. was "going to progress to multiple sclerosis or not." Dr. Bashir arranged for a repeat MRI. Exhibit 1 at 43-46.

The March 23, 2005 MRI showed three small foci of signal abnormality. They showed no mass effect or pathologic enhancement. The interpreting doctor stated that they were "suspicious for a demyelinating process such as multiple sclerosis." Exhibit 7 at 31.

On April 6, 2005, W.C. returned to Dr. Bashir. Dr. Bashir reported that the MRI "showed findings consistent with ADEM." "ADEM" stands for acute disseminating encephalomyelitis. Neil M. Davis, Medical Abbreviations (12th ed. 2005) at 39. Dr. Bashir ordered nerve conduction studies, which were normal, and an EMG, which showed no evidence of denervation. Exhibit 7 at 9-10.[1]

[1] At W.C.'s next appointment with Dr. Darrington, Dr. Darrington reported that W.C. told her that "Dr. Bashir feels that his symptoms could represent an acute [demyelinating] polyneuropathy, which may be secondary to his influenza vaccination last year. However, it could also represent early multiple sclerosis." Exhibit 1 at 5.

At the request of Dr. Bashir, W.C. had another MRI on June 28, 2005. The doctor was able to compare the results of this test to the MRI performed on March 23, 2005. The June 28, 2005 MRI showed the same three lesions that were described three months earlier. Additionally, the doctor reported a "new very ill-defined 7.9 mm focus of signal abnormality is seen." This lesion was the only lesion showing contrast material enhancement. The doctor suggested either acute disseminating encephalomyelitis or multiple sclerosis. Exhibit 7 at 25-26.

Dr. Bashir saw W.C. once more. Dr. Bashir stated that because of new area of enhancement, "I think a diagnosis of clinically supported MS can be made." Dr. Bashir prescribed a medication. Id. at 7. Following this diagnosis, W.C. continued to receive treatment for multiple sclerosis. The details of these visits are generally not relevant to resolving the pending question, which is whether a preponderance of the evidence shows that the flu vaccine caused or aggravated his multiple sclerosis.

Multiple sclerosis is a disorder of the central nervous system. Tr. 54. In multiple sclerosis, parts of the central nervous system are subject to an autoimmune attack, and experience inflammation with resulting demyelination. Tr. 136; see also exhibit C, tab 2 (Bruce D. Trapp & Klaus-Armin Nave, Multiple Sclerosis: An Immune or Neurodegenerative Disorder, 31 Ann. Rev. Neurosci. 247 (2008)) at 247. Multiple sclerosis is a chronic condition. In its chronicity, multiple sclerosis differs from acute conditions, such as transverse myelitis. Tr. 136. The incidence of multiple sclerosis is approximately one case per one thousand. Tr. 137; tr. 252.

For many years, researchers have considered multiple sclerosis to be an autoimmune disease, that is, a disease that starts when the body attacks itself. Although this theory is still under investigation, other theories of pathogenesis are being explored. These alternative theories include the idea that multiple sclerosis is a neurodegenerative disorder. This theory is based, in part, on research showing that inflammation in the central nervous system of mice can be produced without immune dysregulation. Tr. 173-78; exhibit C, tab 1 (Henry F. McFarland & Roland Martin, Multiple sclerosis: a complicated picture of autoimmunity, 8 No. 9 Nature Immunology 913 (2007)); exhibit C, tab 2 (Trapp & Nave).

The cause of multiple sclerosis is not known. Tr. 128; see also tr. 150; tr. 158; tr. 218. It is believed that multiple sclerosis starts when there is a breach in the barrier separating the blood in the circulatory system from the brain. Cells from the immune system cross into the brain, where they mistakenly attack a

component of the central nervous system. This attack leads to inflammation and when the inflammation is healed, a lesion is produced.[2] Exhibit C, tab 2 (Trapp & Nave) at 248-49; tr. 291. When lesions develop in parts of the brain that are referred to as "non-eloquent," the lesion does not cause distinct symptoms. Tr. 69; tr. 143. Consequently, the first clinical manifestation of multiple sclerosis may not develop at the same time as the first lesion. Tr. 314; see also exhibit C, tab 2 (Trapp & Nave) at 249 (stating "much of the disease process is initially clinically silent."). In Dr. Tornatore's words, "we can use the MRI in some cases as evidence that somebody had inflammation in the past. They just didn't clinically recognize it." Tr. 50.

Multiple sclerosis is classified into different types. The most common type of multiple sclerosis, which is the type afflicting W.C., is known as relapsing remitting multiple sclerosis. Tr. 321-22. People with relapsing remitting multiple sclerosis usually have approximately one relapse of multiple sclerosis per year. Tr. 145. Like the cause of the onset of multiple sclerosis, the cause of relapses of multiple sclerosis is not known. Tr. 391.

II. Procedural History

W.C. filed his petition in June 2007. In conjunction with his petition, he filed a set of medical records. Respondent evaluated those records and recommended that compensation be denied. Respondent argued that W.C. had not offered "a reputable medical or scientific theory causally connecting the vaccine to any alleged injury." Resp't Rep't, filed Oct. 1, 2007, at 10.

W.C. attempted to present this theory by submitting a report and associated literature from Dr. Carlo Tornatore. Exhibit 12. Dr. Tornatore has testified in the Vaccine Program on numerous occasions. He is the director of the Multiple Sclerosis Center at Georgetown University Hospital. In this capacity, he follows 2,000 patients with multiple sclerosis and conducts clinical trials researching therapeutic agents for people with multiple sclerosis. He does not directly research the cause of multiple sclerosis. At Georgetown University's Medical School, Dr. Tornatore teaches neurology. He has written more than 50 published articles,

[2] When a lesion is first created, it usually appears on an MRI as an "enhanced lesion." Tr. 254. The duration of enhancement is discussed in the context of analyzing when W.C. developed his lesions. See section III.A.

including some about multiple sclerosis. He has been board certified in neurology since 1991. Tr. 10-13; tr. 111-14; exhibit 13.

In his initial report, Dr. Tornatore expressed the opinion that the influenza vaccination caused W.C.'s multiple sclerosis. To explain how the influenza vaccine can cause multiple sclerosis, Dr. Tornatore relied upon the theory of molecular mimicry, which is discussed below. Dr. Tornatore also cited various medical textbooks and case reports that have reported "an association between influenza vaccine and a number of autoimmune disorders." Additionally, Dr. Tornatore stated that there is a "temporal relationship [between] the vaccination and the onset of symptoms." Exhibit 12 at 13-14.

The filing of Dr. Tornatore's report prompted respondent to seek an expert. Respondent obtained a report from Dr. Arun Venkatesan and submitted it on May 27, 2008. Exhibit A. Dr. Venkatesan is an assistant professor in the Department of Neurology at Johns Hopkins University. He works specifically within the division of neuroimmunology and neuroinfectious diseases. He researches how infections affect the nervous system. Between 2003, when he became a resident in neurology, and 2008, when he first testified in this case, Dr. Venkatesan treated approximately 200 patients with multiple sclerosis. While this case was pending, Dr. Venkatesan chaired a symposium on multiple sclerosis that 100-150 neurologists attended. Topics included the causes of multiple sclerosis and treatments. Tr. 131-34; tr. 189-92; tr. 286-87; exhibit B.

Dr. Venkatesan opined that "the influenza vaccination did not cause" W.C.'s multiple sclerosis. In regard to the theory proposed by Dr. Tornatore, Dr. Venkatesan maintained that "the medical literature does not support a biologically plausible link between influenza vaccination and MS." Exhibit A. Respondent later adopted this position, stating W.C. "has not, to date, offered a reputable medical or scientific theory causally connecting the vaccine to any injury. Petitioner has not demonstrated that Dr. Tornatore's causation theory is sufficiently grounded in science or supported by the medical literature." Resp't Supp. Rep't, filed Sept. 9, 2008, at 3. Respondent also maintained that W.C. had not established "a medically appropriate temporal association between his vaccination and his alleged injury." Id. at 4. Thus, respondent continued to state that W.C. was not entitled to compensation.

Due to the difference in opinions, a hearing was held to receive testimony from Dr. Tornatore and Dr. Venkatesan on November 4, 2008, in Washington, D.C. Dr. Tornatore and Dr. Venkatesan both testified in person.

During this hearing, Dr. Venkatesan stated, for the first time, that lesions that were detected on the December 30, 2004 MRI existed for at least three or four weeks. Tr. 143-45; tr. 347-48. Dr. Venkatesan asserted that studies have measured the duration of enhancement and, according to these studies, the lesions detected on the December 30, 2004 MRI were not new. Id. After the hearing, respondent was instructed to supply the articles on which Dr. Venkatesan relied for this assertion. Order, filed Dec. 1, 2008.

Respondent filed the requested materials. Exhibit D. W.C. was given an opportunity to obtain a supplemental report from Dr. Tornatore, which was filed on March 9, 2009. Dr. Tornatore stated the duration of enhancement was shorter than suggested by Dr. Venkatesan. Therefore, according to Dr. Tornatore, the non-enhanced lesions on W.C.'s December 30, 2004 MRI could have been caused by the December 13, 2004 flu vaccination. Exhibit 27.

The competing views regarding the onset of W.C.'s lesions were the subject of a second hearing, held on November 17, 2009. In this hearing, Dr. Tornatore appeared in person and Dr. Venkatesan appeared by telephone.

Following the second hearing, the parties were encouraged to explore resolving the case. Eventually, the parties determined that continued discussions were unlikely to be productive and a briefing schedule was set. W.C. filed an initial brief, respondent filed one brief, and W.C. filed a reply. With the filing of W.C.'s reply, the case is ready for adjudication.

III. Analysis

Frequently, the analysis in decisions from special masters in the Vaccine Program begins with a review of the three-part test announced in Althen. E.g. Doe/11 v. Sec'y of Health & Human Servs., No. 99-212V, 2008 WL 4899356, at *8 (Fed. Cl. Spec. Mstr. Oct. 29, 2008), motion for review denied, 87 Fed. Cl. 1 (2009), aff'd, 601 F.3d 1349 (Fed. Cir. 2010), cert. denied, __ U.S. __, 131 S.Ct. 573 (2010). This structure makes sense when the parties agree on basic information about the injury. When this circumstance is not present, the analysis may start with a different point. Broekelschen v. Sec'y of Health & Human Servs., 618 F.3d 1339, 1346 (Fed. Cir. 2010) (affirming special master's decision to determine which condition afflicted the petitioner before conducting an analysis of the Althen factors); Doe 60 v. Sec'y of Health & Human Servs., 94 Fed. Cl. 597,

623 (2010) (same), appeal docketed, No. 2011-5004 (Fed. Cir. Oct. 4, 2010). In this case, the preliminary question is whether W.C. suffered from a sub-clinical multiple sclerosis before he received the flu vaccine on December 13, 2004. The answer to this question is yes, W.C. did have sub-clinical multiple sclerosis before his vaccination for the reasons explained in section A, below. This finding is the predicate for an analysis of whether the vaccination significantly aggravated his disease. As discussed in section B, the evidence supports a finding that the flu vaccine did not make W.C.'s multiple sclerosis worse than it would have been.

A. Did W.C. Have Sub-Clinical Multiple Sclerosis Before His Vaccination?

The experts offered different answers to this question. Dr. Venkatesan opined that W.C. had lesions before he was vaccinated. Tr. 143-45; tr. 234; tr. 289. The basis for Dr. Venkatesan's opinion is the result of W.C.'s December 30, 2004 MRI. Dr. Tornatore expressed a contrary opinion. Dr. Tornatore stated that the MRI was not useful in determining whether the lesions were present before the vaccination. Tr. 340-41.

Because the MRI is the foundation for Dr. Venkatesan's opinion, a basic explanation of MRIs follows. MRIs have been used to study the duration of enhancement of lesions and the articles reporting these studies are also discussed. Finally, this knowledge is applied to W.C.'s MRI to determine, on a more likely than not basis, when his lesions began.

An MRI is a tool that produces an image of soft tissues, such as the brain. MRIs are often administered with and without a contrast agent, gadolinium. Gadolinium is injected into the person's blood and should remain within the circulatory system. Gadolinium, however, can reach the brain if there is a breach in the blood-brain barrier. When gadolinium does enter the brain, the lesion appears on an MRI as enhanced. Tr. 51; tr. 141-142; tr. 290; tr. 320-21. After a period of time, the damage to the blood-brain barrier is repaired preventing gadolinium from reaching the brain. When gadolinium stays within the circulatory system, the lesions will not appear as enhanced. A lesion that is not enhanced is considered an older lesion when detected on subsequent MRIs.

Dr. Tornatore agrees with this description of gadolinium enhancement and also agrees that most (approximately 90 percent) of lesions first appear as

enhanced. Tr. 371; tr. 379; see also tr. 286. The dispute between Dr. Tornatore and Dr. Venkatesan is over the duration of an enhancement.

Determining the duration of enhancement is challenging. One problem is that people are reluctant to undergo MRIs frequently. In one study from 1991, people had an MRI on a monthly basis. Exhibit D, tab 4 (Jonathan O. Harris et al., Serial Gadolinium-enhanced Magnetic Resonance Imaging Scans in Patients with Early, Relapsing-Remitting Multiple Sclerosis: Implications for Clinical Trials and Natural History, 29 Ann Neurol 548 (1991)) at 548. This frequency increased to weekly in a study published in 2003 and reported by Francois Cotton. Exhibit 27, tab A (Francois Cotton et al., MRI contrast uptake in new lesions in relapsing-remitting MS followed at weekly intervals, 60 Neurology 640 (2003)). Even a weekly study does not determine the precise number of days that the lesions remained enhanced. As the authors explained, a lesion that appears enhanced on only one weekly MRI scan could have actually been enhanced from 1 to 13 days.

This point from Cotton can be illustrated with a calendar.

May						
M	T	W	T	F	S	S
	1 scan #1	2	3	4	5	6
7	8 scan #2	9	10	11	12	13
14	15 scan #3	16	17	18	19	20
21	22	23	24	25	26	27
28	29	30	31			

Assume that the patient has an MRI performed on three successive Tuesdays, beginning on May 1. The May 1 MRI shows no enhancement. The next MRI is done on May 8 and this MRI does show an enhanced lesion. The enhancement could have started on any date between May 2 and May 8, inclusive. The third MRI is done on May 15 and does not show enhancement. This means that the enhancement could have stopped any time from May 8 to May 14. Thus, the longest period of enhancement of a lesion that appears enhanced only on the May 8 scan is 13 days (May 2 to May 15). The shortest period of enhancement of a lesion that appears enhanced only on the May 8 scan is 1 day (May 8 only).

Importantly, Cotton and his co-authors recognized that the appearance of enhancement on one weekly scan is consistent with enhancement from between 1

and 13 days. Exhibit 27, tab A (Cotton) at 641. Dr. Venkatesan consistently and correctly noted this fact in his testimony. By the same logic, a lesion that is enhanced on two weekly scans may have been enhanced for 8 to 20 days. Tr. 299; tr. 306-09. Dr. Tornatore, on the other hand, incorrectly asserted that the enhanced appearance on two weekly scans meant that the enhancement lasted for 14 days. Dr. Tornatore appeared to refuse to accept the meaning of the Cotton study as conveyed by the authors. Tr. 341; tr. 357-64.

From the observations of 26 patients, Cotton calculated the mean duration of enhancement and the median duration of enhancement. The mean duration of enhancement was 3.07 weeks. The median duration of enhancement was 2 weeks. Exhibit 27, tab A (Cotton) at 642. According to Dr. Tornatore, the median is a more useful measure because the mean permits outlying numbers (such as an enhancement lasting 10 weeks) to skew the result. Tr. 341. The median, in contrast, indicates that one-half of the scans lasted fewer than two weeks and one-half the scans lasted longer than two weeks. Tr. 387-88.

The Cotton study and the other studies allowed Dr. Venkatesan to conclude that the lesions noticed on the December 30, 2004 MRI could not have been caused by the December 13, 2004 vaccination. The December 30, 2004 MRI detected six lesions. Tr. 289; tr. 342. None of the six lesions were enhanced. Exhibit 1 at 27. According to Dr. Venkatesan, if the vaccination caused the lesions, at least one of them should have been enhanced when the MRI was done 17 days after vaccination. Tr. 289.

In reaching this conclusion, Dr. Venkatesan noted that the theory proposed by Dr. Tornatore to explain how the flu vaccine leads to multiple sclerosis requires some time to operate.[3] The administration of the flu vaccine does not lead to the development of lesions immediately. Instead, the flu vaccine triggers a response from the immune system, principally the generation of T-cells. According to Dr. Tornatore's theory, T-cells proliferate, cross the blood-brain barrier, and cause the inflammation in the brain. This inflammation leads to demyelination. See tr. 16-17; tr. 21-23 (Dr. Tornatore's testimony). This process of forming lesions "would take at least a few days and potentially even a week or two. Tr. 302; accord tr. 313

[3] This theory, which is known as molecular mimicry, is discussed more in section III.B.2.

(Dr. Venkatesan).[4] Thus, if Dr. Tornatore's estimate were correct, then the first lesion could have appeared as early as December 16, 2004, and potentially as late as December 27, 2004.

When this information is placed into a calendar for December 2004, it is easy to understand why Dr. Venkatesan's opinion is persuasive.

December 2004						
M	T	W	T	F	S	S
		1	2	3	4	5
6	7	8	9	10	11	12
13 flu shot	14	15	16 early date for lesions to start	17	18	19
20	21	22	23	24 numbness	25	26
27 late date for lesions to start	28	29	30 MRI	31		

It is more probable than not that at least some, if not all, of the six lesions detected on the December 30, 2004 MRI existed before the December 13, 2004 flu vaccination. The number of lesions is important. While Dr. Tornatore's timeline can be compressed to make the lesions develop through the stage in which they would be detectable with enhancement and then through the stage in which they would not be detectable with enhancement within 17 days, such compression might be appropriate if there were only one lesion or two lesions on the chance that the duration of enhancement was less than average. But, with six lesions, there is a greater likelihood that one lesion or more than one lesion would be enhanced for an average amount of time or even a longer than average amount of time.

It is important to emphasize that the standard for finding the duration of W.C.'s lesions, like the standard for finding all facts in the Vaccine Program, is a preponderance of the evidence. Moberly v. Sec'y of Health & Human Servs., 592

[4] The necessity of a medically appropriate interval between vaccination and the onset of a neurological problem has been recognized in other cases in the Vaccine Program. See Bazan v. Sec'y of Health & Human Servs., 539 F.3d 1347, 1352-53 (Fed. Cir. 2008).

F.3d 1315, 1322 (Fed. Cir. 2010); Knudsen v. Sec'y of Health & Human Servs., 35 F.3d 543, 549 (Fed. Cir. 1994) (stating that respondent's burden of proof is the same as petitioner's burden of proof). It is not possible to date the beginning of W.C.'s lesions with absolute certainty, but absolute certainty is not required. Andreu v. Sec'y of Health & Human Servs., 569 F.3d 1367, 1380 (Fed. Cir. 2009); Bunting v. Sec'y of Health & Human Servs., 931 F.2d 867, 873 (Fed. Cir. 1991).

Here, the record including the persuasive testimony of Dr. Venkatesan supports a finding that W.C.'s lesions existed before the vaccination. This finding necessarily means that W.C. cannot prevail on his theory that the flu vaccine caused his multiple sclerosis. Although W.C. cannot be entitled to compensation on this theory, he presented the alternative theory that the flu vaccine significantly aggravated his multiple sclerosis. See Pet'r Br. at 28-31. That theory is discussed in the next section.

B. Did the Flu Vaccine Significantly Aggravate W.C.'s Multiple Sclerosis?

The Vaccine Act authorizes compensation to people whose pre-existing condition is significantly aggravated by a vaccine. 42 U.S.C. § 300aa-11(c)(ii)(I). Significant aggravation means "any change for the worse in a preexisting condition which results in markedly greater disability, pain, or illness accompanied by substantial deterioration of health." 42 U.S.C. § 300aa-33(4).

For cases, such as the present one, in which petitioners assert that a vaccine significantly aggravated a condition not listed on the Vaccine Injury Table, petitioners bear the burden of establishing, by preponderant evidence, six elements. The six elements are:

> (1) the person's condition prior to administration of the vaccine, (2) the person's current condition (or the condition following the vaccination if that is also pertinent), (3) whether the person's current condition constitutes a "significant aggravation" of the person's condition prior to vaccination, (4) a medical theory causally connecting such a significantly worsened condition to the vaccination, (5) a logical sequence of cause and effect showing that the vaccination was the reason for the significant aggravation, and (6) a showing

> of a proximate temporal relationship between the vaccination and the significant aggravation.

Loving v. Sec'y of Health & Human Servs., 86 Fed. Cl. 135, 144 (2009). The last three elements are derived from Althen v. Sec'y of Health & Human Servs., 418 F.3d 1274, 1278 (Fed. Cir. 2005). One special master has recommended evaluating "the last three Loving factors first." Hennessey v. Sec'y of Health & Human Servs., No. 01-190V, 2009 WL 1709053, at *42 (Fed. Cl. Spec. Mstr. May 29, 2009), motion for review denied, 41 Fed. Cl. 126 (2010).

Here, the dispostive factor is the fourth item in the Loving test, which corresponds to the first prong in Althen. This element requires the petitioner to present "a medical theory causally connecting such a significantly worsened condition to the vaccination." For the reasons discussed in section III.B.2 below, W.C.'s evidence is not persuasive. However, before discussing W.C.'s evidence, the criteria for reviewing evidence are presented.

1. Criteria for Reviewing Evidence

Three authorities generally instruct special masters in how to evaluate evidence. They are Congress, the United States Court of Federal Claims, and the United States Court of Appeals for the Federal Circuit. Congress provided some instructions about how special masters should analyze the evidence in enacting the National Vaccine Injury Compensation Act, specifically section 13. Among other provisions, section 13 dictates that the special master should consider "the record as a whole." Section 13 also provides that the special master shall consider "any diagnosis, conclusion, medical judgment or autopsy or coroner's report which is contained in the record regarding the nature, causation, and aggravation of the petitioner's illness, disability, injury, condition or death." Nevertheless, "[a]ny such diagnosis, conclusion, judgment, test result, report, or summary shall not be binding on the special master or court."

The second authority is the United States Court of Federal Claims. Congress authorized the Court of Federal Claims to promulgate rules of procedure for cases in the Vaccine Program. 42 U.S.C. § 300aa−12(d)(2). Collectively, the judges of the Court of Federal Claims have issued the Vaccine Rules. The Vaccine Rules, in turn, provide that the special master "must consider all relevant and reliable evidence governed by principles of fundamental fairness to both parties." Vaccine

Rule 8(b)(1). See Cedillo v. Sec'y of Health & Human Servs., 617 F.3d 1328, 1339 (Fed. Cir. 2010) (interpreting Vaccine Rule 8(b)(1)).

The third authority is the United States Court of Appeals for the Federal Circuit. Decisions by the Federal Circuit are binding precedent. 42 U.S.C. § 300aa–12(e). Within the Vaccine Program, the Federal Circuit expected that special masters would "consider[] the relevant evidence of record, draw[] plausible inferences and articulate[] a rational basis for the decision." Hines v. Sec'y of Health & Human Servs., 940 F.2d 1518, 1528 (Fed. Cir. 1991).

A particular topic on which the Federal Circuit has guided special masters is the process for evaluating the testimony of expert witnesses. In the Vaccine Program, an expert's opinion may be evaluated according to the factors identified by the United States Supreme Court in Daubert v. Merrell Dow Pharmaceuticals, Inc., 509 U.S. 579 (1993). Terran v. Sec'y of Health & Human Servs., 195 F.3d 1302, 1316 (Fed. Cir. 1999). As recognized in Terran, the Daubert factors for analyzing the reliability of testimony are:

> (1) whether a theory or technique can be (and has been) tested; (2) whether the theory or technique has been subjected to peer review and publication; (3) whether there is a known or potential rate of error and whether there are standards for controlling the error; and, (4) whether the theory or technique enjoys general acceptance within a relevant scientific community.

Terran, 195 F.3d at 1316 n.2, citing Daubert, 509 U.S. at 592-95.

After Terran, decisions from judges of the Court of Federal Claims have consistently cited to Daubert. E.g. Snyder v. Sec'y of Health & Human Servs., 88 Fed. Cl. 706, 742-45 (2009); Cedillo v. Sec'y of Health & Human Servs., 89 Fed. Cl. 158, 182 (2009), aff'd, 617 F.3d 1328, 1347 (Fed. Cir. 2010); De Bazan v. Sec'y of Health & Human Servs., 70 Fed. Cl. 687, 699 n.12 (2006) ("A special master assuredly should apply the factors enumerated in Daubert in addressing the reliability of an expert witness's testimony regarding causation."), rev'd on other grounds, 539 F.3d 1347 (Fed. Cir. 2008); Campbell v. Sec'y of Health & Human Servs., 69 Fed. Cl. 775, 781 (2006); Piscopo v. Sec'y of Health & Human Servs., 66 Fed. Cl. 49, 54 (2005).

The reliability of the expert's theory is not presumed. A "special master is entitled to require some indicia of reliability to support the assertion of the expert witness." Moberly, 592 F.3d at 1324. Furthermore, the reliability of an expert's theory affects the persuasiveness of the evidence. Special masters may "inquir[e] into the reliability of testimony from expert witnesses. Weighing the persuasiveness of particular evidence often requires a finder of fact to assess the reliability of testimony, including expert testimony, and we have made clear that the special masters have that responsibility in Vaccine Act cases." Id. at 1325. The finding that an expert's opinion passes a minimal standard of reliability does not require acceptance of that expert's theory because "disputes about the degree of relevance or accuracy (above this minimum threshold [of reliability]) may go to the testimony's weight." i4i Ltd. Partnership v. Microsoft Corp., 598 F.3d 831, 852 (Fed. Cir. 2010), cert. granted, 79 U.S.L.W. 3318 (U.S. Nov. 29, 2010) (No. 10-290).

In evaluating expert testimony and scientific literature, special masters should analyze scientific literature "not through the lens of the laboratorian, but instead from the vantage point of the Vaccine Act's preponderant evidence standard." Andreu, 569 F.3d at 1379. "In other words, a finding of causation in the medical community may require a much higher level of certainty than that required by the Vaccine Act to establish a prima facie case. The special master must take these differences into account when reviewing the scientific evidence." Broekelschen v. Sec'y of Health & Human Servs., 89 Fed. Cl. 336, 343 (2009), aff'd, 618 F.3d 1339.

Generally, the Federal Circuit expects that a special master will present a reasonable basis for rejecting the opinion of one expert. Lampe v. Sec'y of Health & Human Servs., 219 F.3d 1361 (Fed. Cir. 2000); Burns v. Sec'y of Health & Human Servs., 3 F.3d 415, 417 (Fed. Cir. 1993).

2. Evidence

To satisfy the element of presenting a medical theory, W.C. relies upon the opinion of Dr. Tornatore and various medical articles. Pet'r Br. at 21-25, 28-31. Dr. Tornatore presented a theory known as molecular mimicry. This theory is not persuasive in this case because the evidence fails to demonstrate the reliability of molecular mimicry as a way to connect the flu vaccine and multiple sclerosis. The record contains several articles that refute the arguments advanced by Dr. Tornatore.

Molecular mimicry is based upon how the immune system reacts to foreign substances, such as bacteria and viruses. (These foreign substances are known as antigens.) The immune system classifies a virus, for example, as an antigen based upon sequences of amino acids, called peptides. After the virus is recognized, the immune system takes various steps to remove the virus, including the release of T-cells. Tr. 20-21.

From this foundation, the molecular mimicry theory postulates that a similarity in molecular structure between an antigen and portions of the host lead the immune system to turn against the host. According to Dr. Tornatore, portions of the flu vaccine mimic the structure of a component of the central nervous system, myelin basic protein, which is sometimes abbreviated "MBP." Tr. 23-24. This assertion is a basis for Dr. Tornatore's theory linking the flu vaccine to multiple sclerosis.

Molecular mimicry is a well-regarded theory in some contexts. For example, Dr. Tornatore teaches it to medical students. Tr. 46. Medical textbooks refer to molecular mimicry. Tr. 58. Molecular mimicry is generally accepted as the method by which an infection with the streptococcus bacteria can develop into Sydenham's chorea. Tr. 24-26 (Dr. Tornatore). Dr. Venkatesan accepts molecular mimicry as playing a role in Sydenham's chorea. Tr. 147 (Dr. Venkatesan); see also tr. 213.[5] Thus, molecular mimicry can be reliable under some circumstances.

W.C.'s burden is not satisfied with presenting a theory that is reliable in some contexts. "[A] petitioner must provide a reputable medical or scientific explanation that pertains specifically to the petitioner's case." Broekelschen, 617 F.3d at 1345.

Here, Dr. Tornatore offers molecular mimicry to explain how the flu vaccine can serve as the antecedent antigen for the development of multiple sclerosis. To support the reliability of this application, Dr. Tornatore relies primarily upon an article by Kai Wucherpfennig, which is exhibit 19 (Kai W. Wucherpfennig and Jack L. Strominger, Molecular Mimicry in T Cell-Mediated Autoimmunity: Viral Peptides Activate Human T Cell Clones Specific for Myelin Basic Protein, 80 Cell

[5] Dr. Tornatore also mentioned that the measles virus can cause an autoimmune disease in the nervous system. Tr. 26-27. Dr. Venkatesanen was not sure whether this was correct. Tr. 244.

695 (1995)). Tr. 43; tr.105. Secondary support is found in various case reports. Tr. 53-70.

Dr. Wucherpfennig tested a fundamental aspect of molecular mimicry. Dr. Wucherpfennig searched a database containing sequences of proteins to identify various viral and bacterial peptides that appeared to share molecular structure with myelin basic protein. After the database identified candidates, Dr. Wucherpfennig tested these peptides to see if they stimulated the production of T-cells. Exhibit 19 (Wucherpfennig) at 695-96; see also tr. 116-19 (discussing Wucherpfennig's experiment). The results showed that some peptide sequences stimulated a large amount of T-cells. The source of these peptides included herpes simplex virus, Epstein-Barr virus, adenovirus type 12. Another peptide sequence that led to a large response was a particular portion of the influenza A virus. However, three other portions of the influenza virus did not produce a large amount of T-cells. Exhibit 19 at 698-701.

Extending the Wucherpfennig study to support Dr. Tornatore's opinion in W.C.'s case is difficult for several reasons. First, different substances are involved. W.C. received the influenza vaccine. Dr. Wucherpfennig tested the influenza A virus. The difference between the influenza vaccine and the influenza virus could be significant. Different portions of the influenza A virus caused different reactions. Dr. Wucherpfennig commented "The observation that certain viral strains are capable of stimulating MBP-specific T cells while other strains are not may be important in defining the epidemiology of the disease." Exhibit 19 (Wucherpfennig) at 700-01. W.C. has not presented any evidence that the flu vaccine has been tested under conditions like the Wucherpfennig study.

More importantly, there is no evidence that the portions of the influenza virus that mimicked myelin basic protein are the portions of the virus used in the influenza vaccine. Tr. 101. Dr. Tornatore indicated that testing the specific proteins that are found in the flu vaccine could be done "very eas[ily]." Tr. 120. If Dr. Tornatore had performed such a test and if the test confirmed Dr. Tornatore's theory that the molecular structure of the flu vaccine resembles the molecular structure of parts of myelin, then Dr. Tornatore's overall theory that the flu vaccine can cause or aggravate multiple sclerosis would be more likely.

The lack of testing as to whether the flu vaccine has similarity with myelin basic protein does not compel an automatic rejection of Dr. Tornatore's theory, and in this case, Dr. Tornatore's theory has not been rejected solely because he has not tested it. Nevertheless, the lack of testing is another factor against finding that Dr.

Tornatore's opinion is persuasive. See Moberly v. Sec'y of Health & Human Servs., 85 Fed. Cl. 571, 606 (2009) (discussing the lack of testing for petitioner's theory), aff'd, 592 F.3d at 1324 (Fed. Cir. 2010). "[W]hether a theory or technique can be (and has been) tested" is one factor that may be considered in evaluating the expert's opinion. Daubert, 509 U.S. at 593.

An additional concern about relying upon the Wucherpfennig study is that Wucherpfennig conducted his experiments in cell cultures, meaning it is an in vitro study. Tr. 100-01. By way of contrast, an in vivo study uses living subjects. Dorland's Illustrated Medical Dictionary (30th ed. 2003) at 948; tr. 245-46. Dr. Venkatesan stated that extrapolating from the Wucherpfennig in vitro study to a living human being may not be appropriate because human beings are much more complex. For example, a human being has various methods to prevent the immune system from getting out of control. Tr. 153-56. An in vivo study would avoid some of the limitations of an in vitro study. See tr. 200-01.

A study on human beings seems to serve as a check for extrapolating Wucherpfennig to the present case. People with multiple sclerosis were given the influenza vaccine. Two and four weeks after vaccination, their blood was tested to see if they developed an increased number of T-cells that reacted with myelin basic protein. The study found a "lack of increased responses of autoreactive T cells during vaccination." Exhibit A, tab 5 (N.F. Moriabadi et al., Influenza Vaccination in MS: Absence of T-Cell Response against White Matter Proteins, 56 Neurology 938 (2001)) at 943; accord tr. 171 (Dr. Venkatesan discussing this article). The authors stated that their finding "may also reduce concerns about a putative triggering of autoimmune responses by mechanisms such as molecular mimicry." Id. Thus, the Moriabadi article tends to contradict the extension of the Wucherpfennig article, which was cited in the Moriabadi article as reference 26, to the situation of flu vaccine and multiple sclerosis.[6] Consequently, the Wucherpfennig article does not provide a reliable basis for finding that the theory

[6] Dr. Tornatore stated that the Moriabadi study contained a "huge flaw" in that Moriabadi measured gamma interferon and gamma interferon was too limited in that some T-cells could cause multiple sclerosis without producing gamma interferon. Tr. 261-64. This criticism lacks persuasiveness. Dr. Venkatesan explained that gamma interferon was an appropriate measure because the T-cells that are thought to cause disease secrete gamma interferon. Tr. 271. When this testimony was called to Dr. Tornatore's attention during the second hearing, Dr. Tornatore softened his criticism, saying that gamma interferon "is not an unreasonable" cytokine to use. Tr. 396.

that flu vaccine can cause multiple sclerosis is persuasive. In addition to the Wucherpfennig article, Dr. Tornatore cited to various case reports that have reported that acute demyelinating conditions, such as transverse myelitis, have followed vaccinations. Exhibit 13 (Dr. Tornatore's report) at 13-14; see also tr. 53-71 (Dr. Tornatore's testimony about these articles).

Four reasons militate against relying upon these case reports. The weakest reason is that W.C. appears to have relinquished any argument as his briefs submitted after the hearing omit any discussion of these case reports. See Vaccine Rule 8(f)(1). The next reason is that case reports are generally weak evidence of causation because case reports cannot distinguish a temporal association from a causal relationship. See Doe 93 v. Sec'y of Health & Human Servs., No. [redacted], 2010 WL 4205677, at *13 (Fed. Cl. Spec. Mstr. Oct. 20, 2010) (citing cases), motion for review filed (Nov. 8, 2010); see also tr. 94-95 (Dr. Tornatore's testimony about case reports).

The third reason is that the case reports concern neurological diseases other than multiple sclerosis. Dr. Venkatesan asserted that the diseases in the case reports, such as transverse myelitis and acute disseminated encephalomyelitis (ADEM), do not have the same pathology as multiple sclerosis. Tr. 182-86; tr. 236-39. Although Dr. Tornatore agreed that transverse myelitis and ADEM are different diseases, he stated that the diseases were sufficiently similar to multiple sclerosis to make them a valid basis for analogy. Tr. 266-68. Both Dr. Venkatesan and Dr. Tornatore raise fair points. Resolving this dispute is not necessary because more probative evidence is available.

The strongest reason for discounting the various case reports is the collection of studies about flu vaccine and multiple sclerosis submitted by respondent.[7] These studies are entitled to more weight than case reports because the studies are actually about multiple sclerosis, the disease afflicting W.C.. Moreover, these other studies are controlled studies and, therefore, are more probative than case reports.

Respondent submitted three articles that reported how the flu vaccine affects people with multiple sclerosis. One study involved 643 patients and compared whether any relapses occurred in temporal proximity to a vaccination. "This study suggests that commonly administered vaccinations (specifically, against tetanus,

[7] Respondent may introduce evidence in an attempt to undermine the persuasive value of petitioner's evidence. Bazan, 539 F.3d at 1353-54.

hepatitis B and influenza) do not increase the risk of relapse in patients with multiple sclerosis." Exhibit A, tab 1 (Christian Confavreux et al., Vaccinations and the Risk of Relapse in Multiple Sclerosis, 344 No. 5 New England J. of Medicine 319, 324 (2001)). The authors of this study describe the design of this study as offering many advantages and relatively few disadvantages in reaching an informed conclusion. Id. at 324-25; see tr. 161-63 (Dr. Venkatesan's testimony about this article).

In the second study, three health maintenance organizations provided information about 440 case subjects and 950 control subjects. Several different vaccinations were examined. For the influenza vaccine, the odds ratio for developing multiple sclerosis was 0.7. Exhibit A, tab 2 (Frank DeStephano et al., Vaccinations and Risk of Central Nervous System Demyelinating Diseases in Adults, 60 Arch. Neurol. 505, 507 (table 3) (2003)). An odds ratio of less than one means that people who received the influenza vaccine were less likely to develop multiple sclerosis than people who did not receive it. Tr. 164 (testimony of Dr. Venkatesan about odds ratio); tr. 259 (testimony of Dr. Tornatore about odds ratio). The authors of this study reported "We did not find any increased relative risks regardless of the timing of vaccination, indicating that vaccinations do not cause CNS demyelination, nor do they trigger its clinical manifestation in those with subclinical disease." Exhibit A, tab 2 (DeStephano) at 505.

The third study is the most persuasive about W.C.'s claim. In this case, researchers "conducted a multicenter, prospective, randomized, double-blind trial of influenza immunization in patients with relapsing/remitting MS." A study with this design presents very valuable information. See Michael D. Green et al., "Reference Guide on Epidemiology" in Reference Manual on Scientific Evidence 333, 338 (2d ed. 2000) (stating "a randomized trial . . . is considered the gold standard for determining the relationship of an agent to a disease or health outcome."). When a double-blind study is available, this study may be considered in evaluating the reliability on an expert's opinion. Libas, Ltd. v. United States, 193 F.3d 1361, 1368 (Fed. Cir. 1999). Dr. Venkatesan stated that the Miller study was "one of the more rigorous types of studies that can be done in science." Tr. 166.

In this study, 104 patients with relapse-remitting multiple sclerosis were divided into two groups. One group received the flu vaccine and the other received a placebo. The patients were followed for six months to see if they experienced any relapses in the disease. "The two groups showed no difference in attack rate or disease progression over 6 months. Influenza immunization in MS patients is

neither associated with an increased exacerbation rate in the post-vaccination period nor a change in disease course over the subsequent 6 months." Exhibit A, tab 3 (A.E. Miller et al., A multicenter, randomized, double-blind placebo-controlled trial of influenza immunization in multiple sclerosis, 48 Neurology 312, 312 (1997)). This conclusion contradicts Dr. Tornatore's opinion that the December 13, 2004 flu vaccination affected the course of W.C.'s multiple sclerosis.

Dr. Tornatore's assessment of the Miller study is difficult to summarize. Initially, in the context of discussing a case report that mentioned the Miller study, Dr. Tornatore stated that he found that the Miller study "is not relevant to this case." Tr. 98. Later, when Dr. Tornatore was asked to explain why the Miller study was not relevant, Dr. Tornatore stated "I think it has a great deal of relevancy." Tr. 126. In this same context, Dr. Tornatore also cautioned against extrapolating from this study because, according to Dr. Tornatore, the Miller study would not address the situation in which people's multiple sclerosis was actually caused by the flu vaccine. Tr. 125-26.

Dr. Tornatore's point does not ring true. He analogized to case reports that describe what happened to a handful of people. Yet, Dr. Tornatore was not willing to extrapolate from a study with 100 people.

Most, if not all, neurologists follow the conclusions presented in the Confavreaux, DeStephano, and Miller articles. The American Academy of Neurology commissioned the MS Council for Clinical Practice Guidelines to address "the safety of immunization in patients with MS, particularly about the risk of relapse after vaccination." Exhibit A, tab 4 (Oliver T. Rutschmann, Immunization and MS: A summary of published evidence and recommendations, 59 Neurology 1837, 1837 (2002)). These researchers evaluated other studies to develop a "meta-analysis." Tr. 168. After considering a variety of articles, including the Miller study, but not the Confavreux or the DeStephano study, the researchers concluded that "there is definite evidence against a substantial increased risk of MS exacerbation after influenza vaccine." This was a "Level A Recommendation." Exhibit A, tab 4 (Rutschmann) at 1840. Even Dr. Tornatore stated that "we tell all of our MS patients to get the flu vaccine." Tr. 126.[8]

[8] Dr. Tornatore, however, stated that if W.C. were his patient, Dr. Tornatore would recommend that W.C. not receive the flu vaccine. Tr. 126-27.

Collectively, the three large studies (Confavreaux, DeStephano, and Miller) and the recommendation of the committee from the American Academy of Neurology constitute strong evidence against the theory asserted by Dr. Tornatore. Epidemiological studies may be considered, even though petitioners are not required to prove their case with epidemiological evidence. Andreu, 569 F.3d at 1379-80. These studies reinforce Dr. Venkatesan's opinion that the theory offered by Dr. Tornatore is "extremely unlikely." Tr. 149-50.

Dr. Venkatesan did not rule out Dr. Tornatore's theory as medically impossible. Tr. 149. He recognized that, as a matter of theory, molecular mimicry has not been proven false. Actually, both Dr. Tornatore and Dr. Venkatesan recognized that, as a matter of logic, it is impossible to prove that molecular mimicry does not exist. Tr. 384-85 (Dr. Tornatore); tr. 389 (Dr. Venkatesan); see also tr. 259 (Dr. Tornatore).

However, respondent does not bear the burden of establishing that petitioner's theory is impossible and respondent does not bear the burden of identifying an alternative cause for an off-Table injury. Bazan, 539 F.3d at 1353-54. Respondent's failure to identify the cause of W.C.'s multiple sclerosis is consistent with the state of medical knowledge. Doctors do not understand what causes multiple sclerosis initially and do not understand what causes multiple sclerosis to flare. Tr. 128 (Dr. Tornatore); tr. 391 (Dr. Venkatesan). Both Dr. Tornatore and Dr. Venkatesan described advancements in the understanding of multiple sclerosis as worthy of a "Nobel Prize." Tr. 15; tr. 316.

Into this situation in which little is known about multiple sclerosis, Dr. Tornatore posits the theory that the flu vaccine can affect (either cause or aggravate) multiple sclerosis. Strictly as a hypothetical model, molecular mimicry has some appeal. Researchers determined that it merited investigation. When this theory was tested, the flu vaccine was found not to worsen patients' multiple sclerosis. See exhibit A, tab 1 (Confavreux); exhibit A, tab 2 (DeStephano); exhibit A, tab 3 (Miller). The connection between the flu vaccine and multiple sclerosis has been looked for but has not been found. Tr. 157-58.

As the petitioner, W.C. bears the burden of establishing "a medical theory causally connecting such a significantly worsened condition to the vaccination." Loving, 86 Fed. Cl. at 144. The legal standard is a preponderance of evidence, not a medically certain amount of evidence. But, in this case, a preponderance of evidence does not support the persuasiveness of W.C.'s theory for the reasons explained above.

Due to W.C.'s failure to meet his burden of proof on one element, extensive discussion of additional elements is superfluous. This is so even though W.C. emphasizes that Dr. Venkatesan conditionally accepted Dr. Tornatore's assertion that the interval between W.C.'s vaccination and the onset of symptoms of multiple sclerosis, 11 days, is consistent with the theory of molecular mimicry. Pet'r Br. at 27, citing tr. 232. However, establishing a temporal relationship is not sufficient to establish a persuasive medical theory causally connecting a vaccine to an injury. Grant v. Sec'y of Health & Human Servs., 956 F.2d 1144, 1148 (Fed. Cir. 1992). Thus, Dr. Venkatesan's conditional concession about timing does not advance W.C.'s attempt to present, by preponderant evidence, a reliable medical theory.

IV. Conclusion

A preponderance of the evidence shows that W.C. had some lesions indicative of multiple sclerosis before he received the flu vaccine on December 13, 2004. It was only after this vaccination that W.C. experienced symptoms of multiple sclerosis. This sequence of events is the foundation for W.C.'s claim that the flu vaccine significantly aggravated his multiple sclerosis.

Whether the flu vaccine worsens multiple sclerosis has been the subject of medical research. Three different studies have concluded that flu vaccine does not affect multiple sclerosis. No studies showing that the flu vaccine does aggravate multiple sclerosis were introduced. Therefore, the record, when considered as a whole, does not support a finding that W.C. has established, by preponderant evidence, a medical theory causally connecting the flu vaccine to an aggravation of multiple sclerosis. Without persuasive evidence on this point, W.C. cannot prevail. Accordingly, the Clerk's Office is instructed to enter judgment in accord with this decision unless a motion for review is filed.

IT IS SO ORDERED.

s/ Christian J. Moran
Christian J. Moran
Special Master