In the United States Court of Federal Claims
OFFICE OF SPECIAL MASTERS

EDWARD A. SOKOL,	*	
	*	No. 16-1631V
	*	Special Master Christian J. Moran
Petitioner,	*	
v.	*	
	*	Filed: January 9, 2020
SECRETARY OF HEALTH	*	
AND HUMAN SERVICES,	*	flu vaccine, stroke, subarachnoid
	*	hemorrhage (SAH)
Respondent.	*	

Jeffrey A. Golvash, Brenna, Robins & Daley, P.C., Pittsburgh, PA, for petitioner; Voris E. Johnson, Jr., United States Dep't of Justice, Washington, DC, for respondent.

DECISION DENYING ENTITLEMENT[1]

Edward A. Sokol received a dose of the influenza ("flu") vaccine on January 22, 2014, and he developed problems speaking by February 2, 2014. Doctors diagnosed him as suffering a stroke, specifically a subarachnoid hemorrhage. Mr. Sokol contends that the vaccination caused his stroke and seeks compensation through the National Childhood Vaccine Compensation Program. 42 U.S.C. § 300aa–10 through 33 (2012).

[1] Because this decision contains a reasoned explanation for the action in this case, the undersigned is required to post it on the United States Court of Federal Claims' website in accordance with the E-Government Act of 2002. 44 U.S.C. § 3501 note (2012) (Federal Management and Promotion of Electronic Government Services). This means the decision will be available to anyone with access to the internet. In accordance with Vaccine Rule 18(b), the parties have 14 days to identify and move to redact medical or other information, the disclosure of which would constitute an unwarranted invasion of privacy. If, upon review, the undersigned agrees that the identified material fits within this definition, the undersigned will redact such material before posting the decision.

To assist him, Mr. Sokol retained a neurologist, George A. Small, who wrote two reports, exhibits 7 and 9. The Secretary disagreed with Mr. Sokol's claim and retained a neurologist, Steven Messé, who also wrote two reports, exhibits A and C. Both neurologists, as well as Mr. Sokol, testified at a hearing held in Pittsburgh, Pennsylvania, near Mr. Sokol's hometown.

After considering this testimonial evidence and the documentary evidence, the undersigned finds that Mr. Sokol has not met his burden of proof. This is based on: (1) the relatively inferior qualifications of Mr. Sokol's expert, when compared to respondent's expert; (2) weaknesses in Dr. Small's asserted medical theory; (3) failure to establish that the stroke arose in an acceptable time between the vaccination and injury; and (4) the presence of alternative factors that could cause a stroke. See infra Part III.

I. Events in Mr. Sokol's Life

Mr. Sokol was born in 1956. It is likely that Mr. Sokol was born with an aneurysm in his brain. Tr. 67 (Dr. Small), 90 (Dr. Small). An aneurysm is an irregularity in an artery in which the artery balloons. Dorland's Illustrated Medical Dictionary 82 (32d ed. 2012); Tr. 65. Approximately 1-2 percent of people are born with aneurysms in their brains. Tr. 150. There is no allegation that the 2014 flu vaccination caused Mr. Sokol's aneurysm.

As an adult, Mr. Sokol worked as an electrician but stopped working around 2009. Tr. 35. He has not filed any medical records for the period before the vaccination. In the hearing, Mr. Sokol explained that from about 2009 to the vaccination date (January 22, 2014), Mr. Sokol received almost no medical treatment. Tr. 30-31. As discussed below, the lack of treatment does not mean that Mr. Sokol was entirely healthy. He could have been suffering from problems, such as hypertension, that a doctor had not diagnosed due to a lack of medical care. See Tr. 197-98.

In January 2014, Mr. Sokol decided to get a flu vaccine. The vaccination in 2014 was the second flu vaccination in Mr. Sokol's life. Tr. 14.

As previously stated, Mr. Sokol received the flu vaccine on January 22, 2014. Because cold weather increases the risk for hypertension, the weather around this date is relevant in considering the cause of Mr. Sokol's stroke. The temperature on that day in Pittsburgh ranged from a low of negative 5 degrees to a

high of positive 12 degrees. Exhibit 28 at 3.[2] Over the next few days, the temperature warmed, but was still cold. By January 27, 2014, the temperature ranged from 1 degree to 43 degrees. But, on January 28, 2014, the temperature fell to a low of negative 8 degrees and a high of 7 degrees. The temperature then rebounded, reaching a high of 53 degrees on February 1, 2014, with a low of 31 on that day. Exhibit 29 at 3.

Approximately four days after the vaccination, Mr. Sokol started having flu-like symptoms. Exhibit 3 at 8; exhibit 1(a) at 70; Tr. 16. The symptoms lasted about three days, ending by January 30, 2014. Exhibit 3 at 8; Tr. 16; see also Tr. 120.

Mr. Sokol started to have problems talking on February 1, 2014. Exhibit 3 at 8; Tr. 17. On the next day, his daughter brought him to Passavant Hospital. Exhibit 3 at 8; Tr. 19. After imaging studies, doctors diagnosed a stroke. See exhibit 3 at 22; Tr. 21. During his time in Passavant Hospital, the doctors considered giving him a flu vaccination but did not because he had received a flu vaccine two weeks earlier. Exhibit 3 at 45 (showing doctors considered administering the vaccine on Feb. 3, 2014).

Doctors transferred Mr. Sokol to a hospital offering higher level care, Presbyterian University Hospital. Exhibit 1 at 153-54; Tr. 21. Doctors repeated the imaging studies and confirmed Mr. Sokol had suffered a stroke. Exhibit 1(a) at 148-50; Tr. 22.

A stroke, according to Dr. Messé, is an "injury to the brain due to a vascular cause." Tr. 171. Strokes are classified into two types. The more common type (constituting approximately 80% of all strokes) is due to blockages in blood vessels. These strokes are known as "ischemic" strokes. Tr. 171-72.

The less common type of stroke is due to the rupture of a vessel. The rupture can happen in vessels that are within the brain itself, known as an intraparenchymal hemorrhagic stroke. Tr. 172. The rupture can also happen in the area surrounding the brain, the subarachnoid space. Tr. 66, 173-74. Here, Mr. Sokol suffered a subarachnoid hemorrhagic stroke. Exhibit 3 at 8; exhibit 1(a) at 79-80, 149; Tr. 69.

Dr. Small stated that risk factors for subarachnoid hemorrhagic strokes include cigarette smoking and use of drugs that raise a person's blood pressure,

[2] All temperature measurements are in degrees Fahrenheit.

such as cocaine. Tr. 68. These factors did not contribute to Mr. Sokol's case. Dr. Messé added other risk factors that also did not pertain to Mr. Sokol, including female gender, use of alcohol, and family history. Tr. 175. However, Dr. Messé brought out other risk factors that could, as discussed below, increase Mr. Sokol's risk for having a stroke such as increasing age, hypertension, and cold weather. Tr. 175.

According to Dr. Messé's estimate, about one-half of subarachnoid hemorrhage cases occur in people with no risk factor present. Tr. 176.[3] Subarachnoid hemorrhages occur approximately 50,000 times per year in the United States. Tr. 174.

Once Mr. Sokol's subarachnoid hemorrhage was diagnosed, a neurosurgeon, Daniel Wecht, operated on him. The purpose of the operation was to clip the aneurysm. Exhibit 1(b) at 220. In the report from the operation, Dr. Wecht commented: "By the way, the dissection revealed areas of hemosiderin, strongly suggesting that the patient's hemorrhage was not acute, but may have been days ago. This is consistent with the patient's rather nebulous clinical history." Id. at 223. Hemosiderin is a type of iron that comes from blood. See Dorland's at 843. This description of hemosiderin is a critical aspect of Dr. Small's opinion that the flu vaccination caused Mr. Sokol's stroke because, as he states, hemosiderin indicates "chronicity of bleeding," suggesting that onset occurred days before the February 1 diagnosis. Tr. 74.

After the repair of Mr. Sokol's subarachnoid hemorrhage, he remained in Presbyterian Hospital for approximately two weeks. See exhibit 1(a) at 15 (Feb. 2, 2014 note for Mr. Sokol's transfer to rehabilitation). He then went to a rehabilitation facility. See exhibit 1(a) at 11.

When Mr. Sokol was discharged from the rehabilitation facility, he was taking two medications to lower high blood pressure, amlodipine and labetalol. Exhibit 1(a) at 13, Tr. 281. He has continued to take these two medications. Exhibit 15 at 3 (March 3, 2014), exhibit 11 at 6 (July 7, 2017), and exhibit 14 at 1 (April 27, 2018).

During his oral testimony, Mr. Sokol stated that his main problems were with his voice and feeling more tense. Tr. 28.

[3] Dr. Small could not estimate the percentage of subarachnoid hemorrhages associated with some risk factor. Tr. 149-51.

II. Standards for Adjudication

A petitioner is required to establish his case by a preponderance of the evidence. 42 U.S.C. § 300aa–13(1)(a). The preponderance of the evidence standard requires a "trier of fact to believe that the existence of a fact is more probable than its nonexistence before [he] may find in favor of the party who has the burden to persuade the judge of the fact's existence." Moberly v. Sec'y of Health & Human Servs., 592 F.3d 1315, 1322 n.2 (Fed. Cir. 2010) (citations omitted). Proof of medical certainty is not required. Bunting v. Sec'y of Health & Human Servs., 931 F.2d 867, 873 (Fed. Cir. 1991).

Distinguishing between "preponderant evidence" and "medical certainty" is important because a special master should not impose an evidentiary burden that is too high. Andreu v. Sec'y of Health & Human Servs., 569 F.3d 1367, 1379-80 (Fed. Cir. 2009) (reversing special master's decision that petitioners were not entitled to compensation); see also Lampe v. Sec'y of Health & Human Servs., 219 F.3d 1357 (Fed. Cir. 2000); Hodges v. Sec'y of Health & Human Servs., 9 F.3d 958, 961 (Fed. Cir. 1993) (disagreeing with dissenting judge's contention that the special master confused preponderance of the evidence with medical certainty).

Petitioners bear a burden "to show by preponderant evidence that the vaccination brought about [the vaccinee's] injury by providing: (1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of a proximate temporal relationship between vaccination and injury." Althen v. Sec'y of Health & Human Servs., 418 F.3d 1274, 1278 (Fed. Cir. 2005).

III. Analysis

Here, Mr. Sokol has failed to advance a persuasive case for several reasons. First, as a foundational matter, the expert whom Mr. Sokol retained, Dr. Small, has less expertise than the expert the Secretary retained, Dr. Messé. Second, the theory that Dr. Small offers has flaws that tend to reduce the persuasive value of Dr. Small's opinion. Third, Mr. Sokol has not established that his stroke occurred within the time predicted by the theory Dr. Small proposed. Fourth, the presence of alternative causes decreases the likelihood that that the flu vaccination was causal. These are developed below.

A. In the field of stroke, Dr. Messé's qualifications are superior to Dr. Small's qualifications.

Special masters may consider the relative expertise of testifying experts when weighing the value of their opinions. See Depena v. Sec'y of Health & Human Servs., No. 13-675V, 2017 WL 1075101 (Fed. Cl. Spec. Mstr. Feb. 22, 2017), mot. for rev. denied, 133 Fed. Cl. 535, 547-48 (2017), aff'd without op., 730 Fed. App'x 938 (Fed. Cir. 2018); Copenhaver v. Sec'y of Health & Human Servs., No. 13-1002V, 2016 WL 3456436 (Fed. Cl. Spec. Mstr. May 31, 2016), mot. for rev. denied, 129 Fed. Cl. 176 (2016); Bowman v. Sec'y of Health & Human Servs., No. 13-807V, 2014 WL 3486773, at *7 (Fed. Cl. Spec. Mstr. June 17, 2014). In this case, Dr. Messé has more expertise in stroke and presented with a more persuasive demeanor than Dr. Small.

Dr. Small. At the basic level, Dr. Small graduated from Jefferson Medical College in 1988, and became board-certified in psychiatry and neurology in 1993. Dr. Small obtained a specific board certification in electrodiagnostic medicine in 1994. Exhibit 10 (curriculum vitae) at 3; Tr. 43. These qualifications make him competent to express the opinions he expressed.

Within the field of neurology, Dr. Small has focused his practice on treating patients with myasthenia gravis, which is considered an autoimmune disease. Tr. 49. His knowledge about myasthenia gravis gives him some knowledge of immunology (Tr. 141), but he is not an immunologist. Tr. 107.

There are some limitations in Dr. Small's background. He has limited exposure to epidemiology. Tr. 140. He does not act as a peer reviewer for medical journals. Tr. 107.

Dr. Small's presentation while testifying was not as strong as it could have been. He seemed unfamiliar with or unprepared to discuss the important articles. See Tr. 81, 86. He did not always answer questions directly. See Tr. 127 (epidemiology), 157 (clinical experience with patients who received the flu vaccine), 281 (Mr. Sokol's pre-existing hypertension).

Dr. Messé. Dr. Messé graduated from medical school, the University of Michigan in 1998. Like Dr. Small, Dr. Messé became board-certified in psychiatry and neurology (2003). However, their paths diverge as Dr. Messé has obtained a sub-specialization in vascular neurology. Exhibit B (curriculum vitae) at 1-2. Vascular neurology is the field "concerned with the diagnosis and treatment of

cerebrovascular conditions, such as stroke syndrome." Dorland's at 1226; accord Tr. 170.

Dr. Messé's patient population is almost exclusively patients who have suffered strokes. Tr. 169. He teaches other medical professionals about stroke and has written articles about stroke that peer-reviewed journals have published. He was invited to join the Executive Committee of the Stroke Section of the American Academy of Neurology. Tr. 245; exhibit B at 2. Likewise, within the American Heart Association, he was a member of the stroke oversight committee. Exhibit B at 2. In 2011, the American Academy of Neurology awarded him the Michael S. Pessin Stroke Leadership award. Exhibit B at 2; Tr. 245.

As with Dr. Small, Dr. Messé has no special expertise in immunology. Tr. 192, 246. But, unlike Dr. Small, Dr. Messé studied epidemiology and received a certificate for his education. Tr. 246. He also reviews articles for journals. Tr. 170, 245.

Dr. Messé's strong background in stroke may have contributed to his credible presentation while testifying. Dr. Messé was knowledgeable about the topics on which he opined. He conceded weaknesses in studies on which he was relying. He seemed to express his opinions with care to be accurate.

In short, on this topic (stroke), Dr. Messé was a much better witness than Dr. Small. In describing Dr. Messé as "better," the undersigned does not want to communicate that Dr. Small was "bad." Dr. Small did reasonably well. But, Dr. Small could not bring the same degree of expertise on the specific subject of strokes as Dr. Messé.[4] Thus, the undersigned often credits Dr. Messé's opinions in this decision.

B. Dr. Small's theory for how a flu vaccine can cause a subarachnoid hemorrhage has weaknesses.

One element of a petitioner's case is to present "a medical theory causally connecting the vaccination and the injury." Althen, 418 F.3d at 1278. This theory must be sound and reliable. Boatmon v. Sec'y of Health & Human Servs., 941 F.3d 1351, 1360 (Fed. Cir. 2019).

[4] If the injured person suffered from myasthenia gravis, then Dr. Small would be more qualified than Dr. Messé. However, this point is purely hypothetical as Dr. Messé stated that he restricts his testimony to cases involving strokes. Tr. 238.

Dr. Small has presented a theory based upon cytokines. In essence, the vaccination causes the body to produce cytokines, cytokines cause inflammation, and inflammation causes the aneurysm to rupture. Petitioner's brief aptly summarizes the theory:

> in the context of a congenital or preexisting arterial aneurysm, the body's release of these proinflammatory mediators, such as tumor necrosis factor-a, affects arteries by causing their muscular layers to either dilate or contract, changing arterial wall tension in both normal cerebral arteries and those housing aneurysms, which by definition are already weakened structures, and thus vulnerable to rupture by reason of the inflammatory response.

Pet'r's Preh'g Br., filed Jan. 16, 2019, at 6. To support his theory, Dr. Small primarily relied upon an article whose lead author is Daan Backes, exhibit 13.[5]

This theory suffers from various deficiencies as outlined below.

1. *Dr. Small did not establish that inflammation causes stroke.* As Dr. Messé acknowledged, inflammation is associated with stroke. However, whether the inflammation causes a stroke or whether a stroke causes inflammation is not clear. Tr. 203. Dr. Small, on cross-examination, agreed that inflammation can be the evidence of an injury, not the cause of the injury. Tr. 115 (discussing exhibit 18 (Tulamo) at 1).

2. *The theory is too generalized*. In pointing to inflammation as the cause of an aneurysm rupture, Dr. Small opens the possibility that anything that causes inflammation could cause stroke. Tr. 102, 107, 130. As discussed below, cold weather and hypertension are also risk factors for stroke. While the theory that inflammation contributes to stroke could be valid, Dr. Small has not adequately distinguished flu vaccine from any other potential cause for inflammation.

3. *Backes may have reached an inappropriate conclusion regarding flu infection.* This group of researchers investigated whether "the increased incidence of aneurysmal subarachnoid hemorrhage in winter is related to temperature or increased incidence of influenza." Exhibit 13 (Backes) at 737. The foundation for

[5] The complete bibliographical information about the articles cited is found in the appendix.

the study was a set of databases from Holland. For the combined effects of influenza epidemics and decrease in temperature, the authors found an adjusted incidence daily ratio of 1.021 with a 95% confidence interval of 0.98–1.064. Id. at 4 (table 1). The authors concluded: "Influenza epidemics and cold temperatures are associated with an increased risk of SAH." Id. at 743.

Dr. Messé criticized this conclusion. In his view, because the confidence interval includes values less than 1.0, the authors should not have found an increased risk. Tr. 186, 205-06. When the value is 1.0, one factor does not alter the risk of the other. See Tr. 181-82.

Here, although Dr. Messé may technically be correct, the confidence interval barely dips below 1. Thus, it seems, at least at the preponderance of the evidence standard, that this criticism is less significant than the distinction between a flu infection and a flu vaccination.

4. *Backes studied flu infections and Dr. Small did not explain how to extrapolate from a flu infection to a flu vaccination*. The bigger problem with Backes in trying to determine whether flu vaccination can cause subarachnoid hemorrhages is that Backes studied flu infections, not flu vaccinations. Tr. 79. The authors linked flu infection to subarachnoid hemorrhages through inflammation: "A growing body of evidence points to a key role of inflammation in the process of aneurysm rupture. Infection with the influenza virus causes an innate immune response that releases proinflammatory mediators, which lead to symptoms within 2 days." Exhibit 13 (Backes) at 741.

However, the infection with a flu virus prompts a much greater response from the immune system than a flu vaccination. Tr. 101, 108, 119 (discussing exhibit 19 (Hayden)), 223 (discussing exhibit A3 (Smeeth)). Dr. Small appears to have assumed that the inflammation associated with a vaccination could be as detrimental as the inflammation associated with an infection. But, he did not justify this assumption. This gap is especially telling because of the epidemiological studies that are discussed next.

5. *The epidemiological studies on flu vaccination do not show an increased risk for strokes*. Dr. Messé presented three epidemiologic studies that investigated whether people who received the flu vaccine suffered strokes at an increased incidence. Exhibits A1 (Grau), A2 (Siriwardena), A3 (Smeeth); see also Tr. 177-85. They did not find any increased risk, and sometimes found that people who received the flu vaccine suffered fewer strokes (suggesting that the flu vaccine

was actually protective). Dr. Small did not dispute the findings in the epidemiology. Tr. 99, 128.

These studies are not perfect. For example, the studies looked at both ischemic and hemorrhagic strokes. The Grau study finds that flu vaccine is protective against stroke with data suggesting that the flu infection would be associated with approximately 62 percent of all strokes, a rate that the authors describe as "implausibly high." Exhibit A1 (Grau) at 1505. But, these flaws do not diminish the overall point that epidemiology does not support Dr. Small's theory that the flu vaccine causes subarachnoid hemorrhages. Petitioners and their experts bear the burden in the first instance to present a persuasive medical theory explaining how the vaccine can cause an injury. Even if the epidemiologic evidence were excluded, Mr. Sokol would still be required to produce some indicia that Dr. Small's opinion is reliable and persuasive. See Moberly, 592 F.3d at 1324.

For the reasons outlined above, Dr. Small's theory suffers from several weaknesses that ultimately render the theory unreliable for the purposes of establishing a causal connection.[6]

C. Dr. Small did not establish that Mr. Sokol's SAH originated in an appropriate time after the flu vaccination.

If the cytokine-based theory were accepted, then Mr. Sokol would still be required to establish "a proximate temporal relationship between vaccination and injury." Althen, 418 F.3d at 1278. The timing prong actually contains two parts. A petitioner must show the "timeframe for which it is medically acceptable to infer causation" and the onset of the disease occurred in this period. Shapiro v. Sec'y of Health & Human Servs., 101 Fed. Cl. 532, 542-43 (2011), recons. denied after remand on other grounds, 105 Fed. Cl. 353 (2012), aff'd without op., 503 F. App'x 952 (Fed. Cir. 2013). While Dr. Small persuasively defined the medically

[6] In other cases, petitioners have advanced cytokine-based theories with mixed success. See Copenhaver v. Sec'y of Health & Human Servs., No. 13-1002V, 2016 WL 3456436, at *1 (Fed. Cl. Spec. Mstr. May 31, 2016), mot. for rev. denied, 129 Fed. Cl. 176 (2016); Simmons v. Sec'y of Health & Human Servs., No. 11-216V, 2015 WL 6778563, at *4 (Fed. Cl. Spec. Mstr. Oct. 30, 2015); Godfrey v. Sec'y of Health & Human Servs., No. 10-565V, 2015 WL 10710961, at *3 (Fed. Cl. Spec. Mstr. Oct. 27, 2015), mot. for rev. denied, slip op. (Fed. Cl. April 29, 2016); Koehn v. Sec'y of Health & Human Servs., No. 11-355V, 2013 WL 3214877, at *1 (Fed. Cl. Spec. Mstr. May 30, 2013), mot. for rev. denied, 113 Fed. Cl. 757 (2013), aff'd, 773 F.3d 1239 (Fed. Cir. 2014).

acceptable interval, preponderant evidence does not establish that Mr. Sokol's SAH arose in the relevant period.

1. The medically acceptable timeframe for a cytokine-driven response may extend to four days as Dr. Small postulated.

The medically acceptable timeframe depends, at least in part, on the theory being offered. Langland v. Sec'y of Health & Human Servs., 109 Fed. Cl. 421, 443 (2013); Garner v. Sec'y of Health & Human Servs., No. 15-063V, 2017 WL 171384, at *15-16 (Fed. Cl. Spec. Mstr. Mar. 24, 2017). In other words, "the 'etiology' of the disorder determines the appropriate temporal relationship." Veryzer v. Sec'y of Health & Human Servs., 100 Fed. Cl. 344, 356 (2011) (citing Bazan v. Sec'y of Health & Human Servs., 539 F.3d 1347, 1352 (Fed. Cir. 2008)), aff'd, 475 Fed. App'x 765 (Fed. Cir. 2012). Here, as discussed above, Dr. Small has proposed a theory based upon cytokines.

While vaccinations do lead to an increase in cytokines as part of the expected and normal response of the immune system, the increase typically resolves within approximately six days. The strongest support for this statement is a study in which researchers infected 20 volunteers with an influenza virus and measured cytokine levels for eight days. The cytokine levels returned to normal by day 6. Exhibit 19 (Hayden) at 646 (figure 5).

Other evidence suggests that the expansion in cytokines lasts for 48 hours, but these reports hold limited value. For example, Lanza and colleagues measured cytokine levels 48 hours after an influenza vaccination and found an increase. Exhibit 12 (Lanza); see also Tr. 87-88, 110, 124, 192, 207. Lanza did not study cytokines more than 48 hours later. Dr. Small stated that, while the study reflected an elevation of cytokines 48 hours after vaccination, this does not necessarily indicate that the inflammatory response completely ceases at this point. Tr. 160-61 ("[T]hat doesn't mean the inflammatory response is gone, it would mean that that particular inflammatory marker dropped, though."). Backes, the study of influenza infection and strokes, stated that an "[i]nfection with influenza virus causes an innate immune response that releases proinflammatory mediators, which lead to symptoms within 2 days." Exhibit 13 (Backes) at 741; see also Tr. 82.

Although there are issues with establishing onset, discussed below, petitioner's presentation of the Hayden article, coupled with respondent's lack of rebuttal with respect to its findings, show that Dr. Small's proposed timeframe is acceptable. Dr. Small opined that "immune inflammatory response to vaccination would typically manifest and persist 1-4 days post-vaccination," and that Mr.

Sokol manifested symptoms 4 days after vaccination. Exhibit 16 at 3. While this is outside the 48-hour range found in the Lanza study, this is within the 6-day range found in the Hayden study. This grounding in the findings of the Hayden study make this proposition more than mere speculation. See Koehn v. Sec'y of Health & Human Servs., 773 F.3d 1239, 1244-45 (Fed. Cir. 2014) (ruling that the special master was not arbitrary and capricious in finding that the onset of a condition months after vaccination was not consistent with a theory based on cytokines).

2. Dr. Small did not persuasively establish that Mr. Sokol's SAH developed within the relevant time.

To complete the proof on prong 3, Mr. Sokol must present preponderant evidence that his SAH started within the time the cytokine-based theory predicts. This task is challenging as the experts could offer little guidance about when Mr. Sokol's aneurysm ruptured. Dr. Messé was direct in saying that he did not know when the aneurysm ruptured. Tr. 194. When asked twice about the first symptom of Mr. Sokol's SAH, Dr. Small answered inconsistently. He identified both the flu-like symptoms and Mr. Sokol's language problem as the first symptom at different points. Tr. 120, 122. These events occurred on different days, with the flu-like symptoms lasting from January 26, 2014, to January 30, 2014 (four to eight days after the January 22, 2014 vaccination) and the speech problems starting on February 1, 2014 (10 days after vaccination). The flu-like symptoms resolved before Mr. Sokol started having language problems. Tr. 120.

Dr. Small attempted to date the beginning of Mr. Sokol's SAH with Dr. Wecht's finding of hemosiderin during the February 4, 2014 operation to clip the aneurysm. In Dr. Small's opinion, hemosiderin is "old blood" that existed for one week or more before Dr. Wecht's discovery of it during the operation. Tr. 73-74, 91, 95.

Dr. Small seemed to be stretching the usefulness of Dr. Wecht's description. Preliminarily, as Dr. Messé described, hemosiderin is detected through laboratory testing and laboratory testing for hemosiderin is not readily apparent in the record. Tr. 215-17. Thus, Dr. Wecht's use of the term "hemosiderin" might be mistaken.

More significantly, when asked to explain how long the production of hemosiderin takes, Dr. Small did not know. Tr. 153. In contrast, Dr. Messé spontaneously listed the steps that take place to form hemosiderin. Tr. 194-95. In his rebuttal testimony, Dr. Small did not disagree with the process that Dr. Messé described. Tr. 283. Dr. Messé estimated that the production of hemosiderin takes

"usually a month or two . . . maybe two weeks at the very, very earliest." Tr. 194-95. After hemosiderin is produced, hemosiderin can last forever in the body. Tr. 162 (Dr. Small), 195 (Dr. Messé).

Given Dr. Messé's board certification in vascular neurology, the undersigned is inclined to credit Dr. Messé's opinion about an aspect of the circulatory system. If Dr. Messé's estimate that the quickest amount of time for hemosiderin to form (two weeks) is accurate, then the bleed occurred 14 days before Dr. Wecht discovered the blood on February 4, 2014. This date is January 21, 2014, which is one day before the vaccination.

A bleed on January 21, 2014 is not necessarily incompatible with a problem in speaking on February 1, 2014. There can be a lag between the bleeding and the start of neurological symptoms. Tr. 164-65 (Dr. Small), 269-70 (Dr. Messé).

In sum, as Dr. Messé testified: "the timing here is just super difficult." Tr. 268. Some evidence (the hemosiderin) suggests the bleeding started before the vaccination. Other evidence (the onset of speech problems) suggests that the timing occurred too long after the vaccination and cytokine expansion for the cytokines to have caused the rupture. See Tr. 125 (Dr. Small acknowledging that if the speech problems were the first manifestation of the neurologic problem, then the vaccination is less likely to be the cause). Relatively little persuasive evidence suggests that the aneurysm rupture happened in the time Dr. Small's theory predicted. Thus, Mr. Sokol has failed to meet his burden of proof for prong 3.

D. The presence of alternative risk factors for subarachnoid hemorrhages decreases the likelihood that the flu vaccine caused Mr. Sokol's stroke.

Finally, the Secretary has identified two factors that place Mr. Sokol at increased risk for a subarachnoid hemorrhage and Mr. Sokol has not persuasively countered them. In determining whether petitioners have met their burden of proof, special masters may consider all relevant evidence, including evidence that something other than a vaccine may have caused the injury. Doe 11 v. Sec'y of Health & Human Servs., 601 F.3d 1349, 1357-58 (Fed. Cir. 2010). Here, the Secretary has put forward two potential alternative causes: hypertension and cold weather.

Hypertension. The experts agree that hypertension can be a risk factor for an aneurysm to rupture. For Dr. Small, see Tr. 93-95, 132-33, 158; for Dr. Messé, see exhibit A at 4 (Dr. Messé's report), Tr. 197.

The more difficult issue is whether Mr. Sokol suffered from hypertension before he was vaccinated. As mentioned earlier, Mr. Sokol did not file medical records about his health in the years before vaccination because he did not seek medical attention. Tr. 197. This lack of information allows Dr. Small to state that he did not see any evidence that Mr. Sokol suffered from hypertension before the vaccination. Tr. 94.

Once Mr. Sokol did go to the hospital, his doctors placed him on two medicines to control his hypertension. Exhibit 1(a) at 13 (report from discharge from rehabilitation facility).[7] Mr. Sokol thereafter has continued to be prescribed two drugs to lower his high blood pressure. Exhibit 15 at 3 (March 3, 2014); exhibit 11 at 6 (July 7, 2017); exhibit 14 at 1 (April 27, 2018).

This information allows Dr. Messé to infer that Mr. Sokol's hypertension existed before the aneurysm rupture. Tr. 197-98. On cross-examination, Dr. Messé testified that hypertension is "not typically something that appears out of nowhere. It's usually chronic and long-lasting typically if you're requiring multiple medications to control it." Tr. 202. When asked on rebuttal to address Dr. Messé's reasoning, Dr. Small was not responsive. Tr. 282-83.

Based upon this circumstantial evidence, the undersigned finds on a more-likely-than-not basis that Mr. Sokol probably suffered from hypertension before his stroke. This hypertension could explain why he had a stroke.

Cold Weather. Most aneurysmal ruptures occur in cold weather. Exhibit 13 (Backes); Tr. 132, 199. As such, doctors believe that cold weather contributes to the ruptures. Tr. 158. From the date of vaccination through Mr. Sokol's language difficulties, the weather in Pittsburgh was generally cold. Exhibits 28-29. Thus, Dr. Small conceded that the cold weather could have played a role in causing Mr. Sokol's stroke. Tr. 152.

However, at the same time, Dr. Small maintained that the vaccination was a "strong, significant contributor" to the stroke. Tr. 158; accord exhibit 9 at 2. Through his attorney, Mr. Sokol advanced the argument that, assuming that Mr. Sokol had pre-existing hypertension, Mr. Sokol had lived through periods of cold weather with high blood pressure without having a stroke. It was only after Mr. Sokol received the flu vaccination that his aneurysm ruptured. Thus, in Mr.

[7] Mr. Sokol presented to the hospital with hypertension. However, this data point does not necessarily suggest that his hypertension was long-standing as Mr. Sokol might have had elevated blood pressure due to the uncertainty of not knowing what was wrong with him and the anxiety over going to a hospital. Tr. 94.

Sokol's view, because the vaccination was the only new factor, this addition must have caused the stroke. See Tr. 103, 207 (cross-examination of Dr. Messé).

Although this argument has some superficial appeal, it is ultimately not persuasive. The argument resembles the logical fallacy post hoc, ergo propter hoc—that because the rupture happened after the stroke, the stroke must have caused the rupture. As Dr. Messé persuasively explained, the risk factors can explain why Mr. Sokol suffered a stroke. Adding the vaccination is not necessary. Tr. 236.

IV. Conclusion

Mr. Sokol started to experience neurologic symptoms of a stroke approximately 10 days after he received a flu vaccine. Mr. Sokol was hospitalized and required rehabilitation to gain back most, but not all, of his functioning. Mr. Sokol's health problems are unfortunate.

Although Mr. Sokol merits sympathy, he has not established that the flu vaccine caused his stroke. Through an expert who lacked a specialized background in strokes, Mr. Sokol advanced a causal theory that was flawed. The chronology of events in Mr. Sokol's life is not consistent with the appropriate temporal relationship and Mr. Sokol suffered from risks factors other than the vaccination. Therefore, he is not entitled to compensation.

The Clerk's Office is instructed to issue judgment in accord with this decision if a motion for review is not filed.

IT IS SO ORDERED.

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

Appendix of Articles Cited

Daan Backes et al., *Increased incidence of subarachnoid hemorrhage during cold temperatures and influenza epidemics*, 125 J. Neurosurgery 737 (2016), filed as exhibit 13.

Armin J. Grau et al., *Influenza Vaccination Is Associated With a Reduced Risk of Stroke*, 36 Stroke 1501 (2005), filed as exhibit A, tab 1.

Frederick G. Hayden et al., *Local and Systemic Cytokine Responses during Experimental Human Influenza A Virus Infection*, 101 J. Clinical Investigation 643 (1998), filed as exhibit 19.

Gaetano A. Lanza et al., *Inflammation-related effects of adjuvant influenza A vaccination on platelet activation and cardiac autonomic function*, 269 J. Internal Med. 118 (2010), filed as exhibit 12.

A. Niroshan Siriwardena et al., *Influenza and pneumococcal vaccination and risk of stroke or transient ischaemic attack—Matched case control study*, 32 Vaccine 1354 (2014), filed as exhibit A, tab 2.

Liam Smeeth et al., *Risk of Myocardial Infarction and Stroke after Acute Infection or Vaccination*, 351 New England J. Med. 2611 (2004), filed as exhibit A, tab 3.

Rika Tulamo et al., *Inflammatory changes in the aneurysm wall: a review*, 2 J. Neurointerventional Surgery 120 (2010), filed as exhibit 18.