

In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

E-Filed: February 28, 2011; Re-issued March 3, 2011

No. 99-406 V

NATHAN HOUSE,)	PUBLISHED
)	
)	
Petitioner,)	Hepatitis B Vaccine; Crohn's Disease; Theory of Causation Informed by the "New Concept" of Inflamasomes
)	
V.)	
)	
SECRETARY OF THE DEPARTMENT OF HEALTH AND HUMAN SERVICES,)	
)	
Respondent.)	
)	

Clifford Shoemaker, Vienna, VA, for petitioner.

Lisa Watts, Washington, DC, for respondent.

PUBLISHED DECISION DENYING COMPENSATION¹

Campbell-Smith, Special Master

On June 28, 1999, petitioner, Nathan House, filed a petition seeking compensation under the National Vaccine Injury Compensation Program² (the Vaccine Program or the

¹ Because this decision contains a reasoned explanation for the undersigned's action in this case, the undersigned intends to post this decision on the United States Court of Federal Claims' website, in accordance with the E-Government Act of 2002, Pub. L. No. 107-347, § 205, 116 Stat. 2899, 2913 (codified as amended at 44 U.S.C. § 3501 note (2006)). Petitioner's counsel filed a motion to redact the undersigned's decision on March 14, 2011. The undersigned issued a published order denying petitioner's motion to redact on January 11, 2012. Consistent with her published order, the decision is to be published in the original form.

² The National Vaccine Injury Compensation Program is set forth in Part 2 of the National Childhood Vaccine Injury Act of 1986, Pub. L. No. 99-660, 100 Stat. 3755, codified as amended, 42 U.S.C. § 300aa-10 through § 300aa-34 (2006) (Vaccine Act or

Act). Petitioner alleges that as a result of the hepatitis B vaccinations he received on September 9, 1993, October 22, 1993, and February 24, 1994, he “experienced flu-like symptoms, joint pain, diarrhea and fever.” Petition (Pet.) at 1, ¶ 3. He asserts that his symptoms became worse after each vaccination and as a result of the received vaccination series, he has been diagnosed with Crohn’s disease. Id. at 1-2, ¶3.

Having carefully reviewed petitioner’s medical records and the filed scientific articles and having carefully considered petitioner’s testimony as well as the testimony of the parties’ experts, the undersigned concludes that the record as a whole does not support a finding of entitlement to Program compensation. The reasons for this decision are set forth below in greater detail.

I. Procedural History

Petitioner’s claim is one of many claims brought by petitioners after the hepatitis B vaccine was added in August 1997 to the list of vaccines covered under the Program. See 42 C.F.R. § 100.3(c)(2). Record development in this particular case began in 2001, but halted in 2003 when the Office of Special Masters (OSM)—in an effort to address the many claims involving allegations of similar injuries—considered grouping together a number of hepatitis B vaccine cases for coordinated handling through omnibus proceedings. In 2006, OSM’s efforts to conduct various omnibus proceedings for the resolution of related hepatitis B claims were discontinued. At that time, record development in this case resumed.

In October 2006, the undersigned conducted a fact hearing in LaVale, Maryland, to determine when petitioner’s symptoms first began and, on May 3, 2007, issued a Ruling Regarding Onset of Petitioner’s Symptoms. The parties then retained experts and filed expert opinions. The experts testified during a hearing conducted in Washington, DC, in May 2010, and the parties submitted post-hearing briefing for consideration. This case is now ripe for a ruling.

II. The Factual Basis for Petitioner’s Claim

The pertinent factual findings were made in the Ruling Regarding Onset of Petitioner’s Symptoms that issued on May 3, 2007.³ House v. Sec’y of Dept. of Health & Human Servs., No. 99-406V, 2007 WL 5177470 (Fed. Cl. Spec. Mstr. May 3, 2007). They are reviewed briefly here.

the Act). All citations in this decision to individual sections of the Vaccine Act are to 42 U.S.C. § 300aa.

³ The Ruling was issued and electronically filed on May 3, 2007, although the date on the Ruling indicates that it was filed on May 4, 2007.

Notable in petitioner's medical history is his nervous stomach as a child and a family history of both Crohn's disease and colon cancer. Also notable in petitioner's medical history were his episodic reports of symptoms of weakness, nausea, shakiness, vomiting, diarrhea, visual blurring and headaches prior to his receipt of the hepatitis B vaccination series.

Petitioner received his first hepatitis B vaccination on September 9, 1993. He was 23 years of age. Within 12 hours, he experienced cramping and diarrhea, symptoms he promptly reported to his doctor.

Petitioner received his second hepatitis B vaccination on October 22, 1993. He again experienced cramping and diarrhea. He also experienced stomach burning. Petitioner reported the symptoms to his doctor.

On February 24, 1994, petitioner received his third hepatitis B vaccination. The previously reported symptoms of cramping and diarrhea persisted after petitioner's receipt of the third vaccination. While it is not clear from the factual record that the intensity of petitioner's discomfort increased after he received his hepatitis B vaccination series, the undersigned is persuaded that petitioner's symptoms occurred more frequently after his receipt of the vaccination series.

After making the foregoing fact findings based on the medical records and the fact testimony furnished by petitioner and his family,⁴ the undersigned deferred to the parties' respective experts to address the medical significance of the findings.

III. The Parties' Experts

In support of petitioner's claim, he offered the expert opinion of Joseph Bellanti, M.D., a board-certified immunologist. Dr. Bellanti is a professor of Pediatrics and Microbiology as well as the director of the International Center for Interdisciplinary Studies at Georgetown University School of Medicine. Transcript of May 13, 2010 Hearing (Tr.) at 10. He has published over 400 peer-reviewed articles. Id. The chief focus of these publications has been antimicrobial immunity, but a few of Dr. Bellanti's publications have involved "adverse allergic reactions to vaccines and other foreign substances." Id. He has co-authored several book chapters and currently is preparing the fourth edition of his textbook on immunology. Id. Dr. Bellanti has served on numerous national and international committees pertaining to immunology. Id. at 11. The undersigned accepted Dr. Bellanti as an expert in immunology. Id. at 15.

⁴ Petitioner's wife, mother, and sister also testified.

At hearing, Dr. Bellanti stated that, in consultation with gastroenterologists, he has seen and treated patients with Crohn's disease. Id. at 12. Characterizing Crohn's disease as an autoinflammatory disease, Dr. Bellanti opined that the hepatitis B vaccination series that petitioner received produced too many proinflammatory cytokines and, in turn, led to an immunologic imbalance in petitioner that manifested as Crohn's disease. See id. at 16-29.

Acknowledging that the parties differed in their views concerning whether petitioner in fact had Crohn's disease, Dr. Bellanti conceded that he was not qualified to diagnose a gastroenterologic condition and deferred to Dr. Warner's expertise in that area. The nature of petitioner's gastroenterologic problem did not disturb Dr. Bellanti's opinion of vaccine-related causation. But, he explained, his opinion was "more certain" if petitioner were found to have Crohn's disease. Id. at 42, 54, 59.

In refutation of petitioner's theory, respondent offered the expert opinion of Andrew Warner, M.D., a board-certified gastroenterologist. Dr. Warner is currently the chair of the Gastroenterology Division of the Lahey Clinic in Burlington, Massachusetts. Tr. at 61-62. He is also an associate professor at Tufts University School of Medicine and a clinical instructor at Harvard Medical School. Id. at 62-63. His gastroenterologic specialties are Crohn's disease, ulcerative colitis, and inflammatory bowel disease. Id. at 63. About 75 percent of Dr. Warner's time is spent in clinical practice. Id. Annually, he sees nearly 3000 patients, including 800 to 1000 patients in his office, 1200 to 1300 patients for procedures, and a few hundred patients during hospital rounds. Id. When in clinic, he sees 12 to 14 patients with Crohn's disease and up to 20 patients with inflammatory bowel disease daily. Id. at 63-64. He has authored or co-authored 15 to 20 peer-reviewed articles on Crohn's disease and has participated in numerous clinical trials of potential treatments for patients with Crohn's disease and ulcerative colitis. Id. at 65-66. The undersigned accepted Dr. Warner as an expert in gastroenterology. Id. at 66.

Dr. Warner challenged the accuracy of petitioner's diagnosis of chronic Crohn's disease. In his view, petitioner had irritable bowel syndrome prior to his receipt of the vaccine series, experienced a transient response to the first administered vaccine, and later manifested, at most, an extremely mild form of Crohn's disease. Id. at 67-68, 76, 84. Dr. Warner further testified that the administered hepatitis B vaccination series did not cause or aggravate petitioner's ongoing gastroenterologic condition. Id. at 67.

IV. The Applicable Legal Standards

The Vaccine Act authorizes an award of compensation for a vaccine-related injury. 42 U.S.C. § 300aa-10(a). To receive such award, the petitioner must have received a vaccine listed on the Vaccine Injury Table (Table) set forth at 42 U.S.C. § 300aa-14 and 42 C.F.R. § 100.3. If the alleged injury also is listed on the Table and the injury occurred within the time period set forth in the Table, petitioner's claim is deemed

a Table case and a rebuttable presumption of causation attaches. 42 U.S.C. § 300aa-11(c)(1), -13(A)(1)(a). If, however, the alleged injury is not listed on the Table or the injury occurred beyond the identified time frame, petitioner's claim is deemed an off-Table case, and petitioner must prove that his injury was caused in fact by the received vaccine.

Here, petitioner's claimed injury of Crohn's disease is not listed on the Table and thus, he must prove his vaccine claim by providing evidence that shows: "(1) a medical theory causally connecting the vaccination to the injury; (2) a logical sequence of cause and effect showing the vaccination was the reason for the injury; and (3) a showing of a proximate temporal relationship between the vaccination and the injury." Althen v. Sec'y of Dep't of Health & Human Servs., 418 F.3d 1274, 1278 (Fed. Cir. 2005).

To prevail on his vaccine claim, petitioner must show that he would not have been injured but for his vaccination and that the vaccination was a substantial factor in bringing about his injury. Shyface v. Sec'y of Dep't of Health & Human Servs., 165 F.3d 1344, 1352 (Fed. Cir. 1999). Petitioner must present a medical theory that is supported either by medical records or by the opinion of a competent physician. Grant v. Sec'y of Dep't of Health & Human Servs., 956 F.2d 1144, 1148 (Fed. Cir. 1992). Proof of vaccine causation must be supported by a sound and reliable "medical or scientific explanation that pertains specifically to the petitioner's case, although the explanation need only be 'legally probable, not medically or scientifically certain.'" Moberly v. Sec'y of Dep't of Health & Human Servs., 592 F.3d 1315, 1322 (Fed. Cir. 2010) (quoting Knudsen v. Sec'y of Dep't of Health & Human Servs., 35 F.3d 543, 548-49 (Fed. Cir. 1994)); see also Grant, 956 F.2d at 1148 (medical theory must support actual cause). Mere temporal association is not sufficient to prove causation. Grant, 956 F.2d at 1148.

The preponderance of evidence standard under the Vaccine Act requires proof that a vaccine more likely than not caused the vaccinee's injury. Althen, 418 F.3d at 1279. A petitioner may use circumstantial evidence to prove her case, and "close calls" regarding causation must be resolved in favor of the petitioner. Althen, 418 F.3d at 1280.

In evaluating petitioner's vaccine claim, a special master should consider the opinions of petitioner's treating doctors. Capizzano v. Sec'y of Dep't of Health & Human Servs., 440 F.3d 1317, 1326 (Fed. Cir. 2006). Moreover, in evaluating whether a petitioner has presented a legally sufficient medical theory, "the special master is entitled to require some indicia of reliability to support the assertion of the expert witness." Moberly, 592 F.3d at 1324. When the opinion of the expert reflects an extrapolation from existing data and knowledge, and the gap between the science and the opinion proffered is connected "only by the ipse dixit of the expert," the offered opinion may be deemed too speculative. See Gen. Elec. Co. v. Joiner, 522 U.S. 136, 146 (1997).

V. The Bases for the Opinions of the Parties' Experts

Petitioner's expert, a board-certified immunologist, based his theory of vaccine-related causation on a "new paradigm" of immunological disarrangement involving "autoinflammatory diseases." Tr. at 16, 29. Dr. Bellanti testified that "emerging data . . . suggest[s]" that diseases which were formerly described as autoimmune in nature are described more appropriately now as autoinflammatory in nature. Id. at 16. While the characterization of Crohn's disease as an autoinflammatory disease had not yet appeared in textbooks at the time of the expert hearing, Dr. Bellanti asserted that within the six months prior to the conduct of the hearing, the concept of autoinflammatory disease had begun to be discussed as a concept to explore in the immunology community. See id. at 54-56.

A. The Concept of Autoinflammation

Dr. Bellanti explained that autoinflammatory diseases, which first were observed clinically in the 1970s, do not involve the external immune system—which is comprised of mucosal tissues that can be reached through the skin, by inhalation, by ingestion, or through the urinogenital tract—but rather the internal immune system. Id. at 16-17; Petitioner's Exhibit (P's Ex.) 84 at 5 (slide showing the organization of the immune system in the human body)⁵. The internal immune system, which is comprised of the thymus, lymph node, bone marrow and spleen, is the other part of the immune system and involves cell found within the blood. Tr. at 17; P's Ex. 84 at 5.

The internal immune system has two arms, one reflecting innate immunity and the other reflecting acquired or adaptive immunity. Tr. at 17; P's Ex. 84 at 5, 10. The innate system provides a nonspecific mechanism of defense consisting of cells that ingest foreign particles, known as phagocytes. Tr. at 18. Phagocytic cells lack memory and do not recognize foreign particles that have been encountered previously. Id.; P's Ex. 84 at 6. In contrast, the adaptive arm of the immune system is specific and has memory. Tr. at 18; P's Ex. 84 at 6. Made up of both T and B lymphocytes, the adaptive immune system produces a stronger immune response during each encounter with a foreign particle. Tr. at 18. Dr. Bellanti observed that booster vaccines are administered to produce a stronger immune response with each injection and thereby enhance a host's immunity to particular infectious agents. Id. at 19. Dr. Bellanti also observed that the addition of alum, a salt comprised of hydrated potassium and aluminum sulfate, as an adjuvant during the manufacturing process for vaccines is an effective method of further boosting the response of the adaptive immune system. Id. at 20.

⁵ Petitioner's Exhibit 84 is a slide presentation prepared by Dr. Bellanti for the purpose of illustrating the immunological concepts he discussed during his testimony.

Dr. Bellanti testified that “emerging evidence” points to a genetic defect in the innate immune system that appears to be present in a “fair number of patients with Crohn’s [d]isease.” Id. at 23-24. He posited that this genetic defect in the innate immune system allows autoinflammatory diseases to develop and effectively distinguishes autoinflammatory diseases from autoimmune diseases, which are believed to arise from a disturbance in the adaptive immune system, the other arm of the internal immune system that involves specific responses to remembered foreign agents. See id. at 24; P’s Ex. 84 at 6, 14.

Dr. Bellanti explained that cytokines—the proteins produced by both the innate and adaptive immune systems—operate as communication molecules either to promote or deter inflammation. See id. at 25. Immunologic balance is achieved when the proinflammatory cytokines are in balance with the anti-inflammatory cytokines. See id. at 25-26. When immunologic disequilibrium is effected by the presence of too many proinflammatory cytokines, inflammasomes can occur. Id. at 26; P’s Ex. 84 at 22. An inflammasome is the part of a cell that responds to foreign agents by alerting the innate immune system to generate a series of molecular events that produce cytokines that promote inflammation, such as activated interleukin-1 beta (IL-1 β). Tr. at 26; P’s Ex. 84 at 24, 36. This inflammatory immunological process can cause the painful, burning lesions (often red in appearance and hot to the touch) that are characteristic of autoinflammatory diseases. Tr. at 27, 30; P’s Ex. 84 at 25, 27-34.

B. Petitioner’s Theory Regarding How Autoinflammation Caused the Claimed Injury

After generally describing the autoinflammatory process, Dr. Bellanti described how the hepatitis B vaccines that petitioner received triggered an autoinflammatory process that manifested as Crohn’s disease in petitioner.

Dr. Bellanti identified alum and yeast as components of the hepatitis B vaccine that “are known to be handled by the innate [immune] system” in a manner that leads to the production of antibodies, specifically, the anti-yeast antibody known as anti-saccharomyces cerevisiae antibody (ASCA). Tr. at 36. This particular antibody has been found in many patients prior to the onset of their Crohn’s disease but has not been implicated directly in causing the disease.⁶ See id. at 36, 43. Whether petitioner had ASCA antibodies when he received his hepatitis B vaccination series in 1993 is unknown. Id. at 50. But Dr. Bellanti testified that if this antibody were present, a received hepatitis B vaccine would have boosted the immune response because

⁶ Respondent’s expert also observed that the presence of ASCA is not diagnostic of Crohn’s disease. Tr. at 81. Instead, “Crohn’s [d]isease is diagnosed by endoscopic, radiologic, [and] histologic findings in the appropriate clinical setting.” Tr. at 81.

petitioner's adaptive immune system would have recognized the yeast in the hepatitis B vaccine as a previously encountered foreign agent. See id. at 36.

Dr. Bellanti posited that petitioner has a genetic susceptibility in either the innate or the adaptive arm of his internal immune system and that genetic susceptibility renders petitioner "unable to process certain things in that vaccine that trigger an inflammatory reaction." Id. at 35. Upon initiation of an inflammatory reaction in petitioner, tissue damage and immune reactivity directed against petitioner followed, allowing the chronicity of inflammation in petitioner's gastrointestinal tract that provoked a diagnosis of Crohn's disease for petitioner. Id.; see also P's Ex. 84 at 11, 13, 39-46. Dr. Bellanti conceded, however, that agents other than the components of an injected vaccine—such as ingested food or bacteria—also could provoke an inflammatory reaction in a host and precipitate an autoinflammatory disease. Tr. at 29.

Dr. Bellanti asserted that the cramping and diarrhea that petitioner experienced within three days after each administration of the first two hepatitis B vaccines occurred within a time frame that was consistent with and medically appropriate for the immunologic theory of vaccine-related causation that Dr. Bellanti had described earlier in his testimony. Tr. at 52-54.

C. Distinguishing between Irritable Bowel Syndrome and Crohn's Disease

Asserting that petitioner suffered from irritable bowel syndrome rather than Crohn's disease, Dr. Warner, respondent's expert gastroenterologist, testified regarding the difference between irritable bowel syndrome and Crohn's disease. He explained that irritable bowel syndrome, a condition that has many different names, is "a functional disorder" characterized by cramping and diarrhea, urgency to go to the bathroom, occasional constipation, possible abdominal pain, and abdominal bloating.⁷ Tr. at 68; see also Respondent's Exhibit (R's Ex.) D⁸ at 2 (describing the characteristics symptoms of irritable bowel syndrome as "abdominal pain or discomfort accompanied by a disturbed bowel pattern"). Although the underlying cause of irritable bowel syndrome is not known, anxiety and stress are well-recognized triggers for the syndrome. Tr. at 74, 86-87, 91. Accordingly, anti-anxiety medication is prescribed to treat the syndrome. Id. at 91.

⁷ Among the various names for irritable bowel syndrome are nervous stomach, spastic colon, intestinal upset, and intestinal hurry. Tr. at 68.

⁸ The citation for the article filed as Respondent's Exhibit D is M. Simren, et al., Quality of Life in Inflammatory Bowel Disease in Remission: The Impact of IBS-Like Symptoms and Associated Psychological Factors, American Journal of Gastroenterology 97:2 (2002).

Irritable bowel syndrome does not cause Crohn's disease. Tr. at 137. But the two conditions can exist concomitantly. Id. at 115.

Distinguishable from irritable bowel syndrome, Crohn's disease is an autoimmune disorder believed to be triggered by some form of antigenic stimulus that causes immune dysregulation. Id. at 106. The disease is a lifelong one, and its course typically involves periodic flares of more severe symptoms. See Tr. at 123-124. Immunosuppressive medications are used to treat Crohn's disease. See id. at 134. The cause of the disease is unknown. See Tr. at 74.

While the symptoms of irritable bowel syndrome are similar to Crohn's disease, the symptoms of irritable bowel syndrome are subjective and elude demonstrable confirmation. Id. at 70. Contrastingly, Crohn's disease is established by objective findings of inflammatory bowel disease. See id.

A number of testable findings inform a diagnostic determination that a patient is suffering from Crohn's disease. The hallmark feature of Crohn's disease is an ulcerated intestinal lining detectable on imaging of the gastrointestinal tract. Id. at 69-70. The deep ulcerations in the intestinal tract are referred to as "rake ulcers" because they "look[] like someone . . . raked out part of the colon." Id. at 70-71.

Characteristically, seventy percent of patients with Crohn's disease have affected small bowels, and twenty percent have affected colons. Tr. at 77. Of the twenty percent with affected colons, only half have rectal involvement. Id. Therefore, very few Crohn's patients have rectal involvement. Id.

Other findings, such as an elevated sedimentation rate and an elevated presence of C-reactive protein, are further indicative of Crohn's disease. Id. at 69-70. Both findings are made through blood studies, and each is a general marker of inflammation. See id. at 69-70; see also Mosby's Manual of Diagnostic and Laboratory Tests at 197-198, 234-235 (4th ed. 2010).

Inflammation in the intestinal tract of a patient with Crohn's disease also can be confirmed by the presence of granulomata (or granulomas) on biopsied intestinal tissue. Tr. at 77. A granuloma is a "small, nodular, delimited aggregation of mononuclear inflammatory cells . . . usually surrounded by a rim of lymphocytes and often multinucleated giant cells." Dorland's Illustrated Medical Dictionary, at 814 (31st ed. 2007). Granulomata are formed in response to chronic inflammation of body tissue that is triggered by a foreign agent, whether infectious or not. Id.

Over time, chronic inflammation in the intestinal tract of a Crohn's patient causes the architecture of the intestinal lining to become disordered. Tr. at 78. This change in

architecture is easily seen on biopsied intestinal tissue and is referred to in gastroenterologic parlance as the observable “changes of chronicity.” Id. at 77-78.

While the objective measures of Crohn’s disease are well-established, the causal triggers for the disease are not known. See Tr. at 70, 74. It is known, however, that a genetic component is implicated in Crohn’s disease. See id. at 81. While the disease is rarely found in parents and children, the disease is often seen in a distant relative, such as a cousin or aunt, of a Crohn’s patient. Id.

Dr. Warner averred that when the recognized findings of Crohn’s disease are missing in a patient, the accuracy of a Crohn’s diagnosis becomes doubtful. See id. at 81-82.

D. Petitioner’s Test Results Were Normal or Non-Specific

Respondent’s expert Dr. Warner asserts that, after nearly fifteen years of testing and examination, petitioner lacks a record of objective evidence that he suffers from Crohn’s disease that is commensurate in severity with his described gastrointestinal symptoms. Tr. at 73, 75-79. Dr. Warner addressed, with particularity, the deficiencies in the findings reported in petitioner’s medical records.

Petitioner had a number of colonoscopies. His first colonoscopy was performed in 1995, more than a year after petitioner had received his third hepatitis B vaccination. Tr. at 70; P’s Ex. 4 at 1-2. That colonoscopy showed the presence of very tiny superficial ulcers, known as aphthous ulcers, in petitioner’s rectum; the remainder of his colon appeared normal. Tr. at 70; P’s Ex. 4 at 1-2. Dr. Warner explained that aphthous ulcers are nonspecific findings that occur in “all sorts of disorders.”⁹ Tr. at 71. Nearly two years later, in 1997, petitioner had another colonoscopy that showed a mere scatter of “aphthoid-looking” ulcers in an otherwise normal colon. Tr. at 71. Petitioner’s medical records further indicate that his last three colonoscopies, performed in 1998, 2001, and 2009, respectively, were normal. Tr. at 71.

In addition to normal colonoscopies during the twelve year period preceding the hearing in this case, petitioner also had a normal endoscopy performed in 2009. Tr. at 72-73. Petitioner’s complete blood count and sedimentation rate were also completely normal. Tr. at 71.

Petitioner had biopsies performed as well. Significantly, the biopsies were read as showing “mild, acute colitis,” but lacked evidence of chronic changes in the colon. Tr. at

⁹ Dr. Warner further explained that aphthous ulcers are the same small white lesions that appear in the mouth or on the tongue as cold sores. Tr. at 129.

73. No granulomata were ever detected on petitioner's biopsied tissues. Id. at 77. Nor were there any x-rays showing Crohn's disease. Id.

Although several of petitioner's treating doctors characterized petitioner's condition as Crohn's disease, see P's Ex. at 29-30 (Dr. Bayless, gastroenterologist), P's Ex. 81 at 2 (Dr. Chou, gastroenterologist), P's Ex. 20 at 6 (Dr. Lavery, staff surgeon, Department of Colorectal Surgery at Cleveland Clinic¹⁰), P's Ex. 16 at 12 (Dr. Hull, colorectal surgeon¹¹), Dr. Warner asserted that, unlike himself, petitioner's medical examiners did not have all of petitioner's medical records available for review. Tr. at 126. Dr. Warner testified that, contrary to what would be expected of a patient suffering from a grave case of Crohn's disease for a protracted period of time, petitioner had no documented weight loss or evidence of anemia. Id. at 128. Also missing from petitioner's medical records was the type of objective findings of significant and chronic inflammation in the colon that characteristically would accompany a fifteen-year history of severe Crohn's disease as was claimed in this case. Tr. at 71-74. While petitioner's symptoms of enduring diarrhea, cramps, and rectal bleeding hindered his ability to work and impelled him to seek treatment from various doctors, petitioner's test results—when viewed in the aggregate—are inconsistent with a critical case of Crohn's disease. Id. at 71-72, 126.

Based on the scant objective data that petitioner had active Crohn's disease, Dr. Warner doubted the diagnosis of Crohn's disease that appeared in some of petitioner's medical records. See id. at 76, 79, 118-119; see also Petitioner's Exhibit (P's Ex.) 36 at 8. But, noting that there are gradations of Crohn's disease ranging from extremely mild forms of the disease involving minimal, if any, symptoms to severe forms of the disease

¹⁰ In a letter dated May 5, 1997 to Dr. Stasko, Dr. Lavery reports that since 1993, petitioner has had bloody mucous in his stools and diarrhea associated with cramping abdominal pain. P's Ex. 20 at 6. Dr. Warner testified that such symptoms "sound more typical for Crohn's [d]isease" than for irritable bowel syndrome. Tr. at 112-113.

Subsequently, by letter dated November 18, 1997 addressed to Dr. Lavery, Dr. Mark, a gastroenterologist, wrote: "There is some confusion in my mind as to his lack of response to my present medical regimen. . . . I cannot find a dictated report by the colonoscopist to confirm this, not that I doubt your report. I am presently dealing with this healthy, young male who is lifting weights all day long but is yet unable to accept gainful employment." P's Ex. 29 at 21.

¹¹ Dr. Hull noted the presence of severe aphthoid ulcers as well as some edema and loss of vascular pattern in petitioner's mid and distal rectum. P's Ex. 16 at 12. Dr. Warner testified that a finding of aphthoid ulcers was distinguishable from a finding of ulcers in Crohn's patients. See Tr. at 117-118.

that require surgery, Dr. Warner allowed that petitioner may have an extremely mild form of the disease. *Id.* at 76.

Dr. Warner asserted that the episodic symptoms of weakness, nausea, shakiness, vomiting, diarrhea, visual blurring and headaches that petitioner reported after his receipt of the hepatitis B vaccine series were symptoms consistent not only with irritable bowel syndrome but also with the type of transient, self-limited, and nonspecific reaction that can develop in the days following a vaccine administration. Tr. at 82-85. Dr. Warner identified muscle aches, joint aches, low grade fever, and fatigue as types of transient symptoms that could occur in a vaccine recipient in the first day or two after vaccination. *Id.* at 83.

VI. Analysis of Petitioner's Claim

In refutation of petitioner's vaccine claim, respondent's expert questioned whether petitioner's asserted injury is characterized more properly as irritable bowel syndrome or Crohn's disease as petitioner has alleged. Because the resolution of this issue informs the manner in which petitioner's claim is evaluated, the undersigned addresses the issue of the nature of petitioner's injury before turning to the Althen analysis. See Broekelschen v. Sec'y of Dep't of Health & Human Servs., 618 F.3d 1339, 1345-46 (Fed. Cir. 2010) (affirming special master's identification the injury best supported by the evidence prior to applying the Althen test so that the special master could subsequently determine causation relative to the injury).

A. The Nature of Petitioner's Injury

The symptoms of abdominal cramping and diarrhea reported in petitioner's medical records were consistent with the symptoms he related in his testimony. After examining petitioner, a number of petitioner's treating doctors assessed his condition as Crohn's disease even though petitioner's various test findings were minimal.

Petitioner's expert, a qualified immunologist, relied on the recorded diagnostic impressions of petitioner's treating doctors and asserted that petitioner had Crohn's disease. He acknowledged, however, indications in the medical records that petitioner may have had a nervous stomach. Tr. at 42. He testified that he "would defer to [respondent's expert's] judgment." *Id.*

Respondent's expert, an experienced gastroenterologist specializing in the treatment of irritable bowel diseases, expressed his doubts about the correctness of petitioner's Crohn's diagnosis. He questioned whether petitioner suffered from irritable bowel syndrome rather than the irritable bowel disease of Crohn's. He explained that the distinction was a material one because the two conditions require treatment by different medications.

Respondent's expert also provided several articles that addressed the occurrence of irritable bowel symptoms in patients whose inflammatory bowel disease was in remission. As explained in the filed articles, inflammatory bowel disease that is in remission is in a quiescent state rather than a state of active inflammation. See R's Ex. D at 2.

Respondent's expert did allow that the findings noted in the earliest medical records after petitioner's receipt of the hepatitis B vaccine series were consistent with an extremely mild case of Crohn's disease. But missing from petitioner's later medical evaluations and thus, troubling to respondent's expert, were the characteristic changes that occur over an extended course of active Crohn's disease.

Evidence presented to the undersigned about petitioner's medical condition included petitioner's detailed description of his gastrointestinal symptoms, the treating doctors' recorded impressions of petitioner's condition, petitioner's ongoing prescriptions for anti-anxiety medications (to treat irritable bowel syndrome) and immunosuppressive medications (to treat Crohn's disease) as well as respondent's expert's assessment of petitioner's reported test results. Having carefully considered all of the presented evidence, the undersigned is persuaded that a preponderance of the evidence supports a finding that petitioner experienced an extremely mild case of Crohn's disease in addition to severe symptoms of irritable bowel syndrome.

B. Applying Althen

The undersigned turns now to analyze petitioner's claim in accordance with the standards set forth by the Federal Circuit in Althen.

1. The Presented Medical Theory

Prong one of Althen requires petitioner to present a medical theory causally connecting his received vaccination to his injury. Althen, 418 F.3d at 1278. The theory advanced by petitioner must be a biologically plausible one and must explain how the vaccine received by petitioner could cause the sustained injury. See Andreu v. Sec'y of Dep't of Health & Human Servs., 569 F.3d 1367, 1375 (Fed. Cir. 2009). This requirement has been interpreted to present the question of "can [the] vaccine(s) at issue cause the type of injury alleged?" Pafford, 451 F.3d 1352, 1355-56 (Fed. Cir. 2006) (alterations in original).

The proposed theory of causation need not reflect scientific certainty. Moberly, 592 F.3d at 1322. Nor must it be corroborated by medical literature or epidemiological evidence. Capizzano v. Sec'y of Dep't of Health & Human Servs., 440 F.3d 1317, 1325 (Fed. Cir. 2006). The theory, however, must have a scientific basis. A persuasive theory

is a sound, reliable, and reputable one. See Andreu, 569 F.3d at 1379-80; see also Moberly, 592 F.3d at 1322.

Here, petitioner has offered a theory of vaccine-induced inflammation of petitioner's gastrointestinal system that triggered an autoinflammatory process resulting in the development of petitioner's Crohn's disease, or alternatively, irritable bowel syndrome. Petitioner's expert, Dr. Bellanti, stated that his opinion of causation was "more certain" if petitioner were found to have Crohn's disease than if petitioner were found to have irritable bowel syndrome. Tr. at 54.

Dr. Bellanti testified that the presented theory of causation was an emerging theory in immunology. Tr. at 54-55. In response to a question from the court regarding how widely recognized was petitioner's tendered theory, Dr. Bellanti testified that the theory had begun to be discussed in immunological circles "within the last six months to a year." Id. at 55-56. He added that although "[t]hings are happening as we speak," the topic has not been addressed yet in standard textbooks. Id. at 55.

Recognizing the theoretical nature of Dr. Bellanti's causation opinion, Dr. Warner asserted that regardless of whether petitioner's injury is deemed irritable bowel syndrome or a very mild case of Crohn's disease, the condition is not causally related to petitioner's receipt of three hepatitis B vaccines. Dr. Warner stated that the hepatitis B vaccine is not contraindicated for patients with either irritable bowel syndrome or Crohn's disease. Tr. at 40. He further stated that there is no causal link between hepatitis B vaccine and the two conditions in the medical literature. Tr. at 80.

The emerging theory of causation about which petitioner's expert testified at hearing—specifically the inflammatory process believed to trigger diseases formerly described as autoimmune, but now characterized by Dr. Bellanti as autoinflammatory—arises from a clinical observation made nearly forty years ago when subjects who had been exposed to cold temperatures for a thirty minute period developed tender, reddened, skin eruptions that resembled the type of painful, inflammatory lesions that occur in autoinflammatory diseases. See Tr. at 24-25; see also P's Ex. 84 at 16-18. That clinical observation has led to changes in thinking about the immunological process involved in certain autoimmune diseases. Petitioner's expert testified that these changes in thinking have occurred recently and have informed the theory of causation presented in this case. See Tr. at 54-55.

Petitioner's theory is admittedly a novel one. The Supreme Court has offered limited guidance to the lower court charged with the task of evaluating the reliability of novel scientific propositions introduced by experts. In Daubert v. Merrell Dow Pharmaceuticals, Inc., the Supreme Court observed that the reliability of scientific propositions may be tested through submission to the larger scientific community for scrutiny. 509 U. S. 579, 593-594 (1993). Such scrutiny "is a component of 'good

science' in part because it increases the likelihood that substantive flaws in methodology will be detected." Id. The absence of such scrutiny, as revealed by the lack of peer-reviewed journal publications examining the proposition at issue, is "a relevant, though not dispositive, consideration in assessing the scientific validity" of the proposition on which an expert's opinion is premised. Id. at 594.

While the novelty of petitioner's causation theory is a factor for consideration, the undersigned finds the lack of vaccine-related specificity of the posited theory to be the determinative consideration. As Dr. Bellanti explained during his testimony, the received hepatitis B vaccination series was but one of a number of agents that could have led to the autoinflammatory process petitioner holds responsible for his Crohn's disease. See Tr. at 29. Other agents identified as possibly causal were ingested food or encountered bacteria. Id. Petitioner's expert did not explain why three administrations of the hepatitis B vaccine, and none of the other identified agents, triggered the postulated autoinflammatory process in petitioner. Nor did petitioner's expert offer evidence that the administered hepatitis B vaccine series was either "a but-for" causal factor or a "substantial factor" in inducing the proposed course of autoinflammation in petitioner. See Moberly v. Sec'y of HHS, 592 F.3d 1315, 1321-22 (Fed. Cir. 2010) (quoting Shyface v. Sec'y of HHS, 165 F.3d 1344, 1352-53 (Fed. Cir. 1999)) (requiring that a petitioner in a Vaccine Act case show that the received vaccine was "'not only a but-for cause of the injury but also a substantial factor in bringing about the injury'" to prevail). Rather, Dr. Bellanti testified that ingested food, bacteria, or chemicals as well as the components of the hepatitis B vaccine "are all possibilities" for triggering the inflammatory reaction posited to bring about the autoinflammatory disorder of Crohn's disease.¹² Tr. at 29. Dr.

¹² The Federal Circuit instructed that contributing factors must be weighed when concurrent forces are alleged to bring about a single harm. Shyface, 165 F.3d 1344, 1352 (Fed. Cir. 1999). The decision stated:

Some other even which is a contributing factor in producing the harm may have such a predominant effect in bringing it about as to make the effect of the [vaccination] insignificant and, therefore, to prevent it from being a substantial factor. So too, although no one of the contributing factors may have such a predominant effect, their combined effect may . . . so dilute the effect of the [petitioner's] [vaccination] as to prevent it from being a substantial factor.

Id. (quoting Restatement (Second) of Torts § 433 cmt. d)). See also Walther v. Sec'y of the Dept. of & Human Servs., 485 F.3d 1146, 1151, n. 4 ("Where multiple causes act in concert to cause the injury, proof that the particular vaccine was a substantial cause may require the petitioner to establish that the other causes did not overwhelm the causative effect of the vaccine.") In this instance, although Dr. Bellanti identified multiple

Bellanti's assertion that a number of presented causal factors could be equally responsible for causing a petitioner's condition does not advance petitioner's claim, without more, that the received hepatitis B vaccine series was the responsible factor in this case.

Support for petitioner's claim rests primarily with the opinion of causation offered by petitioner's expert, and it is the view of the undersigned that petitioner has not met his burden of preponderant evidence. The opinion put forth by Dr. Bellanti falls short of the "more likely than not" showing of a scientifically sound and reliable theory of causation required for petitioner to prevail. See General Electric Co. v. Joiner, 522 U.S. 136, 146 (1997) (providing guidance that pursuant to Daubert v. Merrell Dow Pharmaceuticals, Inc., 509 U.S. 579 (1993), a court may reject the testimony of an expert "that is connected to existing data only by the ipse dixit of the expert."); see also Terran v. Sec'y of Health & Human Servs., 195 F.3d 1302, 1316 (Fed. Cir. 1999) (recognizing that a special master may assess an expert's testimony using the Daubert factors). Because the proposed theory of vaccine-related causation is wanting, petitioner does not prevail on prong one of the Althen analysis.

2. The Proposed Causal Sequence

Prong two of Althen requires petitioner to establish a "logical sequence of cause and effect" between the received vaccine and the suffered injury. See Althen, 418 F.3d at 1278. Petitioner must show that the vaccine was the reason for (or the but for cause of) the sustained injury. See Pafford 451 F.3d at 1356; Capizzano, 440 F.3d 1317, 1326 (Fed. Cir. 2006); Shyface v. Sec'y of Dep't of Health & Human Servs., 165 F.3d 1344, 1353 (Fed. Cir. 1999). This requirement has been interpreted to present the question of "did the vaccine at issue cause the injury alleged?" Pafford, 451 F.3d 1352, 1356 (Fed. Cir. 2006).

Petitioner need not present evidence of "epidemiologic studies, rechallenge, the presence of pathologic markers or genetic disposition, or general acceptance in the scientific or medical communities to establish a logical sequence of cause and effect . . ." Capizzano, 440 F.3d at 1325. Rather, circumstantial evidence and reliable medical opinions may be sufficient to satisfy the second Althen factor. Capizzano, 440 F.3d at 1325-26; Andreu, 569 F.3d at 1375-1377 (treating physician testimony); see also § 300aa-13(a)(1).

potential causes that might be responsible for the autoinflammatory process that caused petitioner's Crohn's disease, petitioner failed to demonstrate that any of them (including the hepatitis B vaccine) caused the putative injury.

Having found petitioner's theory of general causation wanting, the undersigned briefly addresses petitioner's theory of specific causation. Petitioner's treating doctors did not causally associate petitioner's gastrointestinal problems with his receipt of the hepatitis B vaccine series. Rather, the office notes reflect petitioner's own reported history of his symptoms. The office notes from the doctor visits that took place after petitioner had filed his vaccine claim for compensation further reflect petitioner's personal concern that his hepatitis B vaccinations led to the development of Crohn's disease.

In an effort to assist petitioner, petitioner's expert pointed to petitioner's recurrent symptoms of severe stomach cramping and burning as evidence of inflammatory bowel disease that was caused by petitioner's hepatitis B vaccine series. But over the course of more than twelve years, petitioner's test results fail to show that he suffered from the type of chronic gastrointestinal inflammation associated with the inflammatory bowel disease of Crohn's. Petitioner's theory that an autoinflammatory process led to the development of a serious inflammatory bowel condition is not persuasive absent evidence of any appreciable inflammation of petitioner's colon.

The sequence of cause and effect that petitioner has proposed between his received hepatitis B vaccine series and the development of his gastrointestinal problems contravenes logic and fails to satisfy the second prong of an Althen analysis.

3. The Temporal Relationship

Prong three of Althen requires petitioner to show that "a proximate temporal relationship" exists between the vaccination and the injury. See Althen, 418 F.3d at 1278. Petitioner must present evidence that the injury occurred within a medically acceptable time frame to link the injury to the received vaccine. See Pafford, 451 F.3d at 1358-1359.

Dr. Bellanti discussed the timing between the administered hepatitis B vaccines and the onset of petitioner's gastrointestinal symptoms. He observed that although petitioner began experiencing symptoms of cramping and diarrhea within twelve hours after his first hepatitis B vaccination, he did not report the symptoms to his doctor for two days. Tr. at 52. Dr. Bellanti added that after receiving the second hepatitis B vaccine, petitioner returned to the doctor three days later complaining of a burning sensation in his stomach and green bowels. Id. He further noted that petitioner complained of diarrhea with cramping three days before he received his third hepatitis B vaccine.¹³ Id.

¹³ Although Dr. Bellanti asserted in his testimony that petitioner experienced symptoms of cramps with diarrhea on February 21, 1994, a review of the record reveals that these

Dr. Bellanti testified that “there was a temporal relationship with each of the first two” vaccinations. Id. He commented that he was “not entirely sure about the third one.” Id. But, he asserted, “there was a temporal relationship with the receipt of a vaccine and symptoms worsening.”¹⁴ Id. Dr. Bellanti explained that different time frames are appropriate for different types of immunological responses. See id. at 53. He expressed uncertainty regarding which of the various immunological mechanisms were at work in this case, but he indicated that the timing of petitioner’s symptomatic responses

symptoms were reported on February 21, 1995, nearly one year after petitioner’s receipt of his third hepatitis B vaccine. See Tr. at 52; see also P’s Ex. 41 at 7-8.

¹⁴ The occurrence of cramping and diarrhea within a few days after receipt of the first and second hepatitis B vaccines might be viewed initially as evidence suggestive of a challenge-rechallenge. As explained in Doe/71 v. Secretary of Department of Health and Human Services, “the challenge-rechallenge model is a logical tool used to demonstrate that a vaccine (or any other event) caused an injury. Under this model, an individual who has had an adverse reaction to the initial vaccine dose (the ‘challenge event’) ‘suffers [a] worsening [of] symptoms after a second or third injection’ (the ‘rechallenge event’).” 95 Fed. Cl. 598, 603 (Fed. Cl. 2010) (internal citations omitted). Further examination of the record in this case reveals no record evidence that petitioner experienced any symptoms after receipt of his third hepatitis B vaccine and thus, militates against the application of the challenge-rechallenge model in this case. See P’s Ex. 41 at 7-8. These factual details might explain why petitioner did not assert a challenge-rechallenge theory here.

Petitioner also resisted asserting a claim of significant aggravation, preferring instead to distinguish petitioner’s pre-vaccination symptoms from his post vaccination symptoms. Tr. at 37-38 (attributing his pre-vaccination diarrhea to Valium). The Vaccine Act defines significant aggravation as “any change for the worse in a preexisting condition which results in markedly greater disability, pain, or illness accompanied by substantial deterioration of health.” 42 U.S.C. 300aa-33(4). The undersigned found that the frequency of petitioner’s symptoms increased after his receipt of the hepatitis B vaccine series but made no finding pertaining to whether the intensity of the symptoms increased or worsened after vaccination. Nonetheless, because petitioner failed to satisfy his burden of vaccine-related causation under Althen, a necessary showing to prevail on a significant aggravation claim based on the persuasive guidance provided in Loving v. Secretary of Health and Human Services, 86 Fed. Cl. 135, 143-144 (2009), any significant aggravation claim asserted by petitioner would have been similarly unsuccessful.

in this case would have been consistent with one of the various timeframes that is appropriate for immunological responses.¹⁵ See id. at 53-54.

Notwithstanding Dr. Bellanti's assertion that the timing was medically appropriate for the manifestation of petitioner's gastrointestinal symptoms after his received hepatitis B vaccinations, petitioner's claim necessarily must fail under an Althen analysis. Dr. Bellanti's ambiguity about what type of immunological process was at work in petitioner and correspondingly, what time frame was applicable does not support a finding that the temporal association between petitioner's receipt of the hepatitis B vaccine series and the onset of his symptoms was more likely than not medically appropriate. Petitioner has failed to show that his hepatitis B vaccination series more likely than not led to the development of his Crohn's disease, and without more than a speculative assertion of temporal association, petitioner's vaccine claim cannot prevail. See Grant, 956 F.2d at 1148 (recognizing that a temporal association, without more, is not sufficient to prove causation). See Hennessey v. Sec'y of Dep't of Health & Human Servs., 91 Fed. Cl. 126, 142 (2010) (observing that proposed timing is overly broad and renders any conceivable timing to be an appropriate temporal relationship).

¹⁵ Dr. Bellanti described four types of immunological responses. Each of the four types has a distinct timeframe that is unique to that type of immunologically-mediated response. Without clarity about which type of reaction the proposed causal process involves, the effort to identify a medically appropriate timeframe becomes speculative. Tr. at 53-54.

VII. Conclusion

For the foregoing reasons, petitioner's claim for Program compensation fails. The petition **SHALL BE DISMISSED**, and the Clerk of Court shall enter judgment consistent with this decision.¹⁶

IT IS SO ORDERED.

s/Patricia E. Campbell-Smith
Patricia E. Campbell-Smith
Special Master

¹⁶ Pursuant to Vaccine Rule 11(a), entry of judgment is expedited by the parties' joint filing of notice renouncing the right to seek review.