IN THE UNITED STATES COURT OF FEDERAL CLAIMS

OFFICE OF SPECIAL MASTERS

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ALLISON HAGER,	*	
	*	
Petitioner,	*	No. 01-307V
	*	Special Master Christian J. Moran
v.	*	
	*	Filed: October 15, 2008
SECRETARY OF HEALTH	*	
AND HUMAN SERVICES,	*	hepatitis B vaccine, autoimmune
	*	hepatitis, primary sclerosing
		cholangitis, entitlement
Respondent.	*	
	*	
* *		

Ronald C. Homer and Sylvia Chin-Caplan, Conway, Homer & Chin-Caplan, P.C., Boston, Massachusetts for petitioner;
Althea Davis and Rebecca Trinrud, Department of Justice, Washington, D.C. for respondent.

PUBLISHED DECISION DENYING COMPENSATION[*]

Allison Hager filed a petition seeking compensation under the National Vaccine Injury Compensation Program. 42 U.S.C. §§ 300aa-1 et seq. Ms. Hager claims that the hepatitis B vaccine, which she received in three doses between 1997 and 1998, caused her to suffer autoimmune hepatitis. She further claims that other disorders, including primary sclerosing

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[*] Because this published decision contains a reasoned explanation for the special master's action in this case, the special master intends to post it 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).

All decisions of the special masters will be made available to the public unless they contain trade secrets or commercial or financial information that is privileged and confidential, or medical or similar information whose disclosure would clearly be an unwarranted invasion of privacy. When such a decision or designated substantive order is filed, a party has 14 days to identify and to move to delete such information before the document's disclosure. If the special master, upon review, agrees that the identified material fits within the banned categories listed above, the special master shall delete such material from public access. 42 U.S.C. § 300aa–(12)(d)(4); Vaccine Rule 18(b).

cholangitis and ulcerative colitis, "developed as a consequence of the autoimmune hepatitis." Amended Petition, filed October 10, 2006, ¶ 16.

The evidence demonstrates that Ms. Hager is not entitled to compensation. Preliminarily, the evidence establishes that it is more probable than not that the disease that afflicts Ms. Hager is sclerosing cholangitis, and that Ms. Hager never suffered from autoimmune hepatitis. Regardless of the name of the disease from which Ms. Hager suffers, a preponderance of the evidence establishes that the disease existed before she received any dose of the hepatitis B vaccine. Thus, the hepatitis B vaccine did not cause Ms. Hager's problem. In addition, Ms. Hager has not established a potentially alternative theory that the hepatitis B vaccine significantly aggravated an underlying condition. The reasons for these conclusions are set forth below.

I. Facts

Ms. Hager was born on October 10, 1986.[1] Any health issues for the first 10 years of her life were transient. See Resp't Rep't, filed December 12, 2006.

For reasons explained in section IV.A., below, it is likely that Ms. Hager was already suffering from a disease before November 1997. Ms. Hager received her first dose of the hepatitis B vaccine on November 17, 1997, and the second dose on December 17, 1997. Exhibit 3 at 1-2.

According to the affidavit of Ms. Hager's mother, Allison was healthy until "March or April of 1998. At that time, Allison began to have stomach pains and nausea." Allison's mother also indicates that she brought Ms. Hager to the doctor in the fall of 1998. She does not explain why approximately five months passed without seeking medical attention. Exhibit 4 (Affidavit of Teresa Hager, dated April 28, 2001) ¶ 1. Somewhat inconsistently, Ms. Hager's own affidavit, which was filed relatively late in the litigation, asserts that she was feeling fine in May 1998. Exhibit 26 (Supplemental Affidavit of Allison Hager, dated July 24, 2007) ¶ 2.

Ms. Hager saw her family physician, Dr. Hope Tinker, on September 28, 1998. The notes from this visit indicate that Ms. Hager said that she had been having upper abdominal pain "[s]ince late July [or] early August." Ms. Hager's mother reported a decrease in Ms. Hager's appetite. Dr. Tinker believed that Ms. Hager was suffering from gastritis and prescribed Zantac. Exhibit 1 at 18.

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[1] Originally, Allison Hager was not old enough to prosecute this action on her own. Instead, her mother, Teresa Hager, brought this action on behalf of her daughter. While this case was pending, Allison Hager filed a motion to amend the caption, effectively designating herself as the petitioner. This motion was granted. Whether Ms. Allison Hager or her mother acted as the petitioner does not affect the outcome in this case. Thus, this decision treats Allison Hager as the "petitioner" throughout.

On the next day, September 29, 1998, Ms. Hager received the third dose of the hepatitis B vaccine. Exhibit 3 at 1-2.

Approximately three weeks later, Ms. Hager and her mother returned to Dr. Tinker's office because Ms. Hager was experiencing abdominal pain, nausea and anorexia. Ms. Hager's appetite was better. Dr. Tinker ordered blood tests and increased the Zantac. Exhibit 1 at 17 (report from October 19, 1998).

On October 28, 1998, Ms. Hager and her mother returned to Dr. Tinker's office. They learned that Ms. Hager's blood work showed that her liver enzymes were elevated. Exhibit 1 at 16, 38-39. Dr. Tinker states that Ms. Hager was "first sick [in] late July [or] August." Dr. Tinker also recounts the chronology that by the time Ms. Hager received her third dose of the hepatitis B vaccine, she was "already sick then." Dr. Tinker's assessment included a note that has relevance for this case: "Certainly Sept. HEP B shot could have been contributory to [elevated liver function tests] though rarely reported, have seen before. Doesn't explain initial illness." Dr. Tinker ordered additional tests including a hepatic profile and a repeat of the liver function tests. Exhibit 1 at 16.

On November 5, 1998, Ms. Hager and her mother saw Dr. Jose Barrios, an assistant professor for pediatrics at the University of Missouri Hospital & Clinics. Ms. Hager's mother told him that her daughter was in good health until "3-4 months ago," putting the onset of her troubles in July or August 1998. Dr. Barrios noted that he believed that Ms. Hager's abdominal pain was caused by gastritis. Dr. Barrios also noted her elevated liver function tests. On this issue, Dr. Barrios wanted to follow Ms. Hager clinically and to obtain additional liver function tests to see if the results would change, rather than to obtain a liver biopsy. Dr. Barrios instructed them about various warning signs, including jaundice, that if they were to appear, should prompt a return visit immediately. Exhibit 2 at 3-4.

Although Dr. Barrios recommended that Ms. Hager repeat the liver function tests in a few months, she did not. Exhibit 2 at 17 (report dated September 16, 1999). According to Ms. Hager's mother, she was feeling much better and not taking Zantac. She felt well until late July 1999. Exhibit 4 ¶ 4-5. Between November 1998, and August 1999, nine months passed in which Ms. Hager received no medical treatment.

Around August 1, 1999, Ms. Hager began experiencing a rash. She received different treatments, and, by the time of her visit with an associate of Dr. Tinker on September 14, 1999, the rash had cleared. Exhibit 1 at 8-13; see exhibit 26 (supplemental affidavit from Allison Hager) ¶ 4 (describing illness in early August). During a September 14, 1999 appointment, the doctor noted that Ms. Hager was jaundiced in her eyes. The doctor referred Ms. Hager to a specialist for additional treatment. Exhibit 1 at 8.

Ms. Hager saw Dr. Michael Cooperstock, the same day. After taking her history, Dr. Cooperstock believed that "[i]t is very likely that she has hepatitis, perhaps hepatitis A or C. Far

less likely, might be drug induced hepatitis, lupus hepatitis, or other causes of liver disease." Dr. Cooperstock ordered several tests, including a hepatitis diagnostic panel. Exhibit 2 at 6. The blood work showed that most liver enzymes were elevated, including very high levels for alkaline phosphatase. The lab work also showed that Ms. Hager was not infected with hepatitis A or hepatitis C. Id. at 13-16. When Dr. Cooperstock reviewed these results, he arranged for Ms. Hager to see Dr. Barrios again. Id. at 6.

Two days later, Ms. Hager saw Dr. Barrios. In addition to having a rash, which seems to have reappeared, Ms. Hager was jaundiced and tired. Dr. Barrios requested an abdominal ultrasound to be performed the next day. Exhibit 2 at 17-18.

The ultrasound showed some abnormalities, including a persistently contracted gall bladder and a dilation of the common hepatitic bile duct. Exhibit 2 at 19, 21. Dr. Barrios recommended a liver biopsy by Dr. Tom Foy at Cardinal Glennon Children's Hospital in St. Louis. Exhibit 2 at 21 (report dated September 21, 1999).

Ms. Hager stayed at Cardinal Glennon Children's Hospital from September 23, 1999, to October 1, 1999. When she entered the hospital, she had a macropapular rash over her lower extremities and an enlarged liver. Exhibit 7 at 73-76.

Ms. Hager's blood was tested. Id. at 106. Her test for antinuclear antibodies was positive at 1:160. Id. at 113. Her test for smooth muscle antibodies was also positive. Id. at 115.

While in the hospital, Ms. Hager had more significant tests done. A liver ultrasound on September 23, 1999, showed an enlarged echogenic liver, a normal gallbladder, and some debris in the common bile duct. Id. at 135. On September 24, 1999, Ms. Hager had a liver biopsy. The result of this test was consistent with biliary obstruction and some fibrosis was noted. Id. at 139. She also had an endoscopic retrograde cholangiopancreatography ("ERCP") on September 29, 1999. Id. at 145. An ERCP assists doctors in identifying problems in the liver, gallbladder, bile ducts and pancreas. The ERCP indicated dilatation in the common bile duct. Exhibit 7 at 145. When Ms. Hager was discharged, Dr. Foy believed that any problem was primarily obstructive. Id. at 258. He did not prescribe any medication and he recommended that Ms. Hager follow up with her primary doctor. Id. and at 73-36.

On October 14, 1999, Ms. Hager saw Dr. Barrios. He thought that she had improved but also that she still looked a little yellow. Dr. Barrios ordered tests but the results, assuming the tests were performed, appear not to be included in the medical records. Dr. Barrios also requested that Ms. Hager see Dr. Foy again in two to three months. Exhibit 2 at 22.

On October 25, 1999, Ms. Hager's mother noticed that she appeared more jaundiced. Ms. Hager, herself, was feeling more fatigue, and experiencing some nausea. Consequently, Ms. Hager saw Dr. Akremi on October 26, 1999. Dr. Akremi requested immediate lab work and a referral back to Dr. Foy in St. Louis. Exhibit 1 at 6.

On October 27, 1999, Ms. Hager returned to Cardinal Glennon Children's Hospital. This admission lasted until October 29, 1999. Exhibit 7 at 258. In addition to elevated results for liver function tests, Ms. Hager was jaundiced. She also was nauseous and had an itchy rash over most of her body. Id. at 17. On October 27, 1999, Ms. Hager had another abdominal ultrasound. This test showed mild dilatation in the common bile duct and that her liver was enlarged but about the same size as her previous ultrasound. Id. at 37.

Dr. Foy believed that Ms. Hager had autoimmune hepatitis. A reason supporting this diagnosis is that the results of tests on her blood drawn during her previous admission showed positive results for anti-nucleic antibodies and smooth muscle antibody. Id. at 22, 258; see also id. at 113, 115. Dr. Foy prescribed prednisone and imuran. Id. at 22, 258.

On November 1, 1999, Ms. Hager returned to see Dr. Barrios. Dr. Barrios recorded that the results of the liver function tests, jaundice, her level of activity, and her appetite were all improved. Dr. Barrios stated that he would obtain additional tests. Exhibit 2 at 23.

Dr. Foy indicates that he obtained the results of these tests. He reported that they showed continued improvement. To Dr. Foy, "this is good evidence that at least a component of her liver disease is probably from an autoimmune basis." Dr. Foy also stated that the doctor who performed the ERCP stated that Ms. Hager "did not have [a] biliary tree at this time consistent with sclerosing cholangitis." Exhibit 7 at 259 (letter dated November 12, 1999).

For the next 12 months, Ms. Hager remained relatively healthy. Her medications were occasionally adjusted, and sometimes she missed school. See exhibit 2 at 25-28; exhibit 4 ¶ 9; exhibit 6 at 105. She was not hospitalized during this time.

In November 2000, as part of her on-going monitoring, Ms. Hager saw Dr. Barrios. Ms. Hager said that she was having loose stools. Dr. Barrios attempted to rule out an infectious agent as the cause of the diarrhea. Exhibit 6 at 125. She started to take metronidazole, which is an antibiotic. Although a cause was not found, Ms. Hager returned to normal. Exhibit 6 at 134.

On approximately December 9, 2000, Ms. Hager started having blood in her stools and more diarrhea. She also had abdominal pain. Ms. Hager was admitted to the University of Missouri Hospital in Columbia, Missouri for observations for one day. Exhibit 6 at 134-35, at 158. Her alkaline phosphatase was very high and her aspartate aminotransferase was high. Id. at 176. Dr. Barrious wanted Ms. Hager to return for a bowel endoscopy. Id. at 141.

On December 19, 2000, Ms. Hager had a colonoscopy. Exhibit 6 at 169-72. She was diagnosed with ulcerative colitis. Id. at 173, 188.

On January 3, 2001, Ms. Hager saw Dr. Barrios, whom she had not seen since November 1998. His impression was that Ms. Hager had "ulcerative colitis and probably sclerosing

cholangitis." He continued her medications, which were pentasa and prednisone. Exhibit 6 at 194.

After January 2001, Ms. Hager was hospitalized several times. Sometimes, the doctors interpreted the results of tests as being consistent with a liver problem, not sclerosing cholangitis. See, e.g., exhibit 9 at 475-76 (test on March 29, 2001). Other tests suggested both sclerosing cholangitis and an autoimmune problem affecting the liver. See, e.g., exhibit 9 at 14 (test on January 9, 2002).

In 2004, a doctor stated that although Ms. Hager was initially diagnosed with autoimmune hepatitis, the course of her disease was "more consistent with sclerosing cholangitis." Exhibit 11 at 618.

Ms. Hager's most recent statement indicates that her health varies from day to day. She is on a list to receive a liver transplant. Exhibit 26 ¶ 6-7.

II. Procedural History

On May 21, 2001, Ms. Hager filed a petition seeking compensation along with five exhibits. Over the next three years, Ms. Hager filed more medical records.

While this case was pending, counsel for Ms. Hager, who also represented other petitioners who claimed that the hepatitis B vaccine caused them an injury, and counsel for respondent attempted to establish a structure for resolving the many cases involving the hepatitis B vaccine. Despite good faith efforts over several years, this attempt was not successful.

This case was re-assigned in 2006, and a stay was lifted. Since its re-assignment, this case generally moved at about the same pace as other cases in which a group of petitioners alleged that the hepatitis B vaccine caused them to suffer from autoimmune hepatitis. In total, this group included seven cases in which three different attorneys represent the petitioners. Before the hearing, Ms. Hager filed a statement consenting to the disclosure of information to the parties in these related cases.

Ms. Hager submitted a report from Dr. Bellanti as exhibit 15 on May 26, 2006. Ms. Hager also filed medical literature relied upon by Dr. Bellanti. Later, on July 18, 2007, Ms. Hager filed additional medical literature as exhibits 22 through 25. On October 10, 2006, Ms. Hager submitted an amended petition, which attempted to clarify the scope of her claim.

Once the medical records appeared to be complete, respondent submitted his report, pursuant to Vaccine Rule 4. In this report, dated December 12, 2006, respondent denied that Ms. Hager was entitled to compensation. In conjunction with that filing, respondent also filed expert reports from Dr. Melvin Berger, an immunologist, and Dr. Raymond Koff, a specialist in hepatology. Exhibits A, C. Respondent also filed medical literature cited by Dr. Koff on

February 16, 2007, as exhibits H thru N, and literature cited by Dr. Berger on July 17, 2007, as exhibits O thru W.[2]

In addition to denying that Ms. Hager was entitled to compensation, respondent stated that she "must clarify when the first symptom or manifestation of her condition occurred in order to establish that her petition [was] timely filed." Resp't Rep't at 11. In response to an order, respondent developed this point in a status report, filed on February 26, 2007. Respondent questioned when Dr. Bellanti believed that Ms. Hager's autoimmune hepatitis began and also suggested that the case could be viewed as a significant aggravation case. Resp't Status Rep't, filed February 26, 2007.

On April 3, 2007, a hearing was scheduled to take place on September 17-19, 2007. Several factors contributed to the unusually long time between the scheduling of the hearing and the holding of the hearing. First, petitioners preferred that this group of cases be tried at one time. A single trial is more efficient in terms of saving the time of the attorneys, the doctors, and the Court. Second, two cases required small amounts of additional time to attain the same procedural posture as the other cases. Third, the personal and professional commitments of the many attorneys involved, three doctors and the Court prevented an earlier date for holding the hearing.

The interval of time between the scheduling of the hearing and the commencement of the hearing supported extending to Ms. Hager the opportunity to retain an additional expert. Ms. Hager did not request this opportunity. However, the Court recognized that respondent, but not Ms. Hager, presented a hepatologist, Dr. Koff. The April 3, 2007 order established a schedule for Ms. Hager to file another expert report, and, despite respondent's objection, set a deadline as August 1, 2007 for this report.

Ms. Hager did not file another expert report. The omission of an expert on gastroenterology or hepatology affects the outcome of this litigation. For the reasons explained below, Dr. Koff's opinion that Ms. Hager suffers from primary sclerosing chongalitis was much more persuasive than Dr. Bellanti's opinion that she suffers from autoimmune hepatitis.

While Ms. Hager's opportunity to obtain an expert report was pending, respondent requested that the special master hold a fact hearing and "make findings of fact with respect to the onset of petitioner's condition." Resp't Status Rep't, filed July 10, 2007, at 5. This request was denied without prejudice because respondent could solicit opinions from the doctors testifying at the already scheduled hearing through a series of hypothetical questions and because attempting to conduct a fact hearing between July 10, 2007 (when respondent requested a fact hearing) and September 17, 2007 (when the hearing was scheduled to commence for seven cases) would be problematic.

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[2] Due to a clerical oversight, respondent did not assign the letters E thru G to any exhibit.

The hearing on entitlement took place in two sessions for five petitioners. (Two cases resolved before the hearing.) In the first session, which was held across three days in September 2007, the petitioners presented most of their evidence that the hepatitis B vaccine "can cause" autoimmune hepatitis in general. Respondent disputed this point and presented evidence in response. Tr. 6 through 203. The first session also included testimony about some of the petitioners specifically. For example, Ms. Hager's case was discussed during the first and second days of the hearing. Tr. 204-479.

The second session was held for two days in March 2008.[3] During this session, the parties presented their remaining evidence regarding whether the hepatitis B vaccination can cause autoimmune hepatitis. The second session also completed the discussion of the individual cases.

After the transcript was filed, respondent renewed his motion for a fact hearing. Once again, respondent sought a determination about the onset of Ms. Hager's condition. Resp't Mot. Requesting Fact Hearing, filed July 18, 2008, at 3.

Ms. Hager opposed the motion for a fact hearing. She maintained that her action was timely under either of two different approaches. Ms. Hager argued that her "observable symptoms of autoimmune hepatitis first began in late July or early August of 1998." Pet'r Resp., filed July 28, 2008, at 7. Alternatively, Ms. Hager argued that the third dose of the hepatitis B vaccine, which she received on September 29, 1998, "significantly aggravated an underlying condition. If so, she would be entitled to compensation, and there would be no statute of limitations issue." Id. at 10.

With the filing of those briefs, the case is ready for adjudication.

III. Standards for Adjudication

In this case, the evidence includes conflicting opinions from each party's experts. The persuasiveness of the experts must be evaluated, and the testimony of one side's expert may be rejected when a reasonable basis supports such a rejection. Burns v. Sec'y of Health & Human Servs., 3 F.3d 415, 417 (Fed. Cir. 1993). A decision about the persuasiveness of an expert is virtually not reviewable on appeal. Bradley v. Sec'y of Health & Human Servs., 991 F.2d 1570, 1575 (Fed. Cir. 1993); Sword v. Sec'y of Health & Human Servs., 44 Fed. Cl. 183, 188 (1999) (noting that special masters acquire "specialized knowledge and expertise" to resolve disputes between experts).

[3] The length of time between the two sessions was longer than originally anticipated due to unexpected health troubles in a family member of an expert.

IV. Analysis

The experts reach different conclusions on several points. First, Dr. Bellanti believes that Ms. Hager has autoimmune hepatitis and that her other conditions are sequella to the autoimmune hepatitis. Exhibit 15 at 7. In contrast, Dr. Koff believes that Ms. Hager does not have autoimmune hepatitis. Instead, he thinks that she has either primary sclerosing cholangitis or autoimmune sclerosing cholangitis. Exhibit C at 2. Dr. Berger, respondent's expert, took a middle ground. He states that Ms. Hager has "an 'overlap' syndrome of autoimmune hepatitis . . . with autoimmune sclerosing cholangitis." Exhibit A at 4.

Second, the experts disagree about the cause of Ms. Hager's illness, whatever its name. Dr. Bellanti believes that the hepatitis B vaccine can cause autoimmune hepatitis and that the hepatitis B vaccine did, in fact, cause Ms. Hager's autoimmune hepatitis. Exhibit 15.

Compared to Dr. Bellanti, Dr. Berger and Dr. Koff have different understandings about the role of the hepatitis B vaccination. Dr. Berger believes that for Ms. Hager specifically, the temporal sequence indicates that the hepatitis B vaccination did not cause or exacerbate Ms. Hager's problems. Exhibit A at 6. More generally, Dr. Berger asserts that the evidence does not show that the hepatitis B vaccine can cause autoimmune hepatitis or autoimmune sclerosing cholangitis. Exhibit A at 8. Dr. Koff's opinion is that no evidence shows that the hepatitis B vaccine causes autoimmune sclerosing cholangitis. Dr. Koff also believes that no evidence shows that the hepatitis B vaccine causes autoimmune hepatitis. Exhibit C at 3.

Dr. Bellanti opines that the hepatitis B vaccine "can cause or significantly contribute to the development of autoimmune hepatitis." Exhibit 15 at 7. He offers several related points. First, he presents a syllogistic argument that given (a) it is generally understood that if a wild virus can cause a condition, then the vaccine for that virus can also cause that condition, and (b) the hepatitis B virus can cause autoimmune hepatitis, the logical conclusion is (c) the hepatitis B vaccine can cause autoimmune hepatitis. Second, he presents an argument by analogy. Dr. Bellanti contends that vaccines can cause autoimmune conditions. According to Dr. Bellanti, because autoimmune hepatitis is, as evident by its name, an autoimmune condition, a vaccine can cause autoimmune hepatitis. He attempts to strengthen this analogy by presenting different mechanisms explaining how the hepatitis B vaccine can cause autoimmune hepatitis. Exhibit 15 at 3-7 & tabs A-H; see also exhibit 17-20.

Dr. Bellanti proceeds to a second step. He believes that Ms. Hager's autoimmune hepatitis "was likely due to her hepatitis B immunizations." He reaches this conclusion because "[t]he temporal relationship between her immunizations and the onset of symptoms is medically appropriate and there is no other likely cause identified in the record." Exhibit 15 at 7.

A. What Disease Afflicts Ms. Hager?

Initially, determining what disease afflicts Ms. Hager is necessary because the parties differ on this fundamental issue. A preponderance of the evidence establishes that Ms. Hager suffers from primary sclerosing cholangitis.

A review of basic human anatomy is the framework for discussing autoimmune hepatitis (a disease affecting the liver) and primary sclerosing cholangitis ("PSC") (a disease affecting the biliary system and the liver). A primary function of the liver is to transform food into other substances that other parts of the body need, such as blood clotting proteins. The predominant cells in the liver, called hepatocytes, secrete bile. The bile drains through the left and right hepatitic ducts, which join to form the common hepatitic duct. The common hepatitic duct connects to the gall bladder, where bile is stored, and also connects to the common duct system, which leads to the duodenum, part of the digestive track. Tr. 469-72 (testimony of Dr. Koff); exhibit X (handwritten drawing); see also tr. 46-48, 212-13 (testimony of Dr. Bellanti). The system through which bile is drained is known as the biliary system. See Dorland's Illustrated Medical Dictionary (30th Ed. 2002) at 216.

An inflammation within a bile duct is known as cholangitis. "Primary sclerosing cholangitis" is a "progressive chronic fibrosing inflammation of the bile ducts of unknown cause." Dorland's at 351; see also exhibit 25. In this context "primary" is distinguished from the term "secondary," which means the cholangitis is caused by a known factor, such as abdominal trauma. Exhibit C (Dr. Koff report) at 2, citing Exhibit I (Rupert Abdalian & E. Jenny Heathcote, Sclerosing Cholangitis: A Focus on Secondary Causes, 44 Hepatology 1063-74 (2006)); see also exhibit M (Andrea A. Gossard, et al., Secondary Sclerosing Cholangitis: A Comparison to Primary Sclerosing Cholangitis, 100 Am. J. Gastroenterol 1330-33 (2005)).

Primary sclerosing cholangitis can be further classified into two other conditions, namely, small-duct PSC and large-duct PSC. Exhibit J (Jurgen Ludwig, Small-duct Primary Sclerosing Cholangitis, 11 Semin Liver Dis 11-17 (1991)); exhibit K (Paul Angulo et al., Small-duct Primary Sclerosing Cholangitis; A Long-term Follow-up Study, 35 Hepatology 1494-1500 (2002)). A preponderance of the evidence establishes that Ms. Hager suffers from the small-duct type of PSC. Tr. 445, 466-68.

In some respects, distinguishing between PSC and autoimmune hepatitis is difficult. Ms. Hager introduced articles that state that these two diseases can overlap. Exhibit 17 (Germana Gregorio et al., Autoimmune Hepatitis/Sclerosing Cholangitis Overlap Syndrome in Childhood: A 16-Year Prospective Study, 33 (3) Hepatology 544 (2001)); exhibit 19 (Christoph Schramm and Angspar W. Lohse, Overlap Syndrome of Cholestatic Liver Diseases and Autoimmune Hepatitis, 28 Clinical Reviews in Allergy and Immunology 105 (2005)); and exhibit 25 (Diego Vergani and Giorgina Mieli-Vergani, Primary Sclerosing Cholangitis in The Autoimmune Diseases (Noel R. Rose and Ian J. Mackay eds., 4th Ed. 2006)); see also exhibit H (Nicholas F. LaRusso et al., Primary Sclerosing Cholangitis: Summary of a Workshop, 44 Hepatology 746-64

(2006)) at 750. Dr. Koff, the specialist among the doctors testifying in these cases, recognizes that PSC affects the liver. Tr. 442. The immunologists, Dr. Bellanti and Dr. Berger, had difficulty differentiating between PSC and autoimmune hepatitis. Tr. 225-27 (testimony of Dr. Bellanti), tr. 366-68 (testimony of Dr. Berger).

Despite some similarities, PSC and autoimmune hepatitis are different diseases. Exhibit 17 (Gregorio) at 546 (charts), 550. Results from lab tests provide one non-invasive way of distinguishing between the two diseases. When bile ducts are impaired, the alkaline phosphatase level increases dramatically for PSC. The transaminase levels increase only mildly, at most. Another, more invasive way to diagnose one disease or the other is to obtain a liver biopsy. Tr. 431-32.

For Ms. Hager, a preponderance of the evidence shows that she was suffering from PSC not autoimmune hepatitis. Her liver enzymes in October 1998 showed that Ms. Hager's alkaline phosphatase was three times the normal value. Ms. Hager also had one normal transaminase level and one mildly elevated one. Exhibit 1 at 39. These laboratory results are consistent with significant cholestatic disease, not autoimmune hepatitis. Tr. 377, 421. The test on Ms. Hager's liver enzymes in September 1999 were similar. Exhibit 2 at 13.

In September 1999, Ms. Hager had a liver biopsy. Exhibit 7 at 139. The biopsy showed that Ms. Hager had florid periportal bile duct proliferation, generally meaning a problem in her bile ducts. The biopsy did not show the signs of autoimmune hepatitis such as portal inflammation or lobular inflammation. Tr. 422.

On September 29, 1999, Ms. Hager had another invasive procedure, an ERCP. Exhibit 7 at 145, 258-259. The ERCP indicated an obstruction in the common bile duct. Exhibit 7 at 145. The doctor who ordered the ERCP, Dr. Foy, did not prescribe any treatment but recommended that Ms. Hager follow up with her primary doctor.

These tests underlie the finding that Ms. Hager suffers from PSC. The primary piece of evidence pointing to a contrary result, that Ms. Hager suffers from autoimmune hepatitis, is the report by Dr. Foy, who diagnosed Ms. Hager as having autoimmune hepatitis in 1999. Exhibit 7 at 22, 258.

Although Dr. Foy's diagnosis is entitled to some deference because he was Ms. Hager's treating doctor, his diagnosis is not determinative. 42 U.S.C. § 300aa-13(b)(1) (stating that any "diagnosis [in the medical record] . . . shall not be binding on the special master."). Dr. Foy's determination that Ms. Hager was not suffering from PSC seems to be founded on two possibly mistaken judgments.

Dr. Foy may have refrained from diagnosing Ms. Hager with PSC because her ERCP did not show any lesions. An ERCP can show problems, such as lesions, in large bile ducts. But, ERCPs lack the resolution to show problems in the small bile duct. Tr. 445, 447 (discussing

exhibit H (LaRusso, Primary Sclerosing Cholangitis)), tr. 466 (discussing exhibit J (Ludwig, Small-duct Primary Sclerosing Cholangitis)). Dr. Foy appears to have discounted the possibility that Ms. Hager's sclerosing cholangitis was located in her small bile ducts that cannot be reviewed in an ERCP.

Dr. Foy also could have considered Ms. Hager to have autoimmune hepatitis because she tested positive for certain antibodies, the antinuclear antibody and smooth muscle antibody. Exhibit 7 at 22, 113, 115, 258. However, these antibodies are not specific to autoimmune hepatitis. Tr. 424. These antibodies can be found in other conditions. Exhibit H (LaRusso, Primary Sclerosing Cholangitis) at 753; exhibit L (A.H. Leontine Mulder et al., Prevalence and Characterization of Neutrophil Cytoplasmic Antibodies in Autoimmune Liver Diseases, 17 Hepatology 411-17 (1993)). Thus, Dr. Foy's diagnosis of autoimmune hepatitis cannot rest upon the positive results to the test for various antibodies.

Significantly, two of Ms. Hager's treating doctors indicated that the diagnosis of autoimmune hepatitis was not correct. See exhibit 6 at 194 (record from Dr. Barrios dated Jan. 3, 2001); exhibit 11 at 618 report by Dr. Mary Ann Jackson dated June 18, 2004. Consequently, the opinions of Ms. Hager's treating doctors tend to preponderate in favor of a finding that Ms. Hager suffers from PSC, not autoimmune hepatitis.

The expert opinions also weigh in favor of a finding that Ms. Hager suffers from PSC. Dr. Koff's opinion is entitled to the most weight because he has the most experience with treating diseases of the liver and bile duct. His opinion is that the proper diagnosis for Ms. Hager is PSC. See tr. 429, 441.

Against Dr. Koff's opinion, Ms. Hager could point to the opinion of Dr. Bellanti. Dr. Bellanti's opinion that Ms. Hager suffers from autoimmune hepatitis is very weak for two reasons. First, Dr. Bellanti is an immunologist, not a hepatologist. Second, Dr. Bellanti's opinion is not consistent. Although his report says that Ms. Hager suffers from autoimmune hepatitis, his oral testimony was not as clear. See tr. 214 (stating that Ms. Hager's biopsy is "not classic autoimmune hepatitis").

In sum, although some evidence in the records indicates that Ms. Hager suffers from autoimmune hepatitis, the persuasive evidence establishes that her disease is PSC. Having determined that Ms. Hager is afflicted with PSC, not autoimmune hepatitis, the immediate question becomes whether she has established, by a preponderance of the evidence, that the hepatitis B vaccine caused (or exacerbated) her PSC. The next section explains why Ms. Hager has failed to meet her burden of proof. The following section considers the alternative questions, namely, whether Ms. Hager established, by a preponderance of the evidence, that the hepatitis B vaccine caused or significantly exacerbated autoimmune hepatitis. The answer to these inquiries are also negative.

B. Did the Hepatitis B Vaccine Cause Ms. Hager's PSC?

Ms. Hager presented relatively little evidence - and certainly no persuasive evidence - connecting the hepatitis B vaccine to PSC. A brief review of the procedural history explains how this paucity of evidence developed.

Ms. Hager filed the report of Dr. Bellanti on May 26, 2006. In this report, Dr. Bellanti stated Ms. Hager has autoimmune hepatitis. Exhibit 15 at 7. Dr. Bellanti's report set forth various theories explaining how the hepatitis B vaccine can cause autoimmune hepatitis. Dr. Bellanti's report did not use the term sclerosing cholangitis. Tr. 226.

Shortly after filing this report, Ms. Hager filed an amended petition. Consistent with Dr. Bellanti's report, Ms. Hager sought compensation for autoimmune hepatitis "and all her subsequent disorders developed as a consequence of the autoimmune hepatitis." Am. Pet. ¶ 16.

Dr. Koff, however, disagreed, strongly, with the diagnosis of autoimmune hepatitis. His report concludes that "the liver disease affecting Allison Hager is not autoimmune hepatitis, but either primary sclerosing cholangitis or autoimmune sclerosing cholangitis." Exhibit C at 4.

Dr. Koff's report placed Ms. Hager and Dr. Bellanti on notice that the diagnosis of autoimmune hepatitis was disputed. Ms. Hager was proceeding on a theory that she had autoimmune hepatitis and the autoimmune hepatitis led to the development of PSC. She submitted one article that provides some corroboration for this theory. See exhibit 18 (Ayman A. Abdo et al., Evolution of Autoimmune Hepatitis to Primary Sclerosing Cholangitis: A Sequential Syndrome, 36 No. 6 Hepatology 1393 (2002)).

Ms. Hager, however, did not react in other ways. For example, she did not obtain a report from a doctor who possesses expertise in the field of hepatology roughly equivalent to that of Dr. Koff. She also did not obtain a supplemental report from Dr. Bellanti in which her immunologist offered a theory causally connecting the hepatitis B vaccine to PSC. Ms. Hager did not take these steps although she was given an opportunity. Order, filed April 3, 2007. At the end of the day, Ms. Hager is bound by the choices, actions and omissions of her attorney. Azarkhish v. Office of Personnel Management, 915 F.2d 675, 678 (Fed. Cir. 1990); Swords, 44 Fed. Cl. at 191 (when counsel is not surprised, an additional opportunity to present evidence is not required).

During his testimony, Dr. Bellanti attempted to change the meaning of what he had written. Although his report uses the words "autoimmune hepatitis," Dr. Bellanti stated he should have used the more generic term "autoimmune liver disease." Tr. 229; see also tr. 214 (Dr. Bellanti stating Ms. Hager's biopsy is "not classic autoimmune hepatitis . . . but it could be another form of biliary involvement.").

Dr. Bellanti's change in his opinion about Ms. Hager's diagnosis means that Dr. Bellanti should have changed his report in other ways. (A revised report would have also been the

appropriate procedure to alert the respondent and the special master about Dr. Bellanti's new diagnosis.) Dr. Bellanti's only report in this case does not discuss PSC. Tr. 226; see also exhibit 15. Thus, his report carries almost no persuasive value simply because of the mismatch between Ms. Hager's condition and the premise of the report. (As explained in section IV.C, below, Dr. Bellanti's report has little, if any, persuasive value even if Ms. Hager suffered from autoimmune hepatitis.)

The only type of evidence that the hepatitis B vaccine caused Ms. Hager's PSC is Dr. Bellanti's oral testimony. As mentioned, there is nothing in his report discussing PSC, exhibit 15. The only treating doctor who associated the hepatitis B vaccine with Ms. Hager's condition appears to be Dr. Tinker. See exhibit 1 at 6. Dr. Tinker's statement, however, is not persuasive because she states the vaccination "could have been contributory" without expressing a clear opinion.

Dr. Bellanti's oral testimony that the hepatitis B vaccine can cause sclerosing cholangitis was exceedingly brief. On direct examination, he barely mentions cholangitis at all. In one passage, Dr. Bellanti stated that the "HBV vaccine . . . can cause or significantly have contributed to the development of an autoimmune hepatitis or cholangitis or both." Tr. 220; accord tr. 225 (testimony on cross-examination). However, his opinion with regard to cholangitis was not developed and in the next sentence, Dr. Bellanti stated, again, that Ms. Hager has "autoimmune hepatitis." Id. Beyond these passages, there is almost nothing in the transcript even remotely connecting the hepatitis B vaccine to sclerosing cholangitis.

Section IV.A., above, establishes that Ms. Hager suffers from sclerosing cholangitis. As discussed in this section, Ms. Hager presented barely a scintilla (and maybe not even that much) of evidence that the hepatitis B vaccine causes sclerosing cholangitis. She did not present a medical theory connecting the hepatitis B vaccine to sclerosing cholangitis. As discussed in great detail in section IV.C.2., below, she has not established the appropriate temporal relationship regardless of whether she is diagnosed with sclerosing cholangitis or autoimmune hepatitis. In short, Ms. Hager has not established that she is entitled to compensation.

C. Can the Hepatitis B Vaccine Cause Autoimmune Hepatitis?

Although a preponderance of the evidence establishes that Ms. Hager did not suffer from autoimmune hepatitis at any time, for sake of completeness this alternative argument is addressed as well. Ms. Hager has failed to demonstrate, by a preponderance of the evidence, that the hepatitis B vaccine caused her (assumed) autoimmune hepatitis.

To receive compensation for autoimmune hepatitis, the elements of Ms. Hager's case are familiar. Her

> burden is to show by preponderant evidence that the vaccination brought about [the] 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, 418 F.3d at 1278. Ms. Hager has not established, by a preponderance of the evidence, any of these elements.

1. Medical Theory

Dr. Bellanti presented four theories possibly explaining how autoimmune diseases arise. They are: (a) molecular mimicry, (b) bystander theory, (c) polyclonal activation, and (d) a dysregulation in the function of T-cells. Tr. 24.[4] For the reasons set forth in the following sections, none of these theories presents a reliable explanation of how the hepatitis B vaccine can cause autoimmune hepatitis.

The theory connecting the vaccine to the injury "must be supported by a sound and reliable medical or scientific explanation." Knudsen v. Sec'y of Health & Human Servs., 35 F.3d 543, 548 (Fed. Cir. 1994). To determine whether an expert's theory is reliable a special master may use the factors set forth in Daubert v. Merrell Dow Pharms., Inc., 509 U.S. 579, 594 (1993). Terran v. Sec'y of Health & Human Servs., 195 F.3d 1302, 1316 (Fed. Cir. 1999) (affirming special master's use of Daubert in vaccine program cases). After Terran, decisions from judges of the Court of Federal Claims have consistently cited to Daubert. E.g. De Bazan v. Sec'y of Health & Human Servs., 70 Fed. Cl. 687, 699 n.12 (2000) ("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).

Daubert lists several non-exhaustive factors that may be considered in assessing the reliability of an expert's opinion. Kumho Tire Co., Ltd. v. Carmichael, 526 U.S. 137, 149 (1999). These factors include whether the expert's opinion is well accepted in the relevant community. Daubert, 509 U.S. at 594; see also McDowell v. Brown, 392 F.3d 1283, 1299 (11th Cir. 2004) (affirming district court's exclusion of expert whose theory lacked "testing, peer review, a potential error rate, and general acceptance."); Sullivan v. United States Dep't of Navy, 365 F.3d 827, 834 (9th Cir. 2004) (reversing exclusion of expert whose theory was generally accepted).

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[4] Petitioner's counsel suggested that "loss of tolerance" also constitutes a medical theory. Tr. 26. However, loss of tolerance is not a theory explaining the origins of autoimmune diseases. Loss of tolerance describes the autoimmune disease itself.

A closely related factor is how peer-reviewed articles have evaluated a theory. This point may also be considered in weighing the value of a medical opinion. Id.; see also Merck & Co., Inc. v. Teva Pharmaceuticals USA, Inc., 395 F.3d 1364, 1374 (Fed. Cir. 2005); Libas v. United States, 193 F.3d 1361, 1366-67 (Fed. Cir. 1999); Knight v. Kirby Inland Marine Inc., 482 F.3d 347, 354 (5th Cir. 2007) (stating a lack of textual support may "go to the weight, not the admissibility" of the expert's testimony); Waleryszak v. Sec'y of Health & Human Servs., 45 Fed. Cl. 573, 578-79 (1999), appeal dismissed, 250 F.3d 753 (Fed. Cir. 2000). These factors are useful in evaluating each of the four theories proposed by Dr. Bellanti.

a. Molecular Mimicry

Dr. Bellanti's first theory to explain how the hepatitis B vaccine can cause autoimmune hepatitis is molecular mimicry. Dr. Bellanti stated that among the different theories, he favored molecular mimicry and the fourth-listed theory, a deficiency in T-regulatory cells, as the theories most likely to be valid. Tr. 90, 201. Ms. Hager and Dr. Bellanti have not established, by a preponderance of the evidence, that molecular mimicry is a reliable theory to explain a causal relationship between the hepatitis B vaccine and autoimmune hepatitis.[5]

Molecular mimicry is based upon a premise that some parts of the human body share a sequence of proteins with the foreign substance, here the hepatitis B vaccine. Tr. 23, 130-31; exhibit 23 at 4. This sharing of protein sequences is known as homology. Tr. 171-72.

For the hepatitis B vaccine to cause autoimmune hepatitis via molecular mimicry, cells within the liver must share homology with the hepatitis B vaccine. Tr. 172. The hepatitis B vaccine is a genetically engineered recombinant vaccine consisting of a single protein, the surface antigen. Tr. 84-85, 116. Therefore, comparing the protein sequences in the hepatitis B vaccine to liver proteins would be easier than comparing liver proteins to a more complex vaccine, such as one containing an attenuated virus. See tr. 392-93.

However, despite the possibility that there could be homology between the hepatitis B vaccine and liver proteins, no homology has been found. Tr. 86-87 (Dr. Bellanti), 131, 173 (Dr. Zweiman); 616-17 (Dr. Bellanti). Without establishing this basic postulate, the reliability of molecular mimicry as a viable theory in this case is questionable.

Furthermore, an article presented by respondent's expert, Dr. Zweiman, caused Dr. Bellanti "to seek another explanation." Tr. 203. In the article, a set of researchers vaccinated people who already had chronic autoimmune hepatitis with the hepatitis B vaccine. If the hepatitis B vaccine could cause autoimmune hepatitis, the expected result is an aggravation or exacerbation of the underlying condition. However, the people's condition did not worsen. Tr. 129-30, 184-85; exhibit 1004 (J. Beran, Safety and Immunogenicity of a Combined Vaccine

[5] This decision does not comment upon whether molecular mimicry is a reliable theory connecting other vaccines and other diseases.

Against Hepatitis A and B in Patients with Autoimmune Hepatitis, 13 Cent Eur J Pub Health, 20-3 (2005)). This lack of an adverse consequence undermines the reliability of molecular mimicry as a theory.

Dr. Bellanti agreed. He stated the Beran article "doesn't support molecular mimicry . . . so we have to seek another explanation." Tr. 203; accord tr. 970. Dr. Bellanti's retreat from a theory that he proposed is a poor mark on his credibility as an expert.[6]

b. Bystander Activation

Dr. Bellanti's second theory to explain how the hepatitis B vaccine can cause autoimmune hepatitis is bystander activation, although this theory is not one he prefers. Tr. 24, 90, 201. Dr. Bellanti's explanation of this theory was confusing. He stated that the innocent bystander is "where an immune reaction occurs because of the cytokines and all of the other molecules are being synthesized a normal tissue is involved and damaged." Tr. 24. A preponderance of the evidence does not support a finding that bystander activation is a reliable theory linking the hepatitis B vaccine to autoimmune hepatitis.

Other than Dr. Bellanti's own testimony, Ms. Hager presented little evidence to show that bystander activation is a reliable theory for this case. Dr. Zweiman's testimony supplied some confirmation that researchers have explored bystander activation in experimental models and have found it exists with other substances that stimulate the immune system. Tr. 180. However, Ms. Hager did not present evidence to explain why this theory about some antigens provides information about the hepatitis B vaccine specifically. Because the hepatitis B vaccine contains a single, non-replicating protein, there is no evidence that this antigen causes any bystander activation.

With regard to the hepatitis B vaccine specifically, the Institute of Medicine ("IOM") has investigated the theory of bystander activation and found that this theory is weak. Exhibit 1005 (Institute of Medicine, Immunization Safety Review: Hepatitis B Vaccine and Demyelinating Neurological Disorders (Kathleen Stratton et al. eds. (2002)) 64, 69; tr. 138, 195, 883.

Dr. Bellanti presented no response to the IOM's report, which had been filed before he testified. He was questioned about this report during cross-examination and merely said the IOM has its opinion. Tr. 89. Although given an opportunity to conduct re-direct examination, Ms. Hager's counsel did not. Tr. 109.

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[6] A troubling aspect about Dr. Bellanti's retreat is that respondent presented the Beran article several months before Dr. Bellanti testified. This time was ample for Dr. Bellanti to reconsider his opinion about molecular mimicry. Nevertheless, Dr. Bellanti not only presented molecular mimicry as a theory, he also said it was a theory he "favored." Tr. 90, 201.

Reports from the IOM are favored, although not dispositive, in the Vaccine Program. Cucuras v. Sec'y of Health & Human Servs., 993 F.2d 1525, 1529 (1993) (finding that special master did not abuse his discretion in determinating that a 1991 IOM report was entitled to great weight); Cohen v. Sec'y of Health & Human Servs., Fed. Cl. 94-353V, 1998 WL 408784 *8 (Spec. Mstr. July 1, 1998). Furthermore, Dr. Zweiman explained why he thought the IOM's report is authoritative – primarily because the IOM draws experts from many different fields who are not biased or prejudiced in evaluating the evidence. Tr. 135-36.

Dr. Bellanti may disagree with the IOM's conclusion that the hepatitis B vaccine does not induce bystander activation. However, for Dr. Bellanti's disagreement to be relevant, his opinion must be reliable. Knudsen, 35 F.3d at 548. Reliability, at least in this context, requires that Dr. Bellanti offer some reason for disagreement. For example, a logical argument might be that research conducted after the IOM issued its report in 2002, which the IOM could not have considered, has raised doubts about the IOM's conclusion. But, Dr. Bellanti did not proffer any reasoning. Instead, his response to a question about the IOM's report was to say that the IOM has its "opinion." Tr. 89. Shortly following this passage, Dr. Bellanti again said that the authors of the IOM report "are entitled to their opinion. They are not infallible, and perhaps uninformed." Tr. 97.

Dr. Bellanti's disagreement with the IOM is neither reliable nor persuasive. The context of Dr. Bellanti's use of the term "opinion" is comparable to how people commonly express disputes over matters of style and taste. These can be matters of "opinion." The IOM's study is not an "opinion" in that sense. The IOM examined available data and reached a conclusion. If Dr. Bellanti believes that the IOM was "uninformed," then it is incumbent upon Dr. Bellanti to identify the information that the IOM lacked. Pointing out the fallibility of an investigation without specifying an error does not constitute reliable testimony.

As the party bearing the burden of proving that the hepatitis B vaccine caused autoimmune hepatitis, Ms. Hager was responsible for presenting a reliable theory. Althen, 418 F.3d at 1278 (quoting Grant v. Sec'y of Health & Human Servs., 956 F.2d 1144, 1148 (Fed. Cir. 1992)). Ms. Hager did not. Dr. Bellanti's assertion that the bystander activation theory is a reliable method to explain how the hepatitis B vaccine can cause autoimmune hepatitis is tantamount to a statement ipse dixit. Pursuant to Terran, which affirmed using Daubert in vaccine cases to evaluate an expert's theory, special masters are not required to accept an expert's theory merely because an expert himself said it. Kumho Tire Co., Ltd. v. Carmichael, 526 U.S. 137, 157 (1999) (quoting General Elec. Co. v. Joiner, 522 U.S. 136, 137 (1997)). "[W]ithout more than credentials and a subjective opinion, an expert's testimony that 'it is so' is not admissible." Hathaway v. Bazany, 507 F.3d 312, 318 (5th Cir. 2007) (citation and quotation marks omitted) (affirming district court's decision to exclude testimony of proposed expert). As such, a preponderance of the evidence indicates that bystander activation is not a reliable theory to explain how the hepatitis B vaccine could cause autoimmune hepatitis.

c. Polyclonal Activation

The third theory offered by Dr. Bellanti is known as polyclonal activation. This theory postulates that an antigen, such as the hepatitis B vaccine, stimulates the production of too many B-cells and that these excess B cells lead to autoimmune disease. Tr. 24 (Dr. Bellanti), 881 (Dr. Zweiman).

Other than Dr. Bellanti's own assertions, a minimal amount of evidence supports a finding that polyclonal activation is a reliable theory. First, Dr. Zweiman recognizes that some antigens will stimulate an immune response that is broad-based, not limited to a response against one antigen. Tr. 139. Thus, investigators have looked for polyclonal activation to explain autoimmune disease. Tr. 181. Whether polyclonal activation has actually been found to cause an autoimmune disease is not clear.

The second piece of evidence that lends some support to the polyclonal activation theory is the set of antibodies found in people with autoimmune hepatitis. People with autoimmune hepatitis sometimes have elevated levels of antibodies, but the presence of autoantibodies does not definitively establish that the person has an autoimmune disease. It is extremely important to note that the elevated antibodies have not been found to cause autoimmune hepatitis. Tr. 27, 135, 176, 462 (Dr. Koff), 618 (Dr. Bellanti), 922-23.

Despite some evidence supporting the reliability of the polyclonal activation theory in general, evidence about the hepatitis B vaccine is missing. According to Dr. Zweiman, there is no evidence that the hepatitis B vaccine is an antigen that induces polyclonal activation. Tr. 140, 881-82. The IOM report underlies Dr. Zweiman's opinion. Exhibit 1005 (Institute of Medicine, Immunization Safety Review: Hepatitis B Vaccine and Demyelinating Neurological Disorders (Kathleen Stratton et al. eds. (2002)) at 64, 69.

Dr. Bellanti did not produce any affirmative evidence showing that the hepatitis B vaccine produces polyclonal activation. Because Dr. Zweiman presented his "no evidence" opinion during the first session, the nearly six months between sessions gave Dr. Bellanti sufficient time to counter Dr. Zweiman's assertion. In other contexts, Dr. Bellanti did in fact conduct additional research and presented new articles during the second session. See, e.g., tr. 1204-07. Dr. Bellanti's failure to present rebuttal articles about polyclonal activation strongly suggests that there are no articles showing that the hepatitis B vaccine stimulates polyclonal activation.

Without any information to suggest that Dr. Bellanti's assertion that the hepatitis B vaccine stimulates a "polyclonal activation" of the immune system resulting in autoimmune disease is reliable, Ms. Hager fails to meet her burden of introducing reliable evidence. In short, on the one hand, there is Dr. Bellanti's testimony. This testimony is tempered by his admission that polyclonal activation is not a theory he favors. Tr. 90, 201. On the other hand, there is the testimony of Dr. Zweiman corroborated by the report from the IOM. When the weight of the

evidence so greatly favors one side, a finding that Dr. Bellanti's theory is reliable cannot be made.

d. Dysfunction in T-regulatory cells

Dr. Bellanti's fourth theory for explaining how the hepatitis B vaccine can cause autoimmune hepatitis "involves participation of CD4+ regulatory T cells." Exhibit 15 at 4. This theory involves a deeper understanding of the immune system, and is necessarily more complicated. The complication, however, is not the flaw. The problem with the "theory" is that it is not a theory that postulates how the hepatitis B vaccine can cause autoimmune hepatitis. Instead, the comment about dysfunction in T-regulatory cells is an observation about some people with autoimmune diseases. The observation exists without the hepatitis B vaccine.

To show how Dr. Bellanti's comments do not amount to a theory explaining a causal role for the hepatitis B vaccine, a portion of his report is quoted below. This passage is all that Dr. Bellanti wrote about T-regulatory cells. He states:

> These [T-regulatory cells] have been identified as the cells that maintain immunologic tolerance, the property of the immune system which distinguishes one's own tissues as self from those exogenous materials which are recognized as "non-self." The failure of, or escape from, normal suppression of reactivity against "self" has an essential role in the development of autoimmune disease. Studies suggest that a decrease in the number of regulatory T cells and their ability to expand may lead to autoimmune liver disease.

Exhibit 15 at 4. Noticeably absent from this passage is any reference to vaccines.

Dr. Bellanti's testimony did not fill this gap. He explained how T-regulatory cells function. Tr. 14-19. In doing so, he noted that a current theory to explain the pathogenesis of autoimmune disease is that the regulation of T-cells is not working properly. Tr. 16. Dr. Zweiman offered some limited support for the theory that immunologists believe that problems with T-regulatory cells may lead to autoimmune disease. Tr. 181-82, 1099.

As support for his assertion that a problem with regulatory T cells may contribute to causing autoimmune hepatitis, Dr. Bellanti identified an article by Longhi during the hearing. Tr. 45. Because this article seemed important, the Court introduced it as an exhibit during the hearing. Tr. 1103-04. On cross-examination, Dr. Bellanti tried to clarify his opinion. He stated:

> Whether [T-regulatory cells] produce, you know, specifically, you can say definitively they cause autoimmune hepatitis, I can't say that definitively, but I can say it's my opinion based on my knowledge, putting it all together that they do; that it in some way is related. It's more probable than not.

Tr. 91.

For sake of argument, Dr. Bellanti's assertion that a problem (an imbalance) with the regulatory T cells causes, in some way, autoimmune hepatitis can be accepted. (Dr. Zweiman did not agree with Dr. Bellanti on this point. Dr. Zweiman noted that although a problem with regulatory T cells may be associated with autoimmune hepatitis, it is unclear which came first. It is possible that the autoimmune hepatitis causes the defect in T regulatory cells. Tr. 143, 1131.) But, Dr. Bellanti's assertion again says nothing about the role of the hepatitis B vaccine. Questioning from the Court on the first day of the hearing revealed the hole in Dr. Bellanti's "theory." This passage is quoted at length to demonstrate the limits of Dr. Bellanti's statement:

> THE COURT: The T-regulatory deficiency, I understand you saying that the immune system gets out of balance. Is that right?
>
> THE WITNESS: Yes. There is an imbalance, that's correct.
>
> THE COURT: But is it your theory that something in the hepatitis B vaccine causes the T- cell regulatory deficiency?
>
> THE WITNESS: That isn't known, Your Honor. You know, the publication I think that was referred to in the article simply referred to deficiency in patients with autoimmune hepatitis. Whether it was the cause or the result, it isn't clear.
>
> If you ask my opinion, I would favor it being a preexisting deficiency, but I have no direct evidence for that. That would be speculative.
>
> THE COURT: You mean preexisting, existing before the introduction of the antigen?
>
> THE WITNESS: No. Because of the genetic relationships of the effects of genetic control on the immune system and because of the genetic relationships that are known to occur with patterns of certain HLA types in certain patients with autoimmune disease, this is a distinct possibility.
>
> Whether it will turn out to be, I don't know, but it's very attractive, and it is the center of current research in the field of immunology. This is a very hot field. You know, the regulation of the immune system, how antigen is recognized, processed and delivered determines in all cases the ultimate success or failure of elimination, and that ties in with autoimmune disease, but it's all inferential.
>
> THE COURT: Now, the imbalance in the T-regulatory system would be genetic-based?
>
> THE WITNESS: Yes.
>
> THE COURT: So is it your theory that the introduction of the hepatitis B vaccine would trigger the adverse effects of this imbalance?
>
> THE WITNESS: No, I would say that in certain genetically predisposed individuals, their response to certain vaccines leads to adverse

> effects due to this genetic inability to handle the antigen as that bell-shaped curve -- 95-99 percent of the population.
>
> There is [sic] these outliers that are responding differently, and those are the unfortunate ones that get into trouble with vaccines. There is documentation that there is a T-reg deficiency in autoimmune disease. Whether it's in the case of hepatitis B that was caused by the vaccine, or it was a preexisting condition which led subsequently to their autoimmune disease. I honestly don't know. I would favor that but I have no direct evidence for that.

Tr. 107-09 (emphasis added). As the emphasized portion illustrates, Dr. Bellanti could not connect the hepatitis B vaccine to his belief that an imbalance in T-regulatory cells causes autoimmune hepatitis.

Later testimony did not link the observation in the Longhi article that people with autoimmune hepatitis have an imbalance in their T-regulatory cells with the hepatitis B vaccine. T-regulatory cells were discussed in the context of a particular petitioner, Ms. Rotoli, who did not respond to the hepatitis B vaccine. See, e.g., tr. 620. Yet, no testimony showed how the hepatitis B vaccine connects to an imbalance in T-regulatory cells.

Even after the hearing resumed following a six-month suspension, petitioners did not elicit testimony offering, in any sense, a basis for linking the hepatitis B vaccine with a problem in T-regulatory cells. Dr. Zweiman pointed out that the Longhi article studied people who had autoimmune hepatitis, not people who received the hepatitis B vaccine. Tr. 1100, 1130-32. Dr. Zweiman described the limits of medical knowledge. He stated that "nobody has ever reported whether or not hepatitis immunization induces alteration of immunoregulatory T-cells." Tr. 1132. Dr. Bellanti did not contradict Dr. Zweiman's statement, which seems to be in accord with Dr. Bellanti's testimony quoted at length above.

Petitioner's cause of action is that the hepatitis B vaccine caused autoimmune hepatitis. Dr. Bellanti's statements about the role of the T-regulatory cells are not relevant because no evidence connected a problem with T-regulatory cells to the hepatitis B vaccine. Therefore, statements about T-regulatory cells do not qualify as "a medical theory causally connecting the vaccination and the injury." Althen, 418 F.3d at 1278.

e. Other Arguments in Favor of a Causal Relationship Between the Hepatitis B vaccine and Autoimmune Hepatitis

Dr. Bellanti makes two other observations that he says support a causal relationship, although these observations are not directly tied to any of the four theories discussed above. One is an argument that because the hepatitis B virus can cause autoimmune hepatitis, the vaccine is presumed to be capable of causing the same disease. Another is the argument based on challenge

- rechallenge. Neither observation supports a finding that the hepatitis B vaccine can cause autoimmune hepatitis.

(1) Is the Hepatitis B Vaccine Analogous to the Hepatitis B Virus in Causing Autoimmune Hepatitis?

Dr. Bellanti wrote in his report that because the hepatitis B virus causes autoimmune disease, "it should be assumed that the vaccine [for that virus] can also lead to autoimmunity." Exhibit 15 at 3. Even Dr. Bellanti's choice of words are problematic in that he states that "it should be assumed" that the vaccine is similar to the virus in that it can cause autoimmunity. To "assume" means to take something for granted or without proof. Assumptions are not evidence in vaccine cases.

In his testimony, Dr. Bellanti refined his position to some extent. Tr. 34, 93, 200. There are two problems with Dr. Bellanti's argument. One is the proposition that the hepatitis B virus causes autoimmune hepatitis. The other is whether the hepatitis B vaccine is analogous to the hepatitis B virus.

(a) Does the Hepatitis B Virus Cause Autoimmune Hepatitis?

A preponderance of the evidence establishes that the hepatitis B virus does not cause autoimmune hepatitis. Therefore, Dr. Bellanti errs when he states that "infection with the hepatitis B virus is known to cause autoimmune hepatitis." Exhibit 15 at 3.

Dr. Bellanti offers only a scintilla of support for his statement. Significantly, in his report, Dr. Bellanti did not identify any sources for his proposition. This omission seems inconsistent with a fact that Dr. Bellanti asserts "is known."

In his testimony on the first day of hearing, Dr. Bellanti introduced a textbook to support his statement. Dr. Bellanti cites the third edition of a textbook, The Autoimmune Diseases, edited by Noel Rose and Ian Mackay. Tr. 78-83. This textbook appears to support Dr. Bellanti's assertion. Exhibit 37 (Michael P. Manns et al., Chapter 26: Autoimmune Diseases: The Liver, in The Autoimmune Diseases (Noel R. Rose and Ian R. Mackay, eds., 3d ed. 1998)) at 518.[7]

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[7] Dr. Zweiman criticizes Dr. Bellanti for using the third edition of the Rose and Mackay textbook. Dr. Zweiman observes that a chapter on "Chronic Hepatitis" from the fourth edition of this textbook does not mention the hepatitis B virus causing autoimmune hepatitis. Tr. 144.

This criticism is off base for two reasons. First, this chapter uses the phrase "hepatitis viruses." Although Dr. Zweiman is correct in saying that the hepatitis B virus is not specifically mentioned, the more general term "hepatitis viruses" includes the hepatitis B virus. Secondly, to the extent that Dr. Zweiman is implying that the third edition of the Rose and Mackay textbook is

However, further examination indicates that the textbook's statement was in error. The textbook itself cites two articles. One from 1989 written by Laskus and Slusarczky. (The transcript of the hearing mistakenly shows the first author as "Velascquez.") The other was from 1984, and was written in German by Hopf and Möller.

Current medical knowledge strongly suggests that current doctors would not accept the diagnoses of autoimmune hepatitis from these case reports, which are more than 15 years old. The patient in the German study actually had chronic hepatitis B, not autoimmune hepatitis. Tr. 458-59, 854 (Dr. Koff's testimony). Similarly, the subject of the article by Laskus probably had hepatitis C, not autoimmune hepatitis. Tr. 460, 854.

After learning Dr. Koff's views about the Laskus and Hopf articles, Dr. Bellanti performed more research. He discovered two other articles that, initially, seem to offer some modest support for his assertion that "infection with the hepatitis B virus is known to cause autoimmune hepatitis." (Why Dr. Bellanti did not cite these articles in his initial report was not explained adequately.) However, neither article is persuasive.

In one article, an exacerbation of autoimmune hepatitis was associated with an administration of the Twinrix vaccine. Exhibit 44 (Antal Csepregi et al., Acute Exacerbation of Autoimmune Hepatitis Induced by Twinrix, 11 World J. Gastroenterol., 4114-116 (2005)). Twinrix contains a vaccine against hepatitis A and a vaccine against hepatitis B. Tr. 1035, 1121. Although the presence of another vaccine confounds the analysis, the case report is weak evidence for another reason.

The problem with the Csepregi article is that it is a report about one case. As such, ruling out a possible coincidence is impossible. Case reports have little reliability in establishing causation. See, e.g., McClain v. Metabolife Intern., Inc., 401 F.3d 1233, 1253 (11th Cir. 2005); Meister v. Medical Engineering Corp., 267 F.3d 1123, 1129 (D.C. Cir. 2001); Glastetter v. Novartis Pharmaceuticals Corp., 252 F.3d 986, 989-90 (8th Cir. 2001). The symptoms of autoimmune hepatitis worsen episodically. Exhibit 15, Tab A (Krawitt) at 56; tr. 1145 (Dr. Koff's testimony). A worsening of symptoms may have occurred in the patient reported by Csepregi around the same time after he received the Twinrix. The Twinrix may have not caused the exacerbation of the autoimmune hepatitis. Tr. 1120-23 (Dr. Zweiman testimony); 1145-46, 1149 (Dr. Koff's testimony).

The final article that Dr. Bellanti presented to demonstrate that "infection with the hepatitis B virus is known to cause autoimmune hepatitis," concerns a child from Senegal. Doctors discovered that this child had both a chronic hepatitis B infection and autoimmune hepatitis. Exhibit 50 (Valerio Nobili et al., Co-occurrence of Chronic Hepatitis B Virus Infection

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out-of-date and that the fourth edition eliminates any mention of the hepatitis B virus, respondent should have submitted the corresponding chapter, chapter 26, from the fourth edition. The same chapters from different editions create an apples-to-apples comparison.

and Autoimmune Hepatitis in a Young Senegalese Girl, 18 Eur. J. Gastroenterol Hepatol., 927-29 (2006)). This article, however, provides no information about which condition came first. Therefore, it is speculative to assume that the hepatitis B infection caused the autoimmune hepatitis. The patient may have had autoimmune hepatitis before being infected with the hepatitis B virus. Tr. 1116-20 (Dr. Zweiman's testimony); 1144-45, 1147-48 (Dr. Koff's testimony).

Therefore, at best, Dr. Bellanti identified four articles that minimally support the proposition that the hepatitis B virus can cause autoimmune hepatitis. However, two articles were from the 1980's and, probably, do not represent current medical analysis. The two articles from this decade (Csepregi and Nobili) do not contain any meaningful analysis about causation. Thus, the persuasiveness of these articles is lacking.

Although the articles presented by Dr. Bellanti offer some minimal support for his assertion that "infection with the hepatitis B virus is known to cause autoimmune hepatitis," other evidence contradicts the assertion. The strongest contrary evidence is the scholarly article by Dr. Edward Krawitt, who is generally considered among the world's leading researchers in autoimmune hepatitis. Tr. 813. He wrote a review for the New England Journal of Medicine that all the experts cited. In this article, Dr. Krawitt states that autoimmune hepatitis has been associated with hepatitis A infection and hepatitis C infection. Exhibit 15, tab A, at 54. However, Dr. Krawitt omits the hepatitis B virus. Id.; see also tr. 75-76.

Omitting the hepatitis B virus from the viruses considered as possible triggers for autoimmune hepatitis was intentional. (Hepatitis A, hepatitis B, and hepatitis C are three completely different viruses. Tr. 59, 473-74.) Dr. Koff recounted that between sessions of hearings in these cases, he spoke to Dr. Krawitt and two other experts in autoimmune hepatitis. All three experts told Dr. Koff that they were not aware of the hepatitis B virus causing autoimmune hepatitis. Tr. 989-92. Their statements match Dr. Koff's own statements during the first session of the hearing. Tr. 437. Collectively, this evidence is very persuasive.

Thus, a preponderance of the direct evidence regarding the hepatitis B virus contradicts an assertion that it can cause autoimmune hepatitis. Although Dr. Bellanti can state with a fair degree of support that viruses in general are thought to cause autoimmune diseases in general, this general proposition does not make up for the lack of more specific evidence linking the hepatitis B virus to autoimmune hepatitis.

(b) Is the Hepatitis B Vaccine Analogous to the Hepatitis B Virus?

Even assuming that the hepatitis B virus causes autoimmune hepatitis, Dr. Bellanti's reasoning that "it should be assumed" that the vaccine can cause the same result is questionable. Differences between the hepatitis B vaccine and hepatitis B virus require an analysis rather than an assumption.

The Institute of Medicine offers some general support for Dr. Bellanti's reasoning. The IOM has stated that "the vaccine-adverse event association should be plausible and coherent with current knowledge about the biology of the vaccine and the adverse event. Such information includes experience with the naturally occurring infection against which the vaccine is given, particularly if the vaccine is a live attenuated virus." Exhibit 58 (Vaccine Safety Committee, Institute of Medicine, Adverse Events Associated with Childhood Vaccines: Evidence Bearing on Causality (Kathleen R. Stratton et al. eds. 1994)) at 22.

However, extending this proposition to vaccines, such as the hepatitis B vaccine, that do not contain a "live attenuated virus," is uncertain. Tr. 1127-28 (Dr. Zweiman's testimony). The hepatitis B vaccine does not replicate in the body. Tr. 85-86 (Dr. Bellanti's testimony).

Dr. Bellanti maintains that non-replicating vaccines and vaccines that contain live viruses, which replicate in the body, prompt a similar immune response that can, in rare cases, include an adverse consequence. Tr. 34, 63-64.

During Dr. Bellanti's testimony, he recognized how a vaccine containing a live virus interacts with a person's immune system differs from how a vaccine containing inert material interacts. He was forced to backtrack and to revise his statement to the more general proposition that a person's immune system follows the same steps in responding to a foreign invader regardless of whether the invader is a live virus or a non-replicating protein. Tr. 200, 372, 1128, 1593. This revised statement is accurate. However, its generality provides no information to connect the hepatitis B vaccine and autoimmune hepatitis.

Whether a preponderance of the evidence supports Dr. Bellanti's reasoning is unnecessary to decide. Whether the hepatitis B vaccine is comparable to the hepatitis B virus is relevant in this case only to the extent that the hepatitis B virus is capable of causing autoimmune hepatitis. The preceding section explains that a preponderance of the evidence contradicts this assertion. Therefore, Dr. Bellanti's belief about the hepatitis B virus does not help establish a reliable medical theory.

(2) Challenge - Rechallenge

A second assertion made by Dr. Bellanti to support his overall theory that the hepatitis B vaccine can cause autoimmune hepatitis is that "[t]here are reports in the literature of positive rechallenge where [the hepatitis B vaccine] has been reported to cause various autoimmune conditions." Exhibit 15 at 4.

"A rechallenge event occurs when a patient who had an adverse reaction to a vaccine suffers worsened symptoms after an additional injection of the vaccine." Capizzano v. Sec'y of Health & Human Servs., 440 F.3d 1317, 1322 (Fed. Cir. 2006). Rechallenge can be persuasive evidence that a vaccine is causing an adverse reaction. Tr. 35-36.

Whether literature actually includes cases of rechallenge with the hepatitis B vaccine is not clear. In his report, Dr. Bellanti did not cite any literature for this proposition. Likewise, Dr. Bellanti did not discuss literature about rechallenge in his testimony. See tr. 55-69 (discussing articles). Considering that Dr. Bellanti's report refers to "reports in the literature," his silence on this topic is somewhat surprising (and telling).

Once again, Dr. Bellanti failed to meet the expectations that he himself set. On cross-examination, Dr. Bellanti was asked about rechallenge. Tr. 102-3.

Because the Court's May 31, 2007 order raised this issue specifically, Dr. Bellanti should have expected the question. However, Dr. Bellanti did not know the answer and stated that he needed to review what he submitted. Tr. 103. This evasive answer decreased Dr. Bellanti's credibility.

Furthermore, Dr. Bellanti was questioned about the Beran article. In this study, people with autoimmune hepatitis were given the hepatitis B vaccination. The subjects tolerated exposure to the hepatitis B vaccine without experiencing a worsening of the underlying autoimmune hepatitis. Tr. 199-203, exhibit 1004 (J. Beran, Safety and Immunogenicity of a Combined Vaccine Against Hepatitis A and B in Patients with Autoimmune Hepatitis, 13 Cent Eur J Pub Health, 20-3 (2005)). This article, therefore, is evidence contrary to Dr. Bellanti's unsubstantiated assertion.[8]

f. Summary regarding Medical Theory

Ms. Hager bears the burden of proposing "a medical theory causally connecting the vaccination and the injury." Althen, 418 F.3d at 1278. A theory is not required to be established to a level of medical certainty and does not need to describe the precise biological mechanism. Nevertheless, the theory must have some minimal level of reliability. Knudsen, 35 F.3d at 548; Bunting, 931 F.2d at 873.

Here, through Dr. Bellanti, Ms. Hager offers four medical theories. None of these theories satisfies Ms. Hager's burden of proof. Dr. Bellanti withdrew the molecular mimicry theory primarily because no evidence shows a homology between parts of the hepatitis B vaccine and liver cells that are attacked by autoimmune hepatitis. The IOM has rejected two other theories, bystander activation and polyclonal activation. Dr. Bellanti did almost nothing to justify these two theories, which are theories that, by his own admission, he does not favor, nor did he rebut the IOM's investigation and conclusion. The fourth theory, T-regulatory deficiency, is not really a theory in the sense that it does not involve the hepatitis B vaccine.

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[8] Requesting Dr. Bellanti to substantiate his statement does not violate Althen's statement that experts are not required to produce literature. It was Dr. Bellanti who stated "[t]here are reports in the literature of positive rechallenge." Dr. Bellanti's inability to prove what he wrote implicates his persuasiveness and his veracity.

In addition, Dr. Bellanti offered two other points that, arguably, could support an argument that the hepatitis B vaccine can cause autoimmune hepatitis. However, these too were not persuasive. A preponderance of the evidence shows that the hepatitis B virus has not been shown to cause autoimmune hepatitis. Also, the evidence in this case does not establish examples of positive rechallenge with the hepatitis B vaccine.

For all these reasons, Ms. Hager has failed to meet her burden of establishing, by a preponderance of the evidence, a medical theory connecting the hepatitis B vaccine to autoimmune hepatitis.

2. Timing

Although temporal sequence is listed as the third factor in Althen, discussing it before the second factor makes more sense in Ms. Hager's case. As the petitioner, Ms. Hager bears the burden of establishing the appropriate temporal relationship between the vaccination and the onset of the condition for which she seeks compensation. Pafford v. Sec'y of Health & Human Servs., 451 F.3d 1352, 1358 (Fed. Cir. 2006).

Whether a petitioner meets her burden of establishing the third prong from Althen involves two subsidiary issues. First, after the vaccination, in how much time does the medical community expect an adverse reaction to appear? Second, when did the adverse reaction actually appear?

On both points, Dr. Bellanti's written report provides little, if any, helpful information. It states "[t]he temporal relationship between her immunizations and the onset of symptoms is medically appropriate." Exhibit 15 at 7. This general statement does not say what the time is in which a reaction is expected to occur. Nor does Dr. Bellanti's report state when Ms. Hager's symptoms actually began.

At least for the first sub-issue, during his testimony, Dr. Bellanti provided a more definitive statement. He asserted that a reasonable time to expect a causal relationship is 14 days to 40 days after a vaccination. Tr. 34. Dr. Berger, who testified in regard to Ms. Hager, specifically, agreed that an autoimmune process is likely to take a matter of weeks, not months. Tr. 381-82. Neither party elicited any testimony about the appropriate temporal relationship from the other immunologist who testified on the general causation issue. See tr. 111-203 (Dr. Zweiman). Therefore, Dr. Bellanti's testimony that the appropriate window is 14 - 40 days after vaccination is credited.

On the second issue, when Ms. Hager first experienced an adverse reaction, Dr. Bellanti's testimony is ambiguous. Dr. Bellanti asserts that the temporal relationship is appropriate for two different sequences. First, Dr. Bellanti suggests that the second dose of the hepatitis B vaccine, given in December 1997, caused an autoimmune disease that was first manifest in July 1998. Under this theory, the third dose of the hepatitis B vaccine exacerbated an underlying, but

smoldering, problem. Tr. 230-31, 246. The alternative theory is that the third dose of the vaccine started a brand new disease that became manifest three weeks later. Id., see also tr. 221. Between these two alternatives, Dr. Bellanti did not know which is more correct. Tr. 230.

Determining when Ms. Hager's disease began is difficult. Autoimmune hepatitis can begin insidiously. People can have inflammation in their liver without experiencing any symptoms. Sometimes, the problem in the liver first is detected in an abnormal result on a routine liver function test. Exhibit 15, Tab A (Krawitt at 56-57).

The other (more probable) disease for Ms. Hager is PSC. This condition, too, may appear insidiously. Tr. 369 (testimony of Dr. Berger), 440 (testimony of Dr. Koff), exhibit K (Angulo, Small-duct Primary Sclerosing Cholangitis), exhibit I (Abdalian & Heathcote, Sclerosing Cholangitis).

Thus, under either diagnosis, determining when Ms. Hager's condition began is challenging. The two immunologists who testified about Ms. Hager's case did not state when Ms. Hager's disease began. Tr. 230 (testimony of Dr. Bellanti), 244 (same), 383 (testimony of Dr. Berger).

Although determining a date when Ms. Hager's condition began is difficult, a preponderance of the evidence establishes that Ms. Hager's disease began before the first dose of the hepatitis B vaccine. The primary evidence supporting this conclusion are that Ms. Hager's September 1999 biopsy and her liver ultrasound in September 1999.

The September 1999 biopsy results showed fibrosis, indicating a disease that had been present for more than one year. Fibrosis develops from existing scar tissue, meaning that the disease has been present for a long time. Tr. 209, 212, (Dr. Bellanti), 241, 252 (Dr. Koff), 383 (Dr. Berger); see also tr. 808 (discussing stages of liver disease). The result of the September 1999 biopsy implies that Ms. Hager must have been suffering from a disease for at least one year because if she was suffering from the disease for less than one year, she would not have fibrosis.

Additional information comes from Ms. Hager's liver ultrasound in September 1999. This test showed some enhanced echogenicity. Exhibit 7 at 135. This result is consistent with the beginnings of cirrhosis. Cirrhosis, in turn, indicates that the fibrosis itself has been present "for years." Tr. 435 (testimony of Dr. Koff). Ms. Hager presented no evidence to the contrary. If the cirrhosis develops only after the fibrosis has been present "for years," then a reasonable inference is that the fibrosis itself must have started at least two years earlier. Two years earlier from September 1999 is September 1997. A reasonable inference from the biopsy and the ultrasound is that the onset of Ms. Hager's underlying disease must be no later than September 1997.

The finding that Ms. Hager's disease began no later than September 1997 is based upon the test results and an explanation of the significance of those test results by Dr. Koff. Dr. Koff

provided helpful information about the progression of liver diseases through different stages. Tr. 808. Dr. Koff also interpreted the reports from Ms. Hager's tests. Tr. 435. Although Dr. Koff also testified that Ms. Hager's "disease cannot be dated," tr. 426; he did provide some information about how long Ms. Hager's disease must have been present before the September 1999 ultrasound and biopsy revealed fibrosis and the beginnings of cirrhosis. For purposes of deciding the issues in this case, it is not necessary to make a finding more specific than the disease was present in September 1997.

September 1997 works as a pertinent date because Ms. Hager received the hepatitis B vaccinations only after September 1997. Exhibit 3 at 1-2 (showing vaccinations on November 17, 1997, December 17, 1997, and September 29, 1998).

The combined effect of the chronology of vaccinations and the finding that Ms. Hager began suffering from a disease in September 1997 necessarily means that the hepatitis B vaccines did not cause the disease. Each disease has only one onset. Shalala v. Whitecotten, 514 U.S. 268, 274 (1995).[9]

This finding means that Ms. Hager has not established the third element listed in Althen – the temporal relationship between the vaccination and the onset of her disease. The disease began before the vaccination. Therefore, the vaccines did not cause the disease.

3. Logical Sequence of Cause and Effect

The remaining element from Althen warrants little discussion. The preceding sections have found that Ms. Hager has not presented a reliable theory linking her hepatitis B vaccinations to her disease and that Ms. Hager has not established an appropriate temporal relationship. The reasons supporting the findings that Ms. Hager has not met her burden of proof on those elements also support finding that Ms. Hager has failed to meet her burden of proof on this element as well.

Consequently, even if Ms. Hager is assumed to have suffered from autoimmune hepatitis, she has not established any of the elements required by Althen. For reasons explained in section IV.B., above, she also did not establish that the hepatitis B vaccine caused her sclerosing cholangitis. The only remaining issue in determining whether Ms. Hager is entitled to compensation is whether she established that the hepatitis B vaccine significantly aggravated a pre-existing condition.

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[9] The finding that Ms. Hager's disease existed before she received the first dose not necessarily preclude an award of compensation. She is entitled to recover compensation if she establishes, by a preponderance of the evidence, that the hepatitis B vaccine "significantly aggravated" her underlying disease. 42 U.S.C. § 300aa-11(c)(1)(C)(ii)(I). Section IV.D., below, explains why Ms. Hager has not established this alternative theory.

D. Did Ms. Hager Suffer A Significant Aggravation?

A preponderance of the evidence establishes that Ms. Hager was suffering from sclerosing cholangitis before she received the hepatitis B vaccine. This finding means that Ms. Hager cannot prevail on her theory that the vaccine caused her injury. However, in theory, Ms. Hager could pursue a claim that the hepatitis B vaccine significantly aggravated the underlying sclerosing cholangitis. See 42 U.S.C. § 300aa–11(c)(1)(C)(ii)(I).

1. Procedural Posture

Determining whether Ms. Hager has maintained a significant aggravation claim is important because if she did not, then the issue is waived. Vaccine Rule 8(f). Although a fair argument could be made that Ms. Hager has waived this claim, it is found that she did not.

In Ms. Hager's initial petition, she simply alleged that she was "injured as a result of receiving a Hepatitis B vaccination." ¶ 3.

In November 2004, Ms. Hager filed medical records. One report states that although Ms. Hager was initially diagnosed with autoimmune hepatitis, by 2001, additional developments showed that her "liver disease was felt to be more consistent with sclerosing cholangitis." Exhibit 11 at 618 (report by Dr. Mary Ann Jackson dated June 18, 2004).

The special master ordered Ms. Hager to clarify her cause of action. Ms. Hager responded by stating, in part, that her "medical expert believes that while [Ms. Hager's] diagnosis may have changed, the preceding signs, symptoms, and diagnosis of autoimmune hepatitis are part of the same process that lead to [her] current state of health, including her diagnosis of sclerosing cholangitis, ulcerative colitis, cirrhosis, and hypersplenism." Pet'r Resp., filed Jan. 10, 2005.

In her amended petition, Ms. Hager stated that "[t]he record should be clear; [she] has autoimmune hepatitis." Ms. Hager also maintained that "primary sclerosing cholangitis . . . can also occur as a result of autoimmunity." Am. Pet., filed Oct. 10, 2006, ¶ 14. The amended petition concludes that Ms. Hager "has suffered autoimmune hepatitis as a result of the series of hepatitis B immunizations that she received, and all her subsequent disorders developed as a consequence of the autoimmune hepatitis." Id. ¶ 16.

Dr. Bellanti's report acknowledges that Ms. Hager was diagnosed with ulcerative colitis. However, Dr. Bellanti's concludes that Ms. Hager's "autoimmune hepatitis and associated sequalae were likely due to her hepatitis B immunization." Exhibit 15 at 7.

A fair reading of these pleadings indicates that Ms. Hager did not assert a cause of action that a hepatitis B vaccination significantly aggravated an underlying disease, regardless of whether the disease is considered autoimmune hepatitis or sclerosing cholangitis. Although the

December 3, 2004 order alerted Ms. Hager that medical records indicated that at least one doctor believed that Ms. Hager's diagnosis of autoimmune hepatitis was not accurate, Ms. Hager's amended petition continued to assert that she "has autoimmune hepatitis." Furthermore, the amended petition does not allude to significant aggravation at all.

Although Ms. Hager's pleadings do not assert a significant aggravation theory, respondent identified this possibility. About five months before the first session of the hearing, respondent suggested that the case could be viewed as a significant aggravation case. Resp't Status Rep't, filed Feb. 26, 2007. Ms. Hager did not amend her petition again.

During the hearing, some evidence regarding significant aggravation was introduced. Dr. Bellanti's testimony was muddled. He believed that two sequences were possible. First, the second dose of the hepatitis B vaccination caused autoimmune hepatitis and that the third dose exacerbated the disease. Second, the third dose of the hepatitis B vaccine caused the autoimmune hepatitis. Tr. 219, 221, 229-31. Under either scenario, Dr. Bellanti's medical theory is that one of the vaccines (either the second dose or the third dose) caused the autoimmune hepatitis.

In addition, both of respondent's experts opined about whether a vaccination significantly aggravated an underlying disease. Tr. 382, 385, 437, 441.

Finally, in a brief filed after the hearing, Ms. Hager asserted that she could prevail based upon a theory of significant aggravation. Pet'r Resp., filed July 28, 2008, at 10. This brief appears to be the first time that Ms. Hager filed a pleading alleging a theory of significant aggravation.

Under these circumstances, Ms. Hager has not waived a theory that the hepatitis B vaccine significantly aggravated an underlying disease. The two important factors are (1) respondent's February 26, 2007 status report raised this issue, and (2) some evidence about significant aggravation was introduced during the hearing. In this case, these two factors outweigh the opposing factor, which is Ms. Hager's failure to amend her petition to allege a theory based upon significant aggravation. Notably, Ms. Hager's assertion on July 28, 2008, which is after the hearing, does not contribute to the determination that the significant aggravation theory should be adjudicated on the merit. For example, if there were no evidence in the hearing discussing significant aggravation, Ms. Hager could not fairly claim for the first time that she is entitled to compensation pursuant to that theory. See Swords 44 Fed. Cl. at 191 (when counsel is not surprised, an additional opportunity to present evidence is not required).

2. Evaluation of the Evidence

Very little evidence supports a finding that Ms. Hager met her burden in establishing that a dose of the hepatitis B vaccine significantly aggravated any underlying disease. Consequently, Ms. Hager is not entitled to compensation based upon this theory.

Dr. Bellanti's testimony is not helpful. Dr. Bellanti's theories are that (a) the second dose caused the disease with exacerbation following the third dose, or (b) the third dose caused the disease. Tr. 230-31, 246. Both theories assume that Ms. Hager was not affected by any disease when she received the hepatitis B vaccinations.

However, Dr. Bellanti's assumption does not match the determination that Ms. Hager's disease existed before the before the first dose of the vaccination. See section IV.C.2., above. Therefore, Dr. Bellanti's testimony that the third dose of the vaccination significantly aggravated an underlying condition is not persuasive. When an expert's opinion depends upon facts that are not found to be accurate, the finder of fact may disregard the expert's opinion. nCube Corp. v. Seachange Intern., Inc., 436 F.3d 1317, 1323 (Fed. Cir. 2006); Perreira v. Sec'y of Health & Human Servs., 33 F.3d 1375, 1377 n.6 (Fed. Cir. 1994).

Dr. Bellanti's testimony is also flawed because he did not distinguish the course of her disease as it actually occurred from the course of her disease as it would have occurred if she did not receive the hepatitis B vaccines. See Gruber ex rel. Gruber v. Sec'y of Health & Human Servs., 61 Fed. Cl. 674 (2004) (discussing elements of proof in an on-Table significant aggravation case). This contrast between actual events and "but for" events was especially necessary in this case because both autoimmune hepatitis and sclerosing cholangitis are diseases that wax and wane unpredictably. Tr. 74. If Ms. Hager would have experienced the same symptoms in the absence of the hepatitis B vaccines, then the vaccines did not significantly aggravate her condition. Dr. Bellanti attributes worsening symptoms to a preceding vaccination. In doing so, Dr. Bellanti seems not to appreciate the possibility that the worsening symptoms may have followed a vaccination by a certain amount of time purely by coincidence.

Dr. Bellanti's testimony, by itself, does not establish that Ms. Hager is entitled to compensation pursuant to a theory that the hepatitis B vaccine significantly aggravated an underlying condition. The additional testimony from respondent's experts only weakens Ms. Hager's already tenuous theory. Both Dr. Berger and Dr. Koff opined that the hepatitis B vaccines did not significantly aggravate Ms. Hager's underlying condition. Tr. 382, 385, 437, 441.

Consequently, assuming that Ms. Hager has validly raised a theory that the hepatitis B vaccines significantly aggravated some underlying condition, she has not established a factual basis for her contentions. Therefore, she is not entitled to compensation pursuant to this theory as well.

V. Respondent's Request for a Hearing

As discussed in section II, above (the procedural history), respondent has made several requests for a fact hearing, most recently in a motion filed on July 18, 2008. Respondent argued that a fact hearing was necessary to establish the onset of Ms. Hager's disease. The onset of the

disease has been established in this decision without an additional fact hearing. Therefore, respondent's request for a hearing to determine the onset of the disease is denied.

As stated previously, determining when a person first begins to have sclerosing cholangitis is difficult because a person can have the disease without displaying any symptoms that would prompt medical attention. Exhibit C at 3; tr. 435. (The difficulty in determining the onset is also true for autoimmune hepatitis. Exhibit 15, tab A (Krawitt) at 56.)

Although difficult to determine, a preponderance of the evidence establishes that Ms. Hager began suffering from sclerosing cholangitis by September 1997. The evidence supporting this factual finding comes from two sources, Ms. Hager's liver biopsy and her ultrasound on September 23, 1999. The results from these tests, as interpreted by Dr. Koff, are sufficient to establish the onset of Ms. Hager's disease.[10]

On September 23, 1999, Ms. Hager had a liver ultrasound. This test showed some enhanced echogenicity. Exhibit 7 at 135. This result is consistent with the beginnings of cirrhosis. Tr. 435.

On September 24, 1999, Ms. Hager had a liver biopsy. The result of this test showed some fibrosis. Exhibit 7 at 139. Fibrosis develops from scar tissue, meaning that the disease has been present for a long time. Tr. 209, 212, (Dr. Bellanti), 241, 252 (Dr. Koff), 383 (Dr. Berger); see also tr. 808 (discussing stages of liver disease).

Dr. Koff, the expert in liver diseases, stated "it takes generally years before you can develop sufficient fibrosis to cause portal hypertension and to cause cirrhosis." Tr. 435. Dr. Koff's opinion is persuasive on this point and was not contested.

Consequently, a preponderance of the evidence establishes that Ms. Hager was suffering from her disease, which was previously found to be sclerosing cholangitis, by September 1997. Ms. Hager received the hepatitis B vaccinations on November 17, 1997, December 17, 1997, and September 29, 1998. Exhibit 3 at 1-2. By simple logic, the hepatitis B vaccines did not cause this condition because the disease existed before the vaccinations.

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[10] Respondent's motion suggests that a fact hearing was required because the affidavit from Ms. Hager's mother conflicts with other evidence in this case in that Teresa Hager's affidavit, alone, states that Allison experienced "stomach pains and nausea" in "March or April of 1998." Exhibit 4 (Affidavit of Teresa Hager, dated April 28, 2001) ¶ 1.

For the purposes of determining when Ms. Hager's disease began, obtaining testimony from her mother is not necessary. As explained in the text, the onset of the disease is found based upon tests given to Ms. Hager in September 1999. Whether Mrs. Hager's affidavit is accurate is not relevant to determining the onset of the disease because the presence or absence of stomach pain and nausea in March 1998 is consistent with having sclerosing cholangitis since September 1997.

The determination that Ms. Hager was suffering from sclerosing cholangitis before she received the first dose of the hepatitis B vaccine means that she cannot establish that the hepatitis B vaccine caused the sclerosing cholangitis. Whether this determination affects any claim for attorneys' fees and costs will be resolved, if necessary, after a request for attorneys' fees and costs is made.

VI. Additional Comments Regarding Dr. Bellanti

Sections I-V above of this decision resolve Ms. Hager's case based upon an analysis of the complete record in this case. The complete record includes two different types of evidence — evidence that is generic to the four other cases alleging that the hepatitis B vaccine caused autoimmune hepatitis and evidence that is specific to an individual's case, here Ms. Hager. Some portions of this record, such as Dr. Bellanti's testimony that the hepatitis B vaccine can cause autoimmune hepatitis, are the same as the record in other cases. Consequently, the analysis in section IV.C.1 of this particular case duplicates the analysis in other cases. The analysis of evidence regarding this particular petitioner is set forth in sections I through IV.B., and IV.C.2 through V, above.

Dr. Bellanti's opinion is not persuasive in this case. It also was not persuasive in any of the cases in which petitioners alleged that the hepatitis B vaccine caused autoimmune hepatitis. In every case, his opinion suffered from two significant flaws. First, Dr. Bellanti's written report did not match his oral testimony (section A, below). Second, in terms of addressing either sclerosing cholangitis or autoimmune hepatitis, Dr. Bellanti possessed little knowledge (section B, below). These two points probably contributed to Dr. Bellanti's demeanor, which is discussed in section C, below.

A. Dr. Bellanti's Testimony Failed To Match His Report

Taken on its face, Dr. Bellanti's report indicates that the hepatitis B vaccine can cause – and for these petitioners did cause – autoimmune hepatitis. However, Dr. Bellanti's own testimony does not support what was written in Dr. Bellanti's report. The dichotomy between the words written in Dr. Bellanti's report and words spoken by Dr. Bellanti impairs Dr. Bellanti's credibility. The point, which is repeated several times below, is that Dr. Bellanti could not substantiate the information that was in his own report.

The following six sections provide examples of when Dr. Bellanti's testimony did not match his report. If any one of the topics discussed below were the only time there was a disconnect between Dr. Bellanti's written report and Dr. Bellanti's testimony, perhaps, any discrepancy could be excused as an isolated, innocent error. However, as set forth below, Dr. Bellanti's report contains more than one discrepancy with his oral testimony. The number of places in which Dr. Bellanti's report does not match his testimony amounts to a pattern, suggesting a more significant problem with Dr. Bellanti's credibility.

1. Hepatitis B Virus "Is Known To Cause" Autoimmune Hepatitis

Dr. Bellanti's first point is that an "infection with hepatitis B virus is known to cause autoimmune hepatitis." Exhibit 15 at 3. Although Dr. Bellanti states this fact "is known," a preponderance of the evidence indicates that Dr. Bellanti's statement was in error. See section IV.C.1.e(1)(a), above.

It is curious that in his report, Dr. Bellanti wrote that "infection with hepatitis B virus is known to cause autoimmune hepatitis." Exhibit 15 at 3 (Emphasis added). In describing what the medical community "knows," Dr. Bellanti was implying that there is a general agreement on this point. But, there is no general agreement that the medical community "knows" that the hepatitis B virus causes autoimmune hepatitis.

Dr. Bellanti provided absolutely no basis for this assertion in his report. A more accurate statement is that "four articles associate the hepatitis B virus with the onset (or exacerbation) of autoimmune hepatitis." These four articles, consisting of a single case report each, cannot support the statement that "infection with hepatitis B virus is known to cause autoimmune hepatitis."

Moreover, whether Dr. Bellanti can substantiate his assertion about what "is known" about the relationship between hepatitis B vaccine and autoimmune hepatitis is a question about Dr. Bellanti's veracity. When his written report states that something "is known," Dr. Bellanti should be able to demonstrate the accuracy of his own statement. His failure to prove his assertion with any persuasive evidence suggests that Dr. Bellanti wrote his report without substantiation for his statements at all.

The sequence of events about efforts to establish the basis for Dr. Bellanti's own report at least opens the way for an argument that Dr. Bellanti's report was not written in good faith. Dr. Bellanti's report did not have any citations for his assertion. His only support on the first day of the hearing was the third edition of the Rose and MacKay textbook. Normally, a textbook would be a reliable basis for a statement. However, the Rose and Mackay textbook relied upon two articles that were out-of-date (at least 15 years old). In addition, the Krawitt article, which all experts found to be informative about autoimmune hepatitis, contradicts the Rose and MacKay textbook. After the accuracy of the textbook was called into question, Dr. Bellanti searched for additional literature. But, the articles he presented (by Csepregi and Nobili) were not persuasive. Collectively, all the literature cited by Dr. Bellanti falls well short of establishing that the medical community "knows" the hepatitis B virus causes autoimmune hepatitis.

2. Hepatitis B Vaccine, Autoimmune Disease and Rechallenge

Dr. Bellanti's report also introduced a concept – rechallenge – that he failed to prove. See section IV.C.1.e(2), above.

The misleading nature of Dr. Bellanti's report comes from his failure to substantiate his own assertions. Dr. Bellanti was specifically ordered to be prepared to discuss the rechallenge point because, according to respondent's expert, Dr. Zweiman, none of the articles submitted by Dr. Bellanti supported his report. Order, filed May 31, 2007.

However, when Dr. Bellanti testified, he did not discuss any literature as showing examples of rechallenge. See tr. 55-69 (discussing articles). Considering that Dr. Bellanti's report refers to "reports in the literature," his silence on this topic raises questions about the accuracy of his report.

Besides not discussing examples of rechallenge generally, Dr. Bellanti could not identify any article that shows a rechallenge pattern for autoimmune hepatitis specifically. Tr. 102-03. Because the Court's May 31, 2007 order raised this issue specifically, Dr. Bellanti should have been prepared to answer questions about rechallenge. However, Dr. Bellanti could not answer questions regarding rechallenge and he stated that he needed to review what he submitted. Tr. 103. This evasive answer decreased Dr. Bellanti's credibility and calls into question the truthfulness of Dr. Bellanti's report. If Dr. Bellanti were aware of articles showing that a pattern of challenge and rechallenge links the hepatitis B vaccine and autoimmune hepatitis, Dr. Bellanti would have identified them. (This expectation is reasonable because Dr. Bellanti's report states that "there are reports in the literature. . ." and it was the subject of the May 31, 2007 order.) The failure of Dr. Bellanti to identify any articles strongly suggests that there are none. See tr. 129 (testimony of Dr. Zweiman saying he could not find any articles).

By writing about rechallenge, Dr. Bellanti created an expectation that further evidence on this topic will assist his theory. However, there was little testimony about this topic and what testimony that was elicited from Dr. Bellanti on this point contradicted the argument in his written report. Thus, a question arises as to why Dr. Bellanti introduced rechallenge in his report in the first place.

3. Other Components in the Hepatitis B Vaccine

Dr. Bellanti's report also contains an introductory point that the hepatitis B vaccine contains other components "such as yeast, aluminum and thimerosal." Exhibit 15 at 4. Dr. Bellanti expands on this point by citing articles by Gherardi (Tab B), Grotto (Tab C), and Geier (Tab D) as instances in which authors considered a causal role for these parts of the hepatitis B vaccine.

Once again, Dr. Bellanti's report promised, at least implicitly, more than Dr. Bellanti delivered. During his testimony, Dr. Bellanti explained that yeast, aluminum and thimerosal could prompt a hypersensitivity reaction. But, when questioned by the Court, Dr. Bellanti stated that a hypersensitivity reaction would not lead to autoimmune hepatitis. Consequently, Dr. Bellanti "wouldn't put too much credit on that theory." Tr. 98; accord tr. 609 (Dr. Bellanti's testimony stating that the aluminum, thimerosal and yeast are not "big contributors here.") If Dr.

Bellanti discounts the role of the other components of the hepatitis B vaccine, then the question becomes why did Dr. Bellanti include this statement in his report.

Again the problem is that Dr. Bellanti, himself, expressed doubt about his own theory. It is not a situation in which experts disagreed and one expert was found to be more persuasive than the other. Here, Dr. Bellanti conceded the lack of probative force of his own theory on his own. (Although not necessary for discounting the theory that yeast, aluminum or thimerosal caused an adverse reaction, Dr. Zweiman presented testimony with supporting articles that indicated that these substances have not been found to cause adverse reactions. Tr. 126-28, citing Exhibit 1007 (Lauren D. DiMiceli et al., Vaccination of Yeast Sensitive Individuals: Review of Safety Data in the US Vaccine Adverse Event Reporting System (VAERS), 24 Vaccine 703 (2006)). If Dr. Bellanti believes that these other components are not "big contributors" in these cases, then Dr. Bellanti should not have included them in his report. Their inclusion wrongly implies that they are relevant.

4. Potential Theories That Vaccines Can Cause Autoimmune Disease

Dr. Bellanti's report lists four theories by which vaccines can cause autoimmune disease. These four theories were analyzed and rejected in section IV.C.1, above.

Repeating the reasons for rejecting the four theories is not necessary. But, in the context of discussing Dr. Bellanti's credibility, a few points warrant further review. First, Dr. Bellanti promoted molecular mimicry as the more likely theory. Tr. 90, 201. Yet, when questioned about the specifics of molecular mimicry, Dr. Bellanti retreated. Tr. 86-87 (Dr. Bellanti's testimony that no homology has been found); 203 (Dr. Bellanti's testimony that molecular mimicry does not explain his alleged connection between the hepatitis B vaccine and autoimmune hepatitis). The withdrawal of this theory suggests that Dr. Bellanti failed, when writing his report, to consider what molecular mimicry entails. Instead, the implication is that Dr. Bellanti listed theories without analyzing them in the context of a particular case.

Dr. Bellanti's report also lists, as a theory to explain how the hepatitis B vaccine can cause autoimmune hepatitis, the "participation of CD4+ regulatory cells." This topic is complicated and difficult for someone not trained in immunology to understand.

A theory about CD4+ regulatory cells possibly could been developed to be persuasive, but Dr. Bellanti's oral presentation and written report on this topic were so vague that any potential connection to or substantiation for Dr. Bellanti's theories was lost. In this testimony, Dr. Bellanti cited Dr. Krawitt's article to support a statement that people with autoimmune hepatitis have a deficiency in CD4+ regulatory cells. Tr. 42-43. Dr. Krawitt, in turn, relies upon an article by Dr. Longhi.

In some respects, Dr. Longhi's article demonstrates that Dr. Bellanti appears not to have thought out his presentation. Dr. Bellanti did not cite Dr. Longhi's articles in his report and did

not file a copy of it. However, the Longhi article was discussed much more than any article that Dr. Bellanti actually filed. After the potential importance of Dr. Longhi's article became clear at the beginning of the hearing, the Court obtained a copy of it and filed it as exhibit 1001. Dr. Bellanti would have appeared more prepared if he had cited and discussed this article in his report.

While potentially useful, the Longhi article does not enhance Dr. Bellanti's persuasiveness. The Longhi article has two problems. First, it does not explain whether the deficiency in CD4+ regulatory cells is the cause or the effect of autoimmune hepatitis. See tr. 1131 (testimony of Dr. Zweiman). Second, even if a deficiency in CD4+ regulatory cells were the cause of autoimmune hepatitis, no evidence or theory indicates that the hepatitis B vaccine is the cause of the deficiency in CD4+ regulatory cells.

If Dr. Bellanti's report were more explicit in his reasoning, the gaps in Dr. Bellanti's theory would have been more apparent. By describing CD4+ regulatory cells in general, immunological theory Dr. Bellanti's report fails to connect the CD4+ regulatory cells to the hepatitis B vaccine and autoimmune hepatitis.

5. Literature Attached To Dr. Bellanti's Report

Dr. Bellanti's report also attached eight articles. With one exception, these articles were not helpful. The only relevant article was Dr. Krawitt's article about autoimmune hepatitis. This article did present useful information about the disease, although Ms. Hager does not suffer from this disease.

The remaining articles provided almost no information that advanced Dr. Bellanti's opinion. The article by Gherardi et al. postulates that aluminum in the hepatitis B vaccine can cause a condition called macrophage myofasciitis. Exhibit 15, tab B. But, as discussed above, Dr. Bellanti discounts the role of aluminum in causing autoimmune hepatitis. Tr. 98, 609.

The next article was written by Grotto et al. Dr. Bellanti cited this article to support his assertion that the appropriate amount of time for an adverse reaction to the hepatitis B vaccine is 20-40 days. Tr. 51. Grotto does support this proposition. But, the crucial problem here is that the evidence does not show that petitioners developed their autoimmune hepatitis within 40 days after receiving the hepatitis B vaccine. See section III.A.2.c., above.

The fourth article was written by Geier et al. During Dr. Bellanti's testimony on direct examination, he stated that he "only relied on this secondarily . . . . I didn't put much credit on that one as I did on some of the others, but it's useful." Tr. 55. In Dr. Bellanti's own words, this article should not be given much weight. Dr. Zweiman agrees that the Geier article rests on a shaky foundation, the VAERS database. Tr. 144-46; accord Analla v. Sec'y of Health & Human Servs., 70 Fed. Cl. 552, 558 (2006) (citing cases and indicating "concerns about the reliability of VAERS data").

The fifth article was written by Lilic and Ghosh. This article reports a single case in which the hepatitis B vaccine was associated with transient liver dysfunction. This case report has little value because the liver dysfunction was not autoimmune hepatitis or sclerosing cholangitis. Again, Dr. Bellanti recognized the limited utility of this article. Tr. 56-57.

The sixth article was written by Bogdanos. Dr. Bellanti cited this article for the proposition that the hepatitis B virus is associated with a range of autoimmune responses. Exhibit 15 at tab F; tr. 58. The article does support this general proposition, although the article is based upon a theory that the molecular structure of the hepatitis B virus (not vaccine) mimics the molecular structure of some parts of the body. But, the relevant question is more specific – does the hepatitis B virus cause autoimmune hepatitis, the condition for which petitioners seek compensation. The evidence on this point is scant, at best. See section 1, above. Therefore, this article – even accepting it at face value – does not advance Dr. Bellanti's theories.[11]

The seventh article, which was written by Porobic et al., does not contain any relevant information. This article suggests that the hepatitis B vaccine may induce anti-phospholipid antibodies. However, according to Dr. Bellanti's understanding, anti-phospholipid antibodies do not cause autoimmune hepatitis. Tr. 62-63. Thus, Dr. Bellanti confesses he "only used as a signal." Tr. 61.

The eighth article provided a small amount of support to a theory of molecular mimicry. This theory is based upon a homology between the antigen (the hepatitis B vaccine) and a structure in the body (in this article, the myelin surrounding nerves). But, Dr. Bellanti could not support molecular mimicry for these cases because there does not appear to be any homology between the hepatitis B vaccine and liver tissue. Tr. 86-87, 203; see also tr. 133-36 (testimony of Dr. Zweiman discussing this article).

In sum, five of the articles that Dr. Bellanti presented were not helpful at all. (The only helpful article is by Krawitt on autoimmune hepatitis. To a much lesser degree, the articles by Grotto and Bogdanos weakly supported Dr. Bellanti's opinion.) Again, the point to be emphasized is that at hearing, Dr. Bellanti, himself, indicated that the five articles were not significant. For some articles, Dr. Bellanti discounts the article's relevance explicitly by saying that he used the article as a "signal" or "secondarily." For all the articles, except Krawitt's, the lack of contribution is implicit in the amount of time spent addressing the articles listed in Dr. Bellanti's report. On direct examination, Dr. Bellanti covered his literature in about 15 pages. Then, after the first day of testimony, the articles were not discussed again. By way of contrast, the article by Longhi was discussed repeatedly. The infrequency of testimony about the articles

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[11] Dr. Zweiman disputes the accuracy of the Bogdanos article. Tr. 177. However, this criticism is not relevant in commenting upon the disparity between Dr. Bellanti's written report and his oral testimony. Dr. Bellanti's written report suggests that the Bogdanos article is meaningful. His testimony indicates otherwise.

strongly suggests that they should not have been included with Dr. Bellanti's report in the first place.[12]

6. Discussion Of Temporal Relationship In Dr. Bellanti's Report

Dr. Bellanti's report concludes with a discussion of timing. In every case, the report states "The temporal relationship between [the petitioner's] immunizations and the onset of symptoms is medically appropriate." Exhibit 15 at 7. As discussed in detail in each case, Dr. Bellanti was shown to lack the knowledge to make any statements about the onset. His report, therefore, is misleading and not accurate.

Dr. Bellanti could not state when the petitioner experienced an "onset of symptoms." In Porter, this problem arises because the medical records do not show when the autoimmune hepatitis began. In Rotoli, the problem is that Dr. Bellanti did not understand the report from her liver biopsy, which showed fibrosis.

These problems with Dr. Bellanti's report became apparent only during the hearing. However, Dr. Bellanti (and, arguably, petitioner's counsel) should have realized the limits of his ability. Rereading his report in light of the testimony produces an impression that Dr. Bellanti's report omitted any discussion of when the petitioner's autoimmune hepatitis began to avoid this topic. However, this lack of forthrightness lessens Dr. Bellanti's credibility.

7. Summary: Dr. Bellanti's Report

The preceding six sections illustrate problems with Dr. Bellanti's report. These problems are problems because Dr. Bellanti's own testimony did not corroborate his report. Whether Dr. Bellanti had a reasonable basis for offering his report as originally written will be evaluated if petitioners seek attorneys' fees and costs.

B. Lack of Expertise With Autoimmune Hepatitis and Sclerosing Cholangitis

The preceding section about Dr. Bellanti's report explains how Dr. Bellanti's oral testimony differed from his report for no apparent reason. The situation is different for Dr. Koff's report. This report provided reasons for Dr. Bellanti to re-evaluate his conclusion that the hepatitis B vaccine caused petitioner's autoimmune hepatitis. But, Dr. Bellanti seems to have ignored Dr. Koff's report and did not adjust his report when respondent presented him with new information.

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[12] Articles from peer-reviewed journals are useful when they substantiate the reliability of an expert's opinion. Articles that do not support the expert's opinion are not relevant. Petitioners and Dr. Bellanti should not file irrelevant articles. Submitting irrelevant materials causes the parties and the court to waste time and resources when the articles are reviewed.

To present a reliable, credible and persuasive opinion that the hepatitis B vaccine caused autoimmune hepatitis (or sclerosing cholangitis), Dr. Bellanti should have investigated autoimmune hepatitis and sclerosing cholangitis much more thoroughly. Even if Dr. Bellanti did not adequately research the disease about which he was opining before he wrote his report, he certainly should have been more informed about the disease when he testified.

Although Dr. Bellanti specializes in the field of immunology, his lack of knowledge about diseases of the liver and bile system can be excused only in part. Dr. Koff's report alerted Dr. Bellanti to the salient issues. Dr. Koff also presented articles from peer-reviewed publications to support his opinion. Despite having information from articles cited by Dr. Koff readily available, Dr. Bellanti proceeded as if Dr. Koff's opinion and literature did not exist. This apparent willful blindness happened in every case.

Dr. Bellanti's opinion in each case suffered from one or more significant flaws that are directly tied to his lack of expertise about autoimmune hepatitis. These are not points on which experts typically dispute. Battles between experts are common in vaccine Program cases. See Sword, 44 Fed. Cl. at 188. Rather, Dr. Bellanti's errors concern such fundamental issues over which there was no justifiable dispute that questions about Dr. Bellanti's competence as an expert have arisen.

The list of fundamental errors includes:

Myers	failing to appreciate the difference between autoimmune hepatitis and nonalcoholic steatohepatitis.
Rotoli	failing to appreciate that Ms Rotoli's liver biopsy showed such extensive damage (fibrosis) that the disease must have begun before she received the first dose of the hepatitis B vaccine.
Porter	failing to recognize an alternative cause for her autoimmune hepatitis: minocycline. After Dr. Koff raised this issue, Dr. Bellanti was not prepared to explain why the hepatitis B vaccine was more likely than the minocycline to be the cause.
Torbett	failing to recognize an alternative cause for her autoimmune hepatitis: minocycline. After Dr. Koff raised this issue, Dr. Bellanti was not prepared to explain why the hepatitis B vaccine was more likely than the minocycline to be the cause.
Hager	failing to appreciate the difference between a disease affecting Ms. Hager's liver and a disease affecting Ms. Hager's bile duct system.

As stated, these mistakes are serious. These are errors that directly undermine Dr. Bellanti's opinion. They are also issues on which Dr. Bellanti lacked any effective rebuttal. Therefore, the evidence from each case supports a finding that Dr. Bellanti lacks credibility. However, the repetition of significant errors reinforces the finding that Dr. Bellanti lacked credibility.[13]

C. Dr. Bellanti's Demeanor

The analysis in sections A and B, above, is based upon the written material, primarily Dr. Bellanti's report and the transcript of his testimony. The lack of credibility is apparent on this information alone. But, Dr. Bellanti's demeanor during his testimony strongly reinforces the doubts about Dr. Bellanti's veracity. A fact finder may evaluate an expert's demeanor in determining credibility. Andrew Corp. v. Gabriel Electronics, Inc., 847 F.2d 819, 824 (Fed. Cir. 1988).

Evaluations of credibility by fact-finders who observe testimony are accorded "great deference." Pafford v. Sec'y of Health & Human Servs., 451 F.3d 1352, 1359 (Fed. Cir. 2006); cert. denied, ___ U.S. ___, 127 S. Ct. 2909 (2007); accord Energy Capital Corp. v. United States, 302 F.3d 1314, 1329 (Fed. Cir. 2002).

At several points, Dr. Bellanti's demeanor suggested that he was uncomfortable with the topic being discussed. These included:

1) being evasive during cross-examination about molecular mimicry. Tr. 86

2) being evasive during cross-examination about bystander activation. Tr. 87

3) appearing uncomfortable and not having a better answer when asked about rechallenge. Tr. 103

4) appearing unsettled when asked to discuss his training in gastroenterology. Tr. 106.

5) appearing uncomfortable when providing a summary of his opinion in Ms. Hager's case. Tr. 220.

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[13] During any application for attorneys' fees, the conduct of petitioner's counsel can be evaluated. Dr. Koff's report and literature also alerted counsel to important issues. As an advocate, counsel is responsible for anticipating arguments from the other side and preparing a response. As an officer of the court, counsel is responsible for ending litigation when the likelihood of prevailing is remote. See Perreira v. Sec'y of Health & Human Servs., 33 F.3d 1375, 1376-77 (Fed. Cir. 1994) (affirming special master's decision not to award all attorneys' fees).

6) lacking confidence in his testimony when he stated that Mr. Myers's fevers, chills, headaches were due to the vaccine, and not a virus that was affecting other family members. Tr. 508-09.

7) appearing uncomfortable when admitting that he did not know when Ms. Rotoli's autoimmune hepatitis began but, nonetheless, maintaining that the temporal relationship is appropriate. Tr. 597.

8) appearing unfamiliar with the fact that Ms. Rotoli did not respond to the hepatitis B vaccination. Tr. 606.

9) appearing uncomfortable when informed that Ms. Rotoli's liver biopsy showed moderate fibrosis in her liver. Tr. 607.

10) appearing uncomfortable when asserting that the history of Ms. Porter's autoimmune hepatitis shows that the hepatitis B vaccine, not the minocycline, caused her disease. Tr. 959.

It is probably not a coincidence that this list of instances when Dr. Bellanti's demeanor suggested a weakness in his testimony matches many topics for which his opinion was found not to be credible. Given all the circumstances, a reasonable inference to be drawn from Dr. Bellanti's demeanor is that he was aware that his opinion was flawed, yet he chose to provide it anyway.

D. Overall Conclusion Regarding Dr. Bellanti

A consideration of Dr. Bellanti's report, his testimony, and his demeanor while testifying raises significant concerns not just about Dr. Bellanti's persuasiveness but also his truthfulness. Although this point has been made several times, it bears repeating. The origins about these serious questions are not based upon mere disagreements between experts. Almost every vaccine case involves some dispute between experts. Resolving a reasoned disagreement between experts is a primary function of special masters. Simply finding an expert is not persuasive differs from finding an expert not credible. Here, repeatedly, on significant issues, Dr. Bellanti has presented no credible basis for most (if not all) assertions.

Several times, Dr. Bellanti resorts to describing adverse reactions to the hepatitis B vaccine as "rare cases." Tr. 36-40, 93, 201, 499, 528. Invoking this phrase seems to be equivalent to asking that the requirement for reliable evidence be disregarded. However, even in "rare cases," petitioners bear the burden of presenting evidence to make their experts' theories reliable.

Here, so many questions about the basis for Dr. Bellanti's statements, contained in either his report or his testimony, have led to a question about Dr. Bellanti's veracity. As a professor and published author, Dr. Bellanti should appreciate the need for some evidence to substantiate

his theories. Dr. Bellanti failed to present sufficient evidence that was credible and persuasive to support his statements and opinions. Consequently, Dr. Bellanti's opinion, as a whole, lacks any persuasiveness.

In this case, the quality of Dr. Bellanti's work appears to be inconsistent with previous work. In other cases, Dr. Bellanti has offered opinions that a vaccine caused a particular condition that Special Masters have found persuasive. E.g., Keenan v. Sec'y of Health & Human Servs., No. 99-561V, 2007 WL 1231592 *10 (Fed. Cl. Spec. Mstr. Apr. 5, 2007); Bowes v. Sec'y of Health & Human Servs., No. 01-481V, 2006 WL 2849816 (Fed. Cl. Spec. Mstr. Sept. 8, 2006). For some reason(s), the quality of Dr. Bellanti's work in the present cases fell below what is expected of an expert. In future cases, it is expected that Dr. Bellanti's work, beginning with his report, will again achieve a high quality.

VII. Conclusion

Ms. Hager has not demonstrated, by a preponderance of the evidence, that the hepatitis B vaccinations caused her an adverse consequence, regardless of whether Ms. Hager's condition is diagnosed as primary sclerosing cholangitis or autoimmune hepatitis. If a motion for review is not filed, the Clerk's Office is ordered to file a judgment in favor of respondent.

IT IS SO ORDERED.

S/ Christian J. Moran
Christian J. Moran
Special Master