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

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MARI BOURCHE,	*	
As Personal Representative of the	*	No. 15-232V
Estate of JOSEPH BOURCHE,	*	Special Master Christian J. Moran
	*	
Petitioner,	*	Filed: January 7, 2020
	*	
v.	*	Entitlement, hepatitis B vaccine,
	*	vasculitis, IgA nephropathy,
SECRETARY OF HEALTH	*	endocarditis, vancomycin.
AND HUMAN SERVICES,	*	
	*	
Respondent.	*	
* *		

Andrew D. Downing and Courtney Van Cott, Van Cott & Talamante, PLLC, Phoenix, AZ, for petitioner;
Sherry D. Soanes and Lisa Watts, United States Dep't of Justice, Washington, DC, for respondent.

PUBLISHED DECISION DENYING COMPENSATION[1]

Mari Bourche was married to Joseph Bourche, who was born in 1959. In 2014, Mr. Bourche was suffering from two significant health problems – poor functioning in his kidneys for which he was receiving dialysis and heart trouble for which he had a pacemaker implanted. He received a dose of the hepatitis B vaccine in April 2014. In May 2014, Mr. Bourche suffered a serious infection for which he was hospitalized for five days. In October 2014, Mr. Bourche required

[1] The E-Government Act, 44 U.S.C. § 3501 note (2012) (Federal Management and Promotion of Electronic Government Services), requires that the Court post this decision on its website (http://www.cofc.uscourts.gov/aggregator/sources/7). Anyone can access this decision once it is posted to the website. Pursuant to Vaccine Rule 18(b), the parties have 14 days to file a motion proposing redaction of medical information or other information described in 42 U.S.C. § 300aa-12(d)(4). Any redactions ordered by the special master will appear in the document posted on the website.

another heart operation. Unfortunately, Mr. Bourche declined and eventually died in January 2016.

As the administrator of her deceased husband's estate, Ms. Bourche is pursuing a claim that the hepatitis B vaccination led to the infection, which, in turn, set off a series of events ultimately shortening her husband's life. To assist with her claim, Ms. Bourche retained two doctors, Thomas Zizic, a rheumatologist; and Robert Stark, a cardiologist. Ms. Bourche also presented reports and testimony from a nephrologist who cared for Mr. Bourche, Thomas Mooney.

The Secretary disagreed with the claim that the hepatitis B vaccination caused any adverse consequences to Mr. Bourche. The Secretary also retained two doctors who have the same specialties as the doctors Ms. Bourche retained. These are Mehrdad Matloubian (rheumatologist) and Shane LaRue (cardiologist).

These five doctors as well as Ms. Bourche testified at a hearing on April 23–24, 2018. Following the hearing, the parties submitted additional evidence and post-hearing briefs.

As presented in the testimony as well as in pre-hearing and post-hearing briefs, Ms. Bourche is seeking recovery through a multi-step theory. She maintains the following: (1) the April 23, 2014 hepatitis B vaccination caused Mr. Bourche to develop vasculitis before he entered the hospital on May 23, 2014 by inducing the production of immune complexes, (2) the vasculitic skin lesions allowed bacteria to enter Mr. Bourche's body and this bacterial infection necessitated the hospitalization, (3) bacteria, which the vaccination-induced vasculitic skin lesions permitted, seeded an infection on a heart valve, further weakening Mr. Bourche's cardiac function, (4) this decreased cardiac function was a substantial factor in Mr. Bourche's death on January 16, 2016.

The Secretary challenges Ms. Bourche's theory. The Secretary disputes that the hepatitis B vaccine can cause vasculitis. The Secretary argues that Mr. Bourche developed vasculitis after (not before) the May 2014 hospitalization and further argues that the vasculitis could have been a consequence of the provoking infection or a medication, vancomycin, used to treat the infection. The Secretary disputes the allegation that any vasculitic skin lesion was the portal of entry for the bacteria because the bacteria could have entered Mr. Bourche's body during dialysis. The Secretary questions the sequence of the vasculitis and the heart-valve infection, noting that the infection of the heart valve could have occurred before the vasculitis. Finally, the Secretary contends that the heart-valve infection was not a substantial factor in Mr. Bourche's death.

The evidence does not preponderate in Ms. Bourche's favor. The primary flaw is that the evidence, taken as a whole, shows Mr. Bourche did not form the immune complexes Dr. Zizic's theory predicted. In addition, the evidence does not support a finding that Mr. Bourche developed vasculitis before his hospitalization. Because a finding that Mr. Bourche developed vasculitis before his hospitalization is necessary to link Mr. Bourche's April 2014 hepatitis B vaccination to his subsequent decline in health, the remainder of Ms. Bourche's case becomes untenable. This sequence of events is more compatible with a cause, such as a reaction to vancomycin, other than the hepatitis B vaccination. Finally, Ms. Bourche has not persuasively established that any complication of the hepatitis B vaccination hastened her husband's death. Thus, as explained in more detail below, Ms. Bourche is not entitled to compensation.

I. Events in Mr. Bourche's Life

Due largely to Mr. Bourche's pre-existing conditions, his case presents one of the most challenging and complicated cases the undersigned has reviewed.

A. Pre-existing Kidney Disease

Mr. Bourche's relevant medical history begins a relatively long time before the 2014 hepatitis B vaccination. In 2000, Dr. Mooney began treating Mr. Bourche for a disease known as IgA nephropathy.

IgA nephropathy

The basic meaning of "nephropathy" is a disease of the kidneys. Dorland's Illustrated Medical Dictionary 1241-42 (32d ed. 2012). "IgA" refers to a type of immunoglobulin. Dorland's at 919-21; Tr. 258. In IgA nephropathy, the tubes in the kidneys that filter waste products become inflamed, a condition known as glomerulonephritis. Dorland's at 786; Tr. 379.

The cause of IgA nephropathy is partially known. A person with IgA nephropathy produces abnormal IgA. The specific problem is a defective sugar moiety in a region of the IgA known as the hinge. Because the abnormal IgA is not expected, the body makes antibodies to the abnormal IgA. When the antibodies attack the abnormal IgA, they form immune complexes that clog the tubes in the kidneys leading to kidney damage. Tr. 267-69; see also Tr. 147, 200. For a more in-depth explanation of the pathogenesis of IgA nephropathy, see

exhibit A-8 (Wyatt) at 2404.[2] However, why some people produce abnormal IgA molecules is not known. Tr. 208.

In the context of discussing the pathogenesis of IgA nephropathy, Wyatt links IgA nephropathy to another disease, Henoch-Schönlein purpura ("HSP"). "Patients with Henoch-Schönlein purpura nephritis and those with IgA nephropathy have many of the same laboratory abnormalities . . . and pathological features of renal-biopsy specimens. These similarities have led to proposals that the two entities represent opposite ends of the clinical spectrum characterizing a single disease process." Exhibit A-8 (Wyatt) at 2406. Other evidence also connects IgA nephropathy with HSP. See Tr. 98, 151, 271; exhibit A-9 (Knoppova). As discussed below, later in Mr. Bourche's course, some doctors propose that Mr. Bourche suffered from HSP.

IgA is a chronic condition that medicine cannot cure. Tr. 97, 327. The problem is that the body cannot stop making the defective IgA without a drastic intervention such as a bone marrow transplant. Tr. 330.

One consequence of IgA nephropathy can be hypertension. Tr. 99. As IgA nephropathy progresses, patients require kidney dialysis. Tr. 82, 97.

Dr. Mooney, the nephrologist primarily responsible for treating Mr. Bourche's IgA nephropathy, explained the dialysis process. Tr. 103-10. The dialysis center where Mr. Bourche went is a public place containing approximately 20 chairs. People undergoing dialysis remain in their usual clothes and sit in a reclining chair. A nurse conducts an examination focused on the systems involved in dialysis.

A needle is inserted through a fistula and this needle draws blood out of the patient's arm. A second needle is inserted higher up in the arm to return the cleansed blood to the patient. A dialysis fistula "is a natural connection between an artery and a vein that is covered with your own skin." Tr. 110. With a sterile technique, the insertion of needles is extremely unlikely to introduce bacteria. In the facility that Dr. Mooney supervised, bacterial infections were "extremely rare." Tr. 110.

The removed blood is processed to remove the waste. Dialysis also removes fluids that have accumulated in the patient's body due to the lack of kidney function. The removal of fluids causes dehydration, which is difficult to tolerate.

[2] The complete bibliographical information for all articles cited in the decision appears in the appendix.

The dialysis process can cause itchiness. Tr. 62, 161, 330; exhibit A-1 (Ankudowicz) at 1436. Mr. Bourche experienced itchiness during his dialysis. Tr. 34.

The dialysis process takes approximately four hours. Mr. Bourche required dialysis three times per week. Dr. Mooney or one of his doctor-partners examined patients "pretty rarely," although the doctors were available for more thorough consultations. Tr. 108; see also Tr. 87.

Dr. Mooney initiated dialysis for Mr. Bourche in December 2004. Exhibit 14 at 1. He remained on dialysis until he received a kidney transplant in February 2006. Exhibit 7 at 306.

In October 2009, Mr. Bourche developed shortness of breath, chest pain, hypertensive urgency, a fever, headache, cough and nausea. He underwent a kidney biopsy. Exhibit 9 at 628-29.

Sections of the kidney were stained for immunofluorescence. Immunofluorescence is a process by which a pathologist can determine the presence (or absence) of various antibodies and other components of the immune system. Dorland's at 919. For Mr. Bourche, the pathologist (Patrick Walker) identified IgA and IgM but not IgG. Exhibit 9 at 629. Dr. Matloubian opined that Mr. Bourche was having a recurrence of his IgA nephropathy. Tr. 273, 326, 378.

With respect to the recurrence of IgA nephropathy in Mr. Bourche, Dr. Matloubian's opinion conflicts with the view of Dr. Mooney. Dr. Mooney testified that Mr. Bourche did not have a recurrence of IgA. Tr. 84. Although treating physicians are usually entitled to deference, their views are not sacrosanct. On this point, Dr. Matloubian is more persuasive than Dr. Mooney. First, the biopsy report states under diagnosis "IgA nephropathy, Recurrent." Exhibit 9 at 628. Second, the literature supports the recurrence of IgA nephropathy after a transplant. Exhibit A-8 (Wyatt) at 2408; exhibit A-9 (Knoppova) at 3. Third, Dr. Zizic also supported the idea of a recurrence of IgA nephropathy. Tr. 385 ("[L]et me start off by saying that it would not be surprising to see some IgA deposition in the transplanted kidney.").

The transplanted kidney was removed on September 2, 2011. Exhibit 7 at 95. Dr. Mooney indicated that Mr. Bourche had rejected the kidney. Tr. 65; see

also Tr. 150, 328-29, 386.[3] However, there appears to be no biopsy of the rejected kidney to determine whether the IgA nephropathy had occurred again. Tr. 378.

B. Events from Kidney Removal to Pacemaker Implantation

On April 12, 2012, Mr. Bourche was having a problem with his skin. Tr. 28. He underwent a biopsy and the results were consistent with prurigo nodularis. Exhibit 6 at 9; see also Tr. 160, 274. Prurigo nodularis is "a chronic, intensely pruritic [itchy] form of neurodermatitis… Characteristics include single or multiple, firm nodules that are red, brown, or pink… Scratching or rubbing of the nodules often makes the condition worse." Dorland's at 1539. According to Ms. Bourche, prurigo nodularis is related to chronic kidney disease. Pet'r's Posth'g Br. at 2 n.1.[4]

In November 2012, Mr. Bourche became infected with strep pneumonia. In response, Dr. Mooney sent him to the hospital for treatment with vancomycin. Exhibit 4 at 86; Tr. 123-26.[5] The Secretary argued that the infection was "presumably" related to Mr. Bourche's fistula. Resp't's Posth'g Br. at 2. However, the Secretary failed to cite any opinions of treating physicians to justify this presumption. See Pet'r's Reply at 2.

In this period, Mr. Bourche periodically complained about pain in his abdomen. See Tr. 29, 364. Some of these complaints are reflected in his medical records. E.g., exhibit 10 at 355.

C. Heart History before Vaccination

As alluded to earlier, Mr. Bourche had heart trouble for many years before the vaccination. For example, x-rays from 2011 showed that his heart was abnormally enlarged. Exhibit 7 at 148 ("cardiomegaly"), 270; see also Tr. 416 (discussing enlarged heart in the context of endocarditis). His cardiologist was Dr. Holland, who wrote a report for this case. Tr. 81; exhibit 52.

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[3] In 2015, Mr. Bourche told a doctor that he developed a viral illness on a cruise in 2009, before the kidney removal. Exhibit 72 at 96.

[4] After the hepatitis B vaccination, Mr. Bourche may have had another instance of prurigo nodularis. See exhibit 6 at 11-13; Tr. 331.

[5] During the critical hospitalization in May 2014, Mr. Bourche again received vancomycin. Additional information about that drug is provided in that context below.

By September 2013, Mr. Bourche was not functioning well. Exhibit 8 at 77; Tr. 16; see also Tr. 408-09, 466-68. His heart's ejection fraction was 33 percent. Exhibit 8 at 162-63. "Ejection fraction" refers to "the proportion of the volume of blood in the ventricles at the end of diastole that is ejected during systole. . . . It is normally 65 ± 8 per cent; lower values indicate ventricular dysfunction." Dorland's at 740. To assist him, doctors installed a pacemaker on October 4, 2013. Exhibit 8 at 141-44. This equipment includes two wires that are inserted into the patient's heart and an impulse through the wires synchronizes the heart's beating. Tr. 410, 466.

After installation of the pacemaker, Mr. Bourche functioned much better. Tr. 17. After evaluating Mr. Bourche, Dr. Holland determined that Mr. Bourche's "cardiac condition has improved significantly and that [he is] now ready for transplant from a cardiovascular standpoint." Exhibit 8 at 56 (Jan. 9, 2014); accord Tr. 432, 468-70.

The doctors responsible for coordinating Mr. Bourche's care in advance of a potential kidney transplant evaluated him on April 7, 2014. They found that "he has improved quite a lot, specifically his heart." Exhibit 10 at 403. His status on the transplant list indicates relatively good health because good health is required for a transplant. Tr. 64, 114-15.

D. Other Medical Records from early 2014, before Vaccination

Following the installation of a pacemaker, Mr. Bourche followed up with his cardiologist, Dr. Holland, on January 9, 2014. His ejection fraction was 35-38 percent. Exhibit 8 at 158. This measurement was better than the ejection fraction before the pacemaker, which had been 33 percent.

Dr. Mooney saw Mr. Bourche on February 7, 2014, and recorded that Mr. Bourche looked well and had no complaints. Exhibit 10 at 1527. While Mr. Bourche's brief points out that this medical record does not reflect any skin problems, Pet'r's Posthear'g Br. at 4, Dr. Mooney usually did not examine the skin of his dialysis patients. Tr. 111. Mr. Bourche continued to report abdominal pain. Exhibit 10 at 1525 (Feb. 3, 2014), 1538 (Mar. 17, 2014).

In March 2014, a comprehensive care plan was updated for Mr. Bourche. Here, Mr. Bourche reported that his goals were: (1) to focus his energy on building his automotive business, (2) to enjoy his family, (3) to pursue a transplant, and (4) to travel. Exhibit 10 at 317; see also Tr. 48, 112.

Based upon this information, Dr. Mooney was asked during the hearing to rate Mr. Bourche's health on a scale of 1-10 with 10 being perfect health. Dr. Mooney scored Mr. Bourche as an eight, when compared to other dialysis patients. But, when compared to other men in their 50s, Dr. Mooney gave him a three or four because he was chronically ill. Tr. 114-15.

Through lab testing, doctors learned that Mr. Bourche did not have sufficient antibodies against the hepatitis B virus. Exhibit 7-1 at 6 (Apr. 7, 2014); Tr. 224, 372. Because the Center for Disease Control recommends the hepatitis B vaccine for all dialysis patients, Tr. 84, Dr. Mooney ordered a vaccination.

E. Hepatitis B Vaccine, Vaccination on April 23, 2014, and Remainder of April 2014

The date of vaccination was April 23, 2014, and on that date, one of Dr. Mooney's partners was supervising the dialysis center. Tr. 88; exhibit 10 at 126. Mr. Bourche was itchy. At 17:40, Mr. Bourche was given Benadryl for his itchiness. Exhibit 10 at 1359. This itchiness is not surprising as Mr. Bourche had been itchy previously. See, e.g., exhibit 10 at 1267 (Nov. 8, 2013); Tr. 62, 161, 278, 330. The itchiness relates to the dialysis and is not a manifestation of vasculitis, a condition that later affected Mr. Bourche. Tr. 63, 160, 330.

The dialysis process removed the waste products normally. See exhibit 10 at 1358. Mr. Bourche received the hepatitis B vaccine at 19:30. Exhibit 2 at 1; exhibit 10 at 1359.[6]

The hepatitis B vaccine is manufactured using recombinant DNA technology. This process re-creates the outside structure of the hepatitis B virus without the genetic material of the virus. Thus, unlike an infection with an actual virus or a vaccine containing a live but attenuated virus, the hepatitis B vaccine does not replicate once inside a person's body. Tr. 246; see also Doe 71 v. Sec'y of Health & Human Servs., 95 Fed. Cl. 598, 601 n.3 (2010).

A standard dose of the hepatitis B vaccine contains 20 μg of hepatitis B surface antigen. However, because people receiving dialysis do not create a

[6] The nursing notes created on this date show that Mr. Bourche first received Benadryl at 17:40, and then received the hepatitis B vaccination at 19:30. These records show that Mr. Bourche and Ms. Bourche inaccurately recollected that the hepatitis B vaccination preceded the onset of itchiness. See exhibit 1, ¶ 9; exhibit 63, ¶ 5; Tr. 18.

sufficiently robust response to the vaccination, the dose is doubled, meaning Mr. Bourche actually received 40 µg. Tr. 251, 308.

The hepatitis B vaccine is injected into a muscle. In the muscle, a part of the immune system known as macrophages pick up the antigen and bring the antigen to the draining lymph nodes. This process stimulates B cells to produce antibodies, which would, in the case of infection, attack the hepatitis B virus. Tr. 246-47. The type of antibody to which the hepatitis B vaccine leads is IgG. Tr. 262, citing exhibit A-30 (Siegrist) at 3. The production of IgG takes a few days.

At Mr. Bourche's next dialysis appointment, which took place on April 25, 2014, no complaints were noted. Exhibit 10 at 1360-61; Tr. 85, 202. For example, the medical records do not describe Mr. Bourche having a blister in his mouth. Tr. 203.

F. Health and Hospitalization in May 2014

On May 2, 2014, nine days after the vaccination, Mr. Bourche reported mouth blisters. Exhibit 10 at 127.[7] A blister is a rounded projecting structure. See Dorland's at 226 (referring to bulla and vesicle), 259 (bulla), 2052 (vesicle); exhibit J at 9; Tr. 263. Based on his observations of the blister (or blisters), Dr. Mooney determined Mr. Bourche was reacting adversely to the vaccination. Accordingly, Dr. Mooney entered an allergy to the hepatitis B vaccine in Mr. Bourche's medical chart. Tr. 67, 88, 120. Both Dr. Zizic and Dr. Matloubian recognized this determination, Tr. 162, 336-37, with Dr. Matloubian emphasizing that the treating doctor assumed a causal relationship.

Mr. Bourche's immunity to the hepatitis B virus was retested via laboratory studies reported on May 7, 2014. The results of this testing showed that he produced antibodies to the hepatitis B surface antigen. However, the antigen itself was no longer present in his body. Exhibit 10 at 239; Tr. 210, 226, 308, 333, 373.

Later in May 2014, Mr. Bourche began to become very sick. Tr. 16. While Mr. Bourche was hospitalized, doctors determined that he was infected with bacteria known as *staphylococcus aureus*. Exhibit 9 at 295 (discharge report), 461 (lab report, dated May 26, 2014). *Staphylococcus aureus* "causes serious suppurative infections and systemic disease, including impetigo bullosa,

[7] Mr. Bourche and Ms. Bourche testified a mouth blister (or blisters) had formed within two days of the vaccination. Exhibit 1, ¶ 10; exhibit 63, ¶ 6; Tr. 32; see also Tr. 334. Whether the onset of a blister (or blisters) was two days or nine days does not affect the petitioner's case according to Dr. Zizic. Tr. 164.

staphylococcal pneumonia, and staphylococcal scalded skin syndrome, and has developed resistance to nearly all classes of antibiotics." Dorland's at 1765. Staphylococcus aureus is common on the skin. Tr. 90.

Mr. Bourche's condition during his May 2014 hospitalization is controverted by the parties and their experts. The dispute rests on medical records that are in some respect inconsistent and, in some respect, vague. This inconsistency and vagueness, in turn, allow the parties and their experts to draw different inferences from the same material.[8]

Mr. Bourche arrived at the emergency department of the Boulder Community Hospital by 3:00 in the afternoon on May 23, 2014. Exhibit 9 at 302 (noting he was seen by a provider at 15:01). He reported a one-day history of fever and chills. In his review of symptoms, he had no rash. The physician in the emergency room, Deborah S. Lund, conducted a physical exam and recorded that Mr. Bourche's skin was "warm and dry, no rash." Id. at 303. Dr. Lund's notes also record that he has a hepatitis B vaccine allergy. Id.

After laboratory studies determined that Mr. Bourche had an elevated level of potassium, a condition known as hyperkalemia (see Dorland's at 890), Dr. Lund initiated the standard treatment including "IV fluids, calcium, insulin, glucose and Kayexalate." Dr. Lund talked to one of Dr. Mooney's partners, Dr. Bozeman, "who will arrange for emergent dialysis." Dr. Lund also stated: "The etiology of his fever is unclear. There is no evidence of sepsis at this point. There is no evidence of pneumonia or fistula infection." Id. at 304.

Dr. Lund also gave Mr. Bourche vancomycin. Vancomycin is an antibiotic for severe staphylococcal infections. Dorland's at 2023.

Although the records from the emergency department say "no rash," this notation may be erroneous as three other medical records from this hospitalization mention skin problems. Krystie M. Karageorge, an attending doctor, seems to have seen Mr. Bourche at the end of May 23, 2014, as her report is dictated at 0006 on May 24, 2014. Exhibit 9 at 314. When Dr. Karageorge conducted a physical exam, she described Mr. Bourche's skin as "warm, dry, [and] intact." She also wrote: "There are 2 macular areas present on the right forearm with overlying scabs. No fluctuance is noted. No streaking redness, erythema or increased warmth. Similar areas present over bilateral ankles." Id. at 313. She diagnosed

[8] Although Ms. Bourche witnessed some of these events, her testimony was not very useful due to the lapse of time. Tr. 37-38.

Mr. Bourche as suffering from sepsis. Her plan mentioned, among other points, that Dr. Bozeman was continuing to follow Mr. Bourche.

Dr. Bozeman saw Mr. Bourche on May 24, 2014 and dictated his report at 1448 on that day. The history of present illness that Dr. Bozeman obtained indicates that: "Lately he has had problems with elevated phosphorus levels and sores on his arms and legs. Also, he had an adverse reaction to a hepatitis B booster vaccine 6 weeks ago where he had blisters in his mouth and nose. These have healed but he has been picking at and noticing persistence of the sores on his arms and legs." Exhibit 9 at 321. Dr. Bozeman's history also mentions that a preliminary report of his blood cultures "have grown gram-positive cocci." Id. Dr. Bozeman's physical exam of Mr. Bourche's skin showed that Mr. Bourche "has several papular lesions on his arms and legs, some of which are healed with keloid like scars, some that have more open excoriations and none that appear infected." Id. at 322. The impression and plan from Dr. Bozeman included the following: "It is possible he seeded his bloodstream from the sores that he has had for several months. His fistula appears fine and is not infected. I am concerned given his pacemaker that he could have seeded this." Id.

Annie Meditz, an infectious disease specialist, saw Mr. Bourche on May 24, 2014, and dictated her report at 1549. The history of present illness from Dr. Meditz indicates that Mr. Bourche had been "feeling poorly for a 3 to 4 week period with chronic abdominal pain, . . . [his] symptoms dramatically worsen[ed] on the day of admission with severe fevers, chills and right rigors. He reports that he has had a few skin lesions but otherwise has not noticed any abnormalities of his skin." Exhibit 9 at 315. Dr. Meditz also noted that his blood culture was positive for gram-positive cocci. Like Dr. Bozeman, Dr. Meditz indicated that Mr. Bourche had an allergy to his hepatitis B booster vaccine six weeks ago. Id. at 316 (noting intranasal and oral ulcerations). Dr. Meditz recorded that Mr. Bourche's skin showed that "He has some very small scabbed wounds, 1 on the left forehead, 1 on his ankle. No problems with his graft on his left forearm." Id. The assessment and plan from Dr. Meditz were that Mr. Bourche has "sepsis and is found to have bacteremia with gram-positive cocci. Unclear source. Portal of entry could be related to accessing his graft although his graft does not appear infected. He also has some minor skin lesions that could be portal of entry. Other considerations include pneumonia." Id. Dr. Meditz also recommended that Mr. Bourche have a "more prolonged course of IV antibiotics, i.e. 6 weeks." Id. at 317. Dr. Meditz prescribed vancomycin for him. See exhibit 10 at 131 (June 10, 2014), exhibit 9 at 295 (discharge report).

The main dispute between the parties and their experts is whether the skin lesions were vasculitic. Ms. Bourche contends the lesions were vasculitic (and caused by an adverse reaction to the hepatitis B vaccine).[9] The Secretary counters that the skin problems were not vasculitic. For reasons explained in section III. C below, this position is more persuasive.

Regardless of whether the lesions were vasculitic, the doctors treating Mr. Bourche attempted to determine the portal of entry for the staph bacteria. See Tr. 379 (distinguishing sources of bacteria from portal of entry). Conceivably, as Dr. Meditz explained, the portal of entry could have been either a skin lesion or Mr. Bourche's fistula. Exhibit 9 at 316. Dr. Meditz and Dr. Bozeman each observed the fistula and stated that the fistula did not appear infected. Exhibit 9 at 316, 322. The doctor who discharged Mr. Bourche from the hospital wrote: "Ultimately, the source was unclear . . . ." Id. at 295. The discharging doctor also directed Mr. Bourche to continue to take vancomycin for six more weeks. Id.

Before Mr. Bourche was discharged, his heart was tested via a transthoracic echocardiogram. This echocardiogram did not show any evidence of endocarditis. Exhibit 9 at 451, 295 (discharge report). The ejection fraction was 15-20 percent. Id. at 451.

Mr. Bourche's last visit in May 2014 was an appointment in Dr. Meditz's office on May 28, 2014. Mr. Bourche returned for a follow-up on his methicillin-susceptible *Staphylococcus aureus* ("MSSA") bacteremia, the source of which was unknown. As part of her record of Mr. Bourche's history of present illness, Dr. Meditz referenced her report from May 23, 2014. Mr. Bourche was following up because his current symptoms had worsened. Worsened symptoms included severe abdominal pain that was associated with sweats, anorexia, and loose bowel movements. Mr. Bourche specifically denied a skin rash. He was still taking vancomycin and was anticipated to continue taking vancomycin until July 6, 2014. Exhibit 3 at 33.

When Dr. Meditz conducted a physical exam on his skin and subcutaneous tissue, she found that Mr. Bourche had "no rashes present [and] no lesions present." His skin was also "warm and dry to touch." Id. Dr. Meditz's findings,

[9] Dr. Bozeman wrote that the bacteria could have entered Mr. Bourche's bloodstream "from the sores that he has had for several months." Exhibit 9 at 322. If Dr. Bozeman's May 24, 2014 report of "several months" meant more than 31 days, then Mr. Bourche had sores before the April 23, 2014 vaccination. Under this sequence, the vaccination could not have caused the sores. Tr. 342. However, the more persuasive evidence indicates that Mr. Bourche did not have sores before the vaccination. Tr. 69, 127.

as presented in this May 28, 2014 report, carry significance in the analysis about when Mr. Bourche developed vasculitis. See section III.B, below.

Dr. Meditz diagnosed Mr. Bourche as suffering from bacteremia, among other problems. Her plan included a continued prescription for vancomycin. Exhibit 3 at 34.

G. Health in June – August 2014

While Mr. Bourche saw many doctors in these three months, for purposes of this litigation, the most important appointment was with Dr. Meditz on June 24, 2014. Another important doctor was Steven R. Hong, a dermatologist, who saw Mr. Bourche at least six times.

Before Mr. Bourche saw Dr. Hong, Mr. Bourche went to a different dermatologist, John Fueston, on June 26, 2014. (Mr. Bourche had seen Dr. Fueston as far back as 2012). Mr. Bourche saw Dr. Fueston because he had a rash on his four extremities and his nose. Dr. Fueston recorded that Mr. Bourche is a dialysis patient, who says "his skin does not heal well. He is very itchy, but does not use moisturizes or anti-itch creams." Exhibit 6 at 11. Mr. Bourche also informed Dr. Fueston that he "had a bad reaction a few weeks ago to a hepatitis booster shot resulting in facial swelling, especially his nose. The swelling has resolved, but a circular, raised spot remains." Id.

After obtaining this history, Dr. Fueston conducted "a full skin exam, except for the groin." Id. at 12. Dr. Fueston identified, as lesion B, a 6 mm keratotic papule on the tip of Mr. Bourche's nose. Dr. Fueston also recorded that Mr. Bourche "has a few brown macules and papules on the face, trunk, and 4 extremities. There are many excoriated papules with bruising on the lower extremities and fewer on the upper extremities, shoulders, and back." Id.

Dr. Fueston considered Mr. Bourche as suffering from several possible skin conditions, including prurigo nodularis because Mr. Bourche "admits to scratching his skin." Id. Dr. Fueston also performed a biopsy on skin from the tip of Mr. Bourche's nose. This biopsy revealed that Mr. Bourche had "squamous papilloma with features of lichenification." Id. at 14. Dr. Matloubian explained this was, in layperson's term, a wart. Exhibit A at 4; Tr. 331.

The critical appointment with Dr. Meditz occurred on June 24, 2014. The history of present illness is like Dr. Meditz's report from May 28, 2014, noting that Mr. Bourche suffers from MSSA bacteremia. For "antibiotic therapy," Dr. Meditz recorded that Mr. Bourche's "current antibiotics include: vancomycin. The end

date of antibiotics is anticipated to be 07/06/2014. Side effects of the therapy include: pruritus." Exhibit 3 at 22. Mr. Bourche's current complaints included: "Painful skin lesions on his LE, concerned because they are not healing and have been there for weeks." After Dr. Meditz examined Mr. Bourche's skin and subcutaneous tissue, she found "painful purpuric papules/ulceration[s] on shins bilaterally." Id. at 23.

Dr. Meditz assessed Mr. Bourche as suffering from seven conditions of which the most important was the last listed. Dr. Meditz stated that Mr. Bourche suffered from a rash. She added: "Clinically appears vasculitic, recommended Derm eval – patient already has dermatologist and will make appointment." Id.

After the follow-up appointment with Dr. Meditz on June 24, 2014, Mr. Bourche returned to her on July 2, 2014. While Mr. Bourche's current symptoms had improved, he was complaining of "ongoing abdominal pain (has appointment with GI) and rash on bilateral LE." Id. at 16. Dr. Meditz's inspection of Mr. Bourche's skin and subcutaneous tissue revealed "scattered painful ulcers ½ cm each, primarily on shins – bilaterally." Id. at 17; accord Tr. 293.

The assessment from Dr. Meditz included three items. For the skin rash, Dr. Meditz "took culture today; saw dermatology who felt it was not vasculitis. Took [biopsy] of nose." Exhibit 3 at 17. For the MSSA bacteremia, Dr. Meditz recorded that: "Some of symptoms of fatigue, nausea could be related to vancomycin, which will be [discontinued] within the week. Will discuss with Dr. Holland repeating [transthoracic echocardiogram] in the near future to confirm lack of vegetation in this high risk patient with pacer in place." Id. For the abdominal pain, Dr. Meditz recorded that Mr. Bourche has "appointment with GI. Talked to Dr. Dolan after last visit and reviewed labs including transient increase in [liver function tests]." Id.

The appointment with a gastroenterologist to which Dr. Meditz referred occurred on July 9, 2014. Dr. Robert Dolan performed an upper gastrointestinal endoscopy and colonoscopy. Id. at 5-10. The colonoscopy revealed "[d]iffuse mild inflammation . . . in the entire examined colon." Id. at 10. Dr. Dolan consulted a doctor at Johns Hopkins Medicine, who concurred with Dr. Dolan's finding. With reference to the inflammation, this consultant stated "some of the acute inflammation is within small vessel walls (margination) yet with minimal to absent fibrin and without vascular destruction. Early leukocytoclastic vasculitis, which can be in the colon and be associated with various chronic medical disease or allergic reaction, cannot be excluded . . . ." Id. at 12. Dr. Zizic and Dr. Matloubian explained that margination means the white blood cells are near the

blood vessels, but they have not broken the blood vessel wall. Thus, the colonoscopy did not show vasculitis. Tr. 294, 346, 376.[10]

Vasculitis

The term "vasculitis" means inflammation in the blood vessels. Dorland's at 2026. A leukocytoclastic vasculitis is a hypersensitivity vasculitis. A hypersensitivity vasculitis, in turn, is "a group of systemic necrotizing vasculitides thought to represent hypersensitivity to an antigenic stimulus, such as a drug, infectious agent, or exogenous or endogenous protein; all disorders in this group involve the small vessels. Types include varieties of Henoch-Schönlein purpura and serum sickness." Id. Dr. Zizic provided more information about leukocytoclastic vasculitis. Tr. 150-54.

Doctors divide vasculitis into various types. Some vasculitides affect the skin, some affect the skin plus other organs, and some do not affect the skin at all. Tr. 254. Dr. Matloubian explained a diagnosis of vasculitis requires a biopsy and biopsies will inform the specific type of vasculitis. Tr. 254-55. As Mr. Bourche later had two skin biopsies, details about those results will be discussed in that context.

After the biopsy from the colonoscopy, but before the findings were reported, Mr. Bourche returned to his cardiologist's office as Dr. Meditz had recommended. The physician's assistant for Dr. Holland, Hilary Clark, recorded the following history: "Pt states he was fine until got hepatitis booster right before hospitalization in May. He is very upset about this because had been so much better after BiV-AICD [pacemaker] placed. Broke out in intra and peri-oral ulcers – roof of mouth sloughed off. Then bacteremic -> hospitalized." Exhibit 8 at 50 (July 10, 2014). The history via Ms. Clark continues: "Sent home on IV [antibiotics], started developing leg ulcerations primarily lower extremities but one on back. . . . Finished [antibiotics] 1 week ago." Id.

For more recent problems, Mr. Bourche reported: "Feels overall terribly." Id. His abdominal pain and shortness of breath and leg ulcers "are his main complaint." Id. Ms. Clark's physical exam of Mr. Bourche's extremities showed "Bilat LE [with] mild edema, multiple ulcerations [with] black scab 1-2 mm to 2 cm in size, surrounding eryth[ema] and tenderness. One on upper back. No oozing or discharge." Id. at 52.

[10] Dr. Zizic linked findings of inflammation on the colonoscopy to findings following the autopsy. Tr. 188-94. But, Dr. Matloubian disagreed. Tr. 306-07.

The report, which was signed by Ms. Clark and generated by Dr. Holland, assesses Mr. Bourche with a rash and other nonspecific skin irruption. "Referral to Derm here Dr. Hong for further eval. Was not happy [with] first Dermatology opinion in Longmont . . . These skin lesions are his most bothersome complaint . . . . Unsure if this is venous stasis only (doubt), inflammatory reaction of some kind dermal layer or even vasculitis or new secondary [infection]." Id. at 53. The term "venous stasis" probably refers to "stasis dermatitis," which is a "chronic, eczematous dermatitis caused by venous insufficiency in the lower limb, usually first involving the skin medially near the ankle and sometimes spreading over the entire lower limb; characteristics include edema, pigmentations, and often ulceration." Dorland's at 496.

The report about bothersome skin problems seems consistent with his dialysis record. On July 14, 2014, the dialysis nurse noted: "Pt. has sores to LE bilat[erally]. Pt going to see dermatologist tomorrow." Exhibit 10 at 1432. This note appears to be the first time that vasculitic skin problems were mentioned in the dialysis records after the vaccination. A similar record from a physician at the dialysis center comes from July 16, 2014. This record states Mr. Bourche "has resolving vasculitic rash on LE's, likely sequela of reaction to hep B vaccine when he developed oral ulcers as well . . . No new lesions." Id. at 133. Five days later, the doctor entered a similar report: "LE rash resolving. This [and] GI findings consistent with limited leukocytoclastic vasculitis related to Energex [hepatitis B vaccine reaction]." Id. at 135. Another dialysis center physician on July 30, 2014, wrote: "Looks like skin lesions are a leukocytoclastic type vasculitis, possible from hep B vaccine. He thinks lesions are improving, albeit slowly with topical Rx." Id. at 136.

The first of multiple appointments with dermatologist Steven Hong occurred on July 15, 2014. Because Dr. Hong is a dermatologist, his evaluations of Mr. Bourche's skin condition are very informative.

When Mr. Bourche presented to Dr. Hong, Dr. Hong reported the history of present illness in two parts. For ulcers, Dr. Hong recorded: "legs and arms. Dialysis patient. Got a hepatitis booster, blistered nose, mouth and arms." Exhibit 8 at 47. For the biopsy of Mr. Bourche's nose, Dr. Hong stated "benign." Id. The subjective narrative elaborates that Mr. Bourche had "Hepatitis booster 2 mo ago, broke out mult mouth ulcers. Hosp. for bacteremia and received vancomycin, stopped approximately 7/3/14. Had EGD and colonoscopy 7/9: diffuse gastropathy, mult ulceration colon. I do not have the biopsy results." Id. at 48. This section continues: "Legs inflamed and swollen for about 2 weeks with the

development of mult sores: painful. Saw a Derm in Longmont and told it was stasis derm." Id.[11]

For objective findings, Dr. Hong recorded: "Erythematosus/pitting edematous LE worse on R. Mult sharply marginated hemorrhagic superficial ulcerations, punctuate to approximately 2.5 cm on LE. Few small papules forearms." Id. Based upon this information, Dr. Hong's first assessment was "Probable vasculitis, ? Drug-induced (?vancomycin). I assume this is related to the same process in his colon." Id.

Dr. Hong's plan states that Mr. Bourche "thinks he is getting new ones on his legs so we will biopsy one. A 4 mm crusted papule r shin was excised." Id. at 49. This right shin skin was examined in a biopsy.

Mr. Bourche returned to Dr. Hong's office two days later for a recheck. Under objective, Dr. Hong recorded: "Erythema, edema lower legs much improved, all crusted hemorrhagic ulcers superficial and healing. Path: final pending, sent to Loren Golitz Denver for 2nd opinion. I looked at it and it showed epidermal necrosis with assoc. inflammation but no active vasculitis." Id. at 45 (July 17, 2014). Dr. Hong's assessment was "Still consistent with probable drug-induced cause. Most likely the inflammatory response is all subsiding and in the healing phase." Id.

Dr. Golitz, a dermatopathologist, responded to Dr. Hong on July 18, 2014. His report begins that the clinical impression is "drug induced vasculitis," and notes that Dr. Golitz's reviewed a single glass slide containing multiple skin sections. After reviewing his microscopic observations, Dr. Golitz's impression was: "Leukocytoclastic vasculitis with ulceration, skin, right shin." Id. at 122. Dr. Golitz's commented "the combination of vasculitis with colon involvement raises the possibility of Henoch-Schonlein purpura. A biopsy for direct immunofluorescence microscopy is recommended." Id. Dr. Zizic explained that Dr. Golitz could diagnose vasculitis because he could see "neutrophils in the walls of the vessel." Tr. 172.

[11] Dr. Hong's reference to a painful rash for two weeks is consistent with (a) an onset after the May 27, 2014 discharge for his staph infection, and (b) an onset around the time of Mr. Bourche's follow-up appointment with Dr. Meditz on June 24, 2014. This sequence fits a timeline supporting vancomycin as the cause of the skin problem. However, as Ms. Bourche argues, if Mr. Bourche arrived at the hospital with vasculitis, then the vancomycin did not cause the vasculitis. See Pet'r's Reply at 3.

After Dr. Golitz communicated his impression of the biopsy to Dr. Hong, Dr. Hong reported the possible HSP. Dr. Hong also continued to say that the vasculitis was probably drug-induced. Exhibit 8 at 43 (July 29, 2014), 41 (Aug. 1, 2014), 38 (Aug. 14, 2014). During these visits, the status of Mr. Bourche's skin lesions changed from "resolving" and "healing" to "worse." Because of this decline, Dr. Hong referred Mr. Bourche to a rheumatologist and ordered a second biopsy. Dr. Hong further responded to the decline by prescribing prednisone on August 14, 2014. Id. at 35-38.

These three appointments with Dr. Hong overlap with notes from two other doctors. First, unfortunately, Mr. Bourche's transplant status changed. Exhibit 10 at 246; see also Tr. 129. Second, Mr. Bourche returned to his gastroenterologist, Dr. Dolan. Dr. Dolan recorded that Mr. Bourche "has new skin lesions which may represent leukocytoclastic vasculitis. Earlier he had staph bacteremia, which in retrospect probably was related to his cutaneous lesions. . . . Colonoscopy revealed aphthous-type lesions throughout the entire colon but no active bleeding. Biopsies were possibly consistent with early leukocytoclastic vasculitis." Exhibit 5 at 5 (Aug. 5, 2014); accord Tr. 350. In Dr. Zizic's review of this record, Dr. Zizic emphasizes that the vasculitis was active in the sense of causing new skin lesions. Tr. 176-77.

The skin for Mr. Bourche's second biopsy came from his right foot. The dermatopathologist who interpreted this study, James E. Fitzpatrick, reported the results on August 19, 2014. Exhibit 8 at 121. The skin tissues were subject to direct immunofluorescence. Tr. 172. Direct immunofluorescence help specify the type of vasculitis. Tr. 254. But, the process of interpreting the results of depends, in part, on the subjective interpretation of the person looking at images. Tr. 174-75, 297-98, 348.

Here, Dr. Fitzpatrick reported the following results:

IgG: negative	C3: Negative
IgA: 1+ granular vessels	Fibrin: 3+ granular vessels
IgM: 2+ granular vessels	C1q: Not done

Exhibit 8 at 121.

After this second skin biopsy, Dr. Hong wrote his next report on Mr. Bourche. In the context of an August 22, 2014 recheck of Mr. Bourche's legs, Dr. Hong presented the following objective observations: "hemorrhagic crusted ulcers legs much less erythema, no new ulcerations." Exhibit 8 at 32. Dr. Hong's

assessment was "hypersensitivity vasculitis, ?HSP exacerbated by drug eruption." Id.

Before that visit with Dr. Hong, and while results of the second skin biopsy were pending, Mr. Bourche saw a rheumatologist, Stuart Weisman, on August 18, 2014. Dr. Weisman's report begins by saying that Dr. Mooney had referred Mr. Bourche for systemic vasculitis. Although Dr. Weisman's history of present illness is relatively sketchy, it, nevertheless, recapitulates the important events helpfully. "Has seen Dr. Hong recently – spontaneous ulcers. Started after hepatitis vaccine (developed facial swelling, blisters in nose and mouth). Vancomycin given for sepsis. Developed skin reaction from vancomycin. Much improved. Gastroenterology – multiple ulcers – seen at colonoscopy . . . He was given prednisone last Friday." Exhibit 12 at 15. Under assessment/plan, Dr. Weisman wrote: "I agree that hypersensitivity vasculitis is the most likely diagnosis. Testing for HSP is pending (skin biopsy for IgA deposits). Has improved somewhat with recent prednisone trial, will discuss further with dermatology." Id. at 19.

Henoch-Schönlein Purpura / IgA Vasculitis[12]

Henoch-Schönlein purpura is "sometimes a type of hypersensitivity vasculitis and sometimes of unknown cause, usually seen in children and associated with symptoms including urticaria, erythema, arthropathy, arthritis, gastrointestinal symptoms, and renal involvement." Dorland's at 1557. As Dr. Weisman suggested, "the finding of IgA vascular deposits is the *sine qua non* of HSP and adult IgA vasculitis." Exhibit A-4 (Carlson) at 9. According to this article, on direct immunofluorescence, HSP is an appropriate diagnosis when IgA vascular deposits are "isolated or predominate." Id. at 17 (table 3). However, other sources state that IgA deposits are "dominant." Exhibit A-6 (Audemard-Verger) at 580. "Bacteria, virus or parasitic agents were suspected to trigger the disease in genetically prone individuals, but causative agents and factors remain to be identified." Id.

IgA vasculitis can involve different organs. Tr. 151, 266, citing exhibit A-3 (Fett) at pdf 3. When the IgA vasculitis impairs the kidneys, the results on biopsy of the kidney resembles the biopsies found in IgA nephropathy. Tr. 151.

[12] The term "Henoch-Schönlein purpura" is older. The current term is IgA vasculitis. Exhibit A-6 (Audemard-Verger) at 580; see also Tr. 98. In treating Mr. Bourche, some doctors used the term Henoch-Schönlein purpura (or its abbreviation, HSP), and other doctors said IgA vasculitis.

For Mr. Bourche, after the biopsy of his right foot, he continued to participate in dialysis. Physicians at the dialysis center continued to make notes about his skin condition. On August 20, 2014, a doctor wrote: "Legs / ankles wrapped. [Illegible] [with] ulcers slow to heal." Exhibit 10 at 140. Another doctor, who may have been Dr. Mooney, examined Mr. Bourche's legs on August 25, 2014. Although difficult to read, it appears that the doctor concluded that Mr. Bourche "likely" had "Stevens Johnson [syndrome]" from reaction "[secondary to] hepatitis vaccine." Id.

In the following weeks, the doctors at the dialysis center observed some improvement. His legs had "less edema" on September 3, 2014. Id. at 141. On September 12, 2014, a doctor wrote: "Seen by university [transplant team] on hold until vasculitis resolves. Remains on pred & wounds / ulcers are slowly healing." Id. at 142; exhibit 78 at 70 (duplicate). A doctor, whose handwriting appears to be from Dr. Mooney, wrote on September 22, 2014: "No new skin lesions. Will track down skin [biopsy] results. Would favor tapering of prednisone and avoid further immunization reactions." Exhibit 10 at 143.[13]

Also, by August 2014, Mr. Bourche had consulted attorneys about his claim in the Vaccine Program. See Pet'r's Mot. Interim Fees, filed Jan. 31, 2017, exhibit A (timesheets) at 1.

H. Cardiac Problems – October and November 2014[14]

In October and November 2014, Mr. Bourche suffered significant heart trouble. However, the first medical record in this time came from Dr. Hong on October 6, 2014. The subjective portion begins that Mr. Bourche was following up for IgA vasculitis. Under the objective portion, Dr. Hong memorializes that Mr. Bourche had "mult eschars lower legs, inflammation is mild. Few ulcerations to deep dermis/subcu." Dr. Hong's relevant assessment was "hypersens vasculitis, improved." Exhibit 12 at 45.

During dialysis on October 24, 2014, Mr. Bourche had a rapid heart rate and was sent to the hospital. Tr. 21. A transesophageal echocardiogram detected vegetation on one of his heart valves (a mitral valve), a condition called

[13] As mentioned earlier, Dr. Fitzpatrick reported the skin biopsy results on August 19, 2014. Testing showed, in part, IgG; negative; IgA: 1+; and IgM 2+. Exhibit 8 at 121.

[14] Because Mr. Bourche's history after his August 19, 2014 biopsy contributes less to the outcome of this case, these events are described more cursorily. Nevertheless, the underlying records have been reviewed.

endocarditis. Exhibit 9 at 728-29, 731; Dorland's at 616-17. The ejection fraction had declined to 15-20 percent from the previous measurement in August 2014, which was 30 percent. Exhibit 9 at 811-12; exhibit 8 at 153.

Mr. Bourche remained in the hospital until he could have an operation to repair his mitral valve. During this interim two records are significant. First, Dr. Mooney saw him in the hospital. Dr. Mooney, who was consulted due to his experience in treating Mr. Bourche's end stage renal disease, reported Mr. Bourche's history. With respect to the vaccination, Dr. Mooney provided that Mr. Bourche "had been admitted to Boulder Community Hospital in May. He had hyperkalemia and chest pain. He had reported onset of mouth ulcerations along with upper and lower extremity skin lesions that had started in April. Initially it was felt that the trigger was hepatitis vaccine. During this time, he may have also had a reaction to vancomycin." Exhibit 9 at 738. Dr. Mooney also provided his understanding of Mr. Bourche's skin condition. Dr. Mooney stated that Mr. Bourche's "lesions continued in spite of the mouth ulcerations healing. . . . He was seen by Dr. Hong for evaluation of his dermatologic condition. Skin biopsy revealed a leukocytoclastic vasculitis. In August, he was seen and evaluated by Dr. Weisman. He has been on high-dose prednisone therapy during this time. It is not clear whether the patient has been having new skin lesions or not." Id. at 739. For allergies, Dr. Mooney listed vancomycin, but did not list the hepatitis B vaccine. Id.

Dr. Mooney's assessment begins with a plan for dialysis. Dr. Mooney then discusses Mr. Bourche's other health problems. "He has leukocytoclastic vasculitis on skin biopsy. It is not clear exactly what the trigger was, but originally it was felt to be due to his hepatitis B vaccine. He previously received that without a problem. This is not a finding that I would typically see with IgA nephropathy. He has been on steroid therapy with slow to heal skin ulcerations. . . . It is interesting to note that it is hard to tell whether his vasculitis is still active or not in spite of the slow healing that is going on in his lower extremities." Id. at 740; accord Tr. 351.

The second relevant medical record from the October 2014 hospitalization was created by Myles S. Gruber on October 28, 2014. Dr. Matloubian identified Dr. Gruber as the cardiac surgeon. Tr. 353. Dr. Gruber stated that Mr. Bourche has "numerous vasculitic type ulcers that are chronically infected in both legs." Exhibit 9 at 737.

Also, during this hospitalization, Ms. Bourche took pictures of Mr. Bourche in his hospital bed. One picture shows lesions on his legs, wrapped in plastic. Exhibit 66; Tr. 24, 43.

Mr. Bourche underwent mitral valve surgery on November 5, 2014. Exhibit 9 at 741. After this operation, he functioned much better. Tr. 24, 42, 417, 495.

Following his November 13, 2014 discharge for the mitral valve repair (see exhibit 9 at 741), Mr. Bourche had an episode of atrial fibrillation for which he was treated at a hospital. See exhibit 9 at 918-23. During this hospitalization, Richard K. Halterman consulted on Mr. Bourche's case. Dr. Halterman recorded that Mr. Bourche "did have Staph bacteremia. He was placed on vancomycin. Shortly after that time, he developed a leukocytoclastic vasculitis, with severe skin lesions over his lower extremities." Id. at 928.

I. Health in 2015 – 2016

Mr. Bourche's heart was checked again on January 5, 2015, by a transthoracic echocardiogram. Exhibit 76 at 230; see also exhibit 76 at 180 (Dr. Holland's report of this test). The ejection fraction was 31 percent. Id.

On January 12, 2015, Mr. Bourche saw Dr. Weisman, the rheumatologist whom he had seen in August 2014. Dr. Weisman started his history of present illness by mentioning that Mr. Bourche had a mitral valve repair and feels better in general. Dr. Weisman stated: "His skin ulcers have improved with routine wound care, but lesions persist. No new ulcers have developed. Few small erythematous areas have developed on the arms, legs." Exhibit 12 at 60. Dr. Zizic interpreted this report as showing the development of new lesions. Tr. 219. But, Dr. Matloubian stated this record showed that Mr. Bourche was not developing new lesions. Tr. 303.

Another check of Mr. Bourche's heart happened on March 22, 2015. His ejection fraction was 23 percent. Exhibit 76 at 225.

In spring 2015, Mr. Bourche explored whether other hospitals would place him on a transplant list. Accordingly, he traveled to Cedars-Sinai Medical Center in Los Angeles California to be examined by doctors there.[15]

[15] Although a record from Mr. Bourche's cardiologist, Dr. Holland, references Cedars-Sinai (exhibit 13-2 at 286 [pdf 135]), Ms. Bourche did not file records from Cedars-Sinai until after the hearing. Therefore, the experts did not comment upon records from Cedars-Sinai in their testimony.

Consistent with medical records from other providers, the medical records from Cedars-Sinai are ambiguous about some aspects of Mr. Bourche's health. A cardiothoracic surgeon, Fardad Esmailian, evaluated Mr. Bourche on March 21, 2015. Dr. Esmailian's history noted that Mr. Bourche suffered from vasculitis and had allergies to hepatitis B vaccine and vancomycin. Exhibit 72 at 10-11. The physical exam of Mr. Bourche's skin showed that Mr. Bourche "has an open wound in the right leg which is still healing from August of 2014 secondary to his vasculitis." Id. at 11.

Due to Mr. Bourche's history of anemia, a hematologist / oncologist (Kevin S. Scher) evaluated him on March 25, 2015. Dr. Scher noted that he did not have complete records available to him, but obtained a history from Mr. Bourche. Mr. Bourche recounted: "In April of 2014, he had a hepatitis B vaccine, and after the vaccine suffered with facial swelling, skin breakdown and was diagnosed with a vasculitis. He then developed a staph infection which presumably led to his endocarditis in November." Id. at 69. In accord with this history, Dr. Scher listed "IgA vasculitis" as one of the conditions afflicting Mr. Bourche. Id. Dr. Scher listed the hepatitis B vaccine and vancomycin as allergies. Id. at 70. The physical examination of Mr. Bourche's extremities showed "[m]ultiple lower extremity skin ulcerations, 1+ edema bilaterally." Id.

An infectious disease doctor, Phillip Zakowski, saw Mr. Bourche on March 26, 2015. Mr. Bourche told Dr. Zakowski about his experience with the hepatitis B vaccine. "The patient has a history of receiving hepatitis B vaccine on April 24, 2014 [sic, actually April 23, 2014]. The patient states his face blew up that night, and he developed subsequent skin lesions. He attributes all this to a reaction to the hepatitis B vaccine." Exhibit 72 at 139. Mr. Bourche also spoke to Dr. Zakowski about his skin problems. Mr. Bourche said that he "subsequently had a biopsy of the skin lesion by a dermatologist in Boulder, Dr. Hong. This was diagnosed as vasculitis. He has subsequently been on prednisone." Id. The report from Dr. Zakowski continues to discuss Mr. Bourche's skin problem. "The patient developed multiple skin lesions on his lower extremity. He apparently had bacteremia from this. I spoke with his Infectious Disease physician listed below [Dr. Meditz]. She states that he had MSSA [methicillin-susceptible *Staphylococcus aureus*] bacteremia 05/23, not MRSA [methicillin-resistant *Staphylococcus aureus*]. … Because of a [penicillin] allergy he got 6 weeks of IV antibiotics of vancomycin . . . After this, he felt the skin lesions were worse, and that he was concerned that the vancomycin may have triggered a further inflammatory reaction in his lower extremities." Id. Dr. Zakowski added: "He was felt to have an IgA vasculitis of his skin." Id. at 140.

For the physical examination, Dr. Zakowski was relatively detailed about Mr. Bourche's skin. Dr. Zakowski stated that his examination revealed: "healed old skin lesions, bilateral lower extremity, with the right anterior tibial area, non healed ulcer approximately 1.5 x 1.5 cm with a clean granulating base, and a right dorsum forefoot lesion approximately 1 x 1 without active purulence; skin appearance on bilateral lower extremities suggestive of bilateral vascular changes or vasculitis." Id. at 141. In Dr. Zakowski's discussion, he stated: "A concern of mine would be the lower extremity lesions, whether he has ongoing vasculitis, and his lack of ability to heal, particularly the right anterior tibial one. I will discuss this further with the team." Id.

A nephrologist evaluated Mr. Bourche for a possible kidney transplant on March 25, 2015. Dr. Alice Peng obtained a history that began with Mr. Bourche's IgA nephropathy in 2006. As relevant for this litigation, Mr. Bourche told Dr. Peng that in 2014, he developed vasculitis after a hepatitis B booster. "He developed skin lesions involving all 4 extremities. He then developed a superimposed MRSA infection which was complicated by MRSA endocarditis." Id. at 96. Dr. Peng listed the hepatitis B vaccine has an allergy that caused vasculitis. She did not list vancomycin as an allergy.

As part of her physical examination, Dr. Peng reviewed Mr. Bourche's skin and found that it was "[w]arm to touch with multiple healing shallow ulcers involving the distal extremities." Id. at 99. Based upon all the information available to her, Dr. Peng came to the following recommendation: "Overall the patient does appear to be an appropriate candidate for dual heart and kidney transplant if cleared by the heart transplant team. He would certainly not be a candidate for kidney transplant alone. We will make a final determination of candidacy in recipient selection committee." Id. at 100.

Ultimately, according to notes made by Dr. Holland from a conversation with a Cedars-Sinai doctor, the transplant committee determined that Mr. Bourche was "too high a risk candidate for combined orthotopic heart transplant and current commitment renal transplant. Biggest factors included some degree of fixed pulmonary hypertension, unhealing lower extremity wounds, previous infections, unknown liver status." Exhibit 13-2 at 285 [pdf 135] (Apr. 3, 2015).

By October 2015, Mr. Bourche's heart function had declined so much that hospice was contemplated. Exhibit 43 at 7; see also exhibit 13-2 at 286 [pdf 136]; Tr. 52.

In January 2016, Mr. Bourche was in heart failure. Tr. 189, 358. He died on January 16, 2016, and an autopsy was performed the next day. Exhibit 47 at 19.

The death certificate states severe chronic heart failure caused cardiogenic shock, which led to mesenteric ischemia / necrosis. Exhibit 45; see also Tr. 446 (Dr. Stark's opinion about the death certificate). Following Mr. Bourche's death, Ms. Bourche became the representative of his estate and, in that capacity, became the petitioner. She has continued the litigation, claiming that the hepatitis B vaccine substantially contributed to the development of vasculitic skin lesions that substantially contributed to Mr. Bourche's death.

II. Standards for Adjudication

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

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

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

In weighing evidence, special masters are expected to consider the views of treating doctors. Cappizano v. Sec'y of Health & Human Servs., 440 F.3d 1317, 1326 (Fed. Cir. 2006). The views of treating doctors about the appropriate diagnosis are often persuasive because the doctors have direct experience with the patient whom they are diagnosing. See McCulloch v. Sec'y of Health & Human Servs., No. 09-293V, 2015 WL 3640610, at *20 (Fed. Cl. Spec. Mstr. May 22, 2015). However, the views of a treating doctor are not absolute, Snyder v. Sec'y

of Health & Human Servs., 88 Fed. Cl. 706, 745 n.67 (2009), even on the question of diagnosis, R.V. v. Sec'y of Health & Human Servs., 127 Fed. Cl. 136, 141 (2016), appeal dismissed, No. 16-2400 (Fed. Cir. Oct. 26. 2016).

The views of treating physicians should also be weighed against other, contrary evidence present in the record—including conflicting opinions among such individuals. Hibbard v. Sec'y of Health & Human Servs., 100 Fed. Cl. 742, 749 (2011) (finding that it is not arbitrary or capricious for special masters to weigh competing treating physicians' conclusions against each other), aff'd, 698 F.3d 1355 (Fed. Cir. 2012); Veryzer v. Sec'y of Health & Human Servs., No. 06-522V, 2011 WL 1935813, at *17 (Fed. Cl. Spec. Mstr. Apr. 29, 2011), mot. for rev. denied, 100 Fed. Cl. 344, 356-57 (2011), aff'd without op., 475 Fed. App'x 765 (Fed. Cir. 2012).

This principle comes into play in Mr. Bourche's case because treating doctors reached opposite conclusions about Mr. Bourche. For example, as previously described in section I. A, in October 2009, Dr. Walker, the reviewing pathologist, stated that Mr. B was having a recurrence of his IgA nephropathy. Exhibit 9 at 628. Yet, Dr. Mooney testified that Mr. Bourche did not. Tr. 84. In this situation, deferring to all treating doctors is impossible. Thus, as explained below, the analysis sometimes credits and sometimes rejects statements of treating doctors, but only after considering all the evidence.

III. Analysis

Ms. Bourche has not established her case for four reasons. First, testing in connection with the vasculitis demonstrated that Mr. Bourche did not respond in a way that Dr. Zizic's theory had predicted. Second, although Dr. Zizic had asserted that Mr. Bourche developed vasculitis in early May 2014, relatively close in time to the April 23, 2014 hepatitis B vaccination, a careful analysis of the evidence shows that the vasculitis became manifest near the end of June or beginning of July 2014. These two reasons are the primary reasons for finding that Ms. Bourche is not entitled to compensation and they are independent of each other. The third reason weighs less heavily and depends upon the finding that the vasculitis began near the end of June. This sequence of events makes Mr. Bourche's course more consistent, although not perfectly consistent, with a finding that his vasculitis was a consequence of his staph infection or the vancomycin given for the staph infection. Finally, Ms. Bourche has not established that the endocarditis, regardless of the cause of the endocarditis, hastened Mr. Bourche's death. These reasons are explained in detail below.

A. Mr. Bourche did not respond to the vaccination in a way petitioner's theory or theories predicted

Petitioners should establish, by preponderant evidence, that the vaccinee responded to the allegedly causal vaccines in the way consistent with the theory articulated by their experts. See Hibbard v. Sec'y of Health & Human Servs., 698 F.3d 1355, 1364 (Fed. Cir. 2012); Dodd v. Sec'y of Health & Human Servs., 114 Fed. Cl. 43, 52-57 (2013); La Londe v. Sec'y of Health & Human Servs., 110 Fed. Cl. 184, 205 (2013), aff'd, 746 F.3d 1334 (Fed. Cir. 2014).

Dr. Zizic's theory for how hepatitis B vaccine can lead to vasculitis changed during the litigation. Dr. Zizic's first report presented the theory that the hepatitis B vaccine, which contains hepatitis B surface antigens, combines with antibodies against those antigens to form immune complexes. The antigen-antibody immune complex lodges in the blood vessels, clogging them, and leading to vasculitis. Exhibit 15 at 21. This theory can hold persuasive value. See Fields v. Sec'y of Health & Human Servs., No. 02-311V, 2008 WL 2222141, at *9-10 (Fed. Cl. Spec. Mstr. May 14, 2008) (finding the hepatitis B vaccine can cause a different type of vasculitis through immune complexes). This decision will refer to the theory involving the vaccine-derived hepatitis B surface antigen and hepatitis B antibody immune complex as the "primary" immune complex theory.

Dr. Zizic's second report clarifies his theory, again referencing immune complexes. He wrote: "With the right amount of antigen and antibody, they form complexes that are soluble and circulate in the blood and get deposited in the very small arteries and capillaries that comprise the vascular beds. This is what is seen in vasculitis or l[eu]kocytoclastic vasculitis." Exhibit 44 at 1. Neither Dr. Zizic's first report nor his second report mention the term "molecular mimicry."

Dr. Zizic's third report does use the term "molecular mimicry," but in a strange context. Dr. Zizic uses molecular mimicry to explain how a different vaccine (the flu vaccine) can cause a different disease (rheumatoid arthritis). Exhibit 48 (report dated June 9, 2016) at 5. This passage appears to be copied and pasted from a report intended for a different case. Despite the apparent poor fit in Mr. Bourche's case, Dr. Zizic later included molecular mimicry as one causal theory. He stated: "In summary, the vaccine triggered activation of B and/or T lymphocytes through molecular mimicry, cross-priming, immune complex formation or a combination of these, which because of [Mr. Bourche's] genetic susceptibility, resulted in autoimmunity and the development of vasculitis." Id. at 9.

In the final report before the hearing, Dr. Zizic quoted his third report to explain his theory. He stated: "'Subsequent to the breaking of immunologic tolerance, self-antigens replace the initial inciting foreign antigen (E. G. infectious agent or vaccine) and autoimmune disease develops. Although the infectious agent may be cleared, or a vaccine eventually degraded, since the self-antigens are present all the time, the disease is perpetuated for prolonged periods, and sometimes for life.'" Exhibit 53 at 2, quoting exhibit 48 at 5. Dr. Zizic's fourth report did not use the term "mimicry."

During the hearing, when Dr. Zizic explained his theory, he returned to the primary theory of immune complex formation. See Tr. 153-57. In this context, Dr. Zizic discussed how an infection with hepatitis B virus can lead to problems outside of the kidneys. Dr. Zizic testified: "the hepatitis B virus with its antibody that forms these complexes . . . that end up causing an inflammatory process." Tr. 156. Dr. Zizic further maintained that if the hepatitis B virus could provoke a reaction, then the hepatitis B vaccine could do the same. Notably, during Dr. Zizic's direct testimony he did not discuss "molecular mimicry" at all. See Tr. 221.

Despite the lack of direct testimony, the undersigned asked Dr. Zizic about molecular mimicry. Dr. Zizic clarified that molecular mimicry was not between the hepatitis B surface antigen and the walls of the blood vessels, which is a more typical autoimmune reaction. "It can be any antigen in any cell that has the same amino acid sequence, and once the antibody to that antigen combine and circulate in the blood, they get deposited in the vessels." Tr. 222. Thus, molecular mimicry involving an unidentified cell is a step to producing the immune complexes that lead to vasculitis. This decision will use the term "secondary immune complex theory" to refer to the process in which molecular mimicry precedes the development of immune complexes.

When Dr. Matloubian addressed the primary immune complex theory, he demonstrated that this theory could not explain what happened with Mr. Bourche. The critical fact was that Mr. Bourche's immunity to the hepatitis B virus was retested approximately two weeks after vaccination.[16] This test showed that Mr. Bourche produced, as expected, antibodies to the hepatitis B surface antigen. However, the hepatitis B surface antigen, which came from the vaccine, was no longer present. Exhibit 10 at 239 (May 7, 2014).

[16] This retesting does not typically happen.

In both reports and testimony, Dr. Matloubian persuasively explained that without the continued presence of the hepatitis B surface antigen, Mr. Bourche could not continue to produce the immune complexes that clog the blood vessels. Exhibit A at 13-14; Tr. 307-10. Dr. Matloubian's insight appears to have forced the presentation of the secondary immune complex theory in Dr. Zizic's later reports.[17]

The secondary immune complex theory fares no better. First, under Althen prong one, a petitioner bears the burden of presenting a persuasive medical theory. Boatmon v. Sec'y of Health & Human Servs., 941 F.3d 1351, 1359 (Fed. Cir. 2019) (citing Moberly, 592 F.3d at 1322). The theory that the hepatitis B surface antigen contained in the hepatitis B vaccine resemble some unidentified and unspecified portion of the body and this similarity sparks a cross-reaction was not adequately developed. It is far from persuasive. Caves v. Sec'y of Health & Human Servs., 100 Fed. Cl. 119, 135 (noting that the special master "properly" looked for evidence supporting molecular mimicry in the context of the vaccine and the injury), aff'd without op., 463 Fed. App'x 932 (Fed. Cir. 2012).

Second, even if the secondary immune complex theory worked on its face, the theory leads to the production of immune complexes. Immune complexes, in turn, contain IgG antibodies. Tr. 310-11. But see Tr. 399-401 (Dr. Zizic pointing out that IgG is not present in some situations). Dr. Zizic stated that "[i]n the normal leukocytoclastic vasculitis, they're generally IgG antibodies against the antigen. . . ." Tr. 152. However, when Mr. Bourche's skin biopsy from his right foot was subject to direct immunofluorescence, the vasculitic tissues did not contain IgG. Exhibit 8 at 121. Dr. Matloubian was persuasive when he explained: "So if this [vasculitis in Mr. Bourche] was due to antibodies against the hepatitis B surface antigen forming immune complexes through molecular mimicry or whatever mechanism, I would have expected to have IgG in the skin biopsy, and there is none." Tr. 297-98.

[17] Ms. Bourche argues that "Dr. Zizic's theory is that the Hepatitis B vaccination can induce an autoimmune reaction through the mechanism of molecular mimicry. Unfortunately, at trial, both Dr. Matloubian and Respondent's Counsel devoted much time to a fundamental misunderstanding of Dr. Zizic's theory." Pet'r's Posth'g Br. at 25. To the extent that anyone misunderstood Dr. Zizic's theory, some of the responsibility for the lack of clarify must fall to Dr. Zizic and Ms. Bourche's attorneys. It seems telling that of the two cites to the transcript that Ms. Bourche's brief identifies as places where Dr. Zizic explained his theory, one comes at page 395, the very end of a two-day hearing.

The lack of IgG in Mr. Bourche's skin biopsy undermines the theory that an adverse reaction to the hepatitis B vaccine caused his vasculitis. This reason, by itself, is sufficient to find that Ms. Bourche has not established, by preponderant evidence, that she is entitled to compensation. However, additional reasons support the denial of compensation.

B. Mr. Bourche's Vasculitis Did Not Arise in May 2014 as Dr. Zizic Assumed

The timing prong of Althen actually contains two parts. A petitioner must show the "timeframe for which it is medically acceptable to infer causation" and the onset of the disease occurred in this period. Shapiro v. Sec'y of Health & Human Servs., 101 Fed. Cl. 532, 542-43 (2011), recons. denied after remand on other grounds, 105 Fed. Cl. 353 (2012), aff'd without op., 503 F. App'x 952 (Fed. Cir. 2013).

As to the "medically acceptable" timeframe, the parties seem to have relatively little dispute. Dr. Zizic explained that the formation of immune complexes may take 7 to 14 days. Exhibit 44 at 2. Dr. Matloubian appeared not to challenge this estimate.

Rather, the parties dispute the status of Mr. Bourche's skin generally, and more particularly when he first manifested signs of his vasculitis. According to Ms. Bourche, Mr. Bourche was displaying vasculitis before he entered the hospital for the staph infection on May 23, 2014. Tr. 163-65; Pet'r's Posth'g Br. at 43-44. In contrast, the Secretary maintains that Mr. Bourche did not develop vasculitis until approximately one month later.

Resolution of this issue requires a detailed examination of Mr. Bourche's skin at different times. The evidence, as reviewed below, preponderates in favor of a finding that the vasculitis began near the end of June or beginning of July 2014.

1. Before and During the May 2014 Hospitalization

When Mr. Bourche arrived at the hospital on May 23, 2014, he had some lesions on his skin. Records from three doctors support this finding.

Dr. Karageorge stated that "[t]here are 2 macular areas present on the right forearm with overlying scabs. No fluctuance is noted. No streaking redness, erythema or increased warmth. Similar areas present over bilateral ankles." Exhibit 9 at 313. The term "macular" means the color has changed. Dorland's at 1094. The lack of "fluctuance" suggests that the skin lesion did not contain any liquid content. See Dorland's at 719. Dr. Matloubian interpreted Dr. Karageorge's

report as suggesting that Mr. Bourche was not suffering inflammation or infection. Tr. 283-84.

Dr. Bozeman reported that Mr. Bourche "has several papular lesions on his arms and legs, some of which are healed with keloid like scars, some that have some more open excoriations and none that appear infected." Exhibit 9 at 322. The term "papular" refers to small circumcised superficial solid elevations of the skin. Dorland's at 1373. In contrast to macular, a papular lesion is raised. Exhibit J at 9; Tr. 284. The term "keloid" is a "sharply elevated, irregularly shaped, progressively enlarging scar due to formation of excessive amounts of collagen and in the dermis during connective tissue repair." Dorland's at 978.[18] The term "excoriations" refers to scratches. Dorland's at 657.

The presence of excoriations or scratches on Mr. Bourche's arms and legs is not surprising as the dialysis process often causes dry and itchy skin. In other medical records, Mr. Bourche stated that he scratched his skin. See exhibit 6 at 11 (Dr. Fueston on June 26, 2014, stating Mr. Bourche "is very itchy, but does not use moisturizers or anti-itch creams").

The third doctor who described skin problems during Mr. Bourche's May 2014 hospitalization was Dr. Meditz. She wrote that Mr. Bourche "reports that he has had a few skin lesions but otherwise has not noticed any abnormalities of his skin . . . ." Exhibit 9 at 315. Her description of Mr. Bourche skin was: "he has some very small scabbed wounds. 1 on the left forehead, 1 on his ankle." Id. at 316.

These three reports stand in conflict with the report from the emergency room doctor, Dr. Lund. She stated that Mr. Bourche skin had "no rash." Id. at 303. Dr. Lund's report carries less weight. Dr. Lund created her report in an emergent setting, in which careful reporting of Mr. Bourche's skin condition may not have been at a premium, considering that Mr. Bourche had come to the hospital for fever and chills. Id. at 302. Although not specified in Dr. Lund's report, she may have been looking for new skin problems, different from the skin problem to which Mr. Bourche had become accustomed as a dialysis patient. In addition, the findings of three different doctors corroborate each other and carry, collectively,

[18] Dr. Bozeman's description of Mr. Bourche's rash as "keloid" appears to be the only instance in which the rash was described as keloid.

persuasive value. Also, Dr. Meditz's training as an infectious disease specialist makes her more attuned to skin problems.

Thus, the evidence supports a finding that Mr. Bourche entered the hospital with some skin problems, but these skin problems appear to be typical for a dialysis patient.[19]

2. Skin Condition on May 28, 2014

Mr. Bourche was discharged from the hospital on May 27, 2014. In the relatively short discharge report, the discharging doctor did not mention any problems with Mr. Bourche's skin. Exhibit 9 at 295-96.

The next day, Mr. Bourche had a follow-up appointment with Dr. Meditz. When she reviewed Mr. Bourche's symptoms, he specifically denied any skin rash. Similarly, when Dr. Meditz examined Mr. Bourche, she found "no rashes present [and] no lesions present." Exhibit 3 at 34.

The contrast between Dr. Meditz's May 23, 2014 report to which she referred in her May 28, 2014 report and Dr. Meditz's May 28, 2014 report strongly suggest that Mr. Bourche was not having skin trouble at the end of May 2014. On May 23, 2014, Dr. Meditz recognized and described "some very small scabbed wounds." Exhibit 9 at 316. This documentation demonstrates that Dr. Meditz was attentive to the skin condition of her patient. Thus, it would seem that if Mr. Bourche presented to her with similar skin problems on May 28, 2014, she would have followed this practice and noted them in her report. Instead, she made an affirmative notation that Mr. Bourche had "no rashes." Exhibit 3 at 34.

[19] The mouth blisters (or ulcers) which formed within nine days of the vaccination lasted for a relatively short amount of time. Although Dr. Mooney documented a blister on May 2, 2014, exhibit 10 at 127, there appear to be no other references to a mouth lesion. For example, the doctors who examined Mr. Bourche during his hospitalization for the staph infection did not document any mouth lesions. By June 26, 2014, Dr. Fueston reported that the facial swelling that Mr. Bourche associated with the hepatitis B vaccination had resolved. Exhibit 6 at 11; see also Tr. 282 (Dr. Matloubian acknowledging that the mouth lesion healed on its own).

Dr. Mooney explained that a typical reaction to a medication might be 5-10 days. Dr. Mooney further opined that Mr. Bourche's reaction lasted longer than 10 days because it led to vasculitis. Tr. 119-20. However, for the reasons explained in the text, the hepatitis B vaccination did not cause Mr. Bourche's vasculitis.

3. June – August 2014

Mr. Bourche again saw Dr. Meditz on June 24, 2014. Mr. Bourche complained to her that he was suffering "[p]ainful skin lesions on his LE." Exhibit 3 at 22. He was "concerned because they are not healing and have been there for weeks." Id. After examining Mr. Bourche's skin, Dr. Meditz reported "painful purpuric papules/ulcerations on shins bilaterally." Id. at 23. The term "purpuric" refers to "1. any of a group of conditions characterized by … small hemorrhages in the skin . . . 2. any of several conditions similar to the traditional purpuric group, which may be caused by . . . reactions to drugs." Dorland's at 1557. In Dr. Meditz's assessment of Mr. Bourche's rash, she stated that it "[c]linically appears vasculitic." Exhibit 3 at 23.

Dr. Meditz's description of skin ulcerations as "purpuric" appears to be the first time that a doctor used that adjective. Similarly, Dr. Meditz's tentative diagnosis of vasculitis appears to be the first time a doctor proposed that illness. This fact is a strong reason for finding that the vasculitis started after May 28, 2014, and before June 24, 2014.[20]

Other medical records also support a finding that Mr. Bourche's skin condition worsened in July 2014. For example, in his July 10, 2014 appointment at his cardiologist's office, Mr. Bourche told the physician's assistant, Hilary Clark, that his leg ulcers are one of "his main complaint[s]." Exhibit 8 at 50. Based upon Mr. Bourche's complaint, his unhappiness with his previous dermatologist, and the findings on physical examination, Ms. Clark and Dr. Holland referred Mr. Bourche to a new dermatologist, Dr. Hong. Id. at 53.

The dialysis records also point to an onset of new skin problems in July 2014. The dialysis nurse noted that Mr. Bourche "has sores to LE bilat." Exhibit 10 at 1432. Given that the nursing notes contain complaints about other problems, it seems likely that the first time Mr. Bourche was complaining about significant skin problems during dialysis was on July 14, 2014.[21] Within a few days, doctors

[20] Because Dr. Meditz saw Mr. Bourche multiple times during this critical period, the undersigned directed the parties to seek further information from her. Order, issued April 25, 2018. Unfortunately, however, Dr. Meditz was unable to supply more information about Mr. Bourche. Exhibit 77 (letter from Dr. Meditz's employer representing that she did not have any independent recollection of Mr. Bourche).

[21] For examples of complaints recorded in the nursing notes around this time, see exhibit 10 at 1382 (May 16 – abdominal pain), 1386 (May 21 – shortness of breath on exertion), 1392 (May 28 – abdominal pain, fatigue), 1402 (June 11 – shortness of breath, generalized pain), 1410

at the dialysis center were also noting the skin problems. See exhibit 10 at 133 (July 16, 2014: "resolving vasculitic rash on LE's, likely sequela of reaction to hep B vaccine"), 135 (July 21, 2014: "LE rash resolving . . . consistent with limited leukocytoclastic vasculitis related to" reaction to hepatitis B vaccination).

The non-contemporaneous histories also report that Mr. Bourche developed significant skin problems or vasculitis after he started taking vancomycin. On August 18, 2014, Dr. Weisman recorded: "Vancomycin given for sepsis. Developed skin reaction from vancomycin." Exhibit 12 at 15. On November 13, 2014, Dr. Halterman wrote that Mr. Bourche "was placed on vancomycin. Shortly after that time, he developed a leukocytoclastic vasculitis, with severe skin lesions over his lower extremities." Exhibit 9 at 928. On March 26, 2015, Dr. Zakowski recorded that after taking vancomycin for six weeks, Mr. Bourche "felt the skin lesions were worse, and that he was concerned that the vancomycin may have triggered a further inflammatory reaction in his lower extremities." Exhibit 72 at 139.

The microscopic examinations are also consistent with a finding that the vasculitis developed in either June or early July 2014. Dr. Dolan's colonoscopy from July 9, 2014 did not detect vasculitis because the white blood cells were only at the outside (margin) of the walls of the blood vessels. Exhibit 3 at 12. But, the July 18, 2014 skin biopsy suggested that Mr. Bourche was suffering from "drug induced vasculitis." Exhibit 8 at 122. The August 19, 2014 biopsy, which was subject to direct immunofluorescence, confirmed the vasculitis. Id. at 121.

4. Duration of Active Vasculitis

Regardless of when Mr. Bourche started to manifest symptoms of vasculitis, the parties dispute if or when Mr. Bourche stopped suffering from active vasculitis. "Active" vasculitis refers to a stage in which Mr. Bourche was creating new skin lesions, as opposed to the continuation (or healing) of old skin lesions. For the reasons explained below, the evidence supports a finding that Mr. Bourche did not produce new skin lesions after August 14, 2014, the date when he was prescribed prednisone.

At Mr. Bourche's first appointment with Dr. Hong on July 15, 2014, Mr. Bourche told Dr. Hong that he was getting new lesions. Exhibit 8 at 49. This evidence is slightly more persuasive than the report on July 16, 2014 that,

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(June 23 – lethargy), 1424 (July 4 – abdominal pain), 1450 (July 30 – stomach pain), 1454 (August 4 – abdominal pain, shortness of breath).

according to Mr. Bourche's dialysis doctor, he was not experiencing new lesions. Exhibit 10 at 133-34.

However, it appears that the development of new lesions appeared to pause around this time. On July 17, 2014, Dr. Hong reported that Mr. Bourche's ulcers are "superficial and healing." Exhibit 8 at 45. Based upon Dr. Hong's preliminary review of the skin biopsy, Dr. Hong specifically concluded that Mr. Bourche had "no active vasculitis." Id. The trend that Mr. Bourche's skin lesions were improving (and not developing new ones) continued in the next two appointments with Dr. Hong. Dr. Hong described them as "much improved" (July 29, 2014) and "healing" (August 1, 2014). Id. at 41, 43.

At this point, Mr. Bourche's lesions began to worsen. His gastroenterologist, Dr. Dolan, reported on August 5, 2014, that Mr. Bourche has "new skin lesions." Exhibit 5 at 5. While the report of a gastroenterologist's assessment of skin lesions might be questioned, Dr. Hong, a dermatologist, found that Mr. Bourche's legs were "worse and more painful" on August 14, 2014, with "new small crusted papules." Exhibit 8 at 38. This worsening appears to have prompted Dr. Hong to prescribe prednisone for Mr. Bourche.

After Dr. Hong started Mr. Bourche on prednisone, no treating doctor asserted that Mr. Bourche developed new skin lesions. Instead, Dr. Hong, on August 22, 2014, affirmatively stated "no new ulcerations." Id. at 32. On October 6, 2014, Dr. Hong described some lesions and found that Mr. Bourche's vasculitis was "improved." Exhibit 12 at 45. Dr. Hong did not say whether the lesions were new, nor did he say, "no new lesions."

During the hospitalization for the mitral valve repair, Dr. Mooney had an opportunity to examine Mr. Bourche. Dr. Mooney wrote: "It is not clear whether the patient has been having new skin lesions or not." Exhibit 9 at 739. Dr. Mooney added that Mr. Bourche has been "slow to heal." Id. at 740.

On January 12, 2015, Dr. Weisman, a rheumatologist, stated that Mr. Bourche's "skin ulcers have improved with routine wound care, but lesions persist. No new ulcers have developed. Few small erythematous areas have developed on the arms, legs." Exhibit 12 at 60. Although Dr. Zizic maintained that Dr. Weisman reported that Dr. Weisman discovered new lesions, Tr. 219, Dr. Matloubian's interpretation that Mr. Bourche is not developing new lesions is more persuasive. Tr. 303.

Dr. Matloubian's opinion finds support in a March 6, 2015 evaluation by Dr. Meditz. She found "Multiple LEE wounds initially related to IgA vasculitis but

component of slow healing likely related to low output heart failure." Exhibit 13-2 at 213 [pdf 63]. Dr. Meditz mentioned that Mr. Bourche was going to seek a heart and kidney transplant at Cedars-Sinai.

Two doctors from Cedars-Sinai commented on healing (but not new) lesions. First, a cardiothoracic surgeon stated that Mr. Bourche "has an open wound in the right leg which is still healing from August of 2014 secondary to his vasculitis." Exhibit 72 at 11 (Mar. 21, 2015). Next, an infectious disease specialist reported a "non healed ulcer" on Mr. Bourche's lower right leg. Id. at 141. This problem was significant because the doctor indicated Mr. Bourche's "lack of ability to heal" was a concern in evaluating Mr. Bourche for a transplant. Id.

Finally, on May 19, 2015, Dr. Holland wrote that he had spoken to Dr. Meditz "regarding wound healing. This appears to be progressing but is a slow process." Exhibit 76 at 9.

This evidence collectively supports a finding that Mr. Bourche developed new lesions until approximately July 15, 2014. Then, there was approximately two weeks in which Mr. Bourche did not develop new lesions. Then, from approximately August 1 through August 14, Mr. Bourche developed new and worsening lesions. After August 14, 2014, Mr. Bourche did not develop any new vasculitic lesions.

While the progression of skin lesions carries some consequence for the theory that vancomycin caused Mr. Bourche's vasculitis, the more important finding for evaluating Dr. Zizic's theory that the hepatitis B vaccine caused the vasculitis is that the vasculitis did not begin in early May 2014. As noted above, Dr. Zizic asserted that the vasculitis started with the mouth blister(s) that Dr. Mooney described on May 9, 2014. While Dr. Zizic's estimate of the amount of time for creation of immune complexes appears reasonable, he did not opine that the onset of vasculitis approximately two months after vaccination was also reasonable. Thus, Ms. Bourche has not met the burden of establishing that the vasculitis arose in an appropriate temporal interval.

C. An Onset of Vasculitis in June-July 2014 Makes Explanations, other than the Hepatitis B Vaccination, More Persuasive

In determining whether a vaccine caused an illness, it is "commonsense" that "evidence of other possible sources of injury can be relevant not only to the 'factors unrelated' defense, but also to whether a prima facie showing has been made that the vaccine was a substantial factor in causing the injury in question." Stone v. Sec'y of Health & Human Servs., 676 F.3d 1373, 1379 (Fed. Cir. 2012).

Here, the Secretary, through Dr. Matloubian, has proposed an infection, particularly the staph infection, and vancomycin as alternative explanations. See exhibit A at 9-10.

These proposed alternative explanations rest upon the proposition that the vasculitis Mr. Bourche developed was IgA vasculitis. Because the soundness of this diagnosis is a critical step, see Broekelschen v. Sec'y of Health and Human Servs., 618 F.3d 1339, 1346 (Fed. Cir. 2010), the analysis begins with the question of how to classify Mr. Bourche's vasculitis. Then, the next section discusses the causes for Mr. Bourche's IgA vasculitis.

1. Diagnosis of IgA Vasculitis

The vasculitis that Mr. Bourche developed around June-July 2014 was IgA vasculitis. The basis for this finding is the series of two skin biopsies.

Dr. Golitz interpreted the first skin biopsy, which came from Mr. Bourche's shin, on July 18, 2014. Dr. Golitz commented: "The combination of vasculitis with colon involvement raises the possibility of Henoch-Scholein purpura. A biopsy for direct immunofluorescence microscopy is recommended." Exhibit 8 at 122.

One purpose of the direct immunofluorescence was to look for IgA deposits. Exhibit 12 (Dr. Weisman) at 19. When the direct immunofluorescence was done on the second skin biopsy, which came from Mr. Bourche's right foot, IgA was found. Exhibit 8 at 121. The interpretation of the dermatopathologist was the diagnosis of "vascular IgA, IgM and fibrin." Id.

The finding of IgA on direct immunofluorescence leaves two choices for types of vasculitis – either IgA/HSP or cutaneous small vessel vasculitis. Exhibit A-3 (Fett) at 8 (table 8); Tr. 257. No doctor has proposed that cutaneous small vessel vasculitis fits Mr. Bourche's condition.

Instead, the written reports from the treating doctors point to IgA vasculitis also known as HSP. For example, after receiving the report on direct immunofluorescence, Dr. Hong's assessment was "hypersensitivity vasculitis, ?HSP exacerbated by drug eruption." Exhibit 8 at 32.

Later doctors incorporated "IgA vasculitis" into the histories that they obtained. See, e.g., exhibit 9 at 921 (Josh Emdur on Nov. 24, 2014); exhibit 76 at 32 (Laura Fries for Dr. Holland on Feb. 12, 2015); exhibit 72 at 69 (Dr. Scher on Mar. 25, 2015), 140 (Dr. Zakowski on Mar. 26, 2015).

However, in the course of this litigation, Ms. Bourche presented two witnesses who opined that Mr. Bourche did not suffer from IgA vasculitis. These were Dr. Mooney and Dr. Zizic. Dr. Mooney testified that Mr. Bourche did not suffer from IgA vasculitis. Tr. 62, 128, cited in, among other places, Pet'r's Reply at 8. However, Dr. Mooney's testimony at this point was very conclusory and he was, unfortunately, not asked to address the direct immunofluorescence. Thus, crediting Dr. Mooney's opinion about Mr. Bourche's (lack of) IgA vasculitis is difficult notwithstanding Dr. Mooney's status as a treating doctor.

Dr. Zizic's opinion about IgA vasculitis is not straightforward. In his initial report, Dr. Zizic stated that Mr. Bourche suffered from IgA vasculitis. Exhibit 15 at 5, 20 (postulating HSP as a unifying disorder). But, based upon literature that Dr. Matloubian supplied, Dr. Zizic revised his opinion. Tr. 174.

Dr. Zizic explained that in IgA vasculitis, the amount of IgA found on direct immunofluorescence should be dominant, and Dr. Matloubian agreed with this point. Tr. 173, 348. In Mr. Bourche's case, the person interpreting the direct immunofluorescence rated IgA as 1+ and IgM as 2+. Exhibit 8 at 121. Thus, Dr. Zizic has a fair point that Mr. Bourche did not suffer from IgA vasculitis.

However, Dr. Zizic and Dr. Matloubian also agreed that the process for interpreting direct immunofluorescence is subjective. Tr. 175, 298. Thus, the distinction between 1+ and 2+ is more qualitative than quantitative. Presumably, Dr. Hong, a dermatologist, was aware of how skin biopsies are tested with direct immunofluorescence when he concluded that Mr. Bourche suffered from "hypersensitivity vasculitis, ?HSP exacerbated by drug eruption." Exhibit 8 at 32.[22]

The duration of Mr. Bourche's skin problem is consistent with the expected duration of HSP. As discussed above, Mr. Bourche first manifested skin lesions that could be associated with vasculitis in June 2014, and he continued, with one interruption, to make new skin lesions until being placed on prednisone in mid-August 2014. These slow-healing lesions then persisted until at least March 2015, when he was at Cedars-Sinai.

HSP lesions can last six months or more. Tr. 305 (Dr. Matloubian). Dr. Matloubian's opinion about the duration of HSP lesions was not contested and was supported by some articles. Exhibit A-4 (Carlson) at 5/pdf 3 (bottom right);

[22] No treating doctor appears to have diagnosed Mr. Bourche with IgM vasculitis, the condition that Dr. Zizic proposed in his oral testimony.

exhibit A-6 (Audemard-Verger) at 583 (indicating that the doctors should evaluate an HSP patient with renal problems after three and six months). Thus, the course of Mr. Bourche's health provides some confirmation that he suffered IgA vasculitis.

Mr. Bourche's IgA vasculitis appears linked to his long-standing IgA nephritis. The results of the skin biopsy on his right foot resembled the results of the biopsy of his kidney in October 2009. Both showed the presence of IgA and IgM, but not IgG. Exhibit 9 at 629 (Oct. 6, 2009 - kidney); exhibit 8 at 121 (Aug. 19, 2014 - skin).

People with IgA nephritis, which, strictly speaking, is a disease limited to the kidneys may develop symptoms outside the kidneys and become diagnosed with IgA vasculitis. The underlying pathogenesis of both diseases are the same—the body makes a defective IgA molecule. See Tr. 98-99, 150-52, 271-72.

2. Causes for IgA Vasculitis

Whether the evolution from IgA nephritis to IgA vasculitis is part of the natural course of the disease or whether the evolution requires a distinct trigger is not clear. For Mr. Bourche, Dr. Matloubian proposed two different causes.

The first was Mr. Bourche's staph infection in May 2015. See exhibit A at 9. This aspect of Dr. Matloubian's overall opinion was touched upon only briefly during the hearing. See Tr. 312.

Much more attention during the hearing was directed toward Dr. Matloubian's other possibility, the vancomycin. Dr. Matloubian opined that vancomycin can cause IgA vasculitis. Tr. 312, 365. Dr. Zizic agreed vancomycin can cause IgA vasculitis. Tr. 227. Dr. Mooney agreed, too. Tr. 127-28. Further, although the parties disputed when Mr. Bourche first manifested signs and symptoms of vasculitis, the parties did not controvert Dr. Matloubian's opinion that an onset of vasculitis in late June or early July 2014, when Mr. Bourche was taking the vancomycin, was within the appropriate temporal window to infer that the vancomycin caused the vasculitis. See Tr. 278; Pet'r's Posth'g Br. at 36-37 (asserting that lesions pre-dated vancomycin but not addressing how long it would take lesions to appear after vancomycin).

Treating doctors also suggested that vancomycin caused an adverse reaction in the form of vasculitis. The most prominent example is Dr. Hong. In the report of Mr. Bourche's first visit with Dr. Hong, Dr. Hong first assessment was "[p]robable vasculitis, ? Drug-induced (?vancomycin)." Exhibit 8 at 48. While the

presence of two question marks suggests that Dr. Hong was uncertain about this etiology initially, Dr. Hong became firmer. After Dr. Golitz interpreted the skin biopsy from Mr. Bourche's shin, Dr. Hong stated that the results were "[s]till consistent with probable drug-induced cause." Id. at 45 (July 17, 2014). Dr. Hong carried forward his opinion that the vasculitis was probably drug-induced in successive appointments. Exhibit 8 at 43 (July 29, 2014), 41 (Aug. 1, 2014), 38 (Aug. 14, 2014).

Dr. Hong's assessment appears to underlie the history that Mr. Bourche provided to his rheumatologist, Dr. Weisman, on August 18, 2014. This history that Dr. Weisman obtained includes the passage: "Vancomycin given for sepsis. Developed skin reaction from vancomycin." Exhibit 12 at 15. However, this evidence does not carry much weight because Dr. Weisman seems not to have expressed his own opinion about the origins of the vasculitis. While Dr. Weisman stated he agreed with the diagnosis of "hypersensitivity vasculitis," he did not specify the antigen to which Mr. Bourche was hypersensitive. See id. at 19.

Finally, when Dr. Mooney was treating Mr. Bourche, Dr. Mooney, too, considered the possibility that vancomycin caused the vasculitis. When Dr. Mooney saw Mr. Bourche in the context of being hospitalized for endocarditis, Dr. Mooney prepared a report about Mr. Bourche. Dr. Mooney wrote: "He had reported onset of mouth ulcerations along with upper and lower extremity skin lesions that started in April. Initially it was felt that the trigger was hepatitis vaccine. During this time, he may have also had a reaction to vancomycin." Exhibit 9 at 738 (Oct. 25, 2014).

While Dr. Hong pointed to vancomycin as the probable cause for a drug-induced vasculitis, other treating doctors identified the hepatitis B vaccine as the source of an adverse reaction. This series of doctors begins with Dr. Mooney nine days after vaccination. On May 9, 2014, Dr. Mooney indicated that Mr. Bourche's mouth blisters were due to a reaction to the hepatitis B vaccine. Exhibit 10 at 127. Similarly, during the hospitalization for the staph infection, Dr. Bozeman and Dr. Meditz linked the hepatitis B vaccine to oral ulcers. Exhibit 9 at 321, 316. These opinions may or may not be accurate. But, whether the hepatitis B vaccine caused mouth blisters is not relevant to the outcome of the litigation because Ms. Bourche does not seek compensation for this condition.[23]

[23] Ms. Bourche and Dr. Zizic use the mouth blisters as an initial manifestation of vasculitis. Exhibit 44 at 2. But, for the reasons discussed at length in section III.B above, Mr. Bourche did not begin to suffer vasculitis until June 2014 at the earliest.

The more significant opinions from treating doctors about the adverse consequences of the hepatitis B vaccine arose when Mr. Bourche was having more serious skin problems. In dialysis treatment in July 2014, one physician commented: Mr. Bourche's vasculitic rash was "likely sequela of reaction to hep B vaccine when he developed oral ulcers as well." Exhibit 10 at 133. Another doctor wrote that Mr. Bourche's "limited leukocytoclastic vasculitis [was] related to Energex [hepatitis B vaccine reaction]." Id. at 135. These are the strongest statements supporting vaccine-causation from a treating doctor in the course of treatment.

Other doctors memorialized a sequence of events in which the hepatitis B vaccine preceded the development of vasculitis. See, e.g., exhibit 8 at 47 (Dr. Hong); exhibit 12 at 15 (Dr. Weisman); exhibit 13-1 at 106 (Dr. Ryan's January 28, 2015 note listing hepatitis vaccine as an allergy); exhibit 72 at 69 (Dr. Scher), 139 (Dr. Zakowski), 96 (Dr. Peng listing hepatitis B vaccine as an allergy). However, these carry relatively little (if any) weight because the recitation of a chronological sequence of events is not the same as an opinion regarding causation. Cedillo v. Sec'y of Health & Human Servs., 617 F.3d 1328, 1347-48 (Fed. Cir. 2010); La Londe v. Sec'y of Health & Human Servs., 110 Fed. Cl. 184, 206 (2013), aff'd on other ground, 746 F.3d 1334 (Fed. Cir. 2014); Langland v. Sec'y of Health & Human Servs., 109 Fed. Cl. 421, 439 (2013) (stating that the special master was not arbitrary in finding that the records from treating doctors "reflect no more than intake histories or temporal associations"); Caves, 100 Fed. Cl. at 139-40 (2010).

In the final analysis, the evidence regarding vancomycin is stronger than the evidence regarding hepatitis B vaccine. The primary reason is that the vasculitis developed in late June or early July 2014, which is in the time in which an inference of causation is appropriate for vancomycin, which Mr. Bourche started taking on May 23, 2014. In contrast, an onset of vasculitis near the end of June or beginning July 2014 is approximately two months after the April 23, 2014 vaccination. Dr. Zizic did not present any persuasive testimony to explain why two months would be an appropriate temporal interval. See Tr. 310, 313-14 (Dr. Matloubian explaining that an onset of vasculitis two months after vaccination would be coincidental). Another strong reason for downplaying the hepatitis B vaccine is the pathological similarity between IgA nephritis and IgA vasculitis.

To be sure, the proposition that Mr. Bourche suffered from IgA vasculitis has problems itself. The diagnosis is not perfect as the direct immunofluorescence did not show a dominance of IgA. Further, Mr. Bourche's fluctuating course in which his skin lesions appeared, improved, then worsened may not be entirely

compatible with vancomycin as the cause. But, the Secretary does not bear the burden of presenting a perfect case identifying an alternative cause because Ms. Bourche has not met her initial burden regarding causation. La Londe v. Sec'y of Health & Human Servs., 746 F.3d 1334, 1340 (Fed. Cir. 2014).

D. Ms. Bourche did not persuasively show that the endocarditis contributed to Mr. Bourche's death

The previous three sections explain why Ms. Bourche is not entitled to compensation for the vasculitis that Mr. Bourche suffered. But, Ms. Bourche's petition also includes the theory that the hepatitis B vaccination was a substantial factor in causing Mr. Bourche's death. This theory suffers from the additional flaw that Ms. Bourche has not presented preponderant evidence that the endocarditis further weakened Mr. Bourche's impaired heart such that Mr. Bourche died earlier than expected.

Two metrics to evaluate Mr. Bourche's cardiac function are his ejection fraction and his cardiologist's classification of his functioning. A normal ejection fraction is 65 ± 8 per cent. Dorland's at 740. This chart summarizes results of Mr. Bourche's ejection fractions:

Date	Event	Citation
1/9/2013	TTE: ejection fraction 35-38%	Exhibit 8 at 158
9/3/2013	TTE: ejection fraction 33%	Exhibit 8 at 162-63
10/4/2013	TTE: ejection fraction 10-15%	Exhibit 9 at 260-61
10/4/2013	Pacemaker installed	
11/7/2013	TTE: ejection fraction 35%	Exhibit 8 at 160
4/23/2014	Hepatitis B vaccination	
5/24/2014	TTE: ejection fraction 15-20%	Exhibit 9 at 451
8/14/2014	TTE: ejection fraction 20-30%	Exhibit 8 at 153; Exhibit 76 at 185
10/27/2014	TEE: ejection fraction 15-20%	Exhibit 9 at 811-12
11/5/2014	Mitral valve repair	

11/7/2014	TTE: ejection fraction 15-20%	Exhibit 9 at 808-10
1/5/2015	TTE: ejection fraction 31%	Exhibit 76 at 180, 230
1/28/2015	Hospitalized from Jan. 28, 2015 to Feb. 7, 2015	Exhibit 13-1 at 99-100 (discharge summary)
1/29/2015	TTE: ejection fraction 5-10%	Exhibit 13-1 at 120-21; exhibit 76 at 23 (15%)
2/12/2015	Ejection fraction 31%. Probably incorrect.	Exhibit 76 at 32; exhibit 13-2 at 165 [pdf 15]
3/2/2015	Ejection fraction 23%	Exhibit 76 at 225-26; but see exhibit 76 at 22 (stating today's ejection fraction is 31%)
4/29/2015	TTE: ejection fraction 10%	Exhibit 13-2 at 264 [pdf 114]
5/19/2015	Ejection fraction approximately 20%	Exhibit 76 at 8, 223

Isolating these test results allows for a focused analysis. After Mr. Bourche's pacemaker was installed but before the hepatitis B vaccine, his injection fraction was approximately 35 percent. This number is higher than the ejection fraction about on August 14, 2014, which was about four months after the hepatitis B vaccination. On that date, the ejection fraction was 20-30 percent. Exhibit 8 at 153.[24]

Before Mr. Bourche's November 5, 2014 mitral valve repair, the ejection fraction had declined to 15-20 percent. Exhibit 9 at 811-12 (Oct. 27, 2014). The mitral valve repair did not improve Mr. Bourche's ejection fraction immediately as echocardiograms from November 2014 showed that the ejection fraction ranged

[24] In between, Mr. Bourche had one transthoracic echocardiogram when he was hospitalized for the staph infection. At this time, his ejection fraction was 15-20 percent. Exhibit 9 at 451.

from 5 percent to 20 percent. For an explanation of why the mitral valve surgery does not produce higher ejection fractions, see Tr. 511-14.

However, after more weeks passed, Mr. Bourche's ejection fraction improved. On January 5, 2015, it was 31 percent. Dr. Holland stated: "His ejection fraction is improving. Preoperatively [it] was 5-10[.] Now it is 25-30%." Id. at 180. Of course, it is correct that an ejection fraction of 31 percent is lower than an ejection fraction of 35 percent. Tr. 498 (Dr. LaRue: "[I]t's been testified to that he never got back to that prior level, and I think that's a true statement.").[25]

During the hearing, Ms. Bourche's expert cardiologist, Dr. Stark argued a report of an ejection fraction of 31 percent was anomalous. Tr. 418, 433-34. This argument had some facial plausibility because, then, the record included only a doctor's reference to the ejection fraction, not the actual test result. See exhibit 13-2 at 165 [pdf 15]; Tr. 466, 497-98. However, after the hearing concluded, Ms. Bourche was instructed to obtain additional medical records. These more recently filed records from Dr. Holland include the underlying January 5, 2015 echocardiogram. Exhibit 76 at 230.[26]

Mr. Bourche's ejection fractions roughly correspond to changes in his classification. The New York Heart Association developed a system to classify congestive heart failures based upon how the person feels. Tr. 411-12. In class I, the person feels fine. Tr. 411. In class II, the person has some decrease in function with physical exertion. Tr. 411, 418. In class III, the person has shortness of breath in doing ordinary tasks like walking or getting dressed but can usually breathe easily at rest. Tr. 411, 428-29. In class IV, the person can hardly breathe. Tr. 411.

At various times, Dr. Holland (or Dr. Holland's associate) ascribed a class to Mr. Bourche.

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[25] Dr. LaRue's assessment was made without the benefit of the more recent records filed as exhibit 76.

[26] In narrative reports dated February 12, 2015 and March 2, 2015, Dr. Holland states that Mr. Bourche has an ejection fraction "today of 31%." Exhibit 76 at 22, 32. Both reports seem to carry forward information from Mr. Bourche's January 5, 2015 echocardiogram. When Mr. Bourche had a repeat echocardiogram on March 2, 2015, the ejection fraction was 23 percent. Exhibit 76 at 225-26. Consequently, the undersigned gives little weight to the February 12, 2015 and March 2, 2015 reports that the ejection fraction was 31 percent.

Date	Classification / Note	Citation
8/24/2010	Class II	Exhibit 8 at 117
8/26/2011	Class II-III	Exhibit 8 at 104
8/1/2012	Class III	Exhibit 8 at 100
9/4/2012	Class II-III, improving	Exhibit 8 at 96
2/28/2013	Class III, definitely worse	Exhibit 8 at 90
7/17/2013	Class III	Exhibit 8 at 84
9/3/2013	Class III	Exhibit 8 at 77-78
10/4/2013	Class III	Exhibit 8 at 141
10/4/2013	Pacemaker installed	
10/10/2013	Class III	Exhibit 8 at 68
1/9/2014	Class III	Exhibit 8 at 55
4/23/2014	Hepatitis B vaccination	
7/10/2014	Class III	Exhibit 8 at 53; Exhibit 76 at 1999
8/6/2014	Class III-IV, Class III	Exhibit 76 at 191, 193
8/14/2014	Class III	Exhibit 76 at 186
11/5/2014	Mitral valve repair	
1/6/2015	Class II-III	Exhibit 76 at 180
3/3/2015	Class III-IV, Class III, Class III+	Exhibit 76 at 23
4/3/2015	Class III	Exhibit 76 at 14
5/19/2015	Class III, Class IV, Class IV	Exhibit 76 at 8-9

In this chart, the critical entry is for January 6, 2015. Dr. Holland classified Mr. Bourche as "class II-III." The indication that he was borderline "class II" for the first time since 2011 undermines the argument that endocarditis started a continual decline, leading to his death.

Moreover, after the November 5, 2014 mitral valve repair, Mr. Bourche lived for more than a year until he died on January 16, 2016. This also contributes to a finding that the endocarditis was not a significant factor in Mr. Bourche's death. Tr. 498, 518-19. Instead, Mr. Bourche suffered from other illnesses, including heart problems, which were alleviated by the pacemaker, and his kidney problems for which he still required dialysis. See Tr. 437 (Dr. Stark's acknowledging that people with chronic heart failure and end-stage liver failure have a "shortened life span"), 462 (Dr. LaRue's describing heart failure as following a stair-step—as opposed to linear—pattern). The event that seems to have most closely preceded a substantial decline in Mr. Bourche's heart function was his hospitalization, beginning January 28, 2015. See exhibit 13-1 at 99-100 (discharge summary).

In short, Dr. LaRue's opinion on a more-likely-than-not basis that the endocarditis was not a significant factor in Mr. Bourche's death (Tr. 497, 508, 515) is persuasive. Mr. Bourche's death occurred too remote in time and in the presence of multiple confounding factors to find that the endocarditis was a proximate cause of his death.

IV. Conclusion

In the last two years of Mr. Bourche's life, his medical history was very complicated. He saw many doctors and the reports from these doctors do not agree with each other entirely. However, the evidence preponderates in favor of a finding that Mr. Bourche first manifested vasculitic lesions after he was prescribed vancomycin. This determination, in turn, makes the April 23, 2014 hepatitis B vaccination an unlikely causal contributor to the vasculitis. In addition, the lack of IgG in the biopsy reinforces the conclusion that the hepatitis B vaccination was not to blame for the vasculitis. Finally, regardless of whether the vasculitis contributed to the endocarditis, the endocarditis seems not to have contributed to Mr. Bourche's death.

For these reasons, Ms. Bourche cannot be awarded compensation. Certainly, Mr. Bourche suffered vasculitis. Ms. Bourche, as his devoted wife, suffered along with him. But, special masters cannot compensate cases based upon the emotional appeal.

In the absence of a motion for review filed pursuant to RCFC Appendix B, the clerk of the court is directed to enter judgment herewith.

IT IS SO ORDERED.

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

Appendix[27]

Anna Ankudowicz, Do Patients With End-Stage Chronic Renal Failure Treated With the Use of Hemodialysis Have Health Skin?, 48 Transpl. Proc., 1435 (2016), filed as exhibit A-1.

Alexandra Audemard-Verger, et al., IgA vasculitis (Henoch-Shönlein purpura) in adults: Diagnostic and therapeutic aspects, 14 Autoimmun. Rev. 579 (2015), filed as exhibit A-6.

J. Andrew Carlson, The histological assessment of cutaneous vasculitis, 56 Histopath. 3 (2010), filed as exhibit A-4.

Nicole Fett, et al., Evaluation of adults with cutaneous lesions of Vasculitis, UpToDate (literature review current through Oct. 2016, last updated Apr. 12, 2016), https://www.uptodate.com, filed as exhibit A-3.

Barbara Knoppova, et al., The Origin and Activities of IgA1-Containing Immune Complexes in IgA Nephropathy, 7(117) Front. Immun. 1 (2016), filed as exhibit A-9.

Claire-Anne Siegrist, Vaccine immunology in Vaccines, (Stanley Plotkin et al. eds., 6th ed. 2013), filed as exhibit A-30.

Robert J. Wyatt, et al., IgA nephropathy, 368(25) N. Engl. J. Med. 2402 (2013), filed as exhibit A-8.

[27] This appendix provides bibliographical information for articles this decision cites. However, all articles have been reviewed even if they are not cited.