In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

No. 19-1921V

(to be published)

LAURA PUTMAN, *as parent and natural guardian of B.P., a minor,*	*	Chief Special Master Corcoran
Petitioner,	*	Dated: January 31, 2022
v.	*	
SECRETARY OF HEALTH AND HUMAN SERVICES,	*	
Respondent.	*	

Amy A. Senerth, Muller & Brazil, LLP, Dresher, PA, for Petitioner

Christine M. Becer, U.S. Department of Justice, Washington, DC, for Respondent.

DECISION DENYING ENTITLEMENT[1]

On December 18, 2019, Laura Putman, as parent and natural guardian of B.P., a minor, filed a Petition under the National Vaccine Injury Compensation Program (the "Vaccine Program"[2]), alleging that B.P. developed juvenile idiopathic arthritis ("JIA") due to a measles, mumps, and rubella ("MMR") vaccine administered on November 9, 2017. Petition (ECF No. 1) ("Pet.") at 1–2.

I have determined that the matter could be efficiently and fairly resolved by ruling on the record, and invited briefing on the claim from the parties. Petitioner's Motion, dated July 12, 2021 (ECF No. 28 ("Mot."); Respondent's Brief, dated August 11, 2021 (ECF No. 29) ("Opp."). Now,

[1] This Decision will be posted on the United States Court of Federal Claims' website in accordance with the E-Government Act of 2002, 44 U.S.C. § 3501 (2012). **This means the Decision will be available to anyone with access to the internet**. As provided by 42 U.S.C. § 300aa-12(d)(4)(B), however, the parties may object to the published Ruling's inclusion of certain kinds of confidential information. Specifically, under Vaccine Rule 18(b), each party has fourteen (14) days within which to request redaction "of any information furnished by that party: (1) that is a trade secret or commercial or financial in substance and is privileged or confidential; or (2) that includes medical files or similar files, the disclosure of which would constitute a clearly unwarranted invasion of privacy." Vaccine Rule 18(b). Otherwise, the entire Decision will be available to the public in its current form. *Id.*

[2] The Vaccine Program comprises Part 2 of the National Childhood Vaccine Injury Act of 1986, Pub. L. No. 99-660, 100 Stat. 3755 (codified as amended at 42 U.S.C. §§ 300aa-10–34 (2012)) (hereinafter "Vaccine Act" or "the Act"). All subsequent references to sections of the Vaccine Act shall be to the pertinent subparagraph of 42 U.S.C. § 300aa.

having reviewed the medical record, all expert reports, the parties' briefs, and associated literature, I hereby deny an entitlement award. As discussed in greater detail below, Petitioner has not preponderantly established that the MMR vaccine could (contemporarily with an intercurrent infection) cause JIA, nor does the medical record support the conclusion that the vaccine was the likely cause of B.P.'s JIA.

I. Factual Background

Pre-Vaccination History

B.P. was born at approximately thirty-nine weeks gestation on July 21, 2016 and deemed healthy and developmentally normal. Ex. 2 at 3. No concerns were reported at her first well-child visit at West Virginia University Healthcare Physicians ("WVU") in Martinsburg, West Virginia. *Id*. at 3–5.

B.P. was taken for several additional pediatric visits later that same year, with no significantly concerning issues identified, and she received a number of vaccines without incident. Ex. 2 at 30–32 (August 2016 WVU visit), 52–55 (September 2016 visit, at which time B.P. was administered several vaccines), 74–76, 88–89 (October sick visits for treatment of upper respiratory infection ("URI") and nasal congestion), 99–102 (December 2016 visit, when B.P. received additional vaccines). The same health-care routine—a combination of routine doctor's visits coupled with instances where B.P. was treated for a transient illness—characterized the majority of 2017 as well. *Id.* at 123–26 (February 2017 visit, featuring additional vaccines), 187–90 (April 2017 sick visit), 202–06 (May 2017 well visit), 249 (June 2017 sick visit), 263–67 (one-year well-child visit in August 2017).

Receipt of MMR Vaccine and Development of Subsequent Symptoms

On November 9, 2017, B.P. had her fifteen-month well-child visit. Ex. 2 at 300–04. She was deemed healthy and developmentally-normal, and she now received the MMR vaccine at issue in this case (as well as the varicella vaccine), with no recorded reaction in the following days. *See* Petitioner's Affidavit, filed as Ex. 12 (ECF No. 1-15), at 1 (alleging no symptoms prior to clinical onset of knee problems reviewed below). About two weeks later, B.P. had a sick visit on November 22, 2017, for treatment of an ear infection. *Id.* at 332–35. B.P. was now reported to have experienced some URI symptoms the week before, but they had reportedly resolved. *Id*. at 332.

The following month, however, B.P. began experiencing the symptoms associated with the claimed injury in this case. Specifically, on December 5, 2017, B.P.'s daycare facility contacted Ms. Putman about swelling observed in B.P.'s knee. Ex. 3 at 2. That same day B.P. was taken to MedExpress Urgent Care for right knee swelling. Ex. 4 at 9. An x-ray performed at this time revealed joint effusion and soft tissue swelling, and it was recommended that B.P. treat with over-the-counter pain relievers, and that she see her pediatrician. *Id.* at 10.

The next day, on December 6, 2017, B.P. had a sick visit at WVU for evaluation of the right knee swelling, which was reported to have begun the day prior. Ex. 2 at 345. Although B.P. did not appear to be in pain, she was noted to have an abnormal gait. *Id*. An exam showed right knee effusion but full range of motion and no erythema or tenderness. *Id*. at 347. B.P. was at this point diagnosed with right knee effusion. *Id*. at 348.

B.P. was subsequently taken on December 7, 2017, to see an orthopedist, John Buschman, D.O., at Johns Hopkins Medicine Outpatient Center ("JHM") in Baltimore, Maryland. Ex. 5 at 10. The history from this visit noted that B.P. had been favoring her right leg, and also that she had experienced a runny nose a couple of weeks before and had been on antibiotics for it, but it had since resolved. *Id*. Examination revealed generalized swelling around her right knee, although an ultrasound conducted the same date revealed a normal result. *Id*. at 10–11. B.P. saw Dr. Buschman again on December 14, 2017, and he proposed that she had experienced toxic synovitis in connection with her recent URI, although he also recommended she see a pediatric orthopedist for additional evaluation. *Id.* at 18.

Almost two weeks later, B.P. saw a different JHM orthopedist, John Tis, M.D., on December 18, 2017, and he was informed of the limp that had begun two weeks prior. Ex. 5 at 26. Examination confirmed the limp was secondary to a lack of extension of the right knee. *Id*. at 27. Dr. Tis did not propose a specific diagnosis, but ordered serologic lab work to test for C-Reactive Protein ("CRP") levels and Lyme titers, among other things. *Id*. Lyme AB was negative, CRP was .7 mg/dLv (flagged as high), although her blood work was otherwise unremarkable. *Id*. at 40–41. Dr. Tis also recommended an MRI of B.P.'s knee if her clinical presentation did not improve. *Id.* at 27.

Two days thereafter, on December 20, 2017, B.P. was taken to the WVU emergency room for a fever. Ex. 6 at 141. In providing a history, Ms. Putman reported that B.P. had been experiencing mild swelling and moderate pain in her right knee, along with limping, since December 5, 2017. *Id*. An exam showed warmth and mild swelling in the right knee with pain in the right knee upon extension. *Id*. at 142. In addition, two inflammation biomarkers—CRP and the erythrocyte sedimentation rate ("ESR")—were positive and in the high ranges, although a test for antinuclear antibodies ("ANA") was negative. *Id*. at 143–44. At discharge, B.P. was diagnosed in the ER with acute right knee pain and left otitis media. *Id*. at 144–45.

B.P. next saw a JHM pediatrician, Vineet Sood, M.D., at JHM on December 21, 2017, in follow-up from her ER visit. Ex. 5 at 48. Labs were ordered to test for the presence of a number of antibodies associated with JIA, and Dr. Sood gave the family information about "JRA" (a term often used by medical practitioners interchangeably with JIA). *Id*. at 50–51. The tests performed

by Dr. Sood all yielded normal results. Ex. 8 at 22–23. Dr. Sood did not propose an explanation for B.P.'s presentation or knee-related symptoms.

Treatment for JIA in 2018

B.P. saw Dr. Sood on January 2, 2018, to discuss the recent lab results, and for evaluation of a URI-like symptoms she had been experiencing for a few days. Ex. 8 at 20. B.P. was later taken back to Dr. Sood that same month for pre-MRI consultation, and saw him again for a well-child visit in February 2018. *Id*. at 10–18. At the February visit, Ms. Putman expressed concerns about B.P.'s right knee swelling and painful gait. *Id*. at 13. It was now determined that immunizations would be deferred until after B.P.'s orthopedic testing (although this particular record does not set forth treater speculation that any particular vaccine was associated with B.P.'s knee-related symptoms). *Id*. at 15.

B.P. underwent the planned right knee MRI on February 16, 2018, and it revealed a moderate to large volume joint effusion with diffuse synovitis with epiphyseal cartilage hyperemia and popliteal fossa adenopathy, but no internal derangement. Ex. 5 at 69. The radiologist performing the MRI offered the impression that the results were consistent with "an inflammatory or infectious process, including [JIA] or Lyme arthritis." *Id.* at 70. Several days later, B.P. saw Dr. Sood on February 27, 2018, to discuss her nascent JIA diagnosis, and was scheduled for a visit with a rheumatologist. Ex. 7 at 23, 25. Lab results for CRP were normal, however, and Lyme testing was negative. Ex. 6 at 197.

Pediatric Nurse Practitioner ("PNP") Rachel Connor next saw B.P. in the Rheumatology Department at Children's National Medical Center in Washington, D.C., on February 28, 2018. Ex. 9 at 33–37. The record sets forth a three-month history of a limp and right knee swelling, and notes the MRI findings of synovitis with effusion. *Id*. at 35. Petitioner expressly stated at this time that B.P. "got hep B vaccine 2 weeks prior to the onset of joint symptoms, at which time she also had a URI." *Id*.

Exam showed right knee swelling, mild warmth, incomplete extension, and positive fluid wave, as well as incomplete extension of B.P.'s right elbow. Ex. 9 at 35–36. PNP Connor's diagnosis was oligoarticular JIA with the right knee and right elbow affected. *Id*. at 37. She explained that JIA was a chronic autoimmune condition, and the treatment plan going forward included checking B.P.'s ANA status, checking for uveitis,[3] and starting steroidal shots and other medications specific for JIA. *Id*. B.P. saw Nurse Connor again on March 13, 2018, with a plan to receive a steroid injection in her right knee. *Id.* at 33. At this time, she was reported to have

[3] Uveitis is inflammation of the eye. *Dorland's Illustrated Medical Dictionary* (33d ed. 2020) at 1983 (hereinafter *Dorland's*). It is a secondary symptom associated with oligoarticular JIA. A. Borchers et al., *Juvenile Idiopathic Arthritis,* 5 Autoimm. Rev. 279–98, 281 (2006), filed as Ex. 16 (ECF No. 18-3).

displayed improvement in her mobility and swelling, and less morning stiffness. *Id*. Because of trace effusion revealed in an ultrasound done that day, along with B.P.'s clinical improvement, the steroid injection was postponed. *Id*. at 34. She also saw an ophthalmologist who deemed her not to be experiencing uveitis. *Id.* at 13–14.

Two months later, on May 4, 2018, B.P. saw pediatric rheumatologist Tova Ronis, M.D. Ex. 9 at 28. B.P. still displayed some swelling and a slight limp, she experienced some pain with extreme flexion of her right elbow, and flexion contracture of the right knee. *Id*. at 28–29. Lab results from testing performed at this time now revealed (for the first time since onset) a positive ANA. Ex. 11 at 32. B.P. was diagnosed with oligoarticular JIA, and advised to continue prior treatments as well as start physical therapy ("PT"). *Id*. at 30. She next underwent an initial PT evaluation at the end of May, and participated in eight PT sessions by early August. Ex. 6 at 211, 306. At that time, B.P. displayed full range of motion in her right knee and had met her PT goals, and Ms. Putman opted to hold off on entering a more formal PT program given its cost, requesting instead a home exercise program. *Id*.

Final 2018 Treatment

B.P. returned to Dr. Sood on August 3, 2018, for a two-year-old well visit, and her exam was deemed normal overall, with no comments regarding her prior JIA symptoms. Ex. 7 at 26–28. A few days later, on August 7, 2018, she attended a follow-up visit with PNP Connor. Ex. 9 at 22. Petitioner informed PNP Connor that the family had noticed improvements in B.P., including that she was now able to run, had improved balance, and showed no morning stiffness. *Id*. Ms. Putman did, however, express "concerns about [B.P.] getting her next set of vaccinations as they have another child who had paralysis subsequent to the meningococcal vaccine." *Id*. Lab results from testing performed at this time revealed negative or unremarkable results. *Id.* at 24. PNP Connor recommended splinting for B.P.'s continued knee contracture, and added that "all vaccines can be given according to the regular vaccination schedule" from a rheumatologic standpoint (although live vaccines should be withheld if B.P. ever required future immunosuppressive therapy). *Id*.

Petitioner has filed few records for the subsequent time period through today's date that would shed light on B.P.'s current condition. A November 8, 2018 right knee ultrasound revealed no effusion, and subtle asymmetric increased soft tissue in the region of the right suprapatellar recess that may represent synovial thickening. Ex. 10 at 6. A January 21, 2019 ultrasound of the right knee showed stability from the previous ultrasound. *Id*. at 12. And the record from a February 25, 2019 visit to urgent care for urinary symptoms indicates that B.P. was no longer taking medications for her JIA. Ex. 4 at 16.

II. Expert Reports

A. *Petitioner's Expert – M. Eric Gershwin, M.D.*

Dr. Gershwin, an immunologist, filed three reports. *See* Report, dated July 20, 2020, filed as Ex. 15-1 (ECF No. 18-2) ("First Gershwin Rep."); Report, dated November 30, 2020, filed as Ex. 31-1 (ECF No. 21-2) ("Second Gershwin Rep."); Report, dated May 21, 2021, filed as Ex. 39-1 (ECF No. 27-2) ("Third Gershwin Rep."). Dr. Gershwin opined that B.P.'s JIA was caused by a combination of the MMR vaccine she received in November 2017[4] and her intercurrent URI diagnosed shortly thereafter.

Dr. Gershwin received his bachelor's degree from Syracuse University in Syracuse, New York, followed by his medical degree at Stanford University. Dr. Gershwin Curriculum Vitae, filed as Ex. 30-1 at 1 (ECF No. 18-17) ("Gershwin CV"). He then completed his internship and residency at Tufts-New England Medical Center in Boston, Massachusetts. *Id.* at 2. After completing a fellowship in immunology with the National Institute of Health, Dr. Gershwin became an assistant Professor in Rheumatology and Allergy at the University of California, School of Medicine in Davis, California. *Id.* Dr. Gershwin is now semi-retired—though he continues to work on a "callback" basis at the University of California, School of Medicine in Davis providing consultations for rheumatology and immunology patients. Gershwin CV at 1-2. He currently serves as the editor-in-chief of the Journal of Autoimmunity as well as several other publications focusing on autoimmunity. Gershwin CV at 5-6.

1. First Report: Dr. Gershwin's initial, 13-page report was the longest of the three he submitted, and it sets forth his causation theory in greatest detail.[5] He began with a brief overview of B.P.'s medical history, emphasizing the lack of evidence of any significant or relevant health issues prior to the vaccinations at issue. First Gershwin Rep. at 1. After the November 2017

[4] Although Dr. Gershwin's reports (given the theory espoused) seem to allow for the possibility that *both* vaccines were causal of B.P.'s JIA, Petitioner ultimately only alleges the MMR vaccine to have been causal. *See, e.g.,* Mot. at 1, 10. Otherwise, I do not find that Dr. Gershwin's theory gains or loses strength if the role of the varicella vaccine is disregarded.

[5] This report also features an unfortunate tendency to block-quote lengthy, scientific term-dense passages taken from the authorities Dr. Gershwin relies on—rather than explaining in his own language his opinion, and offering succinct citations for referential support. *See, e.g.*, First Gershwin Rep. at 5–6. This tendency is even more prominent in his subsequent reports, which almost wholly consist of strung-together series of impenetrable, single-spaced citations quoting other scientific or medical literature. *See* Second Gershwin Rep. at 2–6 (out of seven-page report); Third Gershwin Rep. at 1–6 (out of seven-page report).

I have had occasion to hear Dr. Gershwin testify in many Vaccine Program cases, and I find him overall to be qualified to comment on these kinds of claims, as well as helpful in the opinions he offers. But expert reports that merely replicate passages from other sources, without providing persuasive interpretive explanation for their significance or meaning, are unhelpful in making a claimant's case, since they obfuscate rather than illuminate the expert's opinion. Dr. Gershwin, and the Vaccine Program attorneys who retain him, must do better in the future.

vaccinations, by contrast, her JIA symptoms manifested. *Id.* at 1–2. Of particular interest to Dr. Gershwin was B.P.'s URI, which the medical records suggest began on November 15, 2017 (resulting in the ear infection diagnosed a week later). *Id.* at 1. Dr. Gershwin reasoned that B.P.'s exposure to the virus resulting in outward symptoms likely began a few days prior to November 15, 2017—and hence only a few days *after* she received the MMR and varicella vaccines, meaning her exposure to a wild virus infection was "contemporary with the vaccination." *Id.* at 2.

Dr. Gershwin next offered an explanation for JIA and its immune-pathogenic features. JIA, he stated, is a "heterogeneous and multifactorial autoimmune disease characterized by chronic joint inflammation in children with onset ages younger than 16 years." First Gershwin Rep. at 2; Y. Lin et al., *The Pathogenesis of Oligoarticular/Polyarticular vs. Systemic Juvenile Idiopathic Arthritis*, 10 Autoimm. Rev. 482-89 (2011), filed as Ex. 17 (ECF No. 18-4) ("Lin") at 483. Although it has different sub-variants, he proposed that the medical record best supported a diagnosis of oligoarticular JIA for B.P.

One feature of oligoarticular JIA, Dr. Gershwin noted, is the presence of "high numbers of autoreactive T cells" in the joints of affected patients, suggesting the disease process is "antigen-driven," and thus ultimately depends on "activation of the adaptive [or secondary] immune system" response—and making it different from other sub-variants like systemic JIA, where the innate (or primary) immune response more likely explains pathogenesis. First Gershwin Rep. at 2–3; Lin at 483. Ultimately, an aberrant T-cell driven immune response directed at "autoantigens derived from cartilage and other joint-related tissue" would in essence characterize the pathogenesis of the relevant subtype of JIA, with certain T "helper" cells encouraging cytokines and other immune cells responsible for promotion of inflammation (which would in turn explain how the aberrant process would persist over time and become chronic). *Id.* at 4–5. Dr. Gershwin later admitted, however, that the autoimmune response causing JIA was far less understood than comparable conditions like adult rheumatoid arthritis ("RA"). *Id.* at 10.

Besides the above, Dr. Gershwin invoked a theory exceedingly common in Vaccine Program cases—molecular mimicry—as a pathogenic biologic mechanism relevant to explaining how JIA might develop and later manifest clinically. First Gershwin Rep. at 6–9. He agreed at the outset that the existence of homology, or amino acid sequential/structural antigenic similarity with self antigenic sequences/structures, was not enough to cause autoimmune disease, given how common mere sequential homology was in nature (arising from the fact that only 20 amino acids make up all human proteins). *Id.* at 8. He also noted that the "four major criteria" recognized by medical science for when molecular mimicry likely explains an autoimmune disease[6] are

[6] These include (a) evidence of homology/epitope similarity, (b) evidence of cross-reactive antibodies or T cells, (c) a greater epidemiologic link between a particular environmental stimulant (like a vaccine) and the disease in question, and (d) animal model experimentation capable of confirming a pathogenic autoimmune process. First Gershwin Rep. at 8.

"challenging to demonstrate in humans," primarily due to the difficulties in conducting the kinds of testing or experiments that would be necessary to confirm it. *Id.* Nevertheless, science recognizes molecular mimicry's explanatory power for certain autoimmune disease processes, and given what is generally known about how T cells can cross-react with self, it was reasonable to conclude (despite the gaps in science) that an autoimmune disease like JIA could be triggered due to recognition of presenting antigens. *Id.* at 9.

Despite the above (and its somewhat lengthy and dense explication), Dr. Gershwin qualified several of his points regarding the relevance of molecular mimicry herein. For example, he acknowledged that "we do not know what the actual self antigen is in JIA" that would serve as the target for the autoimmune, self-directed attack. First Gershwin Rep. at 6. He also disclaimed the ability in this case to identify homology between *any* vaccine protein components relevant to this case and a self amino acid structure within a relevant human protein,[7] arguing that the "perfect world" in which such evidence could be offered "does not exist"—but also maintaining that molecular mimicry's acceptance as a driver of autoimmune disease limited the impact of this evidentiary absence. *Id.* at 6–7.

Development of any JIA variant is likely attributable to different causal factors. A person's underlying genetic susceptibility is one such factor. First Gershwin Rep. at 3. Oligoarticular JIA is particularly associated with several specific human leukocyte antigen ("HLA") genes (a complex of genes on a specific human chromosome responsible for encoding cell-surface proteins that regulate the immune system).[8] *Id.* at 3, 5–6. Some identified HLA mutations are believed to be causal of JIA given the degree to which they are present in patients with the condition. *Id.* In Dr. Gershwin's opinion, it was highly likely that B.P. was similarly genetically susceptible (although he cited no record evidence corroborating this contention). *Id.* at 9–10. In addition, wild "[i]nfectious agents" are even more important, and (through presentation of foreign antigens) can trigger a T cell-driven adaptive immune response resulting in autoimmune attack on self structures sufficient to manifest in JIA's clinical symptoms. *Id.* Dr. Gershwin specifically identified influenza A, rubella, and parvovirus B19 infections as associated with JIA development (although he admitted that "their pathogenicity . . . is still not well proven"), along with some bacterial infections. *Id.*

Vaccines as well, Dr Gershwin continued, have been associated with JIA or other comparable conditions. For example, he highlighted one study suggesting a "slight increase in risk" of RA or chronic arthritis after receipt of the Hepatitis B, rubella-containing, and varicella vaccines. First Gershwin Rep. at 3; A. Schattner, *Consequence or Coincidence? The Occurrence,*

[7] Dr. Gershwin also admitted that mere amino acid *sequential* homology was unhelpful in the absence of understanding the three-dimensional structure of such antigenic sequences, since a literal "fitting-together" was needed as well for mimicry to result in an autoimmune cross-reaction. First Gershwin Rep. at 7.

[8] *Dorland's* at 854.

Pathogenesis, and Significance of Autoimmune Manifestations After Viral Vaccines, 23 Vaccine 3876-86 (2005), filed as Ex. 18 (ECF No. 18-5) ("Schattner"); J. Ellis, *Possible Environmental Determinants of Juvenile Idiopathic Arthritis,* 49 Rheumatology 411–25 (Oxford, 2010), filed as Ex. 29 (ECF No. 18-16) ("Ellis").

Schattner (a review study of case reports and other studies published between 1966 to 2004 involving purported vaccine reactions) included the MMR vaccine specifically in its analysis, noting that the underlying wild viruses contained therein were rarely associated with autoimmune-driven diseases. Schattner at 3878. However, Schattner also noted that an association between the specific rubella component and "joint reactions" had long been observed, specifically (in a few studies) with acute arthritis/arthralgia or chronic arthritis. *Id.* at 3879, Table 3. Schattner does not, however, mention JIA or RA, neither of which are congruent completely with other forms of arthritis associated with the rubella vaccine component. Ellis discusses an association between some forms of JIA and various infections, citing studies specific to these findings. Ellis at 416–18. It noted, however (as Dr. Gershwin had acknowledged) that explanatory mechanisms for *how* an antecedent infection produced JIA remained "speculative," and its discussion of vaccination as a potential environmental trigger was limited to a single paragraph. *Id.* at 418.

More specific to this claim, a case report observes an exacerbation of a different JIA subtype (systemic JIA) in a child within five days of receipt of a rubella vaccine—although as already noted systemic JIA is not mediated by the adaptive immune system, and the case report's authors expressly noted that they reached no conclusions as to causation. First Gershwin Rep. at 3; S. Korematsu et al., *A Relapse of Systemic Type Juvenile Idiopathic Arthritis After a Rubella Vaccination in a Patient During Long-Term Remission Period,* 27 Vaccine 5041–042 (2009), filed as Ex. 19 (ECF No. 18-6) ("Korematsu"). The child discussed in Korematsu was diagnosed with systemic JIA at the age of two, and was 11 at the time she received a rubella vaccine, developing a fever and rash five days later. Korematsu at 5041. Thus, her experience was facially inapposite to what occurred herein, although Dr. Gershwin still suggested the case report was significant. By contrast, Dr. Gershwin disregarded the value of larger-scale epidemiologic studies in assessing causation, maintaining that the "relatively uncommon" nature of JIA meant that such studies could not be sufficiently powered to measure a causal association. First Gershwin Rep. at 4, 6.

Here, B.P.'s JIA likely developed, in Dr. Gershwin's estimation, due to a confluence of events in which her receipt of the MMR vaccine was a significant factor. He found especially important the fact that the MMR vaccine had been administered shortly before B.P.'s URI. This viral infection coincided with the time that the initial, innate response to the vaccine (which would naturally be characterized by the immune system's release of cytokines, or immune messenger cells) would have occurred. Such cytokines, Dr. Gershwin maintained, play many different roles (from facilitating "antigen presentation" to augmenting the production of antibodies and T cells), and thus serve as "amplifiers of the immune response." First Gershwin Rep. at 10. But cytokines

would also be produced in reaction to the intercurrent infection, working in tandem with the vaccine reaction to trigger a "loss in tolerance to a self antigen" leading to JIA. *Id.* Indeed, the lymph nodes that would have produced the cytokines in reaction to the MMR vaccine "are in the same anatomic location as the lymph nodes of the upper respiratory infection." *Id.*; N. Chatzianodreou et al., *Macrophage Death Following Influenza Vaccination Initiates the Inflammatory Response that Promotes Dendritic Cell Function in the Draining Lymph Node,* 18 Cell Rep. 2427–440 (2017), filed as Ex. 28 (ECF No. 18-15) ("Chatziandreou").

Dr. Gershwin admitted that not all URIs lead to JIA, even ones occurring after vaccination. But he deemed B.P.'s likely genetic susceptibility "critical" to the suspected pathogenic process here, characterizing it as a "host factor" and adding (without citation) that "most cases of [JIA] are preceded by an infection." First Gershwin Rep. at 10. Dr. Gershwin also acknowledged he could offer no study establishing that a URI occurring concurrently with immunization was likely to cause JIA in susceptible individuals (although he again suggested that such research cannot be performed or simply is nonexistent). *Id.*

Dr. Gershwin's First Report also proposed that the timeframe for B.P.'s post-vaccination development of JIA was medically acceptable. Because oligoarticular JIA was in Dr. Gershwin's view likely driven by an adaptive immune process, "it should appear several days to [six] weeks following the antigenic stimulus." First Gershwin Rep. at 3. This timeframe was consistent with the Table claim for chronic arthritis after receipt of the MMR vaccine, which required a showing of onset within 7-42 days. *Id.* at 11. Here, B.P.'s knee swelling was evident within four weeks of vaccination—meaning the actual timeframe for her post-vaccination onset of symptoms was consistent with the time the adaptive process would take to occur. *Id.*

2. Second Report: Dr. Gershwin's next report mostly responded to assertions made by Respondent's initial expert, Dr. Carlos Rose. After reacting in piecemeal form to some of the literature referenced in Dr. Rose's written report, Dr. Gershwin addressed five topics put into contention by Dr. Rose. *See generally* Second Gershwin Rep. at 2-6.

First, Dr. Gershwin defended his earlier contention about the likely incubation period for a URI (which was important to his theory that the immune impact of the MMR vaccine was heightened by the intercurrent infection). Second Gershwin Rep. at 2. Second, he maintained again that cytokines are not only expected to be produced as part of the immune response generally, but that their post-vaccination upregulation in lymph nodes where infections would also be processed (leading to activation therein of B and T cells) had been studied and confirmed (offering a paragraph-long cite from Chatziandreou in support). *Id.* at 2–3; Chatziandreou at 2427, 2436. Chatziandreou, it should be noted, says nothing about the *pathologic* role of cytokines posited by Dr. Gershwin's theory herein. Instead, Chatziandreou sought to explore how innate, immune-response inflammation—mediated by cytokines that are first triggered by the flu vaccine—assists adaptive response B cell-production of antibodies against the flu virus (the ultimate goal of the

vaccine). Chatziandreou at 2429. In other words, Chatziandreou's purpose was to evaluate the mechanisms that make vaccines *effective*, rather than to measure ways they can produce disease processes (as alleged in this case).

Third, Dr. Gershwin reiterated his claim that cytokine upregulation plays an "integral role" in contributing to the development of autoimmune disease—although the literature cited for this contention was not specific to JIA, or the instigation of *any* autoimmune disease due to cytokine upregulation attributable to a vaccine. Second Gershwin Rep. at 3; P. Santamaria, *Cytokines and Chemokines in Autoimmune Disease: An Overview*, 520 Adv. Exp. Med. Biol. 1–7 (2003), filed as Ex. 34 (ECF No. 21-5). In further support of the purportedly pathogenic role of cytokines, he repeated his contention that genetically-susceptible individuals would experience a more pathogenic response to cytokines, pointing to an animal study (referenced within one of the articles he filed) to support the argument. Second Gershwin Rep. at 3–4, *citing* K. Moudgil et al., *Cytokines in Autoimmunity: Role in Induction, Regulation, and Treatment,* 31 J. Interferon Cytokine Res. 695-703 (2011), filed as Ex. 35 (ECF No. 21-6) ("Moudgil"). However, (and like other articles cited on this topic by Dr. Gershwin) although Moudgil does contain summary descriptions of studies showing how cytokines might contribute to specific autoimmune diseases (including RA), it does not reach causation conclusions and says nothing about how a vaccine could over-stimulate the posited disease-encouraging cytokines. Moudgil at 699 (discussing single article involving cytokine as inflammatory mediator in RA).

Finally, the remainder of Dr. Gershwin's second report (and half of it overall) was devoted to three lengthy block quotes from items of literature that he appears to have selected because of what they said about "variation in the immune response" (including the reaction to cytokines produced thereby) after receipt of measles or rubella-containing vaccines like MMR. Second Gershwin Rep. at 4–5 (citations omitted).

3. Third Report: Just as he attempted to rebut points made by Respondent's initial expert, Dr. Gershwin endeavored to do the same in reaction to the expert report prepared by the second defense expert, Dr. Andrew MacGinnitie. First, Dr. Gershwin challenged Dr. MacGinnitie's argument that because the MMR vaccine is live and attenuated, the time in which it would take to produce an immune response would be somewhat longer than Dr. Gershwin's theory allowed. Dr. Gershwin maintained that the vaccine antigens would not remain in the lymph nodes at length, and that live virus vaccine antigens had been detected in the blood "as early as one day post-vaccination." Third Gershwin Rep. at 1. Thus, the cytokine reaction to vaccination could occur earlier than posited by Dr. MacGinnitie.

Second, Dr. Gershwin took issue with Dr. MacGinnitie's purported assertion[9] that a URI would, from an immune standpoint, impact an entirely different lymph node in the body from a peripherally-administered vaccine (thus limiting the potential of cytokine production due to a vaccine interacting simultaneously, and pathogenically, with cytokines whose increase was due to a wild infection). On the contrary, Dr. Gershwin maintained, "the immune response is systemic," and the cytokines upregulated by vaccines could thus interact with other concurrent processes. *Id.* at 2, 3–4.

Dr. Gershwin's last point was to counter Dr. MacGinnitie's argument that no literature existed connecting JIA's pathogenesis to a URI/vaccine combination. Third Gershwin Rep. at 5. Dr. Gershwin repeated his prior position that as a general matter, the inability of epidemiologic evidence to detect highly-uncommon events rendered the absence of such evidence of no regard. *Id.* But he did maintain that an "older Finnish study" in fact provided some support for his opinion. I. Kunnamo, *Infections and Related Risk Factors of Arthritis in Children. A Case-Control Study*, 16 Scand. J. Rheumatol. 93–99 (1987), filed as Ex. 44 (ECF No. 27-7) ("Kunnamo"). Not only, however, is Kunnamo quite old (having been published 35 years ago), but (as the cited portion in Dr. Gershwin's report plainly states) its authors relied solely on a parent questionnaire for 334 children suffering from some form of JIA to confirm a prior URI association. Kunnamo at 93–94. Dr. Gershwin concluded his final report by offering yet another block quote—this one in support of his argument that human diversity of immune response meant that it was extremely difficult to reach predictive conclusions about what factors would, or would not, trigger autoimmune disease (via molecular mimicry in this case). Third Gershwin Rep. at 5–6.

B. *Respondent's First Expert – Carlos Rose, M.D.,*

Dr. Rose, a pediatric rheumatologist, provided a single written report in support of Respondent's position in this case. Report, dated October 14, 2020, filed as Ex. A (ECF No. 20-1) ("Rose Rep."). Dr. Rose accepted B.P.'s oligoarticular JIA diagnosis, but disagreed with Dr. Gershwin's opinion that the MMR vaccine could have been causal.

Dr. Rose is a board-certified pediatric rheumatologist who had a hospital appointment at DuPont Hospital for Children until his recent retirement in June 2020. Rose Rep. at 1–2; CV, filed as Ex. B (ECF No. 20-8) at 3–4. Although he was treating adults with rheumatologic and autoimmune diseases since 1983, beginning in 1989 he began focusing exclusively on pediatric patients with rheumatologic and autoimmune diseases. Rose Rep. at 2. Dr. Rose has published on the topic of JIA, and has recently been studying mechanisms involving the intestinal microbiome and JIA. *Id*. at 2–3. He has lectured locally and at international meetings about JIA. *Id*. He presently

[9] As discussed below, Dr. MacGinnitie later took issue with this assertion, maintaining that Dr. Gershwin misconstrued the point.

holds the title of Honorary Professor of Pediatrics at Thomas Jefferson University in Philadelphia, PA. *Id*. at 1–2.

The first third of Dr. Rose's report contains a detailed review of B.P.'s medical history. Rose Rep. at 4–13. He particularly highlighted her history of URIs, and the fact she received antibiotic treatments at times for her symptoms (including when she experienced the November 2017 URI). *See id* at 6–7. Ultimately, Dr. Rose acknowledges that oligoarticular JIA is the proper diagnosis, adding that the record best supports onset as having occurred on December 5, 2017. *Id.* at 8, 14. He also concludes that B.P. is presently in remission. *Id.* at 13–15. But Dr. Rose proposed that the same record reveals no clinical evidence on JIA in November 2017, as well as the fact that her URI symptoms did not likely manifest prior to the November 13–18, 2017 timeframe (preceding her November 22, 2017 pediatric visit). *Id.* at 16. And he saw no evidence of any post-vaccination reaction that could be attributed to the MMR vaccine. *Id.* at 16–17.

Next, Dr. Rose offered some comments on JIA bearing on Dr. Gershwin's opinion. Although he accepted Dr. Gershwin's general explanation about oligoarticular JIA, he took some issue with claims about its rarity, noting that it is the most common form of JIA, representing about 50 percent of cases. Rose Rep. at 17. He also proposed (drawing upon his own expertise studying the illness) that JIA was not so rare as to be completely outside the analytic or predictive scope of a sufficiently-powered epidemiologic study. *Id.* at 17–18.

More specific to Dr. Gershwin's theory, Dr. Rose disputed the contention that the observation of large numbers of "autoreactive T cells" in the joints of patients with this form of JIA was enough to conclude that its pathogenesis was characterized by "antigen-driven activation of the adaptive immune system." Rose Rep. at 18. He did not disagree that the adaptive immune response played *some* role in JIA's development, but denied that it could be identified as the *main* driver of the disease's pathogenesis (as opposed to a secondary finding). *Id.* To illustrate this point, Dr. Rose observed that a related arthritic disease, ankylosing spondylitis, was known (like JIA) to be associated with a specific (albeit different) HLA genetic variant. *Id.* at 19. Yet, research had suggested that its associative role was attributable *not* to how the mutation impacted the immune response, but more to "an unrelated malfunctioning of the molecule itself" (coded by the variant gene) that resulted in inflammation and disease. *Id.*; R. Colbert et al., *HLA-B27 Misfolding and Ankylosing Spondylitis,* 57 Mol. Immunol. 1–19 (2014), filed as Ex. A, Tab 4 (ECF No. 20-5). The same predominantly-genetic explanation might be applicable to JIA as well.

Moving to the core of Dr. Gershwin's opinion, Dr. Rose offered several objections. First, he noted that the inability to identify the self-antigen that a vaccine's antigens could mimic greatly limited molecular mimicry's explanatory power herein as a general matter (and indirectly suggested that Dr. Gershwin's protests of "how difficult it is to study mimicry" were what impelled

him to offer a theory that did not solely rely on mimicry to explain JIA's vaccine-induced pathogenesis). Rose Rep. at 22–23.

Second, Dr. Rose attacked Dr. Gershwin's contention that the *expected* innate response to a vaccine (which he agreed would result in the upregulation of a variety of cytokines, including some that could be proinflammatory) could be assumed to be pathogenic as well, in the absence of evidence of a "potential synergy with a viral infection to produce a chronic disease like [JIA]." Rose Rep. at 24. He noted in connection with this point that Dr. Gershwin referenced literature that did not at all close this gap, but instead only discussed and addressed *expected* malaise and other post-vaccination reactions attributable to the innate immune response. *See* C. Hervé et al., *The How's and What's of Vaccine Reactogenicity,* 39 NPJ Vaccines 4:1–11 (2019), filed as Ex. A, Tab 5 (ECF No. 20-6) ("Hervé").[10] Hervé mainly reviewed the causes of "reactogenicity"—"a subset of reactions that occur soon after vaccination"—and the factors influencing it, both to educate treaters about what to expect with vaccinated individuals and also to propose subjects for further study that would aid the cause of vaccination. Hervé at 1. Articles like Hervé did not support the conclusion that vaccines could cause a pathogenic response, merely because they induced an immune response that could have transient clinical manifestations.

Wild infections, Dr. Rose maintained, would certainly also cause an innate immune response mediated by cytokines, producing fever or other malaise-associated discomforts. Rose Rep. at 24. But the degree of immune response in that case would not be equivalent to what is experienced in reaction to vaccination (which would inherently be lesser in degree), and thus the fact that vaccinations and infections alike increase cytokine levels was not proof a vaccine could be pathogenic.

Dr. Rose then addressed the assertion that the MMR vaccine could somehow in this case have interacted with B.P.'s intercurrent URI. He took issue with the assumption that the two concurrent external antigenic stimuli would inherently increase pathologic potentiality simply by "meeting" in the same lymph node (where the immune system would process an adaptive response), even questioning that the same lymph node would be implicated (since a different one was more closely located to the vaccine situs than the node that would be associated with a URI). Rose Rep. at 25. He simply found no support for the contention that the infection could play this contributory role, disputing that Chatziandreou truly supported the "amplification" thesis. *Id.*

Dr. Rose also offered an alternative explanation for B.P.'s JIA, based on his own research into the capability of antibiotic medications to cause "dysbiosis,"[11] or a reduction in microbial diversity in the gut, leading to a loss of some of the protections such biodiversity offers individuals.

[10] Petitioner later filed Hervé. *See* Ex. 36 (ECF 21-7).

[11] *Dorland's* at 569.

Rose Rep. at 27–28. Antibiotics are known to change the balance of the intestinal microbiome, encouraging a pathologic state which favors aberrant immune response in distant organs. *Id* at 28. Research Dr. Rose has participated in observed an association between JIA and the receipt of antibiotics to treat benign respiratory infections. *Id.* at 27; D. Horton et al., *Antibiotic Exposure and Juvenile Idiopathic Arthritis: A Case-Control Study,* 135 Pediatrics e334–e43 (2015), filed as Ex. A, Tab 6 (ECF No. 20-7), at 1. Such research suggests that in some cases JIA may develop from *treatment* of a prior infection, rather than the infection itself. And B.P., by Dr. Rose's count, experienced five upper respiratory infections and three courses of systemic antibiotics within six months of the onset of her JIA. Rose Rep. at 28.

Dr. Rose's report concluded by addressing the two remaining elements of causation under *Althen v. Sec'y of Health and Hum. Servs.,* 418 F.3d 1274 (Fed. Cir. 2005). Regarding the "did cause" prong, Dr. Rose disputed that the medical record in this case established that B.P. experienced any "systemic cytokine mediated effects (fever, poor appetite, irritability) or abnormal local cytokine mediated effect (injection site reaction) attributable to the vaccine" and in the days after its receipt. Rose Rep. at 16–17. He thus deemed Dr. Gershwin's contention that cytokine response to the vaccine could have been partially contributable to an aberrant immune response (when the URI's impacts began to be experienced) "highly speculative." *Id*. at 17, 24–25. But with respect to onset and post-vaccination timing, Dr. Rose largely did not contest that B.D.'s onset of JIA occurred in medically acceptable timeframe for an adaptive response, measuring the date of onset of JIA symptoms from the date of vaccination. *Id.* at 18.

C. *Respondent's Second Expert – Andrew MacGinnitie, M.D., Ph.D.*

Dr. MacGinnitie, a pediatric immunologist/allergist, prepared two written reports. Report, dated March 21, 2021, filed as Ex. C (ECF No. 25-1) ("First MacGinnitie Rep."); Report, dated July 26, 2021, filed as Ex. E (ECF No. 30-1) ("Second MacGinnitie Rep."). Dr. MacGinnitie addressed Dr. Gershwin's theory from the perspective of an immunologist, disputing its conclusion that the MMR vaccine could interact with an intercurrent infection to cause JIA.

Dr. MacGinnitie is board-certified in allergy/immunology and pediatrics. First MacGinnitie Rep. at 1–2; CV, filed as Ex. D (ECF No. 25-15). He is an attending physician and Clinical Chief for the Division of Immunology at Boston Children's Hospital, and an Associate Professor of Pediatrics at Harvard Medical School. First MacGinnitie Rep. at 1. Dr. MacGinnitie has over twenty years of experience treating patients with immunological diseases, including reactions to vaccines, and he performs research and publishes peer-reviewed articles on the topics of food allergy, vaccine reaction, and primary immunodeficiency. *Id*. at 2; CV at 12–17.

1. First Report: After summarizing B.P.'s medical history, Dr. MacGinnitie engaged in a succinct analysis of his reaction to Dr. Gershwin's causation theory. First, he considered different aspects of the "can cause" elements of the theory. Dr. MacGinnitie disputed

that any reliable published medical or scientific literature identified vaccination as a "cofactor" in JIA's development, even if a prior infection itself *might* be so associated, adding that he had not himself succeeded in identifying any such evidence on the subject. First MacGinnitie Rep. at 7. To the contrary—relevant epidemiologic studies were unsupportive of a relationship. *Id.*; M. Heijstek et al., *Safety of Measles, Mumps and Rubella Vaccination in Juvenile Idiopathic Arthritis,* 66 Ann. Rheum. Dis. 1384–387 (2007), filed as Ex. C, Tab 8 (ECF No. 25-9) ("Heijstek I"). Heijstek I considered the impact of an MMR vaccine dose on children already diagnosed with JIA (including some with the relevant oligoarticular variant), and found (out of 207 patients) no risk of flares when compared to those not yet vaccinated. Heijstek I at 1384. In addition, in a 60-patient subgroup of subjects that were diagnosed with JIA post-vaccination (and hence more comparable in experience to B.P.), only one developed JIA within a month of vaccination, leading the study's authors to deem that one instance solely a temporal relationship. *Id.* at 1386.

Other subsequent literature has also evaluated the possible adverse impact of an MMR vaccine on JIA patients, but confirmed the absence of worsening of disease course for those receiving the vaccination. *See* M. Heijstek et al., *Effects of the Live Attenuated Measles-Mumps-Rubella Booster Vaccination of Disease Activity in Patients with Juvenile Idiopathic Arthritis: A Randomized Trial,* 309 JAMA 2449–456 (2013), filed as Ex. C, Tab 9 (ECF No. 25-10) ("Heijstek II"). In Heijstek II, 137 Dutch children with JIA (none of whom had yet received the MMR booster), including some with oligoarticular JIA, were studied over a three-year period, with half (randomly selected) receiving MMR boosters in comparison to the other half/control group who did not. Heijstek II at 2449–450. No difference in symptoms flare activity was observed in the vaccinated group when compared to the unvaccinated. *Id.* at 2452–453, 2455.

Dr. MacGinnitie also took issue with the sufficiency of proof offered to establish that JIA could pathogenically proceed in whole or part by the mechanism of molecular mimicry. First MacGinnitie Rep. at 5–6. He noted that the criteria Dr. Gershwin had deemed necessary to attribute causation to molecular mimicry could not be satisfied, since (a) Dr. Gershwin had identified no homologous basis for cross-reactivity between the MMR vaccine's antigens and human protein antigenic targets associated with JIA, (b) no disease-specific T cells or antibodies were identified, (c) there was no greater epidemiologic evidence that would connect the MMR (in the context of an ongoing URI) with JIA, and (d) no animal model studies existed that would permit reproduction of the proposed autoimmune process. *Id.*

Second, certain facts relevant to B.P.'s medical history were inconsistent with the causation theory offered. Dr. MacGinnitie saw no evidence in the record that B.P.'s treaters had connected her vaccinations to her JIA (and a rheumatologist even opined that she should keep to her normal vaccination schedule despite her JIA). First MacGinnitie Rep. at 8. Also, Dr. MacGinnitie proposed that it was "most likely" that B.P. was vaccinated in her thigh—meaning that "the immune response to virus and vaccines would be occurring in distinct lymph nodes," since the

URI she had been diagnosed with would have most likely generated an immune response in one of the *cervical* lymph nodes. *Id.* As a result, Dr. Gershwin's contention that the production of inflammatory cytokines would inherently be magnified by a common lymph node locus for the immune response was not likely (and articles cited in support of the assertion, such as Chatziandreou, did not even discuss the issue of lymph node location as bearing on the extent of cytokine upregulation). *Id.*

Finally, Dr. MacGinnitie challenged the acceptability of the timeframe in which the combination URI and vaccination were purported to have caused pathogenic amounts of cytokines to upregulate and then propagate illness. The MMR vaccine is "live-attenuated," meaning it is "capable of replication after injection and in fact, this property is necessary for generation of a protective immune response." First MacGinnitie Rep. at 6. But this in turn meant a slower cytokine response to the very act of immunizations evidenced by the longer lag time for fever (6-12 days) after receipt of a live vaccine. *Id.* The rash response to MMR vaccine is similarly delayed by a comparable timeframe. W. Orenstein and P. Strebel, *Measles,* 381 N. Engl. J. Med. 349–57, 354 (2019), filed as Ex. C, Tab 6 (ECF No. 25-7) (transient response to MMR vaccination includes rash in some cases, appearing seven to twelve days post-vaccination). Because the cytokines that would trigger these kind of malaise-like clinical manifestations were comparable to what Dr. Gershwin maintained were driving JIA, they would be delayed in production—not "coincident with exposure to the virus which triggered [B.P.]'s URI" beginning a few days post-vaccination. First MacGinnitie Rep. at 6.

2. Second Report[12]: Dr. MacGinnitie's next report addressed four points raised by Dr. Gershwin. First, Dr. MacGinnitie revisited his contention that the fact that the MMR vaccine was a live attenuated vaccine meant the timeframe for an immune response was longer than allowed for by Dr. Gershwin. Second MacGinnitie Rep. at 1-2. In so doing, he addressed Dr. Gershwin's argument that the varicella vaccine (not, of course, the vaccine primarily at issue, although B.P. did receive it at the same time as the MMR) could be "present in the blood within one day of vaccination," maintaining that the scientific support for this argument was weak. *Id.* More pertinent to the causal theory at issue, however, Dr. MacGinnitie also noted that the kind of systematic response that would be associated with cytokine release for the varicella vaccine would still take at least 20 days (and thus still longer than Dr. Gershwin's theory). *Id.* at 2. It was thus impossible for cytokine increases associated with the viral infection B.P. incurred to have occurred at the same time as a vaccine received on November 9, 2017 because by November 22, 2017 the URI had resolved. Second MacGinnitie Rep. at 2.

[12] I note that Dr. MacGinnitie's Second Report was filed at the same time Respondent filed his Ruling on the Record Opposition—somewhat late in the process for consideration of such a document. However, the report itself is brief, and only addresses a few tertiary expert disagreements. Dr. MacGinnitie's core opinion remains his initial report, which was filed well before the Ruling on the Record schedule was set. And Petitioner did not request the opportunity to file a reply, or to add anything else from Dr. Gershwin in reaction to this otherwise late-filed report.

Second, Dr. MacGinnitie defended his contention that the immune response to a concurrent vaccine and infection would likely not be processed by the same lymph nodes. Second MacGinnitie Rep. at 3. Dr. Gershwin, he argued, had assumed the contrary, even though articles filed on Petitioner's behalf, like Hervé, acknowledged "that the specific lymph node is important." *Id.;* Hervé at 2 (observing differences in cytokine expression in lymph nodes specific to where a vaccine is injected, in comparison to nodes adjacent to muscles receiving a placebo). Indirect proof of this contention, he proposed, was further supplied by studies showing that the separation of vaccines from adjuvant, with each injected separately and at different places in the body, "led to diminished antibody responses," revealing that specificity of lymph node was likely important to an immune response. *Id.*

Dr. MacGinnitie further contested the significance of studies offered by Dr. Gershwin to prove viral infections could be associated with JIA, noting that "the larger point is that there is not literature suggesting vaccination can act as a "cofactor" in triggering JIA." Second MacGinnitie Rep. at 4. And he questioned the import of Dr. Gershwin's statements (buttressed with lengthy quotes from primary sources) about "the difficulty of identifying T cell epitopes" (presumably to explain why aspects of Petitioner's theory could not be substantiated). *Id.* What mattered, Dr. MacGinnitie maintained, was that Dr. Gershwin had provided no evidence of "cross-reactive antibodies or T-cell responses" in JIA's pathogenesis. The assertion that they plausibly existed was speculative and could not be tested; if accepted at face value, it meant that "potentially any exposure" to an environmental stimulus could result in autoimmune disease. *Id.* at 5.

IV. Parties' Arguments

A. *Petitioner*

Petitioner's motion largely tracks Dr. Gershwin's opinion in arguing in favor of entitlement, summarizing accurately his general contentions. Mot. at 6–8. After a review of the applicable legal standards, she maintains that she has met each of the three *Althen* prongs. First, she alleges she has (via Dr. Gershwin) offered a reputable medical theory explaining how the MMR vaccine could trigger JIA (here, by immunologically interacting with B.P.'s URI). *Id.* at 11. Second, she established via the medical record that cytokines produced by both the URI (which under other circumstances would be benign) and vaccine interacted to amplify an aberrant immune response, causing an autoimmune response and attacking self (as reflected in B.P.'s initial clinical symptoms). *Id.* at 12. Finally, Dr. Gershwin's theory (in which the autoimmune attack was mediated by an "adaptive immune response" through molecular mimicry) would require a few weeks to manifest symptoms—and this is consistent with B.P. experiencing knee issues within five to six weeks of vaccination. *Id.* at 13.

B. *Respondent*

Respondent contests the appropriateness of an entitlement award in this matter, arguing that Petitioner has not met her *Althen* burden. The first, "can cause" prong is unsatisfied, he maintains, because a reliable theory has not been preponderantly established. Recapitulating Dr. MacGinnitie's opinion, Respondent contests that the criteria for molecular mimicry to set forth a mechanism for autoimmunity are absent—including the lack of an identified mimic on either side of the presumed autoimmune process. Opp. at 14–15. There is, Respondent argues, a lack of evidence connecting a variety of infectious agents with JIA, and the evidence of an MMR vaccine "link" is even less present. *Id.* at 15–17. And the contention that an intercurrent infection could work with vaccination together to increase the aberrant immune response is speculative and/or not bulwarked with sufficient reliable evidence. *Id.* at 20.

The remaining *Althen* prongs are similarly unsupported by a preponderant showing. The "did cause" prong fails, given the lack of treater support for a vaccine-JIA connection along with no medical record proof showing the proposed theory occurring in "real time" to B.P., such as evidence of some systemic reaction to vaccination (which would reflect Dr. Gershwin's view that cytokine upregulation was driving B.P.'s disease course). Opp. at 20–22. The third prong (which focuses on timeframe between vaccination and onset) is also unsatisfied. *Id.* at 23–24. Even if the adaptive immune response does play some role in JIA's course (as Dr. Rose conceded), it is unknown if in fact it pathogenically *drives* JIA in an autoimmune sense. *Id.* at 24. More significantly, Dr. Gershwin's theory is reliant on the vaccine and URI immune responses occurring more or less simultaneously—but in fact (as explained by Dr. MacGinnitie) the MMR vaccine would likely take longer to cause an innate response (which would feature cytokine release) than assumed by Dr. Gershwin, given the vaccine's live-attenuated nature. *Id.* at 24–25. Hence, the two responses would not likely have been concurrent, as Dr. Gershwin assumes. *Id.* at 26.

V. Applicable Legal Standards

A. *Petitioner's Overall Burden in Vaccine Program Cases*

To receive compensation in the Vaccine Program, a petitioner must prove either: (1) that he suffered a "Table Injury"—i.e., an injury falling within the Vaccine Injury Table—corresponding to one of the vaccinations in question within a statutorily prescribed period of time or, in the alternative, (2) that his illnesses were actually caused by a vaccine (a "Non-Table Injury"). *See* Sections 13(a)(1)(A), 11(c)(1), and 14(a), as amended by 42 C.F.R. § 100.3; § 11(c)(1)(C)(ii)(I); *see also Moberly v. Sec'y of Health & Hum. Servs.*, 592 F.3d 1315, 1321 (Fed.

Cir. 2010); *Capizzano v. Sec'y of Health & Hum. Servs.*, 440 F.3d 1317, 1320 (Fed. Cir. 2006).[13] In this case, Petitioner does not assert a Table claim.

For both Table and Non-Table claims, Vaccine Program petitioners bear a "preponderance of the evidence" burden of proof. Section 13(1)(a). That is, a petitioner must offer evidence that leads the "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*, 592 F.3d at 1322 n.2; *see also Snowbank Enter. v. United States*, 6 Cl. Ct. 476, 486 (1984) (mere conjecture or speculation is insufficient under a preponderance standard). Proof of medical certainty is not required. *Bunting v. Sec'y of Health & Hum. Servs.*, 931 F.2d 867, 873 (Fed. Cir. 1991). In particular, a petitioner must demonstrate that the vaccine was "not only [the] but-for cause of the injury but also a substantial factor in bringing about the injury." *Moberly*, 592 F.3d at 1321 (quoting *Shyface v. Sec'y of Health & Hum. Servs.*, 165 F.3d 1344, 1352–53 (Fed. Cir. 1999)); *Pafford v. Sec'y of Health & Hum. Servs*., 451 F.3d 1352, 1355 (Fed. Cir. 2006). A petitioner may not receive a Vaccine Program award based solely on his assertions; rather, the petition must be supported by either medical records or by the opinion of a competent physician. Section 13(a)(1).

In attempting to establish entitlement to a Vaccine Program award of compensation for a Non-Table claim, a petitioner must satisfy all three of the elements established by the Federal Circuit in *Althen,* 418 F.3d at 1278: "(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 proximate temporal relationship between vaccination and injury." Each *Althen* prong requires a different showing and is discussed in turn along with the parties' arguments and my findings.

Under *Althen* prong one, petitioners must provide a "reputable medical theory," demonstrating that the vaccine received *can cause* the type of injury alleged. *Pafford*, 451 F.3d at 1355–56 (citations omitted). To satisfy this prong, a petitioner's theory must be based on a "sound and reliable medical or scientific explanation." *Knudsen v. Sec'y of Health & Hum. Servs.*, 35 F.3d 543, 548 (Fed. Cir. 1994). Such a theory must only be "legally probable, not medically or scientifically certain." *Id.* at 549.

However, the Federal Circuit has *repeatedly* stated that the first prong requires a preponderant evidentiary showing. *See Boatmon v. Sec'y of Health & Hum. Servs.*, 941 F.3d 1351,

[13] Decisions of special masters (some of which I reference in this ruling) constitute persuasive but not binding authority. *Hanlon v. Sec'y of Health & Hum. Servs.*, 40 Fed. Cl. 625, 630 (1998). By contrast, Federal Circuit rulings concerning legal issues are binding on special masters. *Guillory v. Sec'y of Health & Hum. Servs.*, 59 Fed. Cl. 121, 124 (2003), *aff'd* 104 F. Appx. 712 (Fed. Cir. 2004); *see also Spooner v. Sec'y of Health & Hum. Servs.*, No. 13-159V, 2014 WL 504728, at *7 n.12 (Fed. Cl. Spec. Mstr. Jan. 16, 2014).

1360 (Fed. Cir. 2019) ("[w]e have consistently rejected theories that the vaccine only "likely caused" the injury and reiterated that a "plausible" or "possible" causal theory does not satisfy the standard"); *see also Moberly v. Sec'y of Health & Hum. Servs.*, 592 F.3d 1315, 1321 (Fed. Cir. 2010); *Broekelschen v. Sec'y of Health & Hum. Servs*., 618 F.3d 1339, 1350 (Fed. Cir. 2010). This is consistent with the petitioner's ultimate burden to establish his overall entitlement to damages by preponderant evidence. *W.C. v. Sec'y of Health & Hum. Servs.*, 704 F.3d 1352, 1356 (Fed. Cir. 2013) (citations omitted). If a claimant must *overall* meet the preponderance standard, it is logical that they be required also to meet each individual prong with the same degree of evidentiary showing (even if the *type* of evidence offered for each is different).

Petitioners may offer a variety of individual items of evidence in support of the first *Althen* prong, and are not obligated to resort to medical literature, epidemiological studies, demonstration of a specific mechanism, or a generally accepted medical theory. *Andreu v. Sec'y of Health & Hum. Servs.*, 569 F.3d 1367, 1378–79 (Fed. Cir. 2009) (citing *Capizzano*, 440 F.3d at 1325–26). No one "type" of evidence is required. Special masters, despite their expertise, are not empowered by statute to conclusively resolve what are essentially thorny scientific and medical questions, and thus scientific evidence offered to establish *Althen* prong one is viewed "not through the lens of the laboratorian, but instead from the vantage point of the Vaccine Act's preponderant evidence standard." *Andreu,* 569 F.3d at 1380. Nevertheless, even though "scientific certainty" is not required to prevail, the individual items of proof offered for the "can cause" prong must *each* reflect or arise from "reputable" or "sound and reliable" medical science. *Boatmon,* 941 F.3d at 1359–60.

The second *Althen* prong requires proof of a logical sequence of cause and effect, usually supported by facts derived from a petitioner's medical records. *Althen*, 418 F.3d at 1278; *Andreu*, 569 F.3d at 1375–77; *Capizzano*, 440 F.3d at 1326; *Grant v. Sec'y of Health & Hum. Servs.*, 956 F.2d 1144, 1148 (Fed. Cir. 1992). In establishing that a vaccine "did cause" injury, the opinions and views of the injured party's treating physicians are entitled to some weight. *Andreu*, 569 F.3d at 1367; *Capizzano*, 440 F.3d at 1326 ("medical records and medical opinion testimony are favored in vaccine cases, as treating physicians are likely to be in the best position to determine whether a 'logical sequence of cause and effect show[s] that the vaccination was the reason for the injury'") (quoting *Althen*, 418 F.3d at 1280). Medical records are generally viewed as particularly trustworthy evidence, since they are created contemporaneously with the treatment of the patient. *Cucuras v. Sec'y of Health & Hum. Servs.*, 993 F.2d 1525, 1528 (Fed. Cir. 1993).

However, medical records and/or statements of a treating physician's views do not *per se* bind the special master to adopt the conclusions of such an individual, even if they must be considered and carefully evaluated. Section 13(b)(1) (providing that "[a]ny such diagnosis, conclusion, judgment, test result, report, or summary shall not be binding on the special master or court"); *Snyder v. Sec'y of Health & Hum. Servs*., 88 Fed. Cl. 706, 746 n.67 (2009) ("there is

nothing . . . that mandates that the testimony of a treating physician is sacrosanct—that it must be accepted in its entirety and cannot be rebutted"). As with expert testimony offered to establish a theory of causation, the opinions or diagnoses of treating physicians are only as trustworthy as the reasonableness of their suppositions or bases. The views of treating physicians should also be weighed against other, contrary evidence also present in the record—including conflicting opinions among such individuals. *Hibbard v. Sec'y of Health & Hum. Servs.*, 100 Fed. Cl. 742, 749 (2011) (not arbitrary or capricious for special master to weigh competing treating physicians' conclusions against each other), *aff'd*, 698 F.3d 1355 (Fed. Cir. 2012); *Veryzer v. Sec'y of Health & Hum. Servs.*, No. 06–522V, 2011 WL 1935813, at *17 (Fed. Cl. Spec. Mstr. Apr. 29, 2011), *mot. for review den'd*, 100 Fed. Cl. 344, 356–57 (2011), *aff'd without opinion*, 475 F. App'x. 765 (Fed. Cir. 2012).

The third *Althen* prong requires establishing a "proximate temporal relationship" between the vaccination and the injury alleged. *Althen*, 418 F.3d at 1281. That term has been equated to the phrase "medically-acceptable temporal relationship." *Id.* A petitioner must offer "preponderant proof that the onset of symptoms occurred within a timeframe which, given the medical understanding of the disorder's etiology, it is medically acceptable to infer causation." *de Bazan v. Sec'y of Health & Hum. Servs.*, 539 F.3d 1347, 1352 (Fed. Cir. 2008). The explanation for what is a medically acceptable timeframe must also coincide with the theory of how the relevant vaccine can cause an injury (*Althen* prong one's requirement). *Id.* at 1352; *Shapiro v. Sec'y of Health & Hum. Servs.*, 101 Fed. Cl. 532, 542 (2011), *recons. den'd after remand*, 105 Fed. Cl. 353 (2012), *aff'd mem.*, 2013 WL 1896173 (Fed. Cir. 2013); *Koehn v. Sec'y of Health & Hum. Servs.*, No. 11–355V, 2013 WL 3214877 (Fed. Cl. Spec. Mstr. May 30, 2013), *mot. for review den'd* (Fed. Cl. Dec. 3, 2013), *aff'd*, 773 F.3d 1239 (Fed. Cir. 2014).

B. *Law Governing Analysis of Fact Evidence*

The process for making determinations in Vaccine Program cases regarding factual issues begins with consideration of the medical records. Section 11(c)(2). The special master is required to consider "all [ ] relevant medical and scientific evidence contained in the record," including "any diagnosis, conclusion, medical judgment, or autopsy or coroner's report which is contained in the record regarding the nature, causation, and aggravation of the petitioner's illness, disability, injury, condition, or death," as well as the "results of any diagnostic or evaluative test which are contained in the record and the summaries and conclusions." Section 13(b)(1)(A). The special master is then required to weigh the evidence presented, including contemporaneous medical records and testimony. *See Burns v. Sec'y of Health & Hum. Servs*., 3 F.3d 415, 417 (Fed. Cir. 1993) (determining that it is within the special master's discretion to determine whether to afford greater weight to contemporaneous medical records than to other evidence, such as oral testimony surrounding the events in question that was given at a later date, provided that such determination is evidenced by a rational determination).

As noted by the Federal Circuit, "[m]edical records, in general, warrant consideration as trustworthy evidence." *Cucuras*, 993 F.2d at 1528; *Doe/70 v. Sec'y of Health & Hum. Servs.*, 95 Fed. Cl. 598, 608 (2010) ("[g]iven the inconsistencies between petitioner's testimony and his contemporaneous medical records, the special master's decision to rely on petitioner's medical records was rational and consistent with applicable law"), *aff'd*, *Rickett v. Sec'y of Health & Hum. Servs*., 468 F. App'x 952 (Fed. Cir. 2011) (non-precedential opinion). A series of linked propositions explains why such records deserve some weight: (i) sick people visit medical professionals; (ii) sick people attempt to honestly report their health problems to those professionals; and (iii) medical professionals record what they are told or observe when examining their patients in as accurate a manner as possible, so that they are aware of enough relevant facts to make appropriate treatment decisions. *Sanchez v. Sec'y of Health & Hum. Servs.*, No. 11–685V, 2013 WL 1880825, at *2 (Fed. Cl. Spec. Mstr. Apr. 10, 2013); *Cucuras v. Sec'y of Health & Hum. Servs.*, 26 Cl. Ct. 537, 543 (1992), *aff'd*, 993 F.2d at 1525 (Fed. Cir. 1993) ("[i]t strains reason to conclude that petitioners would fail to accurately report the onset of their daughter's symptoms").

Accordingly, if the medical records are clear, consistent, and complete, then they should be afforded substantial weight. *Lowrie v. Sec'y of Health & Hum. Servs*., No. 03–1585V, 2005 WL 6117475, at *20 (Fed. Cl. Spec. Mstr. Dec. 12, 2005). Indeed, contemporaneous medical records are often found to be deserving of greater evidentiary weight than oral testimony—especially where such testimony conflicts with the record evidence. *Cucuras*, 993 F.2d at 1528; *see also Murphy v. Sec'y of Health & Hum. Servs*., 23 Cl. Ct. 726, 733 (1991), *aff'd per curiam*, 968 F.2d 1226 (Fed. Cir. 1992), *cert. den'd*, *Murphy v. Sullivan*, 506 U.S. 974 (1992) (citing *United States v. United States Gypsum Co.*, 333 U.S. 364, 396 (1947) ("[i]t has generally been held that oral testimony which is in conflict with contemporaneous documents is entitled to little evidentiary weight.")).

However, the Federal Circuit has also noted that there is no formal "presumption" that records are accurate or superior on their face when compared to other forms of evidence. *Kirby v. Sec'y of Health & Hum. Servs.,* 997 F.3d 1378, 1383 (Fed. Cir. 2021). There are certainly situations in which compelling oral testimony may be more persuasive than written records, such as where records are deemed to be incomplete or inaccurate. *Campbell v. Sec'y of Health & Hum. Servs*., 69 Fed. Cl. 775, 779 (2006) ("like any norm based upon common sense and experience, this rule should not be treated as an absolute and must yield where the factual predicates for its application are weak or lacking"); *Lowrie*, 2005 WL 6117475, at *19 ("[w]ritten records which are, themselves, inconsistent, should be accorded less deference than those which are internally consistent") (quoting *Murphy*, 23 Cl. Ct. at 733)). Ultimately, a determination regarding a witness's credibility may be required when determining the weight that such testimony should be afforded. *Andreu*, 569 F.3d at 1379; *Bradley v. Sec'y of Health & Hum. Servs*., 991 F.2d 1570, 1575 (Fed. Cir. 1993).

When witness testimony is offered to overcome the presumption of accuracy afforded to contemporaneous medical records, such testimony must be "consistent, clear, cogent, and compelling." *Sanchez*, 2013 WL 1880825, at *3 (citing *Blutstein v. Sec'y of Health & Hum. Servs*., No. 90–2808V, 1998 WL 408611, at *5 (Fed. Cl. Spec. Mstr. June 30, 1998)). In determining the accuracy and completeness of medical records, the Court of Federal Claims has listed four possible explanations for inconsistencies between contemporaneously created medical records and later testimony: (1) a person's failure to recount to the medical professional everything that happened during the relevant time period; (2) the medical professional's failure to document everything reported to her or him; (3) a person's faulty recollection of the events when presenting testimony; or (4) a person's purposeful recounting of symptoms that did not exist. *La Londe v. Sec'y of Health & Hum. Servs*., 110 Fed. Cl. 184, 203–04 (2013), *aff'd*, 746 F.3d 1334 (Fed. Cir. 2014). In making a determination regarding whether to afford greater weight to contemporaneous medical records or other evidence, such as testimony at hearing, there must be evidence that this decision was the result of a rational determination. *Burns*, 3 F.3d at 417.

C. *Analysis of Expert Testimony*

Establishing a sound and reliable medical theory often requires a petitioner to present expert testimony in support of his claim. *Lampe v. Sec'y of Health & Hum. Servs*., 219 F.3d 1357, 1361 (Fed. Cir. 2000). Vaccine Program expert testimony is usually evaluated according to the factors for analyzing scientific reliability set forth in *Daubert v. Merrell Dow Pharm., Inc.*, 509 U.S. 579, 594–96 (1993). *See Cedillo v. Sec'y of Health & Hum. Servs.*, 617 F.3d 1328, 1339 (Fed. Cir. 2010) (citing *Terran v. Sec'y of Health & Hum. Servs.*, 195 F.3d 1302, 1316 (Fed. Cir. 1999). Under *Daubert*, the factors for analyzing the reliability of testimony are:

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

Terran, 195 F.3d at 1316 n.2 (citing *Daubert*, 509 U.S. at 592–95).

However, in the Vaccine Program the *Daubert* factors play a slightly different role than they do when applied in other federal judicial settings—e.g., the district courts. Typically, *Daubert* factors are employed by judges (in the performance of their evidentiary gatekeeper roles) to exclude evidence that is unreliable or could confuse a jury. By contrast, in Vaccine Program cases these factors are used in the *weighing* of the reliability of scientific evidence proffered. *Davis v. Sec'y of Health & Hum. Servs*., 94 Fed. Cl. 53, 66–67 (2010) ("uniquely in this Circuit, the *Daubert*

factors have been employed also as an acceptable evidentiary-gauging tool with respect to persuasiveness of expert testimony already admitted"). The flexible use of the *Daubert* factors to evaluate the persuasiveness and reliability of expert testimony has routinely been upheld. *See, e.g.*, *Snyder*, 88 Fed. Cl. at 742–45. In this matter (as in numerous other Vaccine Program cases), *Daubert* has not been employed at the threshold, to determine what evidence should be admitted, but instead to determine whether expert testimony offered is reliable and/or persuasive.

Respondent frequently offers one or more experts in order to rebut a petitioner's case. Where both sides offer expert testimony, a special master's decision may be "based on the credibility of the experts and the relative persuasiveness of their competing theories." *Broekelschen*, 618 F.3d at 1347 (citing *Lampe*, 219 F.3d at 1362). However, nothing requires the acceptance of an expert's conclusion "connected to existing data only by the *ipse dixit* of the expert," especially if "there is simply too great an analytical gap between the data and the opinion proffered." *Snyder*, 88 Fed. Cl. at 743 (quoting *Gen. Elec. Co. v. Joiner*, 522 U.S. 146 (1997)); *see also Isaac v. Sec'y of Health & Hum. Servs*., No. 08–601V, 2012 WL 3609993, at *17 (Fed. Cl. Spec. Mstr. July 30, 2012), *mot. for review den'd*, 108 Fed. Cl. 743 (2013), *aff'd*, 540 F. App'x. 999 (Fed. Cir. 2013) (citing *Cedillo*, 617 F.3d at 1339). Weighing the relative persuasiveness of competing expert testimony, based on a particular expert's credibility, is part of the overall reliability analysis to which special masters must subject expert testimony in Vaccine Program cases. *Moberly*, 592 F.3d at 1325–26 ("[a]ssessments as to the reliability of expert testimony often turn on credibility determinations"); *see also Porter v. Sec'y of Health & Hum. Servs*., 663 F.3d 1242, 1250 (Fed. Cir. 2011) ("this court has unambiguously explained that special masters are expected to consider the credibility of expert witnesses in evaluating petitions for compensation under the Vaccine Act").

D. *Consideration of Medical Literature*

Both parties filed numerous items of medical and scientific literature in this case, but not every filed item factors into the outcome of this Decision. While I have reviewed all the medical literature submitted in this case, I discuss only those articles that are most relevant to my determination and/or are central to Petitioner's case—just as I have not exhaustively discussed every individual medical record filed. *Moriarty v. Sec'y of Health & Hum. Servs.*, 844 F.3d 1322, 1328 (Fed. Cir. 2016) ("[w]e generally presume that a special master considered the relevant record evidence even though he does not explicitly reference such evidence in his decision") (citation omitted); *see also Paterek v. Sec'y of Health & Hum. Servs.,* 527 F. Appx. 875, 884 (Fed. Cir. 2013) ("[f]inding certain information not relevant does not lead to—and likely undermines—the conclusion that it was not considered").

E. *Disposition of Case Without Hearing*

I am resolving Petitioner's claim on the filed record, as per the parties' request. See Status Report, dated May 7, 2021 (ECF No. 26). The Vaccine Act and Rules not only contemplate but encourage special masters to decide petitions on the papers where (in the exercise of their discretion) they conclude that doing so will properly and fairly resolve the case. Section 12(d)(2)(D); Vaccine Rule 8(d). The decision to rule on the record in lieu of hearing has been affirmed on appeal. *Kreizenbeck v. Sec'y of Health & Hum. Servs*., 945 F.3d 1362, 1366 (Fed. Cir. 2020); *see also Hooker v. Sec'y of Health & Hum. Servs*., No. 02-472V, 2016 WL 3456435, at *21 n.19 (Fed. Cl. Spec. Mstr. May 19, 2016) (citing numerous cases where special masters decided case on the papers in lieu of hearing and that decision was upheld). I am simply not required to hold a hearing in every matter, no matter the preferences of the parties. *Hovey v. Sec'y of Health & Hum. Servs*., 38 Fed. Cl. 397, 402–03 (1997) (determining that special master acted within his discretion in denying evidentiary hearing); *Burns*, 3 F.3d at 417; *Murphy v. Sec'y of Health & Hum. Servs.*, No. 90-882V, 1991 WL 71500, at *2 (Fed. Cl. Spec. Mstr. Apr. 19, 1991).

ANALYSIS

I. Overview of JIA Treatment in Vaccine Program

The experts in this case did not substantively disagree on the nature of JIA. Broadly, it is the juvenile form of RA, with largely the same constellation of symptoms (joint pain and swelling, with secondary impacts on movement, growth, and development). First Gershwin Rep. at 2–3. Although its exact etiologic cause is not well known (and hence the reason its descriptive title includes the word "idiopathic"), JIA is suspected to be driven by an autoimmune process, and is typically chronic (although symptoms may wax and wane). C. Wallace et al., *Preliminary Criteria for Clinical Remission for Select Categories of Juvenile Idiopathic Arthritis,* 31 J. Rheum. 11:2290–294 (2004), filed as Ex. A, Tab 3 (20-4); Ellis at 411. Importantly, there are several different JIA subtypes, with the main ones being systemic, oligoarticular and polyarticular, and each has slightly different presentation characteristics. *See Jimenez v. Sec'y of Health & Hum. Servs.,* No. 17-1190V, 2021 WL 3179643, at *2–3 (Fed. Cl. Spec. Mstr. June 23, 2021) (discussing the specific character of systemic JIA, which includes presenting symptoms of fever and clinical evidence of a macular rash); Ellis at 411.

In this case, there is no dispute that B.P. was properly diagnosed with oligoarticular JIA. It is considered a common subtype and is typically asymmetrical, affecting between one to four joints, mostly in the lower limbs. Rose Rep. at 13–15; First Gershwin Rep. at 3. Onset usually occurs in children between the ages of two and four, and most commonly presents clinically as joint swelling and associated movement issues like limping, rather than with pain. P. Nigrovic et al., *Genetics and the Classification of Arthritis in Adults and Children,* 70 Arthritis & Rheum. 1, 7–17, filed as Ex.

A Tab 2 (ECF No. 20-3), at 11. Systemic manifestations, like fever, rash, or other constitutional symptoms (which are associated with systemic JIA) are not usually present. Rose Rep. at 14; Lin at 483.

There is no consensus to be found in prior Vaccine Program decisions as to the propensity of vaccines generally to cause JIA. Some recent cases alleging a JIA subtype as an injury have resulted in reasoned decisions awarding compensation. *See, e.g.*, *Jimenez,* 2021 WL 3179643, at *26 (Hepatitis A and human papillomavirus vaccines found to have caused teenager's systemic JIA); *Cabrera v. Sec'y of Health & Hum. Servs.,* No. 13-598V, 2017 WL 510466, at *1 (Fed. Cl. Spec. Mstr. Jan. 12, 2017) (DTaP vaccine caused JIA). But the opposite is also the case. *Faup v. Sec'y of Health & Hum. Servs.,* No. 12-87V, 2019 WL 9313600, at *1 (Fed. Cl. Spec. Mstr. June 17, 2019) (DTaP and inactivated polio vaccines not causal of systemic JIA), *mot. for review den'd,* 147 Fed. Cl. 445 (2020).

In *Jimenez,* a special master determined that the two vaccines at issue caused onset within a week of administration. *Jimenez,* 2021 WL 3179643, at *4–5. There, as here, the claimant relied on Dr. Gershwin's expertise (while Respondent countered with an opinion from Dr. Rose), and Dr. Gershwin theorized an aberrant innate (primary immune system) response mediated by overproduction of inflammatory cytokines (as evidenced in part by the petitioner's presenting fever and rash) in a person with a genetic propensity. *Id.* at *13–14. Significantly, however, *Jimenez* not only implicated different vaccines (with literature offered specific to them), but involved a *distinguishable* form of JIA—the *systemic* subtype—which in turn features presenting symptoms (fever and rash) wholly different from what is seen with oligoarticular JIA, plus an older injured party, as well. Indeed, Dr. Gershwin's causation theory in *Jimenez* relied on an aberrant innate response—consistent with the presenting symptoms of systemic JIA (which are not found with oligoarticular JIA). *See also* Lin at 483 ("[m]arkedly distinct clinical and laboratory features of olig/polyarticular JIA and systemic JIA indicate their distinct pathogenesis and immunologic abnormality"). I therefore do not find that *Jimenez* provides useful guidance herein, despite its well-reasoned character.

Cabrera is similarly of low utility in resolving this case, although for different reasons. There as here, the case involved an infant and a non-systemic form of JIA. The injured child also tested positive for an HLA variant associated more with spondyloarthropathies, like ankylosing spondylitis, although the special master did not give that fact significant weight (despite the urging of Dr. Rose, who in that case appeared for Respondent). *Cabrera,* 2017 WL 510466, at *8–9; *see also Godfrey v. Sec'y of Health & Hum. Servs.,* No. 10-565V, 2015 WL 10710961, at *2 (Fed. Cl. Spec. Mstr. Oct. 27, 2015) (discussing HLA as primary risk factor associated with the juvenile form of ankylosing spondylitis), *mot. for review den'd,* 146 Fed. Cl. 70 (2016). Based upon the expert input received (plus an acceptance of molecular mimicry as a pertinent mechanism when discussing toxoid-containing vaccines like DTaP), the special master determined that a reasonable causation

theory (albeit lacking in rigor or detail) had been offered to explain the disease onset in a three-week timeframe. *Cabrera,* 2017 WL 510466, at *14–16. But *Cabrera* also involves a different vaccine, and did not feature any input at all from an immunologist (whereas the present case featured testimony on *both* sides by well-qualified immunologists).

Faup resulted in a determination counter to *Jimenez*, even though the injury was also systemic JIA. *Faup,* 2019 WL 9313600, at *1. *Faup*, however, involved a wholly different causation theory, based upon the contention that the aluminum adjuvant contained in the DTaP vaccine could encourage an aberrant innate response temporally close to vaccination, encouraging the autoinflammation that is believed to propagate systemic JIA. *Id.* at *7–10. Respondent offered a qualified immunologist to oppose the theory, and the special master deemed the causation theory not to have been preponderantly established[14] (although the special master's decision was equally based on the determination that a viral infection the injured child had experienced was a more likely alternative cause). *Id.* at *26. This theory is distinguishable from Dr. Gershwin's theory herein (although the evidence of an intercurrent infection plays into the resolution of the claim, as discussed below).[15]

All in all, what few prior relevant determinations exist provide limited guidance in assessing whether a vaccine could cause a *non-systemic* form of JIA—the type at issue herein. And I have identified no prior reasoned decisions in which the *MMR vaccine* has been found to be causal of *any* subtype of JIA (or RA for that matter).[16] At most, there is a Table claim for "chronic arthritis" after receipt of rubella virus-containing vaccines (meaning the MMR), but the qualifications and aids to interpretation make clear that this specific injury is inconsistent with JIA or RA. 42 C.F.R. § 100.3(c)(5)(C)(2).

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[14] In resolving the motion for review filed in *Faup,* the Court of Federal Claims accepted the petitioner's objection that the *Faup* special master improperly conflated the theory at issue with a more generally discredited theory of "autoimmune syndrome induced by adjuvants," or ASIA, but found that the special master's analysis was otherwise sound and specific to the theory at issue (while also accepting the finding that an alternative cause—a viral infection—better explained the injury). *Faup,* 147 Fed. Cl. at 447–48.

[15] Another somewhat-recent decision also found that a child's systemic JIA was not vaccine-caused. *Koehn v. Sec'y of Health & Hum. Servs.,* No. 11-355V, 2013 WL 3214877 (Fed. Cl. Spec. Mstr. May 30, 2013) (HPV vaccine), *mot. for review den'd,* 113 Fed. Cl. 757 (2013), *aff'd*, 773 F.3d 1239 (Fed. Cir. 2014). Affirmance of the claim's disposition, however, turned largely on the special master's determination that the timeframe for onset was not reliably established, with the Circuit otherwise seeming to embrace the adequacy of the petitioner's "can cause" showing (of an aberrant innate immune response driving the disease's pathogenesis).

[16] At most, in an almost 25-year old decision, a special master rejected the contention that an adult petitioner's RA was caused by the MMR vaccine. *Graves v. Sec'y of Health & Hum. Servs.,* No. 94-444V, 1997 WL 760525 (Fed. Cl. Spec. Mstr. Nov. 25, 1997). *Graves*, however, denied liability based in part on the determination that the petitioner's injury was consistent with RA, rather than the Table injury of "chronic arthritis"—an actionable injury after receipt of the MMR vaccine, but which excludes RA specifically. *Graves* does not contain significant analysis regarding the capacity (in the context of a non-Table claim) of the MMR vaccine to cause RA.

II. Petitioner Has Not Carried her Burden of Proof

A. *Althen* Prong One

Dr. Gershwin's opinion includes several scientifically-reliable points, but these points lack the reliable medical/scientific connective tissue needed to establish a preponderant theory for how the MMR vaccine could cause oligoarticular JIA.

First, Petitioner's causation theory runs afoul in the same way many prior claimants have: by attempting to flip what is known about how vaccines are *expected* to impact the immune system into a theory for pathogenesis. *Martin v. Sec'y of Health & Hum. Servs.,* No. 17-250V, 2020 WL 4815840, at *27 (Fed. Cl. Spec. Mstr. July 17, 2020) ("[m]any other petitioners have similarly attempted to satisfy the first *Althen* prong by arguing, as here, that the intended pro-inflammatory impact of a vaccine . . . can become pathologic. But I have consistently found this argument lacking in sufficient reliable scientific/medical support"). Dr. Gershwin's contentions about cytokine response to vaccination, as bulwarked by reliable literature like Chatziandreou, were medically and scientifically sound. But he has outlined a theory in which the *normal* cytokine upregulation anticipated by vaccination (and even desired, as part of the vaccine's efficacy) becomes aberrant and damaging—without offering the evidence needed to gauge even partly *how this would actually occur*, and what impact it would have (whether on a healthy person or one susceptible to autoimmune injury, as is posited here). The fact that the initial/innate response to vaccination transiently causes increased cytokine levels (a fact that can easily be substantiated by science, as studies often reveal) does *not* imply an aberrant reaction ensues—and it cannot be assumed this has occurred in a petitioner's case, based solely on the subsequent injury.

A related deficiency in the theory is the degree to which it elides the difference between the innate and adaptive "arms" of the overall human immune response—attempting to combine the two into a single pathologic process, but without sufficient evidence of how they would interact to cause JIA. Dr. Gershwin thus states that oligoarticular JIA is likely mediated by autoreactive T cells,[17] and hence reflects an adaptive rather than initial/innate response to vaccination. But if so (and I am assuming this for sake of argument—Dr. Gershwin's evidence is somewhat limited to the contention that the presence of T cells is *detected* in the joints of JIA patients), how does vaccination produce these autoreactive T cells or stimulate their activity? The theory cannot say. It then shifts to consideration of the innate response causing upregulation of cytokines, proposing in a vague

[17] This helps illustrate why decisions finding entitlement in instances of *systemic* JIA are distinguishable. As *Jimenez* makes evident, systemic JIA presents with symptoms reflective of an *innate* immune response—fever and rash, appearing close in time to vaccination. It is thus far more facially likely that this form of JIA is driven by an aberrant/pathologic innate immune response—and in turn, that a vaccine could play a role in that process. Here, by contrast, where the slower-to-occur adaptive response is more implicated in the disease's pathogenesis, more specificity between vaccination and injury needs to be demonstrated.

sense (despite the scientific term-heavy quality of Dr. Gershwin's reports) that they somehow contribute to an inflammatory milieux that later results in a T cell attack. Again, details and reliable connective evidence is lacking. Not enough has been offered to show how the innate response to the MMR vaccine would initiate a disease course. It is of course the case, as often recognized, that petitioners need not offer proof of a scientific mechanism to prevail. But there is not enough of the *other* kind of evidence associating the MMR vaccine to any form of JIA to make up for this absence.

The same goes for Dr. Gershwin's arguments about the adaptive immune response's role in connection with vaccination—and particularly the extent to which he relies on the concept of molecular mimicry (ever-popular in Vaccine Program cases). He seems to propose that some component of the MMR vaccine would cross-react with a JIA self-structure, but is vague in detailing (a) what component of the vaccine is implicated, (b) what evidence exists that JIA is mediated by antibodies to that component, and (c) what that antibody might even be (although I credit the literature that suggests some possibilities). Indeed, Dr. MacGinnitie persuasively observed that the criteria for molecular mimicry proposed *by Dr. Gershwin* are not met. First MacGinnitie Rep. at 5–6. Hence, this reflects yet another case where the general idea of molecular mimicry is asserted on a petitioner's behalf, but without the substantive grounding needed to find it reliably establishes vaccine causation. *Hock v. Sec'y of Health & Hum. Servs.*, No. 17-168V, 2020 WL 6392770, at *27 (Fed. Cl. Spec. Mstr. Sept. 30, 2020) ("[i]n this case (as in countless cases before it), a petitioner has once again hoped that recitation of the phrase "molecular mimicry" will help build a preponderant case on the first *Althen* prong, but without offering robust and reliable scientific or medical evidence suggesting that the concept actually bears on the injury and vaccine at issue" (citations omitted)).[18]

Second, the contention that the immune response to the MMR vaccine could be amplified by the effects of an intercurrent infection was not adequately substantiated. Nothing was provided directly implicating any vaccine, let alone the MMR, in a process combining with a wild infection and resulting in oligoarticular JIA. At most, some evidence (like Schattner)[19] was offered showing an association between viral infections (or the rubella vaccine component) and distinguishable forms of RA, but not enough to establish a fully-reliable connection. No reliable, persuasive proof was offered (beyond the contentions discussed above about cytokine upregulation in the

[18] In fact, even *less* of a showing in support of molecular mimicry has been made here than in other unsuccessful cases, where the expert at least attempted to establish amino acid sequential homology between antigenic components in a vaccine and some target protein in the body proposed as implicated in a relevant disease process. *See, e.g.*, *Pek v. Sec'y of Health & Hum. Servs.,* No. 16-0736V, 2020 WL 1062959, at *5 (Fed. Cl. Spec. Mstr. Jan. 31, 2020) (denying entitlement in claim that flu vaccine caused multiple sclerosis, despite arguments that vaccine components could be demonstrated to possess sufficient homology with proposed target antigens to suggest possibility of autoimmune cross-reaction). Here, Dr. Gershwin simply disclaims the ability to make such a showing at all, while also admitting that sequential homology does not mean a cross-reaction is likely to occur.

[19] Schattner, it should be noted, observed a rubella wild virus connection to *chronic arthritis*, which is consistent with the Table claim, but not enough to prove an MMR-JIA association. Schattner at 3879.

anticipated/normal immune response) to show that infection *plus* vaccination would tip the scales, so to speak, toward an autoimmune pathologic reaction manifesting as JIA. And Dr. MacGinnitie's observations that it could not be assumed the amplification would be more likely due to the same lymph node's processing of a wild infection and vaccine simultaneously were insufficiently answered by Dr. Gershwin.

Third (and as addressed above), there remain numerous holes in Petitioner's theory, preventing the conclusion that it overall "links up" into something preponderant. Thus, no MMR vaccine antigen to drive the putative autoimmune process was identified, and no target self-antigen as the place of cross-reactive attack was named. The rubella vaccine was shown to be associated with a distinguishable condition, chronic arthritis, but not with JIA. In addition, scant evidence—whether in the form of independent literature or expert opinion derived from Dr. Gershwin's research—was offered to show that JIA's pathogenesis is either instigated by cytokine upregulation, or amplified by intercurrent infectious processes.[20] This kind of "back-end" proof (focusing on the end stimuli for oligoarticular JIA) would have aided a theory that lacked much "front-end" support connecting the MMR vaccine more specifically to oligoarticular JIA in the first place.

Respondent has also offered some evidence that undercuts Petitioner's showing of a vaccine association. Heijstek I and Heijstek II both observed no increased risk of a JIA symptoms flare after receipt of the MMR booster (and Heijstek I even saw an extremely low association between vaccination and JIA in a subset of patients whose JIA had not yet been diagnosed). Heijstek I at 1386. Dr. Gershwin's protestations that the rarity of JIA specifically (coupled with the generally-uncommon nature of vaccine injuries) means that this class of evidence merits little to no consideration is wholly unpersuasive. Ample controlling precedent already establishes that special masters may give appropriate weight to reliable epidemiologic studies. *D'Tiole v. Sec'y of Health & Hum. Servs.,* 726 F. App'x 809, 811 (Fed. Cir. 2018) ("[n]othing in *Althen* or *Capizzano* requires the Special Master to ignore probative epidemiological evidence that undermines petitioner's theory"). Here, that evidence does not preclude a better-substantiated showing that the MMR vaccine could be causal, but it weakens what Petitioner did offer.

In response, Petitioner cites to one or two case studies, like Korematsu—which not only involves a single patient (and hence is more likely illustrative of chance or a temporal association), but is wholly-distinguishable circumstances, as well (a child already diagnosed with JIA who received an MMR booster). And it is a kind of evidence usually given less weight in Program determinations in any event. *Crutchfield v. Sec'y of Health & Hum. Servs.*, No. 09-39V, 2014 WL 1665227, at *19 (Fed. Cl. Spec. Mstr. Apr. 7, 2014) ("single case reports of Disease X occurring

[20] I acknowledge that Kunnamo was offered to fill this evidentiary hole, and it facially suggests some link between an antecedent infection and JIA—but its age, along with the fact that the proof of antecedent infection was obtained via survey rather than being confirmed in a scientifically-reliable manner, consistent with a properly-performed study, undercuts the weight to be given to it.

after Factor Y . . . do not offer strong evidence that the *temporal* relationship is a *causal* one—the temporal relationship could be pure random chance"), *aff'd*, 125 Fed. Cl. 251 (2014).

At bottom, Petitioner's theory never arises above a bare form of reasoned speculation. The concept that a vaccine *could* interact with an intercurrent infection, resulting in a pathologic process, is plausible[21]—and an expert with Dr. Gershwin's intelligence and background can in most cases sketch out a theory supporting it, based on accepted immunologic principles, that is not facially absurd. But here, there is exceedingly little reliable evidence establishing that the MMR vaccine *itself* could do so, and/or that the kind of cytokine upregulation postulated as the result of interaction with a concurrent infection would result in JIA (or even drive it pathologically in the first case). The "can cause" prong has not been satisfied.

B. *Althen* Prong Two

Even if I had found that preponderant evidence supported a causal association between the MMR vaccine and oligoarticular JIA, I could not find on the basis of the filed medical record that the vaccine was the likely cause of B.P.'s JIA. To begin, no treaters have proposed that B.P.'s symptoms were associated with the MMR vaccine.[22] And there is no evidence in the record showing that B.P. in fact experienced *any* of the common vaccine malaise-like reactions (fever or other symptoms) that can suggest the start of an immune-mediated illness (or that might have been viewed as suspect by treaters). By contrast, B.P. had a documented URI for which she was treated—followed by an approximately two-week gap before her JIA symptoms first manifested (and hence far closer in time to the URI than vaccination). Thus, while there is a temporal relationship between the receipt of the MMR vaccine and URI, with the former preceding the latter, the record itself reveals nothing to suggest the two *interacted* consistent with Dr. Gershwin's theory—the record does not show, for example, that B.P.'s URI symptoms were unusual or more pronounced (which in turn might support an inference that the immune response triggered by the vaccine initially was subsequently amplified by the infection, as proposed). No other evidence—witness testimony or testing proof—establishes an aberrant immune response.[23]

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[21] Indeed, what is often referred to as a "*Shyface* analysis" in the Vaccine Program involves situations where the greater causal role of vaccine versus some other external factor, like an infection, cannot be differentiated, although it is clear both played a role in the asserted injury, allowing an entitlement finding despite the uncertainty. *Shyface,* 165 F.3d at 1352–53. But here, I do not find that it has been preponderantly established *either* that the MMR vaccine could interact with an intercurrent infection (with identifying which was *more* causal) to cause oligoarticular JIA, or that this did occur in B.P.'s case.

[22] While Petitioner might point to the fact that in February 2018 B.P.'s immunizations were deferred for a period of time, that particular record does not set forth treater speculation that the MMR vaccine was causal of her JIA. Ex. 8 at 15. By contrast, when B.P. later saw PNP Connor in August 2018, it was explicitly recommended that B.P. adhere to her vaccination schedule despite her JIA, and thus without concerns from a rheumatologic standpoint. Ex. 9 at 24.

[23] Dr. Rose's proposal that antibiotic treatments for prior ear infections could have produced dysbiosis in B.P., resulting in JIA, is interesting and plausible, but it has not been preponderantly established by Respondent as an alternative cause in this case.

C. *Althen* Prong Three

The onset of B.P.'s JIA occurred most likely on December 5, 2017, when her swollen right knee and accompanying movement issues were first observed. The 26-day period between that date and her receipt of the MMR vaccine on November 9, 2017, falls within the timeframe for an adaptive immune response to occur under Dr. Gershwin's theory. First Gershwin Rep. at 3, 11. And I find it as general matter to be a reasonable timeframe for an autoimmune process driven by the adaptive/secondary arm of the immune system. Of course, Dr. Gershwin's theory *also* depends on a determination that *before* clinical manifestation of symptoms, B.P.'s URI interacted with vaccination as part of the *innate* response. But as already discussed, the record does not at all reflect onset of such initial symptoms in any way consistent with the theory.[24] Accordingly, the record does not establish an aberrant response occurring in the proposed timeframe prior to symptoms manifestation. And even if I construed Dr. Gershwin's theory as *only* proposing an adaptive, antibody or T-cell driven autoimmune response that was nevertheless vaccine-driven, the fact that symptoms began within in the timeframe for that response do not save the underlying theory from the foregoing analysis. All three *Althen* prongs must be satisfied to prevail, so establishing the third prong does not make up for Petitioner's inability to meet the other two.

[24] Dr. MacGinnitie did make some other persuasive points about the timeframe question, independent of the fact that record evidence shows no aberrant immune response occurred before clinical manifestation of knee swelling. The live and attenuated character of the MMR vaccine meant that an innate response to it might be more delayed than with other vaccine formulations—meaning in turn that the URI (which Dr. Gershwin opined could have begun around the time the vaccine would have elicited an innate response) could not be presumed to amplify the vaccine reaction, since it had likely cleared prior to the time B.P.'s immune system began to react to vaccination. But resolution of this prong does not turn on this argument—and in any event, Petitioner's overall showing remains deficient even were I to find the timeframe prong had been satisfied.

CONCLUSION

Petitioner's claim has not been preponderantly established. I therefore must DENY entitlement in this case.

In the absence of a motion for review filed pursuant to RCFC Appendix B, the Clerk of the Court **SHALL ENTER JUDGMENT** in accordance with the terms of this Decision.[25]

IT IS SO ORDERED.

/s/ Brian H. Corcoran
Brian H. Corcoran
Chief Special Master

[25] Pursuant to Vaccine Rule 11(a), the parties may expedite entry of judgment if (jointly or separately) they file notices renouncing their right to seek review.