OFFICE OF SPECIAL MASTERS

No. 01-0165V

(Filed: July 16, 2004)

LISA ANN PAFFORD and RICHARD LEON PAFFORD PARENTS AND NEXT FRIENDS of RICHELLE LORRAE PAFFORD, a minor Petitioners, v. SECRETARY OF THE DEPARTMENT OF HEALTH AND HUMAN SERVICES, Respondent.	*	TO BE PUBLISHED

Robert T. Moxley, Esq., Cheyenne, Wyoming, for Petitioners.
Melonie J. McCall, Esq., United States Department of Justice, Washington, D.C., for Respondent.

ENTITLEMENT DECISION

ABELL, Special Master:

I. ISSUE

The Court held an entitlement hearing in this case on 8 July 2003. Petitioners allege that the DTaP, MMR and OPV vaccinations, or any component thereof, administered to Richelle Pafford (hereinafter "Richie") on 24 March 1998 resulted in the onset of systemic onset Juvenile Rheumatoid Arthritis, also known as Still's disease. The issue before this Court is simply whether Petitioners' allegation is correct. However, the Court's arrival at its decision was anything but simple. The novel medical theory put forth by Petitioners and their experts created a Serbonian bog of unexplored territory. After wading through and coming out the other side, the Court cannot conclude that Richie's Still's disease was in-fact caused by the vaccinations at issue.

II. PROCEDURAL BACKGROUND

Petitioners have satisfied the requirements for a *prima facie* case pursuant to § 300aa-11(b) and (c) by showing that: (1) Petitioners are valid legal representatives; (2) the vaccines at issue are vaccines set forth in the Vaccine Injury Table; (3) the vaccinations were administered to Richie in the United States; (4) no one has previously collected an award or settlement of a civil action for damages arising from the alleged vaccine-related injury; and, (5) no previous civil action has been filed in this matter. Additionally, the § 300aa-16(a) requirement that the petition be timely filed has been met.

On 8 July 2003, the Court conducted an evidentiary hearing in this matter. The Court heard testimony from Petitioners' medical experts, Dr. Alan S. Levin[1] and Dr. Mark R. Geier,[2] and

[1] Dr. Alan S. Levin earned an M.D. from the University of Illinois (Chicago Medical Center). He is board certified in pathology - clinical pathology and board certified in allergy and immunology. Dr. Levin currently serves as an attending physician in the Department of Medicine at the Mount Zion and University of California San Francisco Hospitals. Dr. Levin has published more than sixty five full length articles and forty five abstracts in peer reviewed medical literature primarily concerning the subjects of immunology, immunopathology, cancer biology, and treatments. Dr. Levin also earned a J.D. from Golden State University and, along with his medical practice, has his own private law practice.

[2] Dr. Mark R. Geier is a geneticist and an obstetrician but is not board certified in the areas of rheumatology, pathology, or immunology, which are at issue in this case. Although the undersigned will, within reason, hear any expert that a petitioner wishes to present, the weight of those experts opining outside of their areas of expertise will be accorded significantly less weight. Because Dr. Geier testified in matters to which his professional background is unrelated, his testimony is of limited value to the court. Notwithstanding such, Dr. Geier opined that the rubella virus contained in the MMR vaccine can produce chronic infection in synovial tissue resulting in the onset of JRA. Transcript at 67. Dr. Geier stated that proof of such would be the presence of the rubella virus in the synovial fluid. *Id*. at 67-68. Regrettably, "the rubella virus was not isolated in any of [Richie's] synovial fluid" because "[n]obody looked." *Id*. at 128. Thus, Dr. Geier's theory, whether plausible or not, cannot be tested in this case and, therefore, will not be considered. Additionally, this Court is concerned at the apparent Procrustean application of Dr. Geier's theory which has been argued on four separate occasions before four separate special masters who, in each case, denied entitlement. *Poulos v. Sec'y of Health and Human Services*, 1994 WL 470622 (Fed. Cl. 1994); *Carter v. Sec'y of Health and Human Services*, 1990 WL 293453 (Cl. Ct. 1990), aff'd, 21 Cl. Ct. 651 (1990); *Muchnik v. Sec'y of Health and Human Services*, 1991 WL 217673 (Cl. Ct. 1991); and, *Boehmer v. Sec'y of Health and Human Services*, 1991 WL 242995 (Cl. Ct. 1991).

Respondent's medical experts, Dr. Carlos D. Rosé,[3] Dr. Melvin Berger[4] and Lawrence H. Moulton.[5] The hearing transcript was filed on 8 August 2003.

Thereafter, the parties filed post-hearing briefs. On 8 October 2003, Petitioners filed their post-hearing brief. On 22 December 2003, Respondent filed a post-hearing brief. Petitioners filed their *sur-response* on 9 February 2004. Thus, the record is complete and ripe for decision.

III. FACTS

Richie was born on 30 January 1993. Petitioners' Exhibit (hereinafter "Pet. Ex.") 1 at 6. She consistently received medical care from Dr. Jay Schmidt throughout her early childhood and there was nothing remarkable about Richie's early development. On 5 August 1993, during a well child exam, Dr. Schmidt administered Richie's first DTP, OPV and Hib vaccinations. Pet. Ex. 3 at 58. On 21 October 1993, Richie received her second DPT, OPV and Hib vaccinations. *Id*. at 53. On 10 May 1994, Richie had a normal well child exam and Dr. Schmidt noted normal development. *Id*. at 46. During the exam, Dr. Schmidt administered Richie's third DTP, MMR and OPV vaccinations as well as her first MMR vaccination. *Id*. On 27 May 1994, Richie developed a faint maculopapular[6] rash on the face, legs and arms that persisted for five days with a negative strep throat culture. *Id*. at 44-45.

During November and December 1997, Richie was treated for otitis.[7] *Id*. at 16-20. On 5 March 1998, Richie saw Dr. Schmidt complaining of a cold and diarrhea. *Id*. at 15. On 12 March

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[3] Dr. Carlos D. Rosé is board certified in adult and pediatric rheumatology. Dr. Rosé graduated *summa cum laude* from the University of Buenos Aires School of Medicine. Dr. Rosé is a staff physician in pediatric rheumatology at The Alfred I. duPont Institute of the Nemours Foundation in Wilmington, Delaware and is a pediatric rheumatology consultant at the Medical Center of Delaware. Additionally, Dr. Rosé served as a consultant to the National Institute of Health by providing expertise concerning the issue of rubella vaccine induced arthritis. He is also a member of the American College of Rheumatology.

[4] Dr. Melvin Berger is board certified in pathology, board certified in pediatrics and board certified in allergy and immunology. Dr. Berger received an M.D. from Case Western Reserve University as well as a Ph.D. in Biochemistry. Dr. Berger currently serves as a professor in pathology and pediatrics at Case Western Reserve University and is the Chief of the Allergy/Immunology/Rheumatology Division, Department of Pediatrics at the Rainbow Babies and Children's Hospital.

[5] Lawrence H. Moulton, Ph.D., is a biostatistician and a faculty member at Johns Hopkins Bloomberg School of Public Health, where he earlier earned his Ph.D. Dr. Moulton earned a bachelor's degree in both statistics and mathematics at the State University of New York at Buffalo and a master's degree at the Texas School of Public Health.

[6] "Both macular and papular, as an eruption consisting of both muscles and papules; sometimes erroneously used to designate papule that is only slightly elevated." DORLAND'S ILLUSTRATED MEDICAL DICTIONARY 971 (27th ed. 1988). DORLAND'S at 1202.

[7] "Inflammation of the ear, which may be marked by pain, fever, abnormalities of hearing, hearing loss, tinnitus, and vertigo." DORLAND'S at 1202.

1998, Richie was seen by Dr. Schmidt for inflamed tonsils with white patches on them and a fever of 101-102 degrees Fahrenheit. *Id*. at 15. A resulting throat culture was negative for Streptococcus.[8] *Id*. at 13-15. On 24 March 1998, Richie had a normal examination showing normal growth and development with a history of normal activity including gymnastics. *Id*. at 11-12. Dr. Schmidt observed that her earlier tonsillitis had resolved, her neck was without lymphadenopathy,[9] her lungs were clear to auscultation,[10] a normal heart rate, a non tender abdomen, and no gross neurological deficits were noted. *Id*. at 11. Richie received a DTaP vaccination, her fourth OPV vaccination, and her second MMR vaccination that same day. *Id*. at 11. On 4 April 1998, Richie developed a fever and complained of neck pain. *Id*. 3 at 5. The next day, Richie's fever had abated but her neck pain continued. *Id*. Richie was taken to Dr. Schmidt's on 7 April 1998 for evaluation and treatment of her symptoms. *Id*. Richie had developed a diffuse pink, macular rash, whitish spots on her tongue (possible Koplik's spots[11]), and complained of limb pain that morning. *Id*. Richie was diagnosed with a vaccine-induced rash and was told to avoid exposure to other people for five days. *Id*.

On 13 April 1998, Richie was taken to the emergency room of the United Medical Center in Cheyenne, Wyoming. Pet. Ex. 5 at 1. She had a temperature of 103.9 degrees Fahrenheit, a blanching red maculopapular rash on the hands involving the palms and soles, on the medial aspects of her upper legs and on her chest and upper abdominal area. *Id*. at 8. Richie was vomiting at intake and refused all intake. *Id*. at 16. On initial examination in the emergency room, Dr. Valerie Bell noted that Richie was tearful and cried wherever touched. *Id*. at 16-17. Dr. Bell noted that "[t]he rash was very viral in character and I did not feel it was related to her immunizations but suggested a CBC[12] to see if it supported the viral picture." *Id*. at 16. By the time Richie was admitted, her temperature was 97.2 degrees Fahrenheit and her rash had greatly diminished. *Id*. She was "playful and happy" and had "no complaints whatsoever." *Id*. Richie tested positive for mycoplasma,[13] which Dr. Bell thought explained her symptoms at the time. Pet. Ex. 4 at 79. On her discharge the following day, Richie was afebrile and "her rash, for the most part, had disappeared." Pet. Ex. 5 at 9.

On 30 April 1998, Richie saw Dr. Bell for recurrence of fever and rash and complaints of

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[8] "spherical gram-positive bacteria occurring in pairs or chains." http://www.cogsci.princeton.edu/cgi-bin/webwn?stage=1&word=streptococcus.

[9] "Disease of the lymph nodes." DORLAND'S at 960.

[10] "The act of listening for sounds within the body, chiefly for ascertaining the condition of the lungs, heart, pleura, abdomen, and other organs, and for the detection of pregnancy." DORLAND'S at 169.

[11] "Small, irregular, bright red spots on the buccal and lingual mucosa, with a minute blueish white speck in the center of each; seen in the prodromal stage of Measles." DORLAND'S at 1569.

[12] "Complete blood count." Neil M. Davis, MEDICAL ABBREVIATIONS: 8600 CONVENIENCES AT THE EXPENSE OF COMMUNICATIONS AND SAFETY, 31 (6th Ed. 1993).

[13] "A bacterium of the class Mollicutes." DORLAND'S at 1085.

increasing joint pain. Pet. Ex. 4 at 79. During the exam Dr. Bell recorded that Richie had a fever of 102.9 degrees Fahrenheit, a painful, swollen right elbow and left knee. *Id*. Neither of the joints, however, were red or hot. *Id*. The rash that Richie had on 13 April 1998 had returned. *Id*. It was "macular, reticular rash on her trunk slightly, prominent on hands, feet and lower legs, and on her thighs on the inner surfaces." *Id*. Dr. Bell "strongly suspected[ed] systemic onset JRA, as the cause of the month long recurrent rash, fever, and discomfort." *Id*. Richie's lab results revealed an elevated sedimentation rate of 80, mild anemia, and a negative ANA[14] and rheumatoid factor tests. *Id*. at 80.

Dr. Bell diagnosed Richie with systemic onset Juvenile Rheumatoid Arthritis, also known as Still's disease. *Id*. Richie was treated with Naprosyn[15] and prednisone[16] with some benefit. *Id*. On 21 May 1998, this diagnosis was corroborated by Dr. Hollister, a pediatric rheumatologist at Children's Hospital in Denver, Colorado. *Id*. at 78. Attempts to wean Richie from the prednisone resulted in recurrent symptoms, and Methotrexate[17] was initiated in September 1998. *Id*. at 55-74.

On 28 January 1999, Richie had continued synovitis[18] despite maximum treatment with Methotrexate. *Id*. at 47. Due to the refractory nature of her Still's disease, it was recommended that a second level arthritis drug, Cyclosporin A,[19] be added to her medication regime. *Id*. at 48. It was determined that Richie would receive the varicella vaccine before starting the Cyclosporin A. *Id*. Over the next year, Richie's disease remained active with recurrent arthritis. *Id*. at 23-46.

IV. DISCUSSION AND ANALYSIS

1. What is Still's disease?

Still's disease is one type of juvenile rheumatoid arthritis ("JRA") and is also known as systemic-onset JRA ("soJRA"). By systemic it is meant that along with joint inflammation it

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[14] "Antinuclear antibody." MEDICAL ABBREVIATIONS at 15.

[15] Naprosyn - a nonsteroidal anti-inflammatory drug (trade name Naprosyn) used in the treatment of arthritis and musculoskeletal inflammation and moderate pain. http://www.cogsci.princeton.edu/cgi-bin/webwn ?stage=1&word=naprosyn.

[16] Predinsone - a dehydrogenated analogue of cortisol (trade names Orasone or Deltasone or Liquid Pred or Meticorten); used as an anti-inflammatory drug in the treatment of arthritis and as an immunosuppressant. http://www.cogsci.princeton.edu/cgi-bin/webwn ?stage=1&word=prednisone.

[17] Methotextrate - toxic antimetabolite that limits cellular reproduction by acting as an antagonist to folic acid; used to treat certain cancers and psoriasis and rheumatoid arthritis. http://www.cogsci.princeton.edu/cgi-bin/webwn ?stage=1&word=Methotextrate+.

[18] "Inflammation of a synovial membrane." DORLAND'S at 1649.

[19] Cyclosporin A is the first of the new generation of immunosuppressive agents with a specific site of action within immune system. http://www.nrdcindia.com/pages/sporin.htm.

typically begins with symptoms and signs of systemic (body wide) illness, such as high fevers, gland swelling, and internal organ involvement.[20] It affects children inflaming the large joints and sometimes retarding bone growth.[21] Mostly, it involves an inflammation of the connective tissue.[22] A dispositive etiology is unknown, but like many other types of arthritis, abnormal immune response, genetic predisposition and environmental triggers, and infectious agents are all being considered.[23]

Still's disease usually begins with systemic symptoms. Extreme fatigue can accompany waves of high fevers that rise daily to 102 degrees Fahrenheit or even higher and rapidly return to normal levels or below. Fever spikes often occur at nearly the same time every day. A faint salmon-colored skin rash characteristically comes and goes and does not itch. Arthritis, with joint swelling, often occurs after rash and fevers have been present for some time. Although the arthritis may initially be overlooked because of the impressive nature of the systemic symptoms, everyone with Still's disease eventually develops joint pain and swelling.[24]

2. Were one or more of the 24 March 1998 vaccinations the cause of Richie's Still's disease?

Petitioners can prove entitlement to compensation under the Program in one of two ways. They can prove entitlement through a statutorily prescribed presumption of causation or, by proving causation-in-fact. First, Petitioners may prove that Richie suffered an injury or condition listed in the Vaccine Injury Table within the statutorily prescribed time period. § 11(c)(1)(C)(i). If Petitioners establish that Richie suffered such injury by a preponderance of the evidence, Petitioners are entitled to a presumption of causation. § 13(a)(1)(A). If Richie qualifies under this presumption, she will be said to have suffered a "Table injury." The burden would then shift to the Respondent to prove that the injury or condition "is due to factors unrelated to the administration of the vaccine described in the petition." § 13(a)(1)(B).

If Petitioners fail to satisfy the requirements under the Act for demonstrating a Table injury, Petitioners may prove by a preponderance of the evidence that the vaccination in question, more likely than not, caused the alleged injury. §§ 11(c)(1)(C)(ii)(I) and (II). This causation-in-fact standard, according to the Federal Circuit, requires proof of a "logical sequence of cause and effect showing that the vaccination was the reason for the injury." *Grant v. Secretary of HHS*, 956 F.2d 1144, 1148 (Fed. Cir. 1992). Once again, if Petitioners are successful in that showing, the burden shifts to Respondent to prove that the injury or condition "is due to factors unrelated to the administration of the vaccine described in the petition." § 13(a)(1)(B).

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[20] http://www.stillsdisease.org/still's_disease_info.htm.

[21] http://www.cogsci.princeton.edu/cgi-bin/webwn?stage=1&word=still%27s+disease.

[22] http://www.dynomed.com/encyclopedia/encyclopedia/arthritis/Juvenile_Rheumatoid_Arthritis.html.

[23] http://arthritisinsight.com/medical/disease/stills.html.

[24] http://www.medicinenet.com/Stills_Disease/page1.htm.

In the present case, Petitioners do not allege that Richie suffered a Table injury. Petitioners allege Richie suffered Still's disease as a result of one or more of the vaccinations she received on 24 March 1998. The Table does not list Still's disease as a recognized adverse event that warrants presumption, thus, Petitioners' claim is one of causation-in-fact.[25]

a. Causation-In-Fact

In order to demonstrate entitlement to compensation in a causation-in-fact claim, a petitioner must affirmatively demonstrate by a preponderance of the evidence that the vaccination in question *more likely than not* caused the injury alleged. *See* 11(c)(1)(C)(ii)(I) and (II); *Grant v. Secretary of HHS*, 956 F.2d 1144 (Fed. Cir. 1992); *Strother v. Secretary of HHS*, 21 Cl. Ct. 365, 369-70 (1990), *aff'd*, 950 F.2d 731 (Fed. Cir. 1991). The Federal Circuit, which summarized the legal criteria required to prove causation-in-fact under the Vaccine Act, requires that every petitioner:

> show a medical theory causally connecting the vaccination and the injury. Causation in fact requires proof of a logical sequence of cause and effect showing that the vaccination was the reason for the injury. A reputable medical or scientific explanation must support this logical sequence of cause and effect.

Grant, 956 F.2d at 1148 (citations omitted); *see also Strother*, 21 Cl. Ct. at 370.

This Court has organized the legal criteria in *Grant* by means of a two-part test. *First*, a petitioner must provide a reputable medical theory causally connecting the vaccination and the injury. *In fine*, can vaccine(s) at issue cause the type of injury alleged? *Second*, a petitioner must also prove that the vaccine actually caused the alleged symptoms in her particular case.

Under the first prong, a petitioner must demonstrate the biologic plausibility of their theory by proffering a scientific pathogenesis underlying the alleged causal relationship. This may be accomplished in a number of ways. Reliability and plausibility of that pathogenesis can be bolstered by providing evidence that at least a sufficient minority in the medical community has accepted the theory as to render it credible. In addition, epidemiological studies and an expert's experience, while not dispositive,[26] lend significant credence to the claim of plausibility. Articles published in respected medical journals, which have been subjected to peer review, are also persuasive. However, publication "does *not* necessarily correlate with reliability," because "in some instances well-grounded but innovative theories will not have been published." *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 509 U.S. 579, 593-94 (1993).

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[25] 42 C.F.R. § 100.3(a).

[26] This first prong of the Court's test meets easily with cases where epidemiological or case study reports are already available. Beginning with this prong is practical when there is epidemiological evidence, for it avoids the tautological reasoning that would result when one attempts to answer *Can It?* without having reports and studies that previously would have answered *Did It?*

The second prong of the causation-in-fact test is difficult to meet but not impossible. A petitioner must show, by a preponderance of the evidence--as this special master is wont to say, a test based on fifty percent and a feather--that the vaccine caused the injuries or symptoms that manifested in this case. A petitioner does not meet this affirmative obligation by merely showing a temporal association between the vaccination and the injury. If petitioners' expert views the temporal relationship as the "key" indicator of causation, the claim must fail. *Thibaudeau v. Sec'y of the HHS*, 24 Cl. Ct. 400, 403 (1991). Rather, a petitioner must explain *how* and *why* the injury occurred. *Strother*, 21 Cl. Ct. at 370; *see also Hasler v. United States*, 718 F.2d 202, 205 (6th Cir. 1993), *cert. denied*, 469 U.S. 817 (1984) (stating that inoculation is not the cause of every event that occurs within a ten day period following it). Ruling out other potential causes is an essential element but does not itself establish causation. Additionally, mere conjecture or speculation does not meet the preponderance standard. *Snowbank Enterprises v. United States*, 6 Cl. Ct. 476, 486 (1984)

b. Applicability of the Two Part test in Richie Pafford's Case

In Richie's case, the Court follows the two pronged causation in fact analysis tailored as: (i) Is it biologically plausible that one or more of the vaccinations in question can cause Still's disease?; and, (ii) Did one or more of Richie's vaccinations result in her Still's disease?

(i) Is it biologically plausible that one or more of the vaccinations in question can cause Still's disease?

Petitioners' expert, Dr. Levin and Respondent's expert, Dr. Rosé, both agreed that an individual that develops Still's disease generally has a genetic predisposition to do so. Transcript (hereinafter "Trans.") at 171, 172, 469 and 471. However, Dr. Berger, another medical expert appearing for Respondent, while not ruling out the possibility of a genetic predisposition, was unwilling to conclude that such was absolutely necessary in contracting Still's disease. *Id*. at 423. Dr. Levin opined that this predisposition can be triggered by vaccinations, Trans. at 171, resulting in an autoimmune[27] mediated inflammatory disorder known as the "activation of a forbidden clone."[28] Pet. Ex. 8 at 3. Dr. Levin asserted that the activation of the forbidden clone is an inflammatory response "causing the release of cytokines[29] which drive the expression and expansion of cells with autoreactive anti-self activity." Id. at 2. Dr. Levin went on to state that "[i]t is well

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[27] Autoimmunity: an abnormal condition in which the immune system develops antibodies against the body's own tissues, causing a reaction that results in an autoimmune disease. http://www.peppypaws.com/Glossary.html.

[28] The Forbidden Clone Theory: a theory that at birth all cells that might react against the body have been eliminated, leaving only cells that will react against foreign substances; when cells that react against the body persist after birth, they can be activated by something and result in an autoimmune disease. http://www.peppypaws.com/Glossary.html.

[29] Cytokine: "a genetic term for non-antibody proteins released by one cell population on contact with a specific antigen, which act as intercellular mediators, as in the generation of an immune response." DORLAND'S at 427-28.

recognized that the symptoms of Still's disease are caused by cytokine expression." Id. at 3. According to Dr. Levin, the release of certain pro-inflammatory cytokines such as Interleuken[30] ("IL")-1, IL-4, and IL-6 trigger Still's disease. Trans. 173. Dr. Levin stated that this has been proven, in that when treating Still's disease, its symptoms can be alleviated by treating the patient with "that particular molecular which tends to be a sponge for certain cytokines," Id. at 174, thereby reducing or removing the cytokines.

Respondent's expert, Dr. Rosé, agreed that "Still's disease has a lot of cytokines circulating," Id. at 468, and that IL-1, TNF Alpha,[31] and IL-6 are "all really big players in the observed symptoms of Still's disease." Id. at 462. Dr. Rosé also added that treating Still's disease patients by trying to reduce certain cytokines "has produced a 70 percent success rate." Id. Finally, Dr. Rosé testified that vaccines induce cytokine production. "Cytokines are produced by the host after receiving the vaccination. If vaccines could not induce cytokines, they could not induce immunity for you to protect against the infectious agent." Trans. at 463. Additionally, Dr. Berger stated that certain cytokines "are important mediators of Still's or systemic-onset JRA" and that it is a matter of excessive and prolonged cytokine production that results in the manifestations of the disease. *Id*. at 421.

Based on the testimony of Petitioners' expert, Dr. Levin and Respondent's experts, Dr. Rosé and Dr. Berger, the Court finds that, by a preponderance of the evidence, it is biologically plausible that one or more of the vaccinations at issue could cause the onset of Still's disease. The experts agree that there is a genetic predisposition to the disease, that a hallmark of the disease is cytokine expression,[32] vaccines induce cytokine expression, and treating such expression reduces the disease's effects.[33]

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[30] Interleukin: "a generic term for a group of protein factors produced by macrophages and T cells in response to antigenic or mitogenic stimulation and affecting primarily T cells." DORLAND'S at 845.

[31] "Tumor necrosis factor [("TNF")] alpha is a cytokine produced primarily by monocytes and macrophages." http://www.arthritis.co.za/tnf.htm.

[32] "Abnormal expression of the three primary inflammatory cytokines (IL-6, IL-1, and TNFα) is characteristic of [systemic onset Juvenile Rheumatoid Arthritis]." Respondent's Exhibit L.

[33] "The Special Master is not required to be a 'potted plant'. . . . Rather, the legislative history of the newly-amended Vaccine Act emphasizes that '[t]he system is intended to allow the proceedings to be conducted in . . . an 'inquisitorial' format, with the [special] master conducting discovery (as needed), cross-examination (as needed) and *investigation*.'" *Hines v. Sec'y. of Health and Human Services*, 21 Fed. Cl. 634, 648 (1990) (emphasis added). Accordingly, the Court, *sua sponte*, researched Dr. Levin's theory and found additional support for his assertions regarding the autoimmune mediated nature of rheumatoid arthritis:

One prevalent theory is that a combination of factors trigger rheumatoid arthritis, including an abnormal autoimmune response, genetic susceptibility, and some environmental or biologic trigger. The primary infection-fighting units are two types of white blood cells: lymphocytes and leukocytes. Lymphocytes include two subtypes known as *T-cell* s and *B-cells.* T-cells have special receptors attached to their surface that recognize the specific antigen. T-cells are further categorized as killer T-cells or helper T-cells (TH cells). Helper T-cells also recognize

(ii) Did one or more of the 24 March 1998 vaccinations in question cause Richie's Still's disease?

(A) Was there a logical sequence of cause and effect?

Dr. Levin testified that the link between the 24 March 1998 vaccinations and Richie's Still's disease is "real, real clear." Trans. at 193. Dr. Levin stated that one or more of the vaccinations administered on 24 March 1998 triggered Richie's genetic propensity to contract Still's disease. *Id*. at 171. This triggering caused an inflammatory response, marked by an increase in cytokine expression, resulting in the disease. *Id*. at 172. Dr. Levin stated that a number of things could have triggered the disease such as surgery or viral illness, *Id*., but "the only factor that seems to be associated with the development of this disease process is the vaccination."*Id*. at 173. Thus, Dr. Levin opines that "[b]ased upon the strong temporal association between the exposure and the disease and in the absence of confounding factors" he believes "to a reasonable degree of medical certainty that the vaccinations that Michelle [sic] Pafford received on 3/24/98 triggered and caused her present autoimmune disorder (Still's disease)." Pet. Ex. 8 at 3.

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antigens, but their role is two fold. They stimulate B-cells and other white cells to attack the antigen. They also produce *cytokines*, powerful immune factors that have an important role in the *inflammatory process*. The actions of the helper T-cells are of special interest in rheumatoid arthritis. For some unknown reason, the T-cells become overactive in rheumatoid arthritis and mistake the body's own collagen as an antigen and trigger a series of immune responses to destroy the false enemy: TH-cells also secrete or stimulate the production of powerful immune factors called *cytokines*. In small amounts, cytokines are indispensable for healing. If overproduced, however, they can cause serious damage, including inflammation and injury in the joints during the rheumatoid arthritis process. They may even be responsible for inflammation that occurs in parts of the body beyond the joints, including fever, shock, and even damage to organs, such as the liver. Important cytokines in the destructive process of rheumatoid arthritis are those known as *interleukins* (ILs) and *tumor necrosis factor* (TNF). Researchers are specifically interested in interleukins 1,6, 9, 10, 11, 12, 15, and 17. (Some of these, such as interleukin-10, may be protective.) Some cytokines play a role in releasing enzymes, such as those known as collagenase and cathepsin L, which destroy collagen. Genetic factors play some role in rheumatoid arthritis, but most experts believe that more than one gene collaborates in the process and that the disease still requires other factors to set it off. Although many bacteria and viruses have been studied, no single organism has been proven to be the primary trigger for the autoimmune response and subsequent damaging inflammation.
http://www.ucdmc.ucdavis.edu/ucdhs/health/a-z/48RheumatoidArthritis/doc48causes.html.

"If lymphocytes produce antibodies or T cell receptors (TCRs) which recognize antigens in our own tissues, then these tissues will be attacked by the phagocytes and will suffer damage. When this happens then we say that the patient is suffering from an autoimmune (Auto - self) disease. It is precisely this scenario that we believe occurs in the autoimmune disease, rheumatoid arthritis. For some reason, which is yet to be discovered, those individuals who suffer from rheumatoid arthritis have immune systems that appear to recognize as foreign some constituents in their joints. B and T lymphocytes enter into the joint and in turn call in the phagocytes - polymorphs and macrophages - to the party. The entry of all these white blood cells into the *joint produces a large number of cytokines* which cause the joint to be painful, result in the joint becoming swollen and slowly cause the damage to the joint which leads it to become disfigured and unable to work properly. The joint damage is caused by the release of special proteins (called proteinases) which destroy the large molecules of which the articular cartilage and bone are composed." http://www.arc.org.uk/newsviews/arctdy/108/cellsbells.htm (emphasis added).

When asked what specific agent in any one of the vaccines was responsible for triggering the reaction that allegedly led to Richie's Still's disease, Dr. Levin could not answer. Dr. Levin testified that "I can speculate" as to which component "but that's as far as I can go, and I don't think anybody can give you a scientifically plausible answer in this particular case" as to which component triggered her reaction. Trans. at 219-20.

However, in his opinion letter filed on 16 April 2002, Dr. Levin asserts that "[i]t is also well established that immune activation caused by DPT vaccinations is in turn caused by the release of the very cytokines that are elevated in Still's disease." Pet. Ex. 8 at 3. This assertion is bolstered by medical literature referenced by Dr. Levin. "Whole-cell pertussis found in diphtheria-tetanus-pertussis (DTP) vaccine can produce symptoms reminiscent of biological responses to circulating proinflammatory monokines such as IL-6, IL-1ß, and TNFα." Pet. Ex. 16 at 1.[34] Although DTP is not a vaccine at issue here, the administration of DTaP also results in enhanced IL-6, IL-1ß, and TNFα stimulation, though resulting levels are less than that induced by DTP. *Id*. at 4. Thus, DTaP stimulates IL-6, IL-1ß, and TNFα expression, which both parties' experts agree are part of the observed symptoms of Still's disease.

When addressing whether there was any evidence that Richie indeed had higher levels of cytokine expression, Dr. Levin explained that at the time of onset, the medical field had yet to develop testing sophisticated enough to identify specific cytokines. Trans. at 214. However, Dr. Levin stated that there were indirect tests performed which did correlate with the clinical symptomatology. *Id*. Specifically, on 13 April 2004, Richie had a high white blood cell[35] count of 26,000, where the normal range is between 4,500 and 12,000 per mcl (microliter). Pet. Ex. 5 at 8; Pet. Ex. 4 at 73. White blood cells secrete cytokines[36] and, accordingly, a high white blood cell count may indicate a corresponding increase in cytokine expression. Trans. at 214.

(B) Temporal relationship*?*

Richie experienced some typical post-vaccinal side effects.[37] On 4 April 1998, eleven days

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[34] Jane Blood-Siegfried et al., *Monokine Production Following in Vitro Stimulation of the THP-1 Human Monocytic Cell Line with Pertussis Vaccine Components*, 18 JOURNAL OF CLINICAL IMMUNOLOGY 81 (1998).

[35] White Blood Cell: "A blood cell that does not contain hemoglobin: a blood corpuscle responsible for maintaining the body's immune surveillance system against invasion by foreign substances such as viruses or bacteria. White cells become specifically programmed against foreign invaders and work to inactivate and rid the body of a foreign substance." http://www.diagnose-me.com/glossary/G788.html.

[36] http://www.diagnose-me.com/glossary/G799.html.

[37] "As with other vaccines, MMR can cause a local reaction with pain and induration at the injection site (CDC, May 1998). Because it is a live virus vaccine, mild illness with symptoms similar to measles, mumps or rubella may occur. About 7-12 days after vaccination, five percent of children develop a fever with temperature greater than 103 degrees, which lasts 1-2 days (Peltola &Heinonen in CDC, May 1998). A transient rash may occur 7-10 days post vaccination in 5 percent of children (due to the measles and rubella components). Transient

after the administration of the vaccines at issue, Richie developed a fever and neck pain. Pet. Ex. 3 at 5. On her visit to Dr. Schmidt's on 7 April 1998, it was noted that Richie had developed a diffuse pink, macular rash, which subsided soon thereafter. *Id*.; Pet. Ex. 4 at 83. Dr. Schmidt noted that the rash appears to be vaccine induced. *Id.* It was also noted that Richie was experiencing fatigue, her upper arm hurt and she had limb pain. *Id*. Thus, at least through the first week of April 1998, the symptoms that Richie experienced do not appear out of the ordinary.

The onset of Richie's Still's disease is apparent some time during the second week of April 2004. On 13 April 2004, Richie presented with a temperature of 103.9 degrees Fahrenheit, a blanching red maculopapular rash on the hands involving the palms and soles, on the medial aspects of her upper legs and on her chest and upper abdominal area. Pet. Ex. 5 at 1. By the time she was admitted to the hospital, her temperature had quickly subsided to 97.2 degrees Fahrenheit and her rash had greatly diminished. *Id* at 16. Such temperature instability fits the profile of Still's disease.[38] Additionally, the transient nature of her rash is common to Still's disease.[39] On 30 April 1998, Dr. Bell noted a recurrence of fever (102.9 degrees Fahrenheit) and rash and complaints of increasing joint pain. Pet. Ex. 4 at 79. At that time, Dr. Bell, in conjunction with other doctors, concluded that Still's disease "is the most likely diagnosis." *Id*. at 80. His diagnosis was corroborated on 21 May 1998 by Dr. J. Roger Hollister, of the Children's Hospital, Rheumatology Clinic. *Id*. at 77.

Petitioner argues that the onset of Richie's Still's disease within a few weeks of the vaccinations at issue strongly suggests a connection between the two. Petitioners' Closing Argument and Memorandum of Law (hereinafter "Pet. Clos. Arg.") at 1-2.[40] As stated *supra*, a temporal

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lymphadenopathy (rubella component) and rare parotitis (mumps component) have also been described (CDC, May 1998)." http://www.corexcel.com/courses/body.immunizations.page9.htm.

Typical "[s]ide effects of the DTaP vaccine are mild and usually last for only a few days after getting the needle. Mild pain, swelling and redness are common at the spot where the needle was given. A few people may get a mild fever, upset stomach, body aches or feel tired for a day or two after the needle." http://www.mpshu.on.ca/Immunization/dTap.htm.

[38] "Patients with Still's disease usually present with systemic (body wide) symptoms. Extreme fatigue can accompany waves of high fevers that rise to 104 degrees F (41 degrees C) or even higher and rapidly return to normal levels or below. A faint salmon-colored skin rash characteristically comes and goes and usually does not itch. . . . Although the arthritis may initially be overlooked because of the impressive nature of the systemic symptoms, everyone with Still's disease eventually develops joint pain and swelling. This usually involves many joints (polyarticular arthritis). Any joint can be affected, although there are preferential patterns of joint involvement in Still's disease." http://stilligans.tripod.com/stills1.htm.

[39] See note 38 *supra*.

[40] The Court is troubled by a portion of Petitioners' counsel's argument during the 7 July 2003 Entitlement Hearing that Richie does not meet the "American College of Rheumatology criteria for the diagnosis of definite systemic onset JRA." Pet. Ex. 56 at 76, and that Richie may have a "JRA-like illness." *Id*. at 77. Until that point in Petitioners' argument and subsequently in Petitioners' closing memorandum, Petitioners' claim Still's disease. Pet. Clos. Arg. at 1-2. Thus, the Court is left perplexed by Petitioners' counsel's late equivocation and finds that it serves

relationship between the alleged injury and the administration of the vaccine is not itself sufficient for Petitioners to meet their burden of proof by a preponderance of the evidence. However, as this Court has previously found, where the claimed injury's manifestation of onset falls within an established time period subsequent to an antecedent or triggering event, the timing of onset is telling.[41]

Here, Petitioners argue that Richie was genetically predisposed to contract Still's disease and that the 24 March 1998 vaccinations triggered its onset. However, Petitioners provide no objective evidence indicating an appropriate time frame in which Still's disease will manifest subsequent to a triggering event. Thus, it appears, at least to this Court, that the timing of onset of Still's disease subsequent to a triggering event is not a telling characteristic of the disease. Accordingly, absent an appropriate time frame, the Court cannot find the mere temporal proximity of the vaccination and injury dispositive.[42]

(C) Were there possible alternative causes*?*

All experts agree that a number of things can trigger Still's disease. Respondent's experts posit that Richie's Still's disease could have been activated by any number of these triggers. However, Respondent puts forth no argument on behalf of any of these triggers beyond asserting their possibility.

Respondent's expert, Dr. Rosé, testified that when a person, such as Richie, has a predisposition for Still's disease, "you may find a lot of potential triggers" for its onset "if you take a good history." Trans. at 466. The day Richie received the vaccinations at issue, the administering pediatrician noted that "[s]he is doing well" and "at the present time is suffering no symptoms of illness." Pet. Ex. 3 at 11. However, on the date of her hospital admission, 13 April 1998, Richie

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only to further cloud Petitioners' claim.

[41] This case stands in contrast to the Court's reasoning in *Kuperus v. Sec'y of Health and Human Services* 2003 WL 22912885, 11 (Fed. Cl. 2003) and *Brown v. Sec'y of Health and Human Services*, 01-0060V at 9 (unpublished). In these cases, the onset of Petitioner's injuries occurred within an appropriate time frame - as described by the medical experts and other objective medical evidence - such that the vaccinations could be considered triggering events.

[42] The only objective evidence concerning the timing of onset subsequent to a preceding event was an exhibit filed by Respondent. Res. Ex. I. In the exhibit, the authors state that Reactive Arthritis is triggered by bacterial infection and that diarrhea within four weeks preceding onset is clear evidence of infection. *Id*. at 679. Therefore, at least in the case of Reactive Arthritis, one could expect to see its onset within a four week time frame of a preceding bacterial infection. Although the Court does not opine on whether Still's disease is a type of Reactive Arthritis, as described in Respondent's Exhibit I, it does note that Richie had diarrhea within four to five weeks preceding the onset of her Still's disease. Pet. Ex. 3 at 15.

tested positive for mycoplasma.[43] Pet. Ex. 5 at 9. Dr. Berger testified that a positive test for mycoplasma could be "interpreted as meaning that she had a recent acute infection," Trans. at 364, and he posited that the mycoplasma could have caused Richie's "tonsillitis that she had about two weeks before the immunization, which had then resolved at the time of the immunization." *Id*.; Pet. Ex. 3 at 11-12. Dr. Rosé testified that the antibody for mycoplasma "rises about three weeks from the infection and it lasts approximately a month, month and a half." *Id*. at 464. Such timing would place any infection causing the production of the mycoplasma antibody around or prior to Richie's vaccination date.

Dr. Levin testified that mycoplasma infections have been known to cause autoimmune diseases. *Id*. at 212. However, Dr. Levin stated that he was "not aware of mycoplasma causing Still's disease." *Id*. Dr. Levin went on to state that "[w]hether the mycoplasma contributed to her [Still's disease] or not, I don't have an opinion, but even if the mycoplasma did, it wouldn't have taken away the causal element of the vaccination." *Id*. "[T]here's no question that she had a reaction to the injections, because that was identified by swelling and inflammation around the injection site. Then she developed the rash, which is certainly not consistent with mycoplasma, and then she developed the arthropathy." *Id*. Respondent has put forth no argument that the mycoplasma was the cause of Richie's Still's disease.

Dr. Berger testified that x-rays of Richie's sinus cavity, taken on 13 April 2004, showed a "thickening of the sinus membranes . . . that could be compatible with a sinus infection." Trans. at 365; Pet. Ex. 4 at 83. Dr. Berger added that "[i]t certainly was not a finding of severe" sinus infection. *Id*. Dr. Rosé testified that the sinus infection or the earlier bout with tonsillitis could have been the cause of the cytokine production. *Id*. at 464. However, neither expert put forth any explanation why these alternative causes were more likely than the vaccinations at issue to have caused Richie's Still's disease.[44]

(D) The Court's summation of its findings.

Articulating an objective analysis for causation in fact is akin to an elusive wraith. As Dean Prosser and the editors of a Torts hornbook have put it:

There is perhaps nothing in the entire field of law which has called forth more

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[43] "A type of small bacteria, which lack the rigid cell walls common to most bacteria. A causative agent of pneumonia in humans and some domestic animals is Mycoplasma pneumonia. Various species are troublesome contaminants of animal cell cultures, in which they may grow attached or close to cell surfaces, subtly altering properties of the cells, but escaping detection unless specifically monitored. One hypothesis is that mycoplasma are capable of causing otherwise unexplained symptoms in humans." www.gulflink.osd.mil/medsearch/glossary/glossary_m.shtml. See also note 13 *supra*.

[44] Of course a respondent does not have the burden to prove a factor unrelated to the vaccination was the cause of injury unless and until the petitioner establishes a *prima facie* case under the Vaccine Act. *See Flores v. Sec'y Health and Human Services*, 52 Fed. Cl. 294 (2002).

> disagreement, or which the opinions are in such a welter of confusion. Nor, despite the manifold attempts which have been made to clarify the subject, is there yet any general agreement as to the best approach.[45]

This Court, as set out in this and numerous past decisions, makes two queries: (1) Can the vaccine(s) cause the injury alleged; and, (2) Did the vaccine(s) cause the injury alleged in this case? Although the theory put forth by Dr. Levin is novel, the Court, as stated *supra*, finds that it is biologically plausible and meets the preponderance of the evidence burden in answering the question "can it."

Answering the question "did it" in this case has presented the Court with considerable consternation. The Court has painstakingly looked for the feather in Petitioners' argument that would tip the scales past the fifty percent threshold. Ruefully, the Court's search was unsuccessful.

The link missing from Petitioners' argument that gave this Court pause was the lack of any defined time period in which one would expect to see the onset of Still's disease subsequent to a triggering event. Without such a defined time period, the link between the vaccinations and the injury is tenuous. This Court has always held that vaccines are not the cause of every event that occurs soon after their administration.[46] Additionally, the medical records indicate within the one month prior to the onset of her injuries, Richie suffered from a cold and diarrhea, Pet. Ex. 3 at 15, inflamed tonsils with white patches on them and a fever of 101-102 degrees Fahrenheit. *Id*. at 13-15. Although the Court does not definitively find that one of these triggered the onset of her Still's disease, the point is that the vaccinations at issue were not the only contemporaneous events. In the end, the Court finds that Petitioners' argument amounts to nothing more than a *post hoc ergo propter hoc* assertion. This is not enough to meet their burden. *See Fricano v. United States*, 22 Cl. Ct. 76, 80 (1991) ("*post hoc ergo propter hoc* . . . is regarded as neither good logic nor good law.").[47]

Whenever the Court decides the merits of a novel medical theory, as is the case here, it runs the risk that such theory, over time, may eventually prove correct. However, the Court can only opine based upon the evidence available. The Court finds that Petitioners have not met their burden of proof that by a preponderance of the evidence the 24 March 1998 vaccinations caused Richie's Still's disease. **Accordingly, compensation must be denied.**

V. CONCLUSION

This petition is **DISMISSED with prejudice**, pursuant to Vaccine Rule 21, for failure to

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[45] PROSSER AND KEETON ON TORTS, 5TH EDITION 263 (1984).

[46] *Hasler v. United States*, 718 F.2d 202, 205 (6th Cir. 1993), *cert. denied*, 469 U.S. 817 (1994).

[47] "[A] showing of biologic plausibility and temporal association is insufficient . . . ." *Huston v. Sec'y of Health and Human Services*, 39 Fed. Cl. 632 (1997).

prove a *prima facie* case for entitlement under the Vaccine Act. In the absence of a motion for review filed pursuant to RCFC, Appendix B, the clerk is directed to enter judgment accordingly.

IT IS SO ORDERED.

Richard B. Abell
Special Master