

*Hi, I am a second-year MD-PhD student and I am eager to share with you my experience meeting the White family. Like all medical students, my dream is to someday become a good doctor – a smart, kind, and good doctor. In medical school, I am learning how to begin with a patient’s chief complaint, elicit a history of the present illness, conduct a physical examination, differentiate the probable diagnosis amongst all possibilities, and propose an assessment and plan of care according to evidence-based medicine. The star of the following story, Sarah White, carries seven diagnoses: pediatric autoimmune neuropsychiatric disorder associated with streptococcus (PANDAS), encephalopathy, postural orthostatic tachycardia syndrome (POTS), autoimmune thyroid disease, scoliosis, small fiber polyneuropathy (SFPN), and chronic inflammatory demyelinating polyneuritis (CIDP). I wonder if a good doctor can read that list, recreate the patient in their mind, and pinpoint the right treatment protocol.*

### Team White

Sarah White was just like any other kid. Growing up in her suburban community near Baltimore and Washington, D.C., Sarah loved art, school, and music, and she could bring the beauty out of just about anything. She was a social butterfly with many friends and she kept a very special place in her heart for pets and animals. Sarah was born to Eileen and Justin White, who met in middle school, became sweethearts in high school, and later got married in the house of Eileen’s grandfather who happened to be a judge. Sarah grew up alongside her older brother, Jack, and younger brother, Brian, all within a few years of each other. Now age 17, Sarah has two dogs that she loves dearly and the talent and portfolio of artwork to become a professional craft artist, but a lot has changed... well... *everything* has changed since Sarah was age 10.

Just two months prior to 4<sup>th</sup> grade, Sarah overcame a strep infection. By the time school started, Sarah was a completely different child. Her mother, Eileen, described her to me as

• *All HIPAA identifiers including unique patient characteristics have been removed or changed* •

suddenly anxious, depressed, and obsessively compulsive. She had separation anxiety, would barely eat, displayed age regression, and became unkind to her younger brother, Brian. She lost all focus in those first months of fourth grade. Between her unusual irritability and rapid loss of weight, Eileen and Justin desperately sought medical help – pediatrics, neurology, infectious diseases, and back to neurology. Three months and three specialists later, it was April 2012 when Sarah received her first diagnosis: PANDAS.

My first visit to the White family’s home was in March 2018. While caught in the rush hour traffic out of Baltimore, I imagined who I was preparing to meet. I had purposefully avoided researching the diagnoses that Eileen had disclosed to me prior to my visit. I was most excited to simply meet this art-loving girl named Sarah. It was easy to identify the house as I pulled up – Eileen had alluded in our emails to the enormous hand-built pirate ship in the corner yard that turns into a haunted house every Halloween. Admission is free, but brave visitors are asked to learn from the White family about PANDAS and to consider donating for Sarah’s expensive intravenous immunoglobulin (IVIG) therapy.

At the front door, I was warmly greeted by Eileen and their two dogs. Pizza was served, and I sat down between Sarah (age 17) and Brian (13). Behind them were floor to ceiling photographs capturing all the fun and silliness of the three kids growing up together. Justin, Eileen, and Jack (19) took their seats around the table, and Eileen took the lead.

Eileen explained PANDAS; she detailed the 27 out of at least 30 symptoms that Sarah had demonstrated over those first tumultuous months. It is believed that PANDAS occurs when a child’s immune system generates a dysregulated response to a strep infection resulting in an autoimmune attack on brain tissue. When I first heard the word “PANDAS,” an image of the animal popped into my head since I had never previously learned about the condition. I must not

have thought too differently from Sarah considering her dozens of colorful drawings of panda bears from over the years; only, her pandas were evil, cannibalistic, smeared with blood, and losing limbs and skin. She chuckled. Her favorite holiday was appropriately Halloween, though she couldn't help but imagine tiny evil panda bears hijacking the switchboard in her brain.

Panda drawings were not the only subject of Sarah's creativity. After dinner, she showed me her room filled with crafts and models. She has created a detailed dollhouse-sized version of the Nightmare Before Christmas Jack Skellington's house. She has also crafted dozens of elaborate and intricate plastic dolls down to the painted buttons on their coats. She even created a beautiful mermaid doll with several hundred scales cut out and glued by hand. Finding the plastic doll's blank smiling face too boring, Sarah transected the head in half and constructed a scarier face on the opposite side. This way, you can rotate between the two depending on your mood.

I learned that after Sarah received her first diagnosis at the age of 10, her parents quickly agreed to the protocol for treatment – antibiotics, then tonsil and adenoid removal if they appear infected. Her removed tonsils and adenoids revealed strep and staph infections, but even after antibiotic treatment her symptoms persisted. Last resort treatment was off-label use of IVIG, costing about \$1,000 per 10 pounds that a child weighs. At 60 pounds, Sarah's family needed to come up with \$6,000. Between savings, family support, and the haunted house fundraisers, it was a team effort for the White family come up with the sum. Two weeks after her IVIG treatment, Sarah was herself again. It was a miracle – albeit short lived.

Meanwhile, her older brother Jack suddenly “fell off the cliff” while in the 8<sup>th</sup> grade. He was struck with extraordinary anxiety and loss of focus, progressing to panic attacks. Years passed in desperate search of help from numerous specialists. Then, Jack suffered what was later called an acute brain injury and was mute for one entire year. Pediatric acute-onset neuropsychiatric

syndrome (PANS) was diagnosed, his tonsils and adenoids were removed, and another bank breaking treatment of IVIG was underway. It did not yield a miracle recovery, and even seven years later Jack has not fully regained his speech abilities and recently received a diagnosis of common variable immune deficiency (CVID). Intellectually Jack is brilliant – learning Russian and navigating computer design programs at a senior undergraduate level. Only after years spent at a small private school for children with learning differences could Jack grow into the brilliant young man that I had the privilege of meeting over this past spring.

Between Sarah and Jack, it is clear to Eileen that an autoimmune etiology is at play. This is paramount to Eileen. Sarah has an over-active immune system and Jack has an underactive immune system. It must be something genetic, and it probably fits within the two-hit hypothesis dominating modern theories of autoimmune pathogenesis. Eileen expressed frustration that no one has ever quite figured out what happened to Jack; that while Sarah's challenges have not been figured out either, at least she has hope in IVIG treatment.

Returning to Sarah, visits were made to otolaryngology, infectious diseases, allergy and immunology, biofeedback, homeopathy, physical therapy, genetics, neuro-development, and cardiology. Sometimes, Sarah's doctors had insurmountable egos and would not value Eileen's input and firsthand experiences against their own clinical reasoning. Oftentimes, when Sarah would speak about her own symptoms, they would be disregarded or generalized. Nearly all the time, Team White would be deemed too medically complex and passed along to another physician. It was a constant battle to convince any physician to dig deeper to help Sarah without having a more concrete diagnosis. And always, medically complex patients are referred to psychiatry. Without a diagnosis, physicians feel that psychotropic drugs or cognitive behavioral therapy may

be the best option. This further frustrated Eileen who knew Sarah's condition was autoimmune and IVIG had clearly helped.

Three years and nine more specialists later, Sarah received her second diagnosis of POTS. At this point, Sarah had developed debilitating fatigue. If she stood for more than 30 seconds she could faint from low blood pressure. Her body lost its ability to regulate automatic functions – heart rate, circulation, pupillary reactions, digestion, temperature, and urination. A shower became impossible because blood would pool in her legs turning them bright red. No medications improved her symptoms and doctors finally attributed it to “something autoimmune.”

Sarah loved school, but school attendance was no longer an option. Teachers nor administrators could understand why she could be so tired without an explanatory diagnosis. Home education had to be started, but her public school system has yet to project a plan for her to receive her diploma through home bound instruction. Eileen's struggle with the public school system is but another challenge alongside her constantly reviewing scientific articles, planning and driving to doctor's appointments, raising funds, and writing letters to senators and delegates.

Currently, Sarah and her family continue their battle for a concrete diagnosis, for IVIG treatment, for insurance coverage, and for a bright future. This past January, Sarah received her third and fourth major diagnoses – SFPN and CIDP – both autoimmune, rare, and nowhere close to encompassing Sarah's challenging and unremitting symptoms, but IVIG is indicated in the treatment of CIDP. This helps justify partial insurance coverage of treatment, but still does not provide a pathway to certain change. In the meantime, Sarah sticks to her studies when she is able and doctor's appointments like a full-time job, channels her passions into crafting and art therapy, and continues to dream of an “after.”

“We’re Team White.” When the whys and hows began to pile up, Eileen White could always fall back on this one poignant phrase. The strength and assertiveness that Eileen conveyed to me across our months of conversations were humbling. This mother and father and little brother have put everything on the line and all dreams aside to navigate an unimaginable set of challenges, obstacles, and uncertainties for two medically complex children. Furthermore, Eileen has spent the past seven years pouring over highly technical scientific literature on any topic related to autoimmunity and her children’s symptoms. It took six years for Sarah to finally receive a diagnosis for which IVIG was indicated. As a medical student entering a doctoral program in molecular microbiology and immunology, I have never felt a greater sense of contradiction: the process behind medical reasoning moves from a set of symptoms to a diagnosis and appropriate treatment, but when appropriate treatment fails the rarities, we are not taught how to work beyond the confines of a diagnosis. The conventional meaning of “treatment” does not account for the flexibility and humility it takes to take care of patients with conditions that challenge a physician’s line of reasoning.

Sarah currently has seven diagnoses. She has seen thirty different physicians in seven years, yet only her pediatrician has stuck by her side through and through. She has advocated on behalf of Sarah to insurance companies to get IVIG covered. She has been willing to think and more importantly, to treat outside of the box of a diagnosis. A great doctor like her is flexible and humble in the face of uncertainty. She is a member of Team White, and not the coach, or worse, the league commissioner. After having learned Sarah’s story and the challenges faced by families like Team White, my one hope would be that someday I could not only be a good doctor, but also a great doctor – a smart, kind, great doctor.