David R. Cox Prize for Rare Compassion Essay

"The Complexities of Medicine Lie Outside Textbooks and Examination Rooms"

I had a one dimensional outlook on medicine: diagnose the patient, treat the patient and then the patient usually gets better. I focused hours and hours of my time memorizing pathways, drugs, common symptoms, and treatments in the hopes that one day I would be competent enough to help my patients. As a medical student learning about the onset, symptoms, pathophysiology, diagnosis, and treatment of diseases I often thought to myself, "how do I handle the increasingly complex nature of medicine?". I later realized that the complexity of medicine lies outside textbooks and examination rooms; the complexity of medicine lies in the three-dimensional effects of a disease on a family.

After I got the email saying that I was matched with a family who had a child with Congenital Central Hypoventilation Syndrome (CCHS) I did a thorough medical literature search of the disease and I explicitly remember coming up with very little information. This was particularly surprising to me because this disease was classified by physicians in the 1960s so it is not a new disease by any means. I then learned that this disease was exceedingly rare; in the world today there are only a couple of thousand cases. I was suddenly conflicted. I felt it was incredibly unfair for people with CCHS to know that the rarity of their disease has effectively slowed the search for a cure, but I also felt the undeniable strength of the utilitarian argument: that the limited resources we have should be focused on diseases like malaria, heart disease or cancer which kills millions of people each year. Each side had valid points and I could not reconcile the two in my mind until many months later.

Medical schools in the US have a limited amount of time to prepare students for the all-important boards (USMLE). Most medical students take their boards after two years of study so the focus is on “high yield” subjects and diseases. The term “high yield” means topics that are most frequently tested on the USMLE. High yield diseases include diabetes, high blood pressure, stroke, heart attack, depression, arthritis, COPD and about a hundred other diseases and syndromes. This is all aimed at building a physician that can recognize and treat the most likely diseases they will see in patients. What the USMLE and thus the curriculum of most medical schools miss, is the impact that diseases have on the daily lives of the individual and the family.

My first interaction with my matched family was a two-hour long video call that was originally supposed to last an hour. I talked with the mother and father about what it was like learning their child had CCHS, the affects on their daily lives, their hopes and fears, the financial burdens, emerging research about the disease, and many other topics. As I listened to their story I started to learn how CCHS affected the family in every aspect of their lives.

“Ashley” knew something was wrong the moment she gave birth. After nine months of a supposed healthy pregnancy, her worst nightmare was happening before her eyes. “John” was quickly taken to the pediatric intensive care unit and placed on a ventilator. Ashley’s husband, “Ryan” was equally shocked and hurried to talk to the doctors to see what was going on. The first night, which should have been a joyous occasion, turned into a night of worrying, sadness, and confusion. The emotions from the first night lasted a second night and then a third and continued for two and a half months. These two and a half months consisted of hundreds of tests, dozens of doctors each

suggesting a different diagnosis, and many hours of waiting. Ashley and Ryan did all they could to understand the process; they read any scrap of medical literature that was related to their baby's symptoms. Their efforts were driven because most of the physicians were too busy running tests to explain what was happening. No one at the hospital communicated effectively what they were doing or what progress had been made or what was planned next, as they hurriedly tried to find a diagnosis.

After almost three months at the hospital, a diagnosis finally was reached. John had a moderate form of CCHS (the Phox2B 20/26 variant). A tracheotomy was done and John was finally taken home from the hospital. When they returned home Ashley felt like she was pushed into a life changing event and wanted to run away. She did not want to be congratulated by anyone. Ryan was more optimistic, regarding the diagnosis as manageable although equally aware that their lives were completely changed from that point forward.

When I learned about the ordeal that the family went through to reach a diagnosis I was appalled at the lack of communication and continuity of care the family received. If I put myself in their shoes I would be equally frustrated. There were probably many reasons why it transpired the way it did. None of the doctors had a clue what John had and this caused a hectic environment. There were systemic failures that inhibited doctors to freely share test results between each other and this combined with the number of doctors involved in John's care led to miscommunication. Many of these problems would have been avoided if there was a single point person, perhaps a nurse, who was in charge of compiling and relaying information from the doctors to the parents. This person would have access to all of John's charts and would have enough experience in the medical field

to translate the medical language. This little change would have made a world of a difference to Ashley and Ryan during the chaotic two and a half months at the hospital.

The family graciously invited me to dinner at their home so that I could learn more about how CCHS affects their daily lives. When normal people fall asleep the medulla oblongata takes control of critical bodily functions such as breathing so that we continue to breathe while asleep. When people with CCHS fall asleep they stop breathing completely and this quickly leads to death within minutes. In the past, this diagnosis was fatal because either the patient died from lack of breathing or lack of sleep. Presently a patient with CCHS is given a tracheostomy which is basically a surgically created hole in the trachea where a ventilator can be plugged in during sleep. The ventilator automatically breathes for the patient. As you can probably imagine this comes with many challenges.

One of the major challenges is monitoring the ventilator and pulse ox every night. The pulse ox is used to monitor John's oxygen levels. The ventilator and pulse ox both have automated alarms when a connection becomes loose or when the oxygen levels becomes dangerously low. This forces Ashley and Ryan to constantly be on alert during the night because if something goes wrong John could very well die. This of course also places a great amount of stress over Ashley and Ryan on a daily basis. Simple tasks such as grocery shopping or going to the bank become a stressful event because Ashley needs to be constantly checking to make sure John is not falling asleep and that his oxygen levels are normal. John's condition makes it incredibly difficult to take family vacations or even go out to eat. The tracheostomy area and ventilator tubes need to be cleaned daily to every few days to reduce the risk of infection. Even so, long term mechanical

ventilation will eventually lead to pneumonia and infections in the vast majority of patients.

CCHS presents special parenting challenges that no ordinary parents have to consider. If John is unable to transition to a less invasive ventilation system he will always have a tracheostomy and that presents a risk that John will be stigmatized as being "different" for his entire life. Ashley and Ryan also have to decide when to tell John about his condition and explain to him why he is different from the other kids. How do you tell a kid that every night there is a chance he might die? When do you trust him to take care of himself and understand the seriousness of his condition? These are the tough questions that keep Ashley and Ryan up at night.

These challenges to daily life are not considered part of the medical side of the disease so healthcare professional are unable to see the whole picture. This leads to conflicts. For example, Ashley and Ryan want John to eventually transition from mechanical ventilation via the tracheostomy to a continuous positive airway pressure (CPAP) machine which only uses a breathing mask. They want this change so that John is not confined forever to a ventilator, to reduce the risk of infection and to lessen the risk that John gets stigmatized and ostracized at school. Ashley and Ryan researched the idea and found out that there are cases of CCHS patients doing very well with a CPAP machine only. John's doctor is very resistant to the idea because using the CPAP machine has a greater risk of failure. Ashley and Ryan wish that healthcare professionals were able to understand the challenges to daily life that CCHS presents and therefore understand why life-long dependence on mechanical ventilation via the tracheostomy is not ideal for the parents or the child. This is why physicians need to understand not only

the disease but how the disease impacts the family as a whole in order to effectively treat the disease and improve quality of life.

The main source of support for Ashley and Ryan come from the CCHS Foundation which is a network of people affected by CCHS who are committed to providing support for each other and supporting research and development for a cure. Ashley has said that the CCHS Foundation was one of the key reasons why she was able to get past the initial feelings of hopelessness and isolation. The CCHS Foundation has also put on conferences every couple of years to spread the word about CCHS and to invite scientists and clinicians to share their progress on CCHS research. The CCHS Foundation provided Ashley and Ryan with a second family that knew exactly what they were going through and that made it a little bit easier to cope with their son's disease.

After my conversations with the family I decided that I wanted to do more than write an essay. I am in the process of creating an elective course at my medical school that will not only teach my peers about rare genetic diseases such as CCHS but also how these diseases affect families as a whole. I believe that if medical students are at least exposed to some rare genetic diseases they will be more compassionate and empathetic towards the special circumstances surrounding rare genetic diseases. I have arranged for Ashley and Ryan to come to one of the classes to share their story and to answer questions.

Raising awareness, although important, is not enough. Ultimately only research provides the hope of a cure and research requires money which brings us back to the problem I addressed earlier. The rarity of CCHS and the limited resources we have means that the vast majority of the money and manpower will be spent on more prominent

diseases such as cancer, heart disease, malaria, etc. I could not find a solution to this problem until I started reading some of the conference abstracts from the CCHS Foundation.

Two of the most promising advances in CCHS treatment research are diaphragm pacing and the use of progesterone. What I noticed about both these advances is that both were adapted from past research and development. The idea of diaphragm pacing comes from a well known technology: cardiac pacemakers. Cardiac pacemakers have been in use since the early 1950s. The idea was that an external electric current could stimulate the heart to beat. This idea was then adapted to the diaphragm (the muscle that controls breathing) to create a diaphragm "pacemaker" that would use electrical currents to stimulate breathing. Progesterone has been in use since the early 1990s to address the decline of natural progesterone levels in the older population. Progesterone has been known to increase the baseline respiratory rate. This knowledge was then used to test the effects of progesterone on CCHS patients and results came back suggesting both short and long-term benefits in spontaneous breathing during sleep.

The best case scenario would be if a big pharmaceutical company decided to spend billions of dollars researching and developing a new drug for CCHS but given the rarity of CCHS it is almost an impossible dream. However the research coming out now about CCHS shows incredible promise and they were all based on past knowledge and drugs that have been readily available for decades. The money available for CCHS research is limited so I propose we use that precious resource in a way that will provide the most utility. I believe any type of research is beneficial however I propose that researchers focus more on how to apply the knowledge we already have into finding

better treatments for CCHS instead of focusing on basic science research regarding how or why CCHS occurs. Let's take a closer look at other drugs that cause a baseline respiratory rate increase and see if they could help with CCHS. Let's look into abdominal displacement ventilation as a non-invasive alternative to life-long dependence on mechanical ventilation via tracheostomy. I believe that my proposal that research should focus on applying past knowledge can be applied to other rare genetic diseases and ultimately provide more utility from the limited resources that rare diseases receive.

This experience has changed how I view diseases. No disease, especially rare genetic diseases, are one-dimensional so the accompanying treatment should not be either. Physicians need to be concerned about not just the diagnosis or treatment of disease but how the disease affects the family and individual as a whole so that they can tailor treatments to improve quality of life. I believe that the best way to increase utility from the limited resources that rare genetic diseases receive is to focus on applying and adapting the knowledge and technology we already have.

Lastly I want to acknowledge the family I was matched with; they took time out of their busy lives to share their story with me and also invited me to their home to gain a better perspective on their daily lives. I truly believe that this family has shaped me to become a better physician and I look forward to the life-long friendships that I have made with them.