What Are Mitochondrial Diseases?

Our Family's Experience

By **Sean Durity**

At six months old, our daughter, Gwendolyn, started making strange-looking flex movements. We took her to the emergency room, where they pronounced these movements as a type of seizure called "infantile spasms." But that was a description, not a diagnosis. It took another 8 months for us to get the diagnosis. A muscle biopsy confirmed the problem -- mitochondrial disease. With that diagnosis, we began a journey into trying to understand what this disease is.

Understanding Mitochondrial Diseases

A diagnosis of mitochondrial disease is like saying someone has cancer. It is too vague to be much use. As there are all types of cancers, there are hundreds of mitochondrial diseases. While some have specific genetic markers and names, many, like my daughter's, do not. And because mitochondria throughout the body can be affected differently, even people with the same genetic problem can have very different outward symptoms. Mitochondrial diseases are still mysteries.

The mystery begins with the mitochondria themselves. Mitochondria are the parts of cells that create energy. They are power plants that take in the breakdown products of food and chemically turn them into ATP. ATP provides about 90% of the energy required for cellular activity. This is a highly complex biochemical process involving dozens of proteins, enzymes, and cofactors. But mitochondria do much more, too. They are intimately involved with many processes to build and break down other chemical building blocks of cells. Their duties vary by the type of cell, and they appear to change as we grow older or experience different biological stresses. Important research to understand these duties is still on-going.

Symptoms of Mitochondrial Diseases

Because of the variety of mitochondrial tasks, it is no wonder that mitochondrial diseases can present themselves so differently. They can impact just certain biological systems or the whole body. Our daughter was primarily affected neurologically with seizures and developmental delay. Others have muscle weakness, gastrointestinal problems, cardiac concerns, breathing trouble, strokes, or a host of other problems. Symptoms can range from mild to severe to deadly. Some mitochondrial diseases are degenerative, while others are relatively static. Doctors tend to pursue a mitochondrial disease theory when multiple systems are involved, when lactate levels are elevated, or when other metabolic possibilities are eliminated.

Diagnosis of Mitochondrial Diseases

Until very recently, suspected mitochondrial diseases were confirmed by an invasive muscle biopsy followed by months of laboratory testing. Within just the last few months, according to Dr. Fran D. Kendall, a mitochondrial specialist in Atlanta, testing can be done with skin cells from the cheek (a buccal swab). Newly expanded DNA testing can detect problems with 700 out of 1,500 mitochondria-related genes.

Causes of Mitochondrial Diseases

Mitochondria have their own DNA separate from the DNA in the cell's nucleus. This smaller DNA contains just 16,569 base pairs compared to 3 billion in nuclear DNA. The mitochondrial DNA (or mtDNA) comes only from the mother. So, some mitochondrial diseases are attributed to maternal inheritance. Mom has a mitochondrial problem and passes it on to her child. This was thought to be the primary transmission mechanism for mitochondrial diseases.

But, Dr. Kendall estimates that 75-90% of pediatric mitochondrial diseases are because of **nuclear** gene defects, not mtDNA. These defects, then are the result of the combination of mom's and dad's genes (autosomal recessive). However, many of these are presumed genetic defects because they have not been positively identified.

Treatment of Mitochondrial Diseases

There are no cures for mitochondrial diseases. In general, the primary treatment is for the secondary symptoms like seizures or GI problems. Gwendolyn tried several seizure medications before we tried the ketogenic diet with a g-tube. Eventually that seemed to stop the seizures, and we removed all seizure medications. She has been basically seizure-free for several years. Her development, though, is still very slow. Now seven years old, she does not sit, stand, walk, or talk.

Many supplements are prescribed as possible treatments to help the energy production of mitochondria. At this point, they are theoretical helps based on what is known of the energy production process. There are not enough clinical studies to prove that they are responsible for any improvements. The commonly prescribed supplements are CoQ10, carnitine, creatine, MCT oil, and lipoic

acid. While there may be anecdotal evidence that these may help some people, they should not be taken without recommendation from a qualified physician.

More helpful is to avoid stresses that can lead to further problems. Since energy production is at a premium, the body must be protected from activities that rob the body of energy. Fasting (more than 8-10 hours) should be avoided. Temperature extremes also stress the body. Viruses and other sickness can be devastating, even leading to a degenerative cycle. So general good health is an important goal.

Living with Mitochondrial Diseases

With no cure and a generally poor prognosis, a mitochondrial disease diagnosis is a painful reality. Multiple specialist doctors, therapists, medical equipment, and the possibility of significant hospital stays (up to hundreds of days per year) are common difficulties. Most families have to learn medical procedures to do at home. All this brings financial, family, schedule, and educational pressures. Sometimes it is hard just to make it through the day. But, as we have learned over the last 6 years, you can experience joy in loving and serving someone who can never repay. Strange as it may sound, we are grateful for all that we have learned with Gwendolyn.

United Mitochondrial Disease Foundation, What is Mitochondrial Disease?