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In This Issue

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The Cornerstones of Mito Management

Contributed by Cristy Balcells, RN, MSN

The process of becoming an advocate for yourself or your child isn't just about fighting insurance battles. It is also, and more importantly, about learning to prioritize and differentiate between what can be managed in the doctor's office and what should be managed by you or those who help you as caregivers.

Recently I was working with a family whose child with Mito was not doing well at all. Evan, their 6 year-old son, was having all sorts of issues that seemed to be spiraling out of control, not the least of which was muscle pain, slurring speech (especially later in the day), and clumsiness. He just didn't seem "himself", and his pale face and marked weakness had his parents very concerned. Their appointment wasn't for a few months when they would be seeing their neurologist, metabolic specialist and GI doctor all in one day.

Concerned, and appropriately so, that Evan was "getting worse because of his Mito", the family wanted to request that bloodwork, MRI, and other tests be given to Evan immediately so that they could understand what was going on. In the midst of their stress and desire to help Evan, they did what they thought that they should, which is to focus on the medical aspect of his disease. Evan's symptoms ARE 99% likely because of his mitochondrial disease, but before invasive (and exhausting, and expensive) testing be performed, it is everyone's responsibility to address the bottom line first.

There IS a very real necessity for careful evaluation and consultation with a physician who knows you or your child when there are any changes. However, there is also a protocol of hydration, nutrition, and rest that should ALWAYS be addressed first – and it should be priority for the family or caregivers. When we know that these three cornerstones are being addressed, we can also feel more confident that the issues that you or your child are having may be related to involvement of a new system or medication, or that we need to look for clues as to why the new symptoms are occurring.

Good, in fact, aggressive, hydration is KEY and can really help many symptoms become more stable. At least 80 ounces of fluid for an adult (G2, the low sugar version of Gatorade is a choice of many patients whom I work with) is important every day, and ideally the fluids are spread out over the day, evening and night as much as possible. Hydration is often overlooked, because the clinical signs of dehydration are subtle. In addition, a truly dehydrated individual who also has mitochondrial disease is a recipe for crisis. Fluids (low sugar fluids, unless otherwise prescribed) can help with many of the symptoms of dysautonomia (autonomic nervous system dysfunction) such as dizziness, blood pressure variability, as well as mental fog, fatigue and even pain.

Nutrition is the second cornerstone, and like hydration can be easily overlooked. Small frequent meals are often recommended, and eating followed by a period of rest is a good idea. A patient with mitochondrial disease should never "fast" (go without food or drink) for a period of several hours without express order from a knowledgeable physician. Some parents and patients find that a pudding made of

cornstarch digests slowly and is a great choice for an evening snack that prevents the body from “starving” during the night. Mitochondria and the cells of your body need food and oxygen in order to function properly – feed them and keep them happy!

Rest doesn’t just need to take place when you or your child gets tired. In fact, like hydration, rest needs to happen BEFORE the slump hits. Keep in mind that basic body functions like digesting food, keeping an ambient body temperature, breathing, talking and thinking DO use energy...so everything needs to be redefined differently than what we typically think of as "an activity". When helping people in the community understand how to help the children and adults in their lives to pace themselves, I often use a battery analogy. If you start out the day with 10 bars of charge, that’s all you’ve got for the entire day. If riding on the hot bus to school takes 3 bars out of a child’s total, was that energy well spent? Walking to the gym or the lunchroom may use up the 2 bars of battery that could have been used to actually enjoy eating or doing an activity. Rest periods are so important - think of it as time to allow those mitochondria to recharge. The key concept here is to eat, drink, and rest BEFORE you feel tired, lightheaded, etc.

Together, we can make the most of the energy we have and learn to live with Mito!.

Cristy Balcells is the full-time executive director of MitoAction.org, a nonprofit dedicated to education, outreach and support initiatives for families affected by mitochondrial disease. Cristy has a Master’s of Science in nursing and public health from University of Virginia and resides in Boston, MA where she helps many children, adults and families learn to navigate the complex journey of mitochondrial disease. Cristy’s youngest daughter, Eva, is five years old and has Leighs disease, allowing Cristy to offer a mother’s insight in addition to solid advice based on research and expert recommendations. An active advocate for the entire mitochondrial disease community, Cristy is well-known for her ability to educate and inspire patients and families on learning to live with mitochondrial disease.

Complex I Defects and Nuclear Genes

Complex I deficiency is the most common cause of respiratory chain defects. However, the gene cause for most complex I respiratory chain defects is rarely identified in this multi-subunit enzyme complex composed of 45 identified parts, 7 encoded for by the mitochondrial genes inherited from mom and 38 nuclear genes passed on through both parents.

Some studies indicate that nuclear genes or those passed on through both parents and associated with a 25% recurrence risk cause 75%-90% of all pediatric mitochondrial disease and, as such, most complex I defects. Pagniez-Mammeri, et.al in a recent article in the journal Molecular Genetics and Metabolism (2009; 96(4) pp196-200) report the detection of nuclear gene mutations in 3 out of 8 complex I patients investigated using what they state is a rapid screening method. Until recent years, while much was known about mtDNA (mitochondrial DNA) little was known about the nuclear genes involved in energy production. More and more clinical diagnostic labs, however, including Baylor and Transgenomic, are now offering a widening array of nuclear gene tests. Other groups, including the Center for Molecular and Mitochondrial Medicine and Genetics at UC Irvine are involved in the basic science of identifying nuclear gene mutations.

Why is this important? Identifying the gene cause for a complex I or other mitochondrial disorder is important to provide the possibility of prenatal diagnosis for carrier couples and to better understand why one complex I defect can present with Leigh disease, a typically more aggressive form of mito disease, and another with a more static course of low tone and developmental delays. Each gene involved in energy production makes a unique protein which subsequently provides a specific function in the energy producing pathway. Identifying and understanding each gene and its function will ultimately lead to treatments for the broad spectrum of mito

You May Not Have a Mito Disorder

Mitochondrial disease may **NOT** be the primary cause of your or your child’s problems despite having undergone expensive, invasive muscle testing. In recent months using the more advanced specialized chromosome microarray study that is non invasive, we have re-diagnosed several patients with a chromosome problem. Detection of a chromosome problem drastically alters a couple’s or family’s recurrence risk, making it likely negligible or close to zero. Ask about arrays and how you and your child may benefit.

These sites will help you to understand and become more informed about clinical research in children...no more second hand information.

www.nhlbi.nih.gov/childrenandclinicalstudies

www.clinicaltrials.gov/ct2/info/understand

Please email us at info@virtualmdpractice.com with your request to continue receiving this newsletter.

disease.

Mito Research: Update on Clinical Trials

A number of researchers are actively seeking patients to participate in various clinical research protocols as they attempt to better define mitochondrial disease. We have established collaboration with a number of groups to better serve our patients and to be actively involved in the ongoing advancement of mitochondrial science.

Any of our patients who elect to participate in these trials will be assisted with enrolling and management by VMP.

Metabolic Consequences of Primary Mitochondrial Disease

Phase III Trial of Coenzyme Q10 in Mitochondrial Disease

Study of Idebenone in the Treatment of MELAS (Mitochondrial Encephalomyopathy, Lactic Acidosis and Stroke-like Episodes)

Details of the studies are:

1. **"Metabolic Consequences of Primary Mitochondrial Disease**". – This NIH sponsored study at Children's Hospital in Philadelphia is recruiting patients with definite biochemical and/or molecular confirmed mito disease to determine if other biochemical markers exist across the spectrum of the hundreds of forms of the disease that will enable improved diagnosis and treatment for patients in general. The group, led by Dr. Marni Falk and her research coordinator, Emily Place, MS, are utilizing PREVIOUSLY collected muscle, skin and blood from diagnosed patients. New blood and/or skin will be requested ONLY if no prior specimens are available.

   WHY IS THIS STUDY IMPORTANT? Finding a common or more easily treated change in all mito patients may lead to new treatment modalities. In addition, it requires release of previously gathered samples for most patients with little or no further testing on enrolled patients. If you wish to enroll contact us at **info@virtualmdpractice.com**

2. **Phase III Trial of Coenzyme Q10 in Mitochondrial Disease** – This study is a multi-center study spearheaded by Dr. Peter Stacpoole at the University of Florida whose aim is to determine in biochemically or molecularly diagnosed mitochondrial patients that supplementation with Coenzyme Q10 at 10 mg/kg/day is safe and more effective in improving outcome than placebo. Patients between the ages of 12 months and 17 years of age with a definitive diagnosis of mitochondrial disease as determined by either molecular or enzyme studies are eligible. All patients entering the trial must, however, be willing to stop ALL medication regimens and supplements other than those deemed medically necessary. The study will be randomized, double blinded and placebos controlled which simply means some people will be taken off of CoQ10, placed on a placebo or have their CoQ dose changed, unbeknownst to them or their caregivers. Exclusion criteria include renal insufficiency, severe anemia and intractable epilepsy. Monitoring will include completion of various questionnaires, objective, standardized measures of motor function and blood work.

   WHY IS THIS STUDY IMPORTANT? Coenzyme Q10 is a staple in the treatment of mitochondrial disease yet much of our information regarding its effectiveness is anecdotal. Once given a diagnosis of mito disease patients are typically started on this supplement and remain on it indefinitely even when it is not clear for a given patient that it is helpful. In light of the out of pocket expense for CoQ10 it is important to determine with objective

measures that it is safe and more effective than placebo. The biggest problem with the study is that most people are unwilling or apprehensive to stop the supplement fearing that while they may not have improved on CoQ10 that they may actually worsen if it is discontinued. If you have stopped or never started taking CoQ10 you would be a perfect candidate for answering this ongoing question. For more information on the trial contact Tracie Kurtz, RN at 888-961-9068.

3. **Study of Idebenone in the Treatment of MELAS (Mitochondrial Encephalomyopathy, Lactic Acidosis and Stroke-like Episodes)** – This NIH study at Columbia University is attempting to determine if treatment of MELAS patients with idebenone results in a decrease in brain lactate levels as measured by magnetic resonance spectroscopy (MRS). Brain lactate is a biomarker associated with disease worsening. MELAS is a progressive and often devastating form of mitochondrial disease commonly associated with the mitochondrial DNA mutation at nucleotide 3243 (the location of the change out of 16,569 pieces that make up the mitochondrial DNA). There is some data to support that Idebenone, an antioxidant and analogue of CoQ10, results in improved neurological function in patients with Friedreich's ataxia, a disease also associated with mitochondrial dysfunction. Patients with MELAS who harbor the 3243 mutation between the ages of 8 and 65 who are found to have elevated brain lactate over a certain threshold on MRS are eligible. Patients also have to be in a stable state with their medications for at least one months prior to the study and must weigh at least 82 pounds. Several exclusion criteria include no stroke like events within two months before entering the study, pregnancy or breast-feeding. Patients will receive either a placebo or idebenone at a dose of 900 mg or 2250 mg per day for one month with follow-up MRS studies to measure brain lactate.

   WHY IS THIS STUDY IMPORTANT? MELAS is almost universally associated with neurological devastation and a poor outcome. No elective treatment is available. Given the data the idebenone may improve neurological outcome in Friedrich's ataxia attempting to determine if this compound proves useful in a devastating form of mito disease as documented by a non-invasive MRS study is a big step in attacking this disorder. If you are interested in this trial please contact Kris Engelstad at 212-305-6834 or Rachel Jerome 212-305-1326.

If you are a patient of VMP and wish to enroll in any of these studies we will assist you to complete all necessary paperwork and other pre-enrollment processes as well as complete any local study requirements.