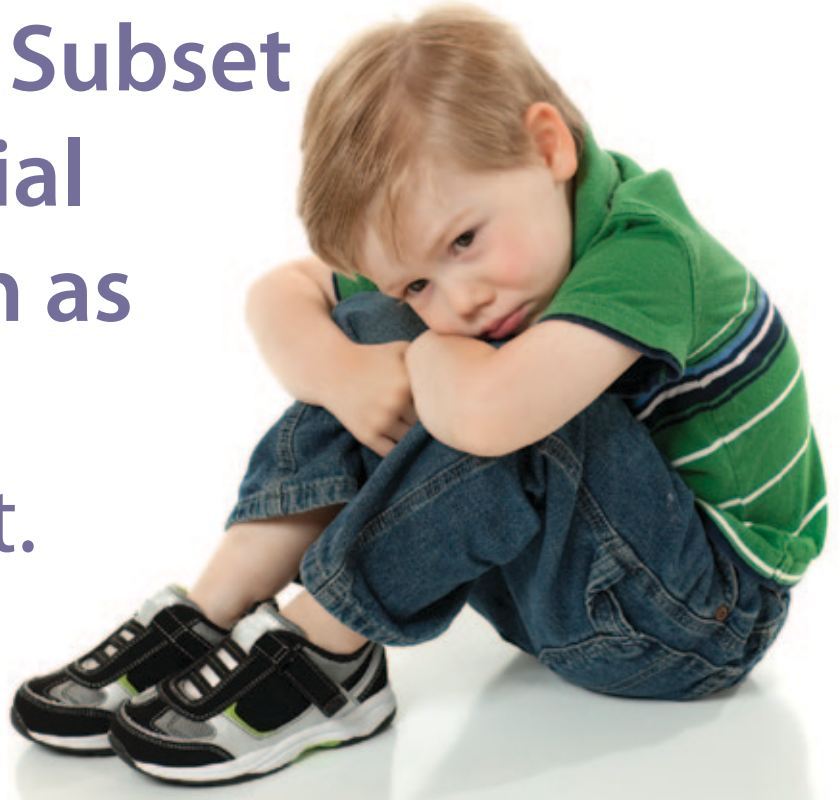


# Has Your Child with Autistic Symptoms Been Properly Screened for a Subset of Mitochondrial Disease Known as OXPHOS? ...Probably Not.



By Alyssa Davi



**Alyssa Davi** is a former special education teacher and is involved in a nonprofit organization called, Parents Ending America's Childhood Epidemic (PEACE), which is sponsoring a parent outreach project known as Epidemic Answers. Please visit [www.epidemicanswers.org](http://www.epidemicanswers.org).

**A**utism secondary to mitochondrial disease (AMD) was once thought to be rare. However, several recent research articles suggest there is a cohort of ASD children with underlying mitochondrial disease. Some geneticists believe that the rate of mitochondrial disease may be as high as 1 in 200 live births,<sup>1</sup> and the United Mitochondrial Disease Foundation (UMDF) states that every 30 minutes a child is born who will develop a mitochondrial disease by age 10.<sup>2</sup> Thus, many children who exhibit ASD symptoms may actually have underlying mitochondrial disease; unfortunately at this time, they are "undiagnosed," and many doctors are unaware of the emerging research. AMD can occur when there are problems within the process known as oxidative phosphorylation.

## What is OXPHOS?

Mitochondrial oxidative phosphorylation, known as OXPHOS, is a new category of autistic spectrum disorder and is a disorder of energy production. It is caused by one or more defects in the oxidative phosphorylation process, resulting in reduced energy production. As a result, the body cannot function properly. If the body has insufficient energy, many adverse physical- and neurological-appearing symptoms may occur. When this medical issue is addressed with appropriate therapeutic protocols, profound improvements occur in some children.

## What are mitochondria and the electron transport chain, and why are they important to the health of your child?

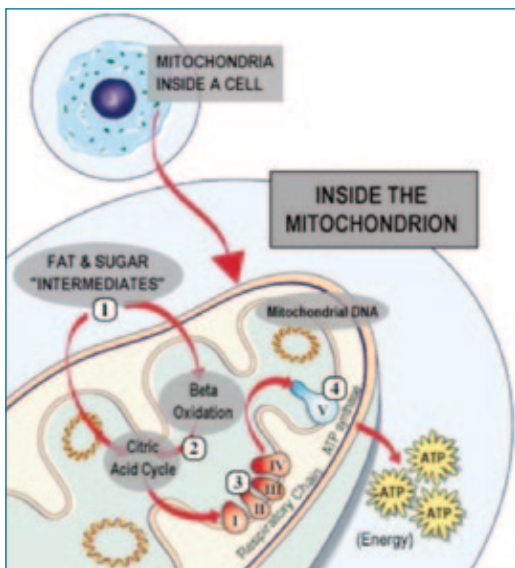
Mitochondria, the "power plants" of the body, make ATP for cellular energy. Mitochondria generate energy for the body, so when there is a breakdown within the mitochondria, the body begins to malfunction. The UMDF website explains:

*Mitochondria exist in nearly every cell of the human body, producing 90 percent of the energy the body needs to function. In a person with mitochondrial disease, the mitochondria are failing and cannot convert food and oxygen into life-sustaining energy. The parts of the body that need the most energy, such as the heart, brain, muscles, [GI system] and lungs are the most affected by mitochondrial disease. The affected individual may have strokes, seizures, gastro-intestinal problems (reflux, severe vomiting, constipation, diarrhea), swallowing difficulties, failure to thrive, blindness, deafness, heart and kidney problems, [poor muscle tone], muscle failure, heat/cold intolerance, diabetes, lactic acidosis, immune system problems and liver disease. An undiagnosed child may exhibit feeding problems, be unable to fight typical childhood infections or have repeated infections and fevers without a known origin. A red flag for mitochondrial disease occurs when a child*

has more than 3 organ systems with problems or when a “typical” disease exhibits atypical qualities.<sup>2</sup>

Mitochondria contain the electron transport chain (ETC), which is made up of five key complexes: Complex I, II, III, IV, and V. The electron transport chain (also referred to as the respiratory chain) transfers electrons to oxygen by means of a process called oxidative phosphorylation. If the mitochondria are not working properly and the electron transport chain begins to break down somewhere along one of these five complexes (or in multiple places along the ETC) the child may begin to exhibit some of the symptoms listed above. Researchers believe that a person can have multiple complexes affected, and it is possible that there may be “a domino effect” in some cases. Disorders of oxidative phosphorylation occur when there is a breakdown within the electron transport chain. Visit this link at Mito Action for a 4-minute video illustrating the workings of the ETC, called “The Way Energy is Made...” <http://www.mitoaction.org/way-energy-made>.

Number three in this image illustrates the location of oxidative phosphorylation and ATP synthesis within a cell. (Image taken from [www.mda.org](http://www.mda.org).)



Both Mito Action and the UDMF list “autistic features” as a symptom of mitochondrial disease or as disorders of energy metabolism. What is less well known is that through good “metabolic manipulation,” many autistic symptoms (such as poor eye contact, lack of social connectedness, gross motor delays and receptive and expressive language deficits) may be reduced or eliminated with a good mito cocktail (a blend of particular therapeutic supplements and medications) specifically targeting energy production and which are aimed at reducing reactive oxygen species using antioxidants.

For some ASD children, a deficiency in

Complex I results in autistic symptoms. Some think that this is a new profile of mitochondrial disease, and it is not neurodegenerative in the same way most mitochondrial diseases were once thought to be. Doctors now believe that this emerging profile of mitochondrial disease can be stable if metabolic stress is controlled and the child receives proper metabolic support. Some knowledgeable in the field even say that these children can be recovered or their symptoms can be stable indefinitely.

**Why is this topic confusing?**

Mitochondrial disease as it relates to autism is confusing because, depending on whom you talk to or what you have read, it has many names and labels. However, all names and labels refer to the same concept.

<b>Mitochondrial Disease</b> Disorder of Energy Metabolism	<b>Mitochondrial Disorder</b> Disorder of Bioenergetics
<b>Mitochondrial Dysfunction</b> Mitochondrial Myopathy	<b>Mitochondrial Oxidative Phosphorylation (known as OXPHOS)</b> Mitochondrial Cytopathy
<b>Autism secondary to Mitochondrial Disease (AMD)</b> Respiratory Chain Disorder	<b>Disorder of Energy Production</b> Enzyme Deficiency

**Why is screening for OXPHOS/AMD important in children labeled ASD?**

Screening for underlying mitochondrial disorders is important because the children clinically look and act the same as other ASD children. Recently, Oliveira and colleagues published a population-based survey of school age children with ASD. They found that 7% of those who were fully tested met criteria for definite mitochondrial respiratory chain disorders and were also clinically indistinguishable from other children with ASD. This work is notable because it suggests that mitochondrial disorders of energy production may be present in a substantial percentage of children with ASD.<sup>3</sup> Therefore, if your child exhibits features of mitochondrial disease in conjunction with ASD symptoms, screening for OXPHOS should be considered.

**Why is early screening for OXPHOS/AMD important for your child?**

There may be a cohort of ASD children with undiagnosed mitochondrial disease, and early treatment of mitochondrial problems may improve outcome. Doctors in the field of mitochondrial medicine now believe that management of symptoms can occur in some children. Unfortunately, children with ASD or regressive ASD are not being regularly evaluated for issues of energy production, even when the symptoms and red flags for OXPHOS are present. Early identification of these children

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may improve their overall outcome if they start the correct mito cocktail sooner rather than later.

Another study published in November 2008 by doctors in the field of mitochondrial medicine reported, “Although all patients’ initial diagnosis was idiopathic autism, careful clinical and biochemical assessment identified clinical findings that differentiated them from children with idiopathic autism. These and prior data suggest a disturbance of mitochondrial energy production as an underlying pathophysiological mechanism in a subset of individuals with autism.”<sup>3</sup>

Because problems within mitochondria have been very difficult to diagnose, it is common to meet people within the mito community who have spent 10 years (or more) getting an accurate diagnosis. The times may be changing, thanks to the hard work of mitochondrial experts.

For children who have not had a clinical response to other treatments and who have the labs suggestive of OXPHOS, this treatment option is worth pursuing. Although some ASD children may have tried various biomedical treatments for metabolic abnormalities suggestive of mitochondrial dysfunction, they may not have used the combinations of supplements and medications at the dosages recommended by mito specialists. For some children, it may take a long time to realize the full benefits as the slow, steady, cumulative, and synergistic effect of the whole cocktail helps augment Complex 1 deficiency.

**Who should be screened for OXPHOS?**

Symptoms of mitochondrial disease are highly variable and range from mild to severe. The following are features and symptoms that physicians should consider:

1. abnormal fatigue / exercise intolerance
2. developmental stagnation or regression after a viral illness, fever, or vaccine
3. regression following surgery, sedation, or anesthesia
4. poor muscle tone, muscle weakness, or motor incoordination
5. an episode of sudden ataxia (a sudden motor regression at a later age)
6. difficulty handling temperature changes (heat or cold), suggesting autonomic temperature control issues
7. unexplained GI issues (not related to allergies)

Dr. Bruce Cohen, an expert in mitochondrial medicine from the Cleveland Clinic, has listed the following possible problems associated with mitochondrial disease when children exhibit symptoms across 3 or more organ systems.

**Possible Symptoms Associated with Mitochondrial Disease**

Organ system	Possible problem
Brain	developmental delays, mental retardation, dementia, seizures, neuropsychiatric disturbances, atypical cerebral palsy, migraines, strokes
Nerves	weakness (which may be intermittent), neuropathic pain, absent reflexes, dysautonomia, gastrointestinal problems (GI reflux, dysmotility, diarrhea, irritable bowel syndrome, constipation, pseudo-obstruction), fainting, absent or excessive sweating resulting in temperature regulation problems
Muscles	weakness, hypotonia, cramping, muscle pain
Kidneys	renal tubular acidosis or wasting resulting in loss of protein, magnesium, phosphorous, calcium and other electrolytes
Heart	cardiac conduction defects (heart blocks), cardiomyopathy
Liver	hypoglycemia (low blood sugar), liver failure
Eyes	visual loss and blindness
Ears	hearing loss and deafness
Pancreas and other glands	diabetes and exocrine pancreatic failure (inability to make digestive enzymes), parathyroid failure (low calcium)
Systemic	failure to gain weight, short stature, fatigue, respiratory problems including intermittent air hunger, vomiting

Taken from *Mitochondrial News*, Fall 1997 issue

More red flag symptoms can be found at [www.mitosoc.org](http://www.mitosoc.org) as well as [www.umdff.org](http://www.umdff.org).





### Which health care provider should order the screening labs for OXPPOS?

This is an interesting question because there are too few skilled health care providers in the field of autism and mitochondrial medicine. If you have an excellent pediatrician, then this may be your best choice for getting the initial screening labs completed. A biomedical physician may also be able to help you complete the screening labs. And of course, a geneticist, specialist in inborn errors of metabolism, or mitochondrial specialist could request the labs.

Mitochondrial disease has been historically difficult to diagnose since it resembles so many other things.<sup>2,4</sup> It is in your child's best interest to go to a doctor who is an expert in the field of mitochondrial medicine. You can find an excellent provider list, with hospital affiliation, on the Mitochondrial Medicine Society website at [www.mitosoc.org](http://www.mitosoc.org).

### What screening labs should be requested?

Many children with an overlapping diagnosis of mitochondrial disease and ASD have an elevated lactate level as well as elevated alanine/lysine ratios. At this time, metabolic screening does not occur routinely in autistic patients, thereby delaying early identification and the start of treatments to improve some children's outcomes.

**The Mitochondrial Medicine Society lists the following as metabolic screening labs for mitochondrial disease:**

- Basic Chemistries
- Liver Enzymes and Ammonia
- Complete Blood Count
- Creatine Kinase
- Blood Lactate and Pyruvate
- Qualitative Plasma Amino Acids
- Quantitative Urinary Organic Acids
- Plasma Acylcarnitine Profile

There are several important things to mention regarding metabolic labs:

1. Blood lactate levels should be drawn without a tourniquet in a free flowing venipuncture for proper results.
2. Pyruvate requires special handling to be processed correctly. It should be immediately deproteinized and assayed because pyruvate is an unstable compound.
3. To ensure proper handling of these labs, you may want to speak with the phlebotomist in advance and make an appointment for your child to make sure these labs are properly processed.
4. The results of metabolic labs may vary somewhat based on a child's overall health (good or bad) at the time the blood is drawn. The best time to do metabolic labs is when the child is slightly under the weather (or during a time of regression)

but not so sick that the lab draw becomes an additional metabolic stress to the child. You are most likely to catch the nature of the child's underlying metabolic abnormalities when your child is "slightly decompressed." Make sure your child is well hydrated (with plenty of water) prior to the blood collection.



Free carnitine and total carnitine levels should also be checked via blood and urine because relative carnitine deficiency is common in children with ASD.

In a study completed in 2004, "100 children with Autism were evaluated for serum carnitine levels and the conclusion was that 83% of the subjects had total and free carnitine levels below the reference norm."<sup>5</sup> This study is highly suggestive that a large number of autistic children have a relative carnitine deficiency.

However, if a child has been taking an over-the-counter carnitine prior to the lab (which many biomedical doctors do recommend), this may falsely elevate the carnitine levels and elevate them within the normal reference range when, in fact, they may have been low prior to supplementation. There have been many anecdotal accounts of children doing much better symptomatically on prescription brand Carnitor® or generic brand Levo-carnitine compared to over-the-counter carnitine supplements.

### What lab results suggest OXPPOS?

The Mitochondrial Medicine Society lists the following lab results as "Findings Suggestive of Mitochondrial Dysfunction."<sup>6</sup>

Findings Suggestive of Mitochondrial Dysfunction		
Amino Acids (plasma/CSF)	Organic Acids (urine)	Acylcarnitines (plasma)
Elevated alanine	Elevated TCA intermediates	Low free carnitine
Alanine/Lysine ratio > 3	Elevated Ethylmalonate	Elevated acyl:free carnitine ratio
Elevated glycine, proline, tyrosine, or sarcosine	Elevated 3-methylglutaconate	Elevations suggesting disrupted fatty acid oxidation

If screening labs are completed and there appear to be abnormalities suggestive of OXPPOS, it is important to see a specialist in inborn errors of metabolism, genetics, or mitochondrial medicine.

### What are the treatment options?

OXPPOS is not thought to be curable at this time, but there is dramatic symptom improvement in some children once appropriate treatments are started. Many physicians start with Tishcon brand coenzyme Q10 and/or pharmaceutical grade creatine (not over-the-counter brands as they may be toxic). Mito cocktails may also



include the B-complex vitamins thiamine (B1), riboflavin (B2), B6, B12, pantothenic acid (B5), and biotin; antioxidants (e.g., alpha lipoic acid, vitamin C, vitamin E); Leucovorin Calcium®, Carnitor®, Neotine, and more.<sup>7</sup> Always consult your physician before beginning any new treatments.

For more information about treatments used for mitochondrial disease, visit:

- The Cleveland Clinic website under mitochondrial disease: [http://my.clevelandclinic.org/disorders/mitochondrial\\_disease/hic\\_mitochondrial\\_disease.aspx](http://my.clevelandclinic.org/disorders/mitochondrial_disease/hic_mitochondrial_disease.aspx)
- “Mitochondrial Vitamin Cocktails – A guide for Parents” written by Acton Compounding Pharmacy: <http://www.mitoaction.org/files/mito%20cocktail%20brochure%202010.pdf>
- “The Dosing Debate: CoQ10 and Creatine in mitochondrial disorders”: <http://www.mitoaction.org/blog/the-dosing-debate-coq10-and-creatine-mitochondrial-disorders>
- “Updates on Mitochondrial Disease Treatment Approaches”: <http://www.mitoaction.org/blog/update-mitochondrial-disease-treatment-approaches>
- “A Modern Approach to the Treatment of Mitochondrial Disease”: [www.mitosoc.org](http://www.mitosoc.org) and access this article on the home page

#### How is the mitochondrial cocktail different from biomedical intervention for mitochondrial dysfunction through a biomedical physician?

That is an excellent question. It is not entirely different, but it is different in several ways.

First, the mito cocktail uses more bioavailable versions of supplements and cofactors (and some at much higher doses). Increased bioavailability is generally beneficial to a patient population that has difficulty metabolizing and absorbing food, nutrients, and medications. There are now several formulas of CoQ10, creatine, and riboflavin (B2) specifically designed for someone with a mitochondrial myopathy. Over-the-counter carnitine and folate supplements may not be bioavailable enough for some children with disorders of energy production. Some may do better on pharmaceutical grade carnitine (Carnitor®) and/or folinic acid (Leucovorin Calcium®), so this should be discussed with your physician.

Second, mito specialists’ cofactor and dosage recommendations have been chosen based on information gathered from treating more typical mitochondrial disease over several decades.<sup>7</sup>

Therefore, their cocktails are specifically targeted for this patient population and are specifically targeting the metabolic pathways that are necessary for energy production.

Both groups agree on the critical need to reduce oxidative stress using antioxidants that in turn reduce reactive oxygen species (ROS). This remains an important and central part of the treatment protocol, similar to that of biomedical physicians, and both groups agree that there may be a synergistic effect when antioxidants are combined.<sup>17,8,9,10</sup> A combination of vitamin E, vitamin C, and ALA is often used to reduce oxidative stress in these patients.

The most exciting thing about this emerging research is that it opens up diagnostic testing and some treatment options to people who have been unable to afford out-of-network biochemical practitioners who are generally paid out-of-pocket and often not reimbursable by insurance companies. This information also has the potential to help countless children whose parents are unwilling to step outside of the mainstream medical model for the treatment of their child with autism.

#### Why aren’t doctors routinely screening for OXPHOS in children labeled ASD?

There is a lack of information and knowledge about mitochondrial disorders within the mainstream medical community for three reasons.

First, mitochondrial disease was once thought to be very rare, which we now know is not true.<sup>1,2</sup> Mitochondrial disease is now implicated in many other disease states including depression, mood disorders, bipolar disorder, schizophrenia, Alzheimer’s, Parkinson’s, diabetes, neurodegenerative diseases, and even some cancers.<sup>14,11,12</sup>

Second, the field of mitochondrial medicine and science is in its infancy. As a result, most doctors have had little (or no) training in this area. In addition, the Mitochondria Research Society website states that “Many mitochondrial diseases are so new that they have not yet been mentioned in the medical textbooks or in the medical literature.”

Third, the medical paradigm within which all children are currently being evaluated needs to change. Global developmental delay and early marked motor delay have now become “a red flag symptom” for potential underlying mitochondrial disease. In 2008, eight experts in the field of mitochondrial medicine published an article stating that, “64% of patients [with disorders of energy production] were delayed in attaining early developmental milestones and 32% were five or more standard deviations later than the mean in walking independently.”<sup>3</sup> But it is not standard practice or currently required by the American Academy of Pediatrics to do **any** metabolic testing on a child who has a profound global developmental delay or a marked gross motor delay. Those children are often just

“Both groups agree on the critical need to reduce oxidative stress using antioxidants that in turn reduce reactive oxygen species (ROS).”

referred to developmental therapists, which is important but does not address the underlying medical issues causing the developmental delays. Therefore, this medical paradigm desperately needs to change. This is really the greatest challenge at this point in time.

**What kind of diet is best for children with OXPPOS?**

Like other children, children with OXPPOS need a diet that is balanced and healthy. "Optimizing the number and quality of calories has been shown to improve mitochondrial health in these patients."<sup>7</sup> The leading doctors in mitochondrial medicine are advocating minimal meats and no (or limited) animal fats containing fatty acids and cholesterols. Diets high in omega-6 and 9 fatty acids and low in omega-3 oils tend to be pro-inflammatory, and one goal is to reduce inflammation in children with autism and disorders of energy production. Flaxseed oil and fish oils should be considered to improve and maintain healthy membranes surrounding mitochondria. The UMDF has stated that in some patients adding fat in the form of medium chain triglycerides (MCT) may be helpful. Medium chain triglycerides of 8 to 10 carbons long are easier to metabolize (turn into energy) than the longer chain triglycerides (those with 12-18 carbons) because they do not require carnitine to be transported into the mitochondria. For more information about MCT oil visit, [www.umdf.org](http://www.umdf.org).

It is important to maximize your child's fruit and vegetable intake, and some experts are advocating for a Mediterranean diet with nothing white in color (no refined sugar or white flour) and eating mainly fish and beans as the source of dietary protein. Some children do best eating five small meals a day as opposed to the more typical three larger meals daily.<sup>2,7</sup>

In addition, it is advantageous to remove foods that may promote oxidative stress. This includes avoiding MSG (monosodium glutamate) found in Chinese food, nitrites/nitrates, foods with preservatives, dyes, food allergens, and genetically-modified foods (in particular, non-organic soy and corn, which has a high likelihood of being GMO).

It is critical for children with mitochondrial disease to stay well hydrated and avoid fasting

for long periods of time as this can disrupt their delicate metabolic balance. So, make sure to pack water and a snack for any outing.

Any diet modifications made to a child's diet should be monitored by your physician, a registered nutritionist, or a metabolic nutritionist, because a low fat diet is sometimes contraindicated in some children with mitochondrial disease.<sup>2</sup>

**What precautions should be taken with OXPPOS children?**

Children with a mitochondrial diagnosis often receive special care during times of acute illness because they need to avoid dehydration and additional metabolic stress.

1. Children with OXPPOS require special care during times of dehydration. If an OXPPOS child is in a state of acute dehydration, he or she should be brought to the hospital for IV fluids, but it is important that these children do not receive a "lactated ringer" on the IV as most children with OXPPOS already have elevated blood lactate levels, and this could be detrimental to their overall well-being. They may also receive D5, D10 dextrose (D20 in severe cases) and sometimes IV carnitine (if available) to help control metabolic stress. These precautions are important because they may prevent complications (such as neurological regressions) associated with illness and fever in these children.<sup>13,14,15</sup>
2. Children with OXPPOS often have emergency protocol letters. Emergency protocol letters are extremely helpful when or if there is an emergency or illness requiring a trip to the emergency room. This is helpful because, as stated before, many doctors are not knowledgeable about the issues surrounding mitochondrial disease and this will help advocate for proper care of your child in an emergency situation.
3. Children with OXPPOS should avoid certain medications. There are known contraindications to



**Effects of Medication on Mitochondrial Function:**

<p><b>Acetaminophen:</b> Depletes glutathione; increases reactive oxygen species (ROS); inhibits OXPPOS</p>	<p><b>Anti-psychotics:</b> Inhibits OXPPOS</p>	<p><b>Aminoglycosides antibiotics (e.g., gentamicin):</b> Toxic to mitochondria Impair mtDNA translation<sup>7</sup></p> <p><b>Erythromycin:</b> should generally be avoided.</p>	<p><b>Aspirin:</b> Sequesters CoA inhibition of and uncoupling of oxidative phosphorylation<sup>7</sup></p>	<p><b>Depakote, Depakene, (Valproic acid):</b> Depletes carnitine; inhibits Beta Oxidation; inhibits urea cycle; sequesters CoA</p>	<p><b>Iron:</b> In some cases, increase radical oxygen species (ROS) and damages mitochondria<sup>2</sup></p> <p><b>SSRIs:</b> Complex 1 inhibitor</p>
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“ Children with OXPHOS should be given a special anesthesia protocol (known as a Malignant Hypothermia protocol) to prevent complications during all medical procedures requiring anesthesia and/or sedation. ”

some medications. These medications can further damage mitochondria and should be avoided in children with mitochondrial disease, if possible.<sup>2,7</sup> In some cases, these medications cannot be avoided, but this should be discussed with your health care provider so an informed decision is made. An important new webcast featuring Dr. Katherine Sims of MassGeneral Hospital and covering a multitude of medications and their effect on mitochondrial function can be found on the Mito Action website at <http://www.mitoaction.org/blog/medication-exposures-mitochondrial-toxicity>.

4. Children with OXPHOS should be given a special anesthesia protocol (known as a Malignant Hypothermia protocol) to prevent complications during all medical procedures requiring anesthesia and/or sedation.  
If your child is going under anesthesia for any reason and you suspect OXPHOS, make your pediatrician aware of the risks with anesthesia and sedation in this patient group. A copy of the anesthesia protocol used for children with mitochondrial disease can be found at [www.umdf.org](http://www.umdf.org) and is called "Anesthesia and Mitochondrial Cytopathies."<sup>13,14</sup> Knowing if your child has the symptoms or biochemical markers for OXPHOS prior to a procedure requiring anesthesia or sedation is in your ASD child's best interest. Children with mitochondrial disease often have elevated lactate levels. Therefore, it is important that these children DO NOT receive IV's with lactated ringers, as they already have elevated lactic acid levels and this can cause additional problems.

5. Children with OXPHOS need to control metabolic stress as much as possible. Doctors are advocating for the control of environmental factors that increase metabolic stress in children diagnosed with mitochondrial disease. This includes helping your child:
  - maintain good overall nutritional status and adequate hydration;
  - get enough rest and sleep daily;
  - avoid physiological stressors;
  - control body temperature (i.e., make sure they don't get too hot or too cold);
  - avoid fasting; and,
  - prevent infections.<sup>2,4</sup>
 Children with OXPHOS should also avoid exposure to second-hand smoke due to the carbon monoxide.<sup>2</sup>
6. Children with OXPHOS need to exercise regularly.  
Perhaps the single best thing a child with mitochondrial disease can do is exercise regularly. This can be a challenge, however, in children with mitochondrial disease because they often experience fatigue and muscle weakness. "Exercise is one of the few proven methods for improving mitochondrial functioning and decreasing the burden of unhealthy mitochondria. Graded endurance exercise can improve exercise tolerance as well as biochemical enzyme activity and mutation burden."<sup>7</sup> However, overexertion and dehydration should be avoided. Having an accurate diagnosis of OXPHOS allows you to better manage the daily life of your child for the best overall outcome. It also allows you to monitor the progress of researchers in this area so you can get the latest treatments for your child as soon as they become available.

#### Adverse Effects of Anesthesia on Mitochondrial Function

Medication	Biochemical & Clinical Effects on Mitochondrial Function
Barbiturates	Inhibits Complex I activity at high levels
Benzodiazepines	Inhibits adenosine nucleotide translocase
Propofol and /or Lipid Carrier	Inhibits mitochondrial function
Halothane	Increased risk for heart rhythm disturbances
Nitrous Oxide (chemical formula is N2O)	Neurotoxic, possibly by increasing nitric oxide production, which inhibits cis-acotinase and iron-containing electron transport enzymes; affecting energy production
Non-depolarizing Agents	Increased sensitivity to the paralytic effects and prolonged responses reported
Local Anesthetics	Bupivacaine uncouples oxidation and phosphorylation

Table taken from [www.umdf.org](http://www.umdf.org), written by Dr. Cohen, Dr. Shoffner and Dr. DeBoer.

#### What does the future hold?

There are now several well-respected mainstream doctors in the field of mitochondrial medicine advocating for identifying and treating children who have OXPHOS within the autism community.<sup>3,7,10,11</sup> These doctors are the unsung heroes in this fight for better, more appropriate treatments for these children.

Most of the mitochondrial diagnostic testing available at this time is imprecise and invasive. At the UMDf 2009 symposium in Virginia, a leading expert stated that skin punch biopsies are thought to be approximately 50% inaccurate, a frozen muscle biopsy approximately 30% inaccurate, and a fresh muscle biopsy approximately 15% inaccurate. Due to the fact that these testing procedures often yield false negative results and all three are invasive, with muscle testing requiring sedation and/or anesthesia which has inherent risks in OXPHOS children, several researchers are working to develop less invasive testing. These include buccal/cheek swab testing, micro-organic breath analysis, and laser technology to analyze



the skin as alternative mitochondrial diagnostic testing.<sup>16</sup> The hope is that over time one of these less invasive tests will make screening for OXPHOS easier and more accurate.

At this time, several specialists are advocating for a “clinical diagnosis” based on suggestive lab work and clinical response to the mito cocktail over more invasive procedures and testing such as a muscle biopsy. This is due to the fact that a positive muscle biopsy (or a “confirmed” mitochondrial diagnosis) does not change the treatment, which would still remain a mito cocktail.

Not all children will be helped by the mito cocktail, and not all ASD children will have the lab markers for OXPHOS, so it is not a “one size fits all” solution. But for many children who have the biochemical markers for OXPHOS, some will have benefits from the treatment protocols.<sup>7</sup>

### How should you best advocate for your child if you want screening labs for OXPHOS done?

1. Get informed and stay informed. New research is being published as the field of mitochondrial medicine is emerging. Know what information is being discussed in the mito community. The Mitochondrial Medicine Society, Mito Action and UMDF websites are excellent sources of up-to-date and accurate information on mito.
2. Write out a list of symptoms that your child exhibits that are also consistent with the OXPHOS profile and present this list to your doctor. The endnotes of this article have several important articles that any doctor who has ASD patients should read.
3. Advocate for your child. A well-read, informed, and organized parent is much harder to dismiss. Due to the fact that there is a lack of information within the mainstream medical community regarding disorders of energy production, education needs to be a goal of families who have children diagnosed.

There are two main goals:

- The first goal is getting pediatricians to take a more proactive approach to requesting metabolic testing/screening on kids who have atypical symptoms such as fatigue, global developmental delay, or marked early motor development delays.
- The second goal is getting pediatricians to complete screening labs for OXPHOS immediately after any developmental regression or developmental stagnation is observed by a parent in their child.

If parents begin to request screening for their child who exhibits these symptoms, perhaps this paradigm can slowly be changed.

This article is meant to be a resource to share

with your physician to advocate for proper screening of a child for disorders of energy production when the clinical features of OXPHOS exist. Several excellent clinician guides exist and links to these documents can be found in the reference section of this article to share with your physician.

Autistic symptoms in children with disorders of energy production are no longer being considered a static disease state that cannot be improved upon. This is a critical and important paradigm shift within mainstream medicine. Under the care of a specialist, dramatic improvements can be made through metabolic manipulation using supplements and medications in some children.

As parents become more aware that mitochondrial impairment is involved in the etiology of some autism spectrum disorders, it is my hope that more children will have proper metabolic screening and evaluations for problems involving energy production.

In the next issue of *The Autism File*, I will share the journey of several ASD children undergoing evaluations for mitochondrial disease, details about their symptoms, their current treatment plans, and the children’s responses to the mito cocktail.

I wish every child improved health.

“Children with mitochondrial disease often have elevated lactate levels. Therefore, it is important that these children DO NOT receive IV’s with lactated ringers, as they already have elevated lactic acid levels and this can cause additional problems.”

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### Resources for physicians:

Mitochondrial Disease: A Practical Approach for Primary Care Physicians. <http://pediatrics.aappublications.org/cgi/content/full/120/6/1326>

Clinicians Guide to the Management of Mitochondrial Disease: A Manual for Primary Care Providers <http://www.mitoaction.org/guide/table-contents>

Mitochondrial and Metabolic Disorders- A Primary Care Physician’s Guide <http://biochemgen.ucsd.edu/mmdc/ep-toc.htm>

Dr. Mark Korson, Chief of the Metabolic Program at Tufts New England Medical Center, speaks about Mitochondrial Disease and Patient Challenges (5-minute video) <http://www.youtube.com/mitoaction#play/all/F38FD8F6D9124E1B-all/1-zf3eYRGpko>

Think Mitochondria (1997) Mitochondrial Evaluation Worksheet can be found at [www.umdf.org](http://www.umdf.org), page 13

[http://www.umdf.org/atf/cf/%7B858ACD34-ECC3-472A-8794-39B92E103561%7D/think\\_mitochondria.pdf](http://www.umdf.org/atf/cf/%7B858ACD34-ECC3-472A-8794-39B92E103561%7D/think_mitochondria.pdf)

Palmieri L, Persico AM. (2010 May 8). Mitochondrial dysfunction in autism spectrum disorders: Cause or effect? *Biochim Biophys Acta*. [Epub ahead of print] <http://www.ncbi.nlm.nih.gov/pubmed/20441769>

### Websites of interest:

The Mitochondrial Medicine Society [www.mitosoc.org](http://www.mitosoc.org)

Mito Action [www.mitoaction.org](http://www.mitoaction.org)

United Mitochondrial Disease Foundation (UMDF) [www.umdf.org](http://www.umdf.org)

Mitochondria Research Society [www.mitoresearch.org](http://www.mitoresearch.org)