

# THE JOURNEY FROM ASD TO A MITOCHONDRIAL DISEASE DIAGNOSIS:

## Symptoms, testing, treatments & responses to a mitochondrial cocktail—Families' Stories—Part II

(Part I: Has Your Child with Autistic Symptoms Been Properly Screened for a Subset of Mitochondrial Disease Known as OXPPOS? ...Probably Not.)

By Alyssa Davi



**Alyssa Davi** is a former special education teacher and is involved the nonprofit organization Parents Ending America's Childhood Epidemic (PEACE), which is sponsoring the parent outreach project Epidemic Answers. Please visit [www.epidemicanswers.org](http://www.epidemicanswers.org) or you can contact Alyssa at [Alyssa@epidemicanswers.org](mailto:Alyssa@epidemicanswers.org).

As discussed in part I of this series, there is an overlapping cohort of children who exhibit ASD symptoms and who have underlying mitochondrial disease. Disorders of energy production or defects of oxidative phosphorylation are emerging as a new category of ASD and are being called many different names, including OXPPOS (mitochondrial oxidative phosphorylation), mitochondrial complex I deficiency, and autism secondary to mitochondrial disease (AMD).

Many of the leading mitochondrial specialists (neurologists and geneticists) now acknowledge that there is a group of ASD children whose labs and symptoms are suggestive of mitochondrial disease. This is important because a few years ago many specialists did not think this was possible. It is worth noting that that one day was devoted to discussing this link as well as to mitochondrial research and treatments at the 2010 United Mitochondrial Disease (UMDF) Symposium in Arizona.

In this article, I first provide some background information about mitochondrial disease and explain what goes in a "mito cocktail" (a therapeutic combination of supplements and medications), and then I discuss several children's developmental profiles. The first two children received their ASD label first but are now diagnosed with mitochondrial disease, presumed complex I. I identify these children's symptoms, testing, suggestive lab work, treatments, and responses to the mito cocktail. Then, I give details of another child trying the mito cocktail including their symptoms and responses to the cocktail.



### Identifying Mitochondrial Disease

Mitochondrial disease should be considered when a child has more than 3 organ systems with problems.

Mitochondrial symptoms in ASD children may include:

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 an allergy)

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

*Above top: Will, summer 2010  
Next page, top: autonomic temperature control problems*

The Mitochondrial Medicine Society lists the following lab results as suggesting mitochondrial dysfunction:

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

### The mito cocktail

The treatment for disorders of energy production is a mito cocktail aimed at increasing cellular energy production and reducing oxidative stress, which in turn reduces reactive oxygen species (ROS).

A top mitochondrial specialist at the 2010 United Mitochondrial Disease Symposium has listed the following as a possible starting mito cocktail. Many ASD children with an overlapping mitochondrial diagnosis (or suspected mitochondrial dysfunction) are taking this cocktail and are seeing developmental benefits over more traditional biomedical treatments.

coenzyme Q10 (CoQ10)  
L-carnitine (prescription or pharmaceutical grade, not over the counter/supplement)  
vitamin B-2 (riboflavin)  
alpha lipoic acid  
creatine monohydrate (pharmaceutical grade, not over the counter/supplement as this can be toxic to children)  
vitamin D and calcium

#### For some:

L-arginine  
folinic acid (Leucovorin Calcium, a prescription medication)  
Some specialists prefer vitamin C and vitamin E over alpha lipoic acid as the primary antioxidant component; however, in an attempt to reduce reactive oxygen species, all specialists recognize the need for an antioxidant component for children with disorders of energy production.

For more information on current accepted treatments for mitochondrial disease please read, "A Modern Approach to the Treatment

of Mitochondrial Disease" in *Current Treatment Options in Neurology* (2009).  
<http://resources.metapress.com/pdf-preview.axd?code=d872354q672090mq&size=largest>

### PROFILES

The following are two children's developmental profiles identifying symptoms, testing, suggestive lab work, treatments, and responses to the mito cocktail.

#### PROFILE #1

**Child's name:** Will

**Current age of child:** 3 years, 2 months old

**Age of ASD diagnosis:** 2 years, 6 months old

**ASD label given to child:** pervasive developmental disorder – not otherwise specified (PDD-NOS)

**Coexisting diagnosis:** Gastroesophageal (GE) reflux, high human herpesvirus six (HHV-6) levels with reoccurring fever blisters, clinically diagnosed mitochondrial disease complex I

**Prenatal complications:** mother needed Darvocet due to pain from uterine fibroids, unplanned C-section

**Post-natal problems:** jaundiced, tongue tied, respiratory wheezing, and reflux. He often arched his neck and head backwards during and following feedings.

**Relevant family history:** only child, family history of diabetes on the paternal side

**Early history/First signs of developmental problems:** restless, didn't sleep well, arched back, reflux (starting at 3-4 months old), content to



sit, not particularly active, "a little late meeting all developmental milestones," limited babbling, sensitive to temperature (overheated or got cold easily), sleeping area needed to be the "perfect temperature," good eye contact, loved to be held until 12 months old, Starting at 2 months old, following each set of vaccinations, Will was fussy and had a low grade fever.

At 12 months, he experienced his first sharp regression following MMR, varicella, pneumococcal and HiB vaccines. He had noticeably less energy, began to spin himself in circles, spun stacking rings for long periods of time, rolled around on the ground, began staring at floor and objects for long periods of time, exhibited a strong insistence on routines, did not respond to a parent speaking to him, lost the ability to wave goodbye and hello, had a language regression (lost "mama" and "dada,") became obsessed with fans, opened and closed doors repeatedly, became more mood liable ( unable to transition easily from mother to caregivers and was very clingy), unable to go out in public because he was bothered by crowded, noisy spaces, and had great difficulty sitting still in a stroller or shopping cart.

At 34 months, he had second sharp regression following anesthesia after replacement of ear tubes and removal of adenoids. Post anesthesia, Will had facial swelling that persisted on and off for a month, rolled around the floor moaning in pain, moaned in his sleep, and lost his appetite. His anesthesia regression was the red flag to investigate a mitochondrial disorder.

“ Mitochondrial disease should be considered when a child has more than 3 organ systems with problems. ”

# DOES THIS REMIND YOU OF YOUR CHILD?

## Gross motor development symptoms:

- slightly delayed in meeting motor milestones; sat up at 7 months, crawled at 10.5 months, walked at 14 months
- exhibits low tone, muscle weakness, exercise intolerance (often needs to be carried instead of walking independently) and exhibits fatigue (increased in heat)
- motor incoordination: awkward gait, bumps into things, unsteady on feet, trips easily (cannot walk well in sandals) and has difficulty walking on/navigating uneven surfaces
- difficulty getting up and down stairs safely and independently at 3 years old

## Fine motor symptoms:

- appears to be within normal limits at this time

## Communication symptoms:

### Oral motor symptoms:

- feeding difficulty with tongue movements
- difficulty with oral motor exercises
- cannot lick food off lips, cannot stick out tongue on demand

### Articulation:

- words sound garbled, poor articulation, difficult to understand

### Expressive language:

- severe expressive speech delay, using one word at a time at age 3 years old, approximately 100- word vocabulary

### Receptive language:

- appears to be within normal limits at this time

### Pragmatics:

- understands that language is reciprocal, will respond, back and forth
- able to read nonverbal cues – knows when someone is upset or angry (and often responds to these emotions in others around him)

## Cognitive development and problem solving:

- appears to be within normal limits at this time
- knows letters, numbers, shapes, colors, body parts, animals, may be exhibiting some early reading, and has a high interest in phonics, words and numbers

## Self help/daily living skills:

- difficulty dressing self, feeding self, and potty training

## Play skills:

- play skills are affected by how well he feels on a given day
- can build tall towers with blocks, do wooden puzzles on days he feels well
- throws toys, can't concentrate, is easily frustrated and will lay around and push buttons on electronic toys over and over again on days he does not feel well

## Personal social skills symptoms:

- exhibits empathy and concern for others, hugs and hold hands with peers
- learning how to interact with others, share, potty training skills
- social skills are directly affected by how well he feels on any given day
- can play peek-a-boo and smile at people on a good day, whereas ASD kids would not; this always puzzled developmental pediatricians as he seems to have a lot of ASD symptoms but not the consistent social symptoms one would expect

## Sensory symptoms:

- tactile defensive – improvements have been made in this area: can tolerate stickers on face, wiping his face, putting his face in water to blow bubbles
- screeches loudly when other children sing
- exhibits symptoms of proprioceptive dysfunction (including seeking out deep pressure) and occasionally has sound sensitivity

## Attention symptoms:

- difficulty following directions
- ability to focus on a task/toy intermittently, based on how he's feeling on a given day

## Feeding symptoms:

- exhibits feeding problems;

### Solids:

- gagging on food and difficulty chewing
- food consumption waxes and wanes, small frequent meals seem to work best
- difficulty swallowing certain textures
- need to break up foods (crackers) for him to eat so he won't gag
- self limits protein, especially red meat and chicken and limits sweets

### Liquids:

- self-limits fluid consumption; often need to syringe feed fluids to keep him hydrated when he's sick and also when he's well (frequently use syringe to feed fluids/Pedialyte)
- does not appear to recognize when he's thirsty, great difficulty controlling the rate of liquids while swallowing

## Allergy/food sensitivities/current diet:

- positive IgE, immune mediated allergy to egg white
- IgG food sensitivity/intolerance testing underway at this time
- Symptoms of food sensitivity to corn and soy include red ears and cheeks, hyperactive after eating
- Gluten, casein, soy, corn, egg free diet, only organic, non-GMO foods
- low sugar (due to glucose metabolism issues)

## GI symptoms/ bowel symptoms:

- as an infant, history of arching back after drinking fluids and eating a meal, in the middle of a feeding and afterwards (made feedings difficult)
- GE reflux
- yellow stool, some undigested food
- occasional diarrhea, gas, and stomach cramping
- history of *Clostridium difficile*

## Immune system symptoms:

- chronic fluid in the ears resulting in an approximately 30 percent hearing impairment, two confirmed ear infections resulting in two courses of antibiotics
- initial set of tubes at 21 months, one confirmed ear infection after this set of tubes
- second set of tubes at 34 months old, also removed adenoids at the same time.
- low total IgG and subclass I and II IgG, indicating poor immune function

## Physical symptoms:

- currently small for his age (but never "failure to thrive") 37.5 inches tall, 31 pounds
- hasn't felt "well enough" to do much therapy routinely

## Current therapies and educational placement:

- speech therapy, 30 minutes 2 times weekly (speech remains his area of greatest developmental need, so his speech therapy will increase soon)
- occupational therapy, 2 hour sessions, 3 times weekly
- early education special education pre-school, fully self-contained, student/teacher ratio 9:2, 3 hours a day, Monday through Friday (for school calendar year)

## Will's red flag symptoms for mitochondrial involvement:

- exercise intolerance
- abnormal fatigue
- developmental regression after 12-month vaccinations (including MMR and varicella)
- regression after ear tube placement and adenoid removal; could not stand up post anesthesia, acted as if he was in pain; moaning, no energy, extremely weak, tired and fussy, lips swelled periodically
- poor muscle tone, muscle weakness, motor incoordination
- an episode of sudden ataxia, post anesthesia
- difficulty handling temperature changes: in the cold, his fingers turned purple and in the heat he easily overheated and got very red faced
- hypoglycemia
- GI issues (not related to allergy)

**Biomedical interventions:**

Will has been doing biomed for approximately 1 year. During that time, the following biomedical interventions were most helpful: mito cocktail, Pepcid for reflux, probiotics, trimethylglycine (TMG) and methyl B-12 injections (every 3 days) in combination with folinic acid, one course of Zithromax for the treatment of pediatric autoimmune neuropsychiatric disorders associated with streptococcal infection (PANDAS), coconut oil to treat fever blisters as well as short term use of *Flagyl/Saccharomyces boulardii* for *C. difficile*.

He did not tolerate systemic prescription antifungals (diflucan or ketoconazole) or antivirals (Valtrex). These worsened his symptoms, so they were stopped. He seems to be very sensitive to prescription medications and multivitamins. Vitamins are given individually.

**Testing:**

Initial metabolic screening labs for mitochondrial impairment were completed by Will's local developmental pediatrician after the anesthesia regression. These tests included a blood lactate and pyruvate, urine organic acids, plasma amino acids, acylcarnitine profile and creatine kinase. His results were as follows:

**Elevated urine organic acids:**

elevated succinic acid, methylsuccinic acid, adipic, suberic, sebacic

**Elevated amino acids:**

- extremely elevated alanine/lysine ratio (greater than 7.5)
- elevated glycine
- low creatine kinase

Will was then referred to the Division of Metabolism at Kennedy Krieger Institute in Baltimore, MD, for a more formal assessment of mitochondrial metabolism under several physiological conditions; overnight fasting, 4-hour fasting, and 2-hours postprandial (after mealtime) selected to elicit specific metabolite patterns in mitochondrial complex I deficiency and related candidate metabolic disorders.

Will had the following testing protocol done at Kennedy Krieger Institute:

**Collection 1:** Morning fasting sample (overnight 14-hour collection)

- urine organic acids
- quantitative plasma amino acids
- blood lactate level

- comprehensive metabolic panel
- CRP (C-reactive protein)
- serum selenium

**Collection 2:** 4-hour fasting (pre-lunch)

- quantitative plasma amino acids
- creatine kinase
- blood lactate level
- comprehensive metabolic panel
- coenzyme Q10
- vitamin E levels
- lipid profile
- CBC with differential
- RBC total lipid fatty acid profile

**Collection 3:** 60-to-90 minutes after a 0.75 g/kg protein lunch postprandial collection (after mealtime)

- quantitative urinary organic acids (anytime up to 4 hours after lunch)

For a copy of Dr. Richard Kelley's autism secondary to mitochondrial disease (AMD) physician guide (which includes this testing protocol) please visit: [http://www.epidemicanswers.org/wp-content/uploads/2010/05/Dr.-Richard-Kelly-Autism\\_Mitochondrial\\_Disease.pdf](http://www.epidemicanswers.org/wp-content/uploads/2010/05/Dr.-Richard-Kelly-Autism_Mitochondrial_Disease.pdf)

Will recently received his test results from Kennedy Krieger. After the testing was completed, Will was diagnosed mitochondrial complex I deficiency, a common finding in ASD children who have defects in oxidative phosphorylation. Will's report states, "Due to the mitochondrial abnormalities in Will's lab work, a diagnosis of complex I deficiency is appropriate and secure enough to dictate treatment and obviate the need for muscle biopsy to 'confirm' the diagnosis."

In addition, it was discovered that Will most likely has "a mitochondrial disorder that impairs gluconeogenesis or effects insulin regulation in a way that depresses his blood glucose level during fasting."

**Lab results suggestive of mitochondrial complex I deficiency:**

- high levels of glycine, alanine, and an especially high alanine to lysine ratio
- elevated lactate (in plasma and urine) and an increased AST/ALT ratio (liver function tests)
- abnormal acylcarnitine profile, suggestive of disruptions in fatty acid metabolism

Often, the biochemical findings in ASD children with overlapping defects of oxidative phosphorylation are quantitatively



Will, summer 2010

mild and individually would have questionable (or doubtful) significance. However, taken together, they present a biochemical profile consistent with a diagnosis of a mitochondrial disorder, and a positive clinical response to the supplements and medications used to treat mitochondrial disease further supports this diagnosis.

“ Often, the biochemical findings in ASD children with overlapping defects of oxidative phosphorylation are quantitatively mild and individually would have questionable (or doubtful) significance. However, taken together, they present a biochemical profile consistent with a diagnosis of a mitochondrial disorder, and a positive clinical response to the supplements and medications used to treat mitochondrial disease further supports this diagnosis. ”

**Current mitochondrial cocktail:**

The following is the mitochondrial cocktail that Will (31 pounds) is currently taking:

Medication/Supplement	Dose	Response
L-carnitine (prescription liquid, not tablets as it's better absorbed)	generic liquid Carnitor® called levo-carnitine  500 mg; 2 times daily	<ul style="list-style-type: none"> <li>● marked improvement in fine motor skills</li> <li>● improved oral muscle tone</li> <li>● better swallowing and chewing/less gagging after 8 week trial</li> <li>● improvement in energy level</li> <li>● gross motor gains</li> </ul>
Creatine monohydrate	Cytotine® by Solace Nutrition 2.5 ml; 2 times daily	<ul style="list-style-type: none"> <li>● improvement in expressive language after 2 weeks</li> </ul>
CoQ10	Tishcon Quinogels® 50 mg; 1 time daily	<ul style="list-style-type: none"> <li>● after long term use, cognitive gains</li> <li>● helped with recovery from anesthesia regression</li> </ul>
Riboflavin (B2)	Cyto B2® by Solace Nutrition 50 mg 2 times daily	
5 methyltetrahydrofolate	Prothera's Methylfolate® – 1000 mcg/day	
Additional antioxidants	vitamin E, 400 IU/day vitamin C, 250 mg/day	
Calcium	1000 mg/day	
Vitamin D	1000 IU/day	

“ Will had limited developmental progress until the mitochondrial cocktail was started. Prior to this, the family was frustrated that he was a “nonresponder” to most biomed interventions. ”

Will had limited developmental progress until the mitochondrial cocktail was started. Prior to this, the family was frustrated that he was a “nonresponder” to most biomed interventions. With the mito cocktail, the family has seen slow, steady progress across all developmental areas. Will has had a dramatic response to liquid levocarnitine. They saw a marked improvement in his energy levels and also saw significant improvements in fine and gross motor skills. The family realized the true benefits of levocarnitine in their son when it was removed for 3 days prior to the testing protocol at Kennedy Krieger. Will’s mom reported, “He went downhill fast. Each day he had less and less energy. On the day of the testing, he couldn’t get out of his stroller [he was so fatigued] and previously he was running around playing like a typical 3-year-old.”

Will also had a significant and

notable response to Cytotine® made by Solace Nutrition. Cytotine® is creatine monohydrate and is considered a medical food. It is being used by children and adults with mitochondrial disease and is dosed by weight. Will’s mom reports the following expressive language improvements on Cytotine®: “He had an increased desire to talk within 2 weeks of starting this supplement. He said ‘mama’ and ‘dada’ for the first time in 15 months (since his initial regression post MMR and other vaccinations) after being on Cytotine® for 3 weeks. His language continues to grow every day, and he is now able to ask for food items without grunting. He can say all his ABCs, 123s, shapes and colors. While we knew he knew these things before, he was unable to say them. Prior to this supplement, we would hear a word once and never hear it again. Now once we hear a word, it’s here to stay.”

When I asked Will’s mom if she was glad

she tried the mito supplements she replied, “YES!! The mito supplements have been the main source of Will’s improvement, especially Carnitor®. For other parents, if your child just ‘doesn’t feel well’ a lot, and you have no idea why, you must try a mito cocktail. This is especially true in nonverbal children with low energy levels who appear to not feel well, have feeding issues and low muscle tone. If that describes your child, a mito cocktail and testing for mito issues is a must.”

**Will’s current diagnosis is mitochondrial complex I deficiency.**

Due to the fact that Will has a history of poor anesthesia response resulting in neurological decline and severe fatigue, the family has also requested an “emergency protocol letter” regarding anesthesia, IV placement, and fever or infection management used for children with mitochondrial disease; during these times, these children require special care

to reduce metabolic stress. This emergency protocol letter, written and signed by Will's physician, will help them advocate for proper care of their child in the event of an emergency. It discusses the accepted management practices of children with mitochondrial disease during anesthesia, IV placement, fever or infection.

The following are links to anesthesia, IV placement, fever and infection protocols in children (and adults) with mitochondrial disease.

Anesthesia and Mitochondrial Cytopathies, at [www.umdf.org](http://www.umdf.org)  
[http://www.umdf.org/atf/cf/%7B858ACD34-ECC3-472A-8794-39B92E103561%7D/anesthesia\\_mitochondrial\\_cytopathies.pdf](http://www.umdf.org/atf/cf/%7B858ACD34-ECC3-472A-8794-39B92E103561%7D/anesthesia_mitochondrial_cytopathies.pdf)

Procedures or Surgery Requiring Sedation or Anesthesia, at [www.mitoaction.org](http://www.mitoaction.org)  
<http://www.mitoaction.org/files/protocol-general-surgery-eating-not-disrupted.pdf>

Fever or When Infection is Suspected, at [www.mitoaction.org](http://www.mitoaction.org)  
<http://www.mitoaction.org/files/protocol-fever-and-infection.pdf>

Information for Anesthesiologists and Surgeons for Operative and Preoperative Care of Patients with Mitochondrial Disease.

<http://www.epidemicanswers.org/wp-content/uploads/2010/05/Dr-Richard-Kellys-Mito-Anesthesia-document.pdf>

## PROFILE #2

**Child's name:** Aidan

**Current age of child:** 14 years old

**Age of ASD diagnosis:** 2 years old

**ASD label given to child:** PDD-NOS at age 2, currently labeled high functioning autism

**Coexisting diagnosis:** attention deficit disorder (ADD), mood disorder, generalized anxiety disorder, clinically diagnosed mitochondrial disease complex I (and possibly complex III)

**Prenatal complications:** none

**Post-natal problems:** took a long time to keep body temperature stable post birth

**Relevant family history:** only child, family history of diabetes, mood disorders, bipolar disorder, type 2 diabetes, Myelodysplastic Syndromes (also known as pre-leukemia), suspected mitochondrial disease on the maternal side, rheumatoid arthritis on the paternal side

“ Neuro-psych testing done 3 weeks after surgery revealed significant drop in all areas of functioning, raising a huge red flag for mitochondrial disease. ”

### Early history/First signs of

**developmental problems:** feeding issues, cried halfway through feeding (fatigue when nursing), reflux as an infant  
 Loss of language, began memorizing videos, no longer wanted to have books read to him, stopped understanding receptive language, excessive temper tantrums, had severe reactions to each set of vaccinations, causing increased irritability and long periods of sleeping

At 17 months old, the MMR, DTaP, HiB caused a high fever that lasted 3 weeks, high white blood cells, loss of skills started at 17 months old and continued until shortly after age 2

Severe diarrhea started at 20 months, lost all language by age 2.

At 13 years old, he suffered a sharp

regression following surgery and sedation using Propofol® and Ketamine®. Aidan was put under anesthesia for what was thought to be appendicitis, but it turned out to be low lobe pneumonia that was confirmed through a chest x-ray.

His symptoms post anesthesia included very delayed waking, low O2 levels, persistent fever for 4 days, and he did not wake up for most of that time. He lost 8 pounds as he could not eat and was vomiting bile. Cognitive and physical decline noted post anesthesia as well as severe mood worsening with panic attacks, depression, and severe auditory processing problems. Neuro-psych testing done 3 weeks after surgery revealed significant drop in all areas of functioning, raising a huge red flag for mitochondrial disease.



Aidan

# DOES THIS REMIND YOU OF YOUR CHILD?

## Gross motor development symptoms:

- met (and exceeded) early motor milestones, sat up at 4 months, crawled at 7 months, and walked at 12 months
- heat intolerance and exercise fatigue present at age 5, Aidan's family first began to strongly suspect mitochondrial disease at this time
- currently exhibits low tone, muscle weakness, exercise intolerance, motor incoordination and fatigue, issues make it difficult for Aidan to participate in regular school gym classes and to join in age-appropriate sports and social events
- high heat/temperatures currently increase his fatigue and exercise intolerance and too much physical activity at one time causes a "physical crash" (he's physically unable to move much at all post-exercise, his body just runs out of energy) and often results in him becoming very emotional
- During a recent viral illness, was unable to walk

## Fine motor symptoms:

- fine motor delay and exhibits upper trunk weakness. This symptom has been present since pre-school.
- a now has excellent keyboarding skills which help with the demands of school.

## Communication symptoms:

### Oral motor symptoms:

- fairly clear articulation, early development and currently

### Expressive language:

- nonverbal at age 2, slowly regained language with biomedical interventions and therapies

### Receptive language:

- severe auditory processing disorder starting at age 18 months old and worsened again post anesthesia exposure at 13 years old, has gotten substantially better with mitochondrial supplements

### Pragmatics: (social language use):

- aware of tone of voice and body language in others
- understands reciprocal nature of language
- has had retrieval and syntax issues, mito cocktail has been very helpful in these areas

## Cognitive development and problem solving:

- has many cognitive delays and scattered skills; it is very difficult to get an accurate picture of his cognitive levels because his skills fluctuate greatly, based on his

energy levels and his wellness/health on a given day

- continues to improve across all areas of academics
- ADD is a hindrance to learning

## Giftedness

- started to read at age 2, excellent memory for facts in areas of special interest

## Self help/daily living skills:

- Currently, he can self-dress, read, write, make himself a snack/sandwich, make a phone call and is potty trained

## Play skills:

- acts like a much younger child but enjoys studying animation techniques, planning his animation projects, and studying history

## Personal social skills symptoms:

- wants friends very much, but he is shy and is aware of his deficits, which often make him avoid socializing with age-appropriate peers
- enjoys playing with children a few years younger
- has always been empathetic, very emotionally connected and physically affectionate

## Sensory symptoms:

- a history of sound sensitivity and some occasional smell aversion/sensitivity

## Attention symptoms:

- attention deficit remains an issue unless he is involved in an area of special interest

## Feeding symptoms:

- exhibits feeding problems:

### Solids

- self-limits protein and craves mostly carbs and fat

### Liquids

- drinks a lot throughout the day and craves salty foods

## Allergy/food sensitivities/current diet:

- symptoms of food sensitivity to gluten include diarrhea and abdominal pain, casein and soy cause behavioral changes, including rage
- gluten free, casein free, soy free, only organic, non-GMO foods

## GI symptoms/ bowel symptoms:

- severe diarrhea began at 20 months and continued until 4 years of age; many food intolerances, allergies and GI/abdominal pain present as a young

child, diarrhea finally resolved following endoscopy where he received IV secretin

- severe constipation from age 5 until age 9, only resolved after Aidan started a colitis medication, Pentasa®
- gut is much improved but is still intolerant of gluten, casein, and soy

## Immune system symptoms:

- chronic ear infections from age 4 months old until age 5, got two sets of tubes and many courses of antibiotics, had no issues with anesthesia during those procedures.
- became ill every time he was exposed to other children, public play spaces, and other children at school
- misses 40 days of school per year (on average), due to illness (he appears to be sickly compared to other ASD children)
- currently troubled with reoccurring sinus infections

## Physical symptoms:

- small for his age 5'4" 110 pounds

## Current therapies and educational placement:

- historically, he received ABA at a specialized autism preschool (but progress was always hindered by chronic illness)
- from ages 9-11 he had a 1:1 aide at a school
- will be going into the 8th grade in the fall
- was placed in a nonpublic setting last year, with 30 hours of IEP services and will be attending school in a nonpublic school setting again next year

## Current challenges

- puberty (and anesthesia regression) brought mood issues that have proven tough to manage

## Aidan's red flag symptoms for mitochondrial involvement:

- exercise intolerance
- abnormal fatigue
- developmental regression after high fever triggered by MMR, DTaP and HiB at 17 months old
- developmental stagnation and regression following surgery and sedation using Propofol® and Ketamine®
- poor muscle tone, muscle weakness, motor incoordination
- difficulty handling hot/cold temperature, sometimes shiver when it's not cold
- unexplained GI motility issues; severe diarrhea, followed by severe constipation ongoing for years

**Biomedical interventions:**

Aidan has been doing biomed since age 2.5. During that time, he saw some positive benefits with the following biomedical interventions: yeast protocols, IV glutathione and IV secretin. He did not tolerate chelation, even at a very low dose of DMSA and transdermal DMPS. It actually worsened his symptoms, so it was stopped.

Biomedical interventions that were most helpful to Aidan were the mito cocktail, GI medications, diet restrictions, and antibiotics for the treatment of PANDAS.

**Testing:**

Initial metabolic screening labs for mitochondrial disease were completed by a neurologist when Aidan was 6 years old. At that time, the family was told that Aidan did not have supportive labs for mitochondrial disease, despite the family's suspicions.

Eight years after the initial testing and a striking anesthesia regression, the family revisited the idea that mitochondrial disease might in fact be the reason for Aidan's persistent fatigue, ASD symptoms, chronic illness, and regression after anesthesia. It was then that he was finally diagnosed with mitochondrial disease, 8 years after his initial metabolic workup.

A mitochondrial diagnosis finally makes sense of Aidan's symptoms across many different organ systems and his significant positive response to the mito cocktail, at age 14, is further evidence that he has an impairment in mitochondrial energy production.

**Lab results suggestive of mitochondrial complex I deficiency:**

- extremely elevated alanine/lysine ratio
- slightly elevated CPK
- abnormal acylcarnitine profile, suggestive of disruptions in fatty acid metabolism
- low free and total carnitine labs
- urine amino acids showing mild ketosis

Over the years, Aidan had many small benefits from biomed from those that were mainly mitochondrial support supplements aimed at increasing energy production at a cellular level and reducing oxidative stress. He had a dramatic response to liquid

<b>Current mitochondrial cocktail:</b>		
The following is the mitochondrial cocktail that Aidan (110 pounds) is currently taking:		
Medication/Supplement	Dose	Response
L-carnitine (prescription)	generic liquid Carnitor® called levocarnitine-  2000 mg/daily  (oral tabs caused GI irritability and adverse mood swings)	<ul style="list-style-type: none"> <li>● increased expressive language</li> <li>● increased energy</li> <li>● improved cognitive skills</li> <li>● improved focus</li> <li>● increased body language and use of slang</li> </ul>
creatine monohydrate	Not taking	
CoQ10	Tishcon Quinogels® (ubiquinol)- 200 mg/daily  (hyperactivity if given more than 200 mg daily)	<ul style="list-style-type: none"> <li>● increased energy</li> <li>● general feeling of well being</li> <li>● decreased complaints of heart racing</li> </ul>
Riboflavin (B2)	Cyto B2® by Solace Nutrition 50 mg 2 times daily	
Leucovorin Calcium® (folic acid medication)	5 mg/day given at bedtime	<ul style="list-style-type: none"> <li>● more present/seemed better</li> </ul>
Alpha Lipoic Acid (ALA)	200 mg/daily	<ul style="list-style-type: none"> <li>● steady blood sugar</li> <li>● increased expressive language</li> </ul>
Additional antioxidants-	vitamin E; 200 IU 2x/daily vitamin C; 1000 mg 3x/day	
Calcium	will begin soon	
Vitamin D	2000 IU/day	

levocarnitine. His energy levels increased and he had a significant improvement in expressive language, which included word-retrieval skills, and his auditory processing has also improved since starting this cocktail. Aidan's mother states, "My son used to get sick every couple of weeks before starting the cocktail. He complained not only about his physical fatigue but mental fatigue and said his words were stuck in his head." She continued, "I am glad we tried the mito supplements because my child looks so much better. He is able to speak and function better. Best of all, he is able to tell us he feels stronger in every way."

**Aidan's current diagnosis is classic mitochondrial ASD, complex I.** This family's treatment strategy now focuses

on increasing cellular energy production, reducing oxidative stress, and making sure that psychiatric medications and other medications do not inhibit energy production or oxidative phosphorylation, which is already an issue.

Aidan's mother states, "Knowing that he has mitochondrial disease explains many things in Aidan's history that did not make sense to us, and it gives us a solid foundation for every decision we make for him now. It is absolutely pivotal in helping ensure stable health and developmental progress moving forward. It impacts all the decisions we make for him, from medical decisions, to therapies, to daily management. As a family with a diagnosed child, we now need to focus on physician education, so his condition can be better

“Aidan’s mother states, “Knowing that he has mitochondrial disease explains many things in Aidan’s history that did not make sense to us, and it gives us a solid foundation for every decision we make for him now.”



• biomedical

“ Once we started the mito cocktail, his constipation improved so much that we were able to take him off of his laxative (magnesium) for the first time in over a year! It felt like a huge burden had been lifted because we had been battling constipation since he was about 3 months old. For the first time in his life, Sergio is able to have little back and forth conversations with us which has alleviated so much frustration because he is able to express his needs, likes, and dislikes. What stands out to me most is that Sergio is an active member of our family now, instead of a passive observer. ”

understood by all specialists and doctors, not just mitochondrial experts. We need his local physicians to see beyond his autistic symptoms to his underlying mitochondrial disease.”

**OTHER PROFILES**

Several other families who have children on the spectrum with suspected mitochondrial dysfunction are also trying the mito cocktail medications and supplements under the supervision of their biochemical physicians. Many children are having significant positive developmental gains on these medications and supplements aimed at increasing cellular energy production and reducing oxidative stress.

One family is Sergio’s. Sergio is currently 3 years old and was diagnosed with ASD at 18 months old. His family history is noteworthy for mood disorder, depression, ulcerative colitis, Alzheimer’s, Parkinson’s, and an extensive family history of type II diabetes for 3 generations. He has one older sister, Alexa, who is neurotypical; however, she has a history of poor anesthesia response.



He is currently on a gluten-, casein-, soy-, and corn-free diet that consists mainly of organic fruits, vegetables, and meats as well as non-GMO foods. He exhibits the following symptoms that may be due to mitochondrial disease: GI

The following is the mitochondrial cocktail that Sergio (26 pounds) is currently taking under the supervision of his biomedical physician:		
Medication/Supplement	Dose	Response
L-carnitine	prescription levocarnitine tablets- 330 mg; 3 times daily	● improvement in chronic constipation
Creatine monohydrate	Neotine®	Will begin soon
CoQ10	Tishcon MitoMedica H2Q® (ubiquinone) 100 mg; 1 time daily	● improved fatigue; energy level more consistent throughout the entire day
Riboflavin (B2)	Tishcon MitoMedica Riboflavin mini-capsule®- 100 mg/day	Will begin soon
Leucovorin Calcium® (folinic acid medication)	5 mg/day	● moved very quickly from one-word labeling to conversational speech; speech is clearer; sentences are more well formed and thought out
Additional antioxidants	vitamin E, 400 IU/day vitamin C, 500 mg/day	Will begin soon ● improvement in constipation
Calcium	170 mg/day	
Vitamin D	3000-5000 IU/day	during winter season; currently not taking

Above top: Sergio and his sister, Alexa. Next page: Sergio

dysmotility (chronic constipation), poor muscle tone, muscle weakness, motor incoordination, and intermittent fatigue.

Sergio has made significant developmental progress since he was first diagnosed at 18 months old. His mother states, "Although we had made some great strides with diet changes and homeopathic remedies, we still did not have a solution for his chronic constipation and speech delay, which had plagued him from the beginning. Once we started the mito cocktail, his constipation improved so much that we were able to take him off of his laxative (magnesium) for the first time in over a year! It felt like a huge burden had been lifted because we had been battling constipation since he was about 3 months old. For the first time in his life, Sergio is able to have little back and forth conversations with us which has alleviated so much frustration because he is able to express his needs, likes, and dislikes. What stands out to me most is that Sergio is an active member of our family now, instead of a passive

observer. We love having our little boy back and we are excited to see what additional developmental gains the next mito supplements will bring."

The mito cocktail these 3 children are currently taking has been chosen based on information gathered from treating more traditional mitochondrial disease over several decades. I have listed specific brands, not to endorse them, but to make families aware that certain brands (both supplements and medications alike) have been specifically chosen by physicians for their enhanced bioavailability which has significant benefits in a patient population that has difficulty metabolizing and

absorbing food, nutrients, and medications, in general.

For children with symptoms across 3 or more organ systems (low muscle



tone, marked motor impairment, fatigue, unexplained medical issues including; developmental regression from a "trigger" such as a fever, illness or anesthesia, a sudden episode of ataxia or unexplained GI symptoms) metabolic screening for mitochondrial disease is an appropriate avenue to pursue.

However, getting to a mitochondrial oxidative phosphorylation biochemical diagnosis is not easy, in many cases. That is why it is important to go to a doctor who is knowledgeable about mitochondrial disease. The Mitochondrial Medicine Society web site lists these physicians as knowledgeable about mitochondrial

disease: <http://www.mitosoc.org/blogs/diagnosis/providers>

Very recently, the American Academy of Pediatrics (AAP) put out a policy statement recommending that chromosomal microarray testing be done on children who are "globally developmentally delayed." This is a step in the right direction; however, it is my opinion that they should also complete metabolic screening labs for mitochondrial disease. A primary goal of families that have children diagnosed with mitochondrial disease is to help educate pediatricians and other specialists so they can complete screening labs on children with the "early warning signs" of mitochondrial disease so that metabolic support (in the form of a mito cocktail) can be started as early as possible to improve developmental and cognitive outcomes in these children.

At the 2010 UMDF conference, buccal swab and saliva testing for mitochondrial disease was discussed. This type of testing is new, painless, much easier and less invasive than other testing procedures and gaining in its accuracy. Watch for information on the development of this technology in the coming months/years.

Thank you to these wonderful families (and other families also trying the mito cocktail) for sharing your child's symptoms, treatments and responses to the mito cocktail and for giving so generously of your time, which is already in very high demand. I wish every child improved health.  
***"Do not go where the path may lead. Go instead where there is no path and leave a trail." Emerson***

**The following links are for Primary Care Physicians to help with initial testing, referrals, diagnosis and management of a patient with suspected Mitochondrial Disease.**

Mitochondrial and Metabolic Disorders- A Primary Care Physician's Guide

<http://biochemgen.ucsd.edu/mmdc/ep-toc.htm>

Mitochondrial Disease: A Practical Approach for Primary Care Physicians

<http://pediatrics.aappublications.org/cgi/content/full/120/6/1326>

A Modern Approach to the Treatment of Mitochondrial Disease  
<http://www.springerlink.com/content/d872354q672090mq/?p=fd9ba0ec0d2a4789b9d74c7daf763fa0&pi=2>

Clinicians Guide to the management of Mitochondrial Disease: A Manual for Primary Care Providers

<http://www.mitoaction.org/guide/table-contents>

## Disclaimer

Information is not provided as medical advice. Parents/patients should research all information given. Every person's physiology is unique. All information provided should be discussed with the patient's personal physician and/or autism or other specialist appropriate to the symptom(s) or body system(s) involved in their individual situation, who provides the patient with regular medical oversight, monitoring, and lab testing, and who keeps up-to-date on the most recent research and interventions. Beginning any significant biomedical or other interventions that may impact physiology or making changes to an established regimen should be discussed with the patient's physician in advance.

Supplements and brands mentioned in the preceding article do not indicate endorsement by this magazine, but rather are a relation by the author of what others have recommended or done.

## Autism and Mitochondrial Disease related articles

1. Weissman JR, Kelly RI, Bauman ML, Cohen BH, Murray KF, et al. (2008). Mitochondrial Disease in Autism Spectrum Disorder Patients: A Cohort Analysis. *PLoS ONE* 3(11):e3815. doi:10.1371/journal.pone.0003815. <http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=2584230>
2. Oliveira G, et al. (2005). Mitochondrial Dysfunction in Autism Spectrum Disorders: A Population-Based Study. *Developmental Medicine and Child Neurology*, 47:185-189. [http://www.ncbi.nlm.nih.gov/pubmed/15739723?ordinalpos=1&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed\\_ResultsPanel.Pubmed\\_RVBrief](http://www.ncbi.nlm.nih.gov/pubmed/15739723?ordinalpos=1&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_RVBrief)
3. Filipek PA, Juranek J, Nguyen MT, Cummings C, Gargus JJ. (2004). Relative Carnitine Deficiency in Autism. *Journal of Autism and Developmental Disorders*, Vol. 34, No. 6, 615-623. <http://www.ncbi.nlm.nih.gov/pubmed/15679182>
4. Winter SC, Szabo-Aczel S, Curry CJ, Hutchinson HT, Hogue R, Shug A. (1987). Plasma carnitine deficiency. Clinical observations in 51 pediatric patients. *Am J Dis Child*, Jun;141(6):660-5 <http://www.ncbi.nlm.nih.gov/pubmed/3578191>
5. Palmieri L, Persico AM. (2010). Mitochondrial dysfunction in Autism Spectrum Disorders: cause or effect? *Biochem Biophys Acta*. <http://www.ncbi.nlm.nih.gov/pubmed/20441769>
6. Rossignol DA, Bradstreet JJ. (2008). Evidence of Mitochondrial Dysfunction in Autism and Implications for Treatment. *American Journal of Biochemistry and Biotechnology*. 4(2):208-217 <http://www.scipub.org/fulltext/ajbb/ajbb42208-217.pdf>
7. Poling JS, Frye RE. (2009). Mitochondrial Disorders and Autism. *The Autism File*, issue 31. [www.autismfile.com](http://www.autismfile.com)
8. Poling JS, Frye RE, Shoffner J, Zimmerman AW. (2006). Developmental Regression and Mitochondrial Dysfunction in a Child with Autism. *J Child Neurol*. 21(2):170-172. <http://www.ncbi.nlm.nih.gov/pubmed/16566887>
9. Medscape News, (2008) Mitochondrial Dysfunction May Play a Role in Autistic Spectrum Disorders Etiology. American Academy of Neurology 60th Annual Meeting: Abstract IN1-1.004. Presented April 13, 2008. <http://www.medscape.com/viewarticle/573004>
10. Shoffner, J, Hyams L, Langley GN, et al. (2008). Oxidative Phosphorylation (OXPHOS) Defects in Children with Autistic Spectrum Disorders. Platform Session: Integrated Neuroscience: Autism. [http://www.abstracts2view.com/aan2008chicago/view.php?nu=AAN08L\\_IN1-1.004](http://www.abstracts2view.com/aan2008chicago/view.php?nu=AAN08L_IN1-1.004)
11. Shoffner, J, Hyams L, Langley GN, et al. (2009). Fever Plus Mitochondrial Disease Could Be Risk Factors for Autistic Regression. *J Child Neurol*. OnlineFirst 000(00)1-6. <http://www.ncbi.nlm.nih.gov/pubmed/19773461>
12. Dr. Marvin Natowicz, Genomic Medicine Institute Lerner Research Institute, The Cleveland Clinic, Cleveland, OH. <http://www.lerner.ccf.org/gmi/natowicz/>
13. Parikh S, Saneto R, Faulk MJ, Ansel I, Cohen BH, Haas, R. (2009). A Modern Approach to the Treatment of Mitochondrial Disease. *Current Treatment Options in Neurology* 11:414-430 <http://resources.metapress.com/pdf-preview.axd?code=d872354q672090mq&ize=largest>
14. Anselm I. (2009). Updates on Mitochondrial Disease Treatment Approaches, audio web cast, Mito Action website: [www.mitoaction.org](http://www.mitoaction.org) <http://www.mitoaction.org/blog/update-mitochondrial-disease-treatment-approaches>
15. Kendall F. (2008). The Dosing Debate: CoQ10 and Creatine in Mitochondrial Disorders, audio web cast, Mito Action website: [www.mitoaction.org](http://www.mitoaction.org) <http://www.mitoaction.org/blog/the-dosing-debate-coq10-and-creatine-mitochondrial-disorders>
16. Medical Foods for Mito. CoQ10, creatine monohydrate, cytochrome c. (2010). Audio webcast. Mito Action website: [www.mitoaction.org](http://www.mitoaction.org) <http://www.mitoaction.org/blog/medical-foods-mito>
17. Tarnopolsky MA. (2008). The Mitochondrial Cocktail: rationale for combined nutraceutical therapy in mitochondrial cytopathies. *Adv Drug Deliv Rev*. 60 (13-14):1561-7
18. Rodriguez MC, MacDonald JR, Mahoney DJ, Parise G, Beal MF, Tarnopolsky MA. (2007). Beneficial effects of creatine, CoQ10, and lipoic acid in mitochondrial disorders. *Muscle Nerve*. 35(2):235-42.
19. Siciliano G, Volpi L, Piazza S, Ricci G, Mancuso M, Murri L. (2007). Functional Diagnostics in Mitochondrial Diseases. *Biosci Rep*. 27(1-3):53-67.
20. Tarnopolsky MA, Raha S. (2005). Mitochondrial myopathies: diagnosis, exercise intolerance, and treatment options; *Med Sci Sports Exerc*. 37(12):2086-93.21. Rae C, Digney AL, McEwan SR, Bates TC. (2003) Oral Creatine monohydrate supplementation improves brain performance: a double-blind placebo controlled, cross-over study. *Proc Biol Sci*. 270 (1529):2147-50.
21. Davi A. (2010). Has Your Child with Autistic Symptoms Been Properly Screened for a Subset of Mitochondrial Disease Known as OXPHOS? ... Probably Not. *The Autism File*, issue 36 (pdf file available at [www.epidemicanswers.org](http://www.epidemicanswers.org)).
22. Leib S, Davi A. (2010). Mitochondrial Oxidative Phosphorylation (OXPHOS) Dysfunction: A newly emerging category of Autistic Spectrum Disorder, Information for Primary Care Providers. MitoAction website. <http://www.mitoaction.org/files/OXPHOS%20awareness%20for%20local%20pediatricians-%20updated%20Feb.%202010.pdf>

## Websites for further information

[www.mitosoc.org](http://www.mitosoc.org)  
[www.mitoaction.org](http://www.mitoaction.org)  
[www.umdf.org](http://www.umdf.org)

List of mitochondrial disease doctors/specialists (with hospital affiliation) can be found at: <http://www.mitosoc.org/blogs/diagnosis/providers>