



## Questions From 2015-2017

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Living with mitochondrial disease presents many twists and turns, and a maze of questions. UMDf is pleased to offer answers to some of those questions as taken from Ask the Mito Doc<sup>SM</sup> at [www.umdf.org](http://www.umdf.org).

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**Q:** My Great Plains **Labs report** shows that I have Mitochondria dysfunction. What do you think about that blood test?

**A:** The Great Plains Laboratory is not a traditional/commercial lab. Their interpretations do not align with how mitochondrial and metabolic physicians interpret metabolic test results. We do not know what to do with these results. For many patients with these abnormalities on the Great Plains testing - nothing concrete is seen on traditional tests. **Sumit Parikh, MD**

**Q: Inheritance question:** My mother in law has Chronic Progressive External Ophthalmoplegia(CPEO). No genetic testing was ever done for her two boys (one being my husband). Could my husband be a carrier and be asymptomatic? And -my main question -could he therefore pass it on to his offspring?

**A:**CPEO is often a sporadic disorder caused by mtDNA deletions. However, there are also autosomal dominant forms of the disease. You need to determine the genetic etiology for your mother-in-law and once that is known, you can address the possible recurrence risk for your husband and subsequently your children. **Fran D. Kendall, MD**

**Q:** My daughter has **Complex IV / Leigh's**. Is it normal for her to start losing her hair? She recently had blood work and nothing showed out of her norm so doctors are stunned because they are not familiar with the illness.

**A:** No. But, hair loss can be reflective of multiple other issues to include poor nutrition and general poor health. *Fran D. Kendall, MD*

**Q:** My currently 2.3 year old has **hypotonia**. We did genetic testing and received a result of: Variant of unknown significance in the MT-TV M.1647 TA (otherwise known as Leigh's). While she has lost a lot of her mobility, she is stable. She is currently on a mito cocktail of Levocarnitine, Leucovorin, Ubiquinol, Biotin and a 7.5 mg of Liquid B-Complex by Natures Answer. I am concerned that the B-Complex I am using contains PABA. I am considering switching her to a more natural product such as Buried Treasure Brand Liquid B Complete or the Tropical Oasis Liquid B Complex, but neither have been reviewed by the FDA and I don't know if these supplements are legitimate. I would appreciate your advice on a suitable solution and dosage for my little one. After reading many of the posts I have also seen creatine, alpha-lipoic acid, and magnesium 400- 800 mg and I'd like to know your thoughts about adding these supplements to the current cocktail. Thank you.

**A:** In regards to **supplement or vitamin therapies** for mitochondrial disease - we do not have evidence to show that any of these are effective. However, they are generally low risk and can sometimes make a difference in our patients - and so they are tried - sometimes one-at-a-time or sometimes as a combination or "cocktail." Depending on the physician you see - each one may have their own preferences. Alpha lipoic acid, creatine, CoQ10 as ubiquinol, carnitine, leucovorin and B-complex vitamins are some of the most popularly used supplements. L-Arginine is tried if there is a history or risk of strokes. The list of things that could be tried is long. The truth is that these may not help so it may not be worth continuing them endlessly. If there are no benefits noted after 3-6 months - it may be worth streamlining the vitamins given to a crucial 2 or 3. We hope that future research provides us with better guidance on which supplements may work better for specific patients. *Sumit Parikh, MD*

**Q:** My 6 year old daughter is diagnosed with **PDHD E1**. Her caregiver was just told she has mononucleosis. I know this can last for up to six weeks. What precautions should I take with her caring for my daughter? Do I need to suspend her until it has completely cleared, or for a shorter period of time? Is there extra risk for someone with mitochondrial disease when contracting mono? What should I watch out for?

**A:** Mononucleosis is spread from person to person by direct contact through saliva. As such, coming into close contact with somebody with the disease makes you at risk for contracting the infection. While good handwashing and use of gloves and mask would reduce the transmission possibility, to be completely safe, you may wish to find another caregiver until the infection has resolved. Although some patients with a host of mitochondrial diseases do have low immunoglobulin levels making them more prone to infection, the primary risk for infection contraction in mitochondrial disease patients is the metabolic instability that occurs when they get sick. I would recommend that you speak to your caregiver, and your local providers to determine your best option for managing the situation. *Fran D. Kendall, MD*

**Q:** I have epilepsy, cardiac, endocrine, muscular and gastric issues. My daughter has asthma gastric issues cvs severe abdominal and regular migraines we are both the second child the other people in our family have been fairly healthy we know she has a mito disease just not sure which one. Is it possible that we can be a swinging door so to speak where I got some symptoms and she have separate symptoms but basically have the same disease?

**A:** Yes, clinical symptoms can vary between mother and daughter who have the same mutation. This is most often seen in mtDNA related diseases. There is something that is called heteroplasmy where the percentage of mutation can vary from one child to the next or from mother to her offsprings. This is less so in disease caused by nuclear DNA mutations, but still symptoms can vary in generations depending on the which chromosomes the defect lies in, e.g. X-chromosome. Other nuclear mutations are most often not seen in one generation and then the next generation unless the other parent has the same mutation- pretty rare. I would suggest getting testing, as there are some pretty interesting medications being used in clinical trials for certain disease. **Russell Saneto, DO, PhD**

**Q:** I have had tests for mitochondrial disease and on my genome everything was positive and I thought that was the end of the concern of having a form of mitochondrial disease. A more in depth testing has come back showing evidence of cox deficient fibers and they are now checking for s specific mutation that my uncle was diagnosed with which I believe will take months before I know any more. Having cox deficient fibers showing in a test. Does that mean I have a mitochondrial condition? Or can it show up in perfectly healthy individuals as well? Thank you for your time.

**A:** Without knowing the specifics of your case (or your age) - I can try and provide some general information. I am presuming that you mean your "genome testing" came back normal when you say that it was "positive." I would be curious to know what DNA test you had - as there is no one mitochondrial DNA test and even if all available DNA testing in blood is completed - we are only able to confirm a mitochondrial disease diagnosis in patients where we are highly suspicious of one about half of the time. The muscle biopsy is often sent for a variety of tests - some where we look at the muscle under a microscope - but additional tests of how mitochondria are working (biochemical tests) and how the mitochondrial DNA looks (Genetic tests) are also routinely performed. You mention "COX-deficient fibers." In this situation - the mitochondria look different under the microscope. This finding can be seen in mitochondrial disease, as a part of normal aging and in other genetic and muscle/ nerve disorders - so it is a non-specific finding by itself. This piece of information would be used by your physician along with other test findings to help decide the likelihood of your having a primary mitochondrial disorder. **Sumit Parikh, MD**

**Q:** My daughter is 8 years old, and was diagnosed with CUD when she was about 3 months. She has been taking L-Carnitine since she was 4 months old. Lately she has had symptoms of extreme hunger.

She even goes so far as to sneak food in her room, eat it and hide the evidence. She has also been having stomach pain, and burps that smell like rotten eggs, and at times nausea, vomiting, and diarrhea. Do you think that any of these symptoms have to do with her CUD?

**A:** These are not symptoms of CUD per se. However, the odor and GI and some of the GI symptoms may be due to carnitine. Excess appetite could be a symptom of low blood sugar, but it would be unusual with good metabolic control. You should contact your metabolic physician for an appointment.

**Jerry Vockley, MD, PhD**

**Q:** What are the prospects for genetic therapy using CRISPR/Cas9 gene editing technology to treat mitochondrial disease? It seems that mitochondrial diseases that are the result of a single autosomal genetic mutation (e.g., those involving mitochondrial aminoacyl-tRNA synthetases) are well suited to CRISPR and that CRISPR technology is on the cusp of moving from the realm of academic research to the realm of practical treatment.

**A:** CRISPR/Cas9 (more generally known as gene editing) technology is indeed a promising prospect for correcting genetic disorders, including those causing mitochondrial disease. In fact, the UMDF is already sponsoring a research project to explore gene editing of the mitochondrial chromosome. While exciting, it must be kept in mind that any clinical use is still likely years away. **Jerry Vockley, MD, PhD**

**Q:** I am 48 and have **LHON plus**. I have been having horrible GI issues as well as many other issues for six months, still trying to get resolved. Fever, chills, weight loss, extreme abdominal and back pain, malnutrition, black stools, nausea, heartburn, and more. My palliative nurse found thrush yesterday. I'm worried about an infection throughout my entire body now but can't get my doctor to respond. Any advice I can print and pass on for urgently testing and treating an infection such as thrush that could be candida in the blood stream? Thank you.

**A:** A systemic fungal infection is very serious and can certainly be deadly so it is unlikely that this is causative for this patient's issues. She definitely needs to seek assistance from her local doctor.

**Fran D. Kendall, MD**

**Q:** Through **genetic testing using a sample of a muscle biopsy** taken 4 years prior, I have been told I have a large single 12kb mitochondrial deletion with a heteroplasmy level. My assumption is since my symptoms have progressed significantly since the muscle biopsy, my heteroplasmy level has increased over time. I am an adult whose main symptoms include muscle fatigue/weakness throughout body and muscle fasciculations which have progressed with time, light-headedness/mental fatigue as well as focus issues/blurry vision occasionally in one eye primarily. Exercise appears to lower my baseline (creating what seems to be more significant fatigue and weakness which never gets better). My questions are as follows: I was curious if any of the medicine being tested in current pharmaceutical trials (Stealth Biotherapeutics, Reata Pharmaceuticals, etc.) could be beneficial to someone who has such a large

single deletion (i.e., with having so much genetic material deleted in a percentage of mitochondria, is it still theoretically/physically possible to still somehow receive benefit from these medications being tested)? Are there any treatments recommended for adults with large single mito dna deletions? I am taking supplements (CoQ10 - 300mg morning and 300mg at night, Creatine 5 grams/day, Vitamin E 400 IU/day, Vitamin C 500 mg/day, Vitamin B2 100 mg/day, Vitamin D3 2000 IU/day, Alpha lipoic acid 300 mg morning and 300mg night) which don't seem to help. I have tried light exercise which seems to permanently lower my baseline after engaging, which I notice a few days later after engagement. Is muscle fasciculation, typical with those having large single deletion in mitochondria? Any research of large single mitochondrial dna deletions that I should follow? Any doctors in US that specialize in adult patients with large single deletion in mitochondria? Thanks very much. I would greatly appreciate all or any subset of these questions answered. Please let me know if you need any additional information.

**A:** I am sorry to hear about your medical condition. Currently, as far as I know, the only clinical trial looking at mitochondrial myopathy is the study by REATA. The Stealth study has closed but what we hear, they will be having a Phase III study on their medication opening soon. You can always check [clinicaltrials.gov](http://clinicaltrials.gov) and look for mitochondrial disease studies. Since your heteroplasmy is so low, likely the normal mtDNA present should be working and providing enough energy. There are no studies showing any vitamin therapy to be universally helpful (Cochran Report). Certainly, in any particular patient the vitamins may give some help. Muscle fasciculation is rare in mitochondrial disease and mostly only seen in young children with mtDNA depletion syndromes. Muscle fasciculations are often seen in other types of myopathies, especially ALS. But there are benign forms seen in viral illness. At your age, I would follow the mtDNA induced CPEO literature as single deletion disorders expressed during adult age ranges are usually related to CPEO. I do not know of any physician specializing in large mtDNA deletions." **Russell Saneto, DO, PhD**

**Q:** Recent labs (OAT) support that my 7 year old autistic son has at least some degree of mitochondrial dysfunction (high succinic, methylglutaric, and ketone and fatty acid oxidation). He responded well to Levocarnitine (990 mg twice per day), which also improved GI motility even though it continues to be a problem. He also takes 200 mg of ubiquinol per day and 1 gram of vitamin C twice per day with good results. He continues to struggle with hypotonia related issues: he has extreme difficulty pedaling a bike with training wheels, becomes exhausted after biking a few feet, unable to bike up slight inclines, unable to balance, etc. Per his doctor's recommendation, I recently began supplementing him with 1000 mg of kre-alkalyn twice per day. I have noticed some improvement with his speech with this and it also seems to have a calming effect. However, the improvements last for 2 hours maximum. I believe that he would benefit from a much higher dose eventually. My big concern is that the creatine supplementation has made him physically weaker and exhausted. Any idea of why this could be?

**A:** I am sorry to hear about your son. There are no universal treatments that are beneficial for all patients with mitochondrial disease. This is unfortunate and many of us are trying our best to uncover best treatments for this disorder. In a recent review article, in a very well respected journal The Cochrane Collaboration, a review of the literature was performed on creatine and its use in muscle dystrophies and metabolic myopathies (which would include mitochondrial myopathies). The authors

looked at all studies investigating the effects of creatine on muscle performance. There was no significant effect on metabolic myopathies. So, although in some patients a beneficial effect might be seen, overall there is no significant effect on the majority of patients. So, what you are noticing with your son sounds very much like there is little benefit and maybe even a loss of muscle performance. This would be congruent with what the review study in the Cochrane Collaboration reported. I am sorry.

**Russell Saneto, DO, PhD**

**Q:** My 6 year old son has been diagnosed with **respiratory chain enzyme complex IV deficiency**. We are in Dublin, Ireland and we are going to attend a neurologist soon. Is this particularly rare and if so should I push to be seen abroad (US/ UK) where bigger numbers are treated. I am a cancer nurse and can find very little info on this particular deficiency. Thank you.

**A:** I am sorry to hear about your son. It is somewhat difficult to answer your question just based on complex IV deficiency. As an isolated electron transport chain complex, complex IV is not the most common defect we see. However, if the genetic etiology of the complex IV defect is known, then it might be very helpful. For instance, if the deficiency is due to mutations in the SURF1 gene (this gene helps the assembly of complex IV), then this is one of the most common nuclear mutations causing Leigh syndrome. However, there are multiple other genes, both genes from the nucleus and mitochondrial DNA that can alter complex IV activity and give rise to disease. As a group, complex IV disorders are very heterogeneous in their clinical presentation and possible course. Knowing the possible genetic etiology of your son's complex IV might be helpful in knowing the next best steps. There are large mitochondrial centers in the UK, Newcastle and Cambridge come to mind. These larger Institutions may know of possible clinical trials that might benefit your son in your region, so I would keep a look out for possible treatment trials. In the US there is an internet site, <https://clinicaltrials.gov> that list the current trials in the US. Although many genes that are involved in complex IV are known, there are likely genes that remain unknown. I do hope for the best for your son. **Russell Saneto, DO, PhD**

**Q:** My 33 year old daughter abruptly **lost most of her vision** simultaneously in both eyes 5 years ago. MS was ruled out, NMO was feasible, and then she was found to have the **LHON 11778** mutation, heteroplasmy. However, her neurologist suggested NMO was the root cause because of small spinal lesions and neuro-symptoms though blood NMO antibody was negative. Three years ago she suddenly started having severe headaches and a year ago abruptly presented with episodic muscle knots and severe pain, urinary retention, muscle weakness, exercise intolerance, unexplained weight loss, tachycardia, neuropathy, and worsening vision. MS and NMO have been discarded and MRIs actually show fewer lesions. LHON plus is thought to be the cause. Pain level and incapacity can be severe, especially during 'episodes'. Tizanidine and Lyrica help some but she needs better management. Is it worth testing for other mito disorders? What should she be tested for in order to determine an appropriate mito cocktail? She's taking idebenone and Ubiquinol but hasn't seen a marked improvement. She's seen two mito docs but this is so rare both have not seen a case and are uncertain.

**A:** The core neurological features are extremely likely to be due to the LHON mutation. MS-like

features are more common in women likely because women have a higher propensity for auto-immunity. In fact, we have seen several people with true proven mitochondrial mutations (such as this case) with positive NMO antibodies and oligoclonal bands; consequently, it is likely that the mitochondrial disorder predisposes to auto-immunity (We know that mitochondrial damage can activate the inflammasome). I would not be looking for other genetic disorders for the LHON is the likely culprit and explains most of this. Pain medications are many and need to be carefully managed by a neurologist with expertise in pain or another pain specialist. Mitochondrial medications for LHON are coenzyme Q10 + alpha lipoic acid + vitamin E + creatine monohydrate - we also add VITALUX for LHON patients. I would also consider acute MS/LHON if there are sudden acute flare ups of the neurological deficits (not pain but urinary retention, stroke-like episodes, etc.) and imaging abnormalities that change. **Mark Tarnopolsky, MD, PhD, FRCP(C)**

**Q:** My niece (sister's daughter) was diagnosed by muscle biopsy with Mitochondrial Disease, she was 18 months at diagnosis and over a year behind developmentally. Since then she has improved remarkably and caught up to all milestones for her age. Other than being quite petite and less athletic than her sister, she has no symptoms. Her neurologist believes it is a mild to moderate case and my sister has decided not to pursue any more genetic testing which would reveal what specific type of Mito she has. I am 39 and after repeated miscarriages am pursuing **IVF** in the hopes of starting a family. My doctor feels strongly I should be tested for Mito before IVF. I went to see a genetic counselor, but they had little to offer since I do not know what type my niece has. I scheduled an appointment at Stanford some time ago to investigate Mito, but unfortunately the wait is quite long and my appointment is not until the end of the year. I do not want to hold up IVF any longer due to my advancing age (it took 4 months just to get the IVF process started), but I am at a loss for what to do next. My questions are 1) what are the chances that I am a carrier? 2) What type of testing would you recommend I do, and can my fertility doctor order these labs? 3) If I do turn out to be a carrier, what are my options during IVF to minimize risk?

**A:** Based on the information you provided, it is possible that your niece does not have a mitochondrial disorder or has a reversible form that can sometimes occur. Without knowing what caused her issues at a genetic level - there is no testing that would be recommended for you - especially if you are otherwise well and asymptomatic. Without knowing the genetic cause of her disorder - we cannot offer specific information as to whether you are a carrier. Meeting with a genetic counselor could help go over some of this information in more detail and they may be able to offer you a little more.

**Sumit Parikh, MD**

**Q:** Here is the link from Michael J. Fox Foundation. Is there a link between CVS with Mito? Mito problems...all together? My daughter has CVS with possible Mito. (Our ins. wouldn't pay for test). My youngest daughter has Hypothyroidism, and I have Parkinson with CVS characteristic. My mom (still living) has Parkinson with the same characteristic. Are they all connected?

**A:** At one time it was felt that CVS was a definite mitochondrial disease; however, in most cases there is at most a higher risk for CVS amongst certain types of mitochondrial DNA variants. Given the strong

family history it would be worth getting the mom with PD and CVS tested with a muscle biopsy and mtDNA sequencing just to make sure that there is no rare mtDNA variant counting for this cluster of medical issues. **Mark Tarnopolsky, MD, PhD, FRCP(C)**

**Q:** It is suspected that I have Mitochondrial Disease and was looking into **the mtSEEK and nucSEEK** testing, however, I was told that these tests are 50% likely to find something that will change management and improve care. Are there tests besides the mtSEEK and nucSEEK that provide more definitive answers for Mitochondrial Disease?

**A:** For suspected mitochondrial disease, most of the commercially available genetic tests have at best a 50% yield (likely to find something). It is much less likely that a positive gene test will also change management and improve care. We do not have specific therapies based on gene mutation for the majority of the mitochondrial disorders; gene therapy is just now in clinical trials for disorders such as LHON. **Sumit Parikh, MD**

**Q:** I have a levo **carnitine deficiency along with B12 and CoQ10 deficiency** since Christmas of 2015. I have had spontaneous compartment syndrome in both arms 5 times to the point I almost lost my arms. is there a correlation between the two?

**A:** Carnitine deficiency, if secondary to a fatty acid oxidation disorder, could lead to increased muscle breakdown and sometimes compartment syndrome. Carnitine deficiency can also occur due to nutritional issues. In that case it is less likely to be a cause of your symptoms. It would be worth determining why you have carnitine deficiency. Vitamin B12 deficiency and CoQ10 deficiencies, if not dietary, can also be due to select metabolic diseases, though they are less likely to cause muscle breakdown or compartment syndrome. **Sumit Parikh, MD**

**Q:** My granddaughter has **Leigh's Disease**. She had no breathing problems until she had surgery for a g tube. During that surgery she was administered propofol and ringers lactate; of which, I have read are absolute no no's. Since then, she has not been able to breathe on her own. After surgery she coded and had metabolic acidosis. I am convinced that all of this is connected. Please let me know your thoughts.

**A:** I am sorry to hear about your granddaughter. Leigh syndrome is complex and very difficult to treat due to multiple reasons, one of which is the many different ways to get the disease. There are likely over 70 different genes that can cause Leigh syndrome, which suggests that each patient can be somewhat different from each other depending on the reason for the disease. This also means that likely the response to various medications can be different as well. Before we understood that Propofol could impact mitochondrial function, we used it for muscle biopsies and other procedures and there were only

some patients with mitochondrial disease to have problems post anesthesia. Still, in parts of the country and world, Propofol is still used for sedation in patients with mitochondrial disease. Whether using it to place a G-tube caused your granddaughters problems after surgery is difficult to know without knowing more about the etiology of the disease and other clinical factors at the time of the surgery. In addition, the stress of surgery could have also placed your granddaughter at risk for worsening disease, which is really hard to factor in how much of this stressor might have played into the worsening of her disease. Unfortunately, there is no way to tell you for sure how much using Propofol and Lactated Ringers contributed to her worsening. I am sorry that your granddaughter has had such an outcome.

**Russell Saneto, DO, PhD**

**Q:** Could you please confirm that “oxidative myopathy” falls under a **mitochondrial myopathy**? A 61 year old family member, with a history of fibromyalgia, RA, migraines, mitral valve prolapse (with MV repair and replacement 11 years apart) and cold- induced asthma recently had a right heart catheterization/ stress test to assess for pulmonary hypertension. The diagnosis was oxidative myopathy. Who specializes in this disease...Neuromuscular? Rheumatology? Endocrinology?

**A:** I don't know what this term means, but it certainly doesn't diagnose mitochondrial disease. I think it's likely to be a non-specific term that reflects muscle deconditioning. Sounds like a cardiologist is the first stop. If that's who did the testing in the first place, then I'd try a neurologist who specializes in neuromuscular disorders. **Jerry Vockley, M.D., Ph.D.**

**Q:** I have a 16 year old son with **mitochondrial myopathy**. He is diagnosed with hyper nasality, his palate is not functioning properly, and he is becoming very difficult to understand and always sounds nasal. Doctor is recommending surgery to build up his palate. He uses a bipap at night. I am not finding any information on successes or failures with this type of surgery. Does anybody know if the results from this surgery are long lasting or only temporary solution? This surgeon has only done about 10 of this type of surgery and none on patient with mitochondrial myopathy. Any insights would be most welcome, as I am not hugely in favor of surgery, but my son is desperate for some relief. Thanks

**A:** The response to surgery is more likely dependent on the surgeon's experience, how your son has tolerated anesthesia and surgery in the past and the type of mitochondrial disease. Mitochondrial myopathy is not a diagnosis - is the genetic cause known? This information may help us better understand what the response to surgery might be. You may also want to consider a 2nd opinion from another surgeon to see if you receive a similar recommendation. **Sumit Parikh, MD**

**Q:** Hello, I have been really sick for about 16 months now and it has finally been narrowed down to **autonomic neuropathy** and some clotting disorder. Both believed to be autoimmune in nature but not definitive (I am currently going through chemotherapy to suppress my immune system). I recently had my COQ10 levels checked and they were rather low (.30 mg/L) is this indicative of a mitochondrial disease causing my issues or can low COQ10 occur due to other factors not related to mitochondrial disease? Thank you very very much for your time! Sincerely.

**A:** I am sorry to hear about your clinical problems. Your question about COQ10 levels. Can you tell us how these were checked- serum levels or intracellular leukocyte levels. There is some difference of opinion about what CoQ10 levels might reflect. Here is my view: If levels were taken from the former then likely just nutritional intake and likely not related to a CoQ10 synthesis problem. If the CoQ10 were related to an intracellular leukocyte level, then this might be related to a CoQ10 synthesis problem, and therefore the possibility of a mitochondrial disorder related to the CoQ10 level. One needs to investigate this latter finding in more depth to really prove it is a primary CoQ10 synthesis disorder. For instance, gene testing or muscle levels of CoQ10. I think that supplementation with CoQ10 might be used in either case and would advise to talk with your mitochondrial specialist.

**Russ Saneto, DO, PhD**

**Q:** My son is 13 and disabled. In 2013, we received his diagnosis of **Phelan McDermid Syndrome** via Whole Exome Sequencing. He has a mutation on his SHANK3 gene. During his sequencing, it was also discovered that he has 2 mutations on 2 Mito DNA genes. He is Homoplasmic for a m.644 A>G variant of unknown significance in the MT-TF gene. He is also heteroplasmic for a m.3198 A>T variant of unknown significance in the MT-RNR2 gene. The heteroplasmy is approximately 23%. Due to finding his other mutation on his SHANK3 gene, we stopped investigating if the Mito mutations were part of his problems/disability. Currently, he is experiencing extreme fatigue that has become debilitating. Fatigue is not a symptom of his other syndrome and I'm wondering how I can determine if his mito mutations are causing additional problems for him (or are benign) and what/how possibly to help him with his fatigue. Thank you for your assistance.

**A:** Sorry to hear about your son's fatigue. When we see such a symptom, we would want to ensure that treatable sources of fatigue such as iron or vitamin D deficiency, thyroid dysfunction and sleep disorders including obstructive sleep apnea are evaluated for. In regards to the mitochondrial DNA variants, you should meet with a genetic counselor to discuss these and consider maternal testing. If the homoplasmic variant is present in you, it is more likely to be benign. The heteroplasmic variant may require further investigation and study, especially if only found in Samuel. I would recommend following up on these. Sumit Parikh, MD

**Q:** I present with multiple symptoms of Mitochondrial Disease. EMG and muscle biopsy indicate the disease may be present. A genetic blood test was done, 2 of them specific for the eyes because that was the first real problem I was having, sporadic vision issues...my neurologist said the test came back negative. Could I still have this condition? Main complaints muscle soreness and very weak after 4-5 hours of being awake. My doctor said nothing she can do for me. Your thoughts please and thanks. I just want some direction so I can feel better.

**A:** Sorry to hear about your health problems. From the limited information that you've provided, you may have mitochondrial disease or dysfunction but you may not have it either since no definitive diagnosis was made. The most reliable diagnosis would be by DNA testing because it's the most specific

and the least one to be affected by artifact (like muscle biopsy) or biochemical markers and symptoms which are usually nonspecific, i.e. they can be seen in other diseases, not necessarily mitochondrial. Or you could have mitochondrial dysfunction secondary to something else. If you have time and desire, read my latest article (attached) which is a bit detailed but you'll get an idea. You probably had a limited genetic testing (mito DNA and/or nuclear mito genes). What you've described as 2 variants "specific for eyes" may be benign and I'd need to see which specific ones but they likely don't explain everything so unlikely to be definitive diagnosis. You can have Whole Exome Sequencing (WES) which tests the entire DNA (20,000 genes) which could give you an answer (see the booklet giving a good description of this test). In my practice, autoimmune diseases can present with mito symptoms, so see a rheumatologist. Another problem could be food allergies which you may not be aware of so see an allergist. You should check your blood sugar when you feel weak and plasma cortisol because some people may have adrenal insufficiency. You probably had your thyroid checked already. You can try ubiquinol for energy at this link (best brand for the best price): <http://www.amazon.com/ActiveQ-Softgels-Ubiquinolantioxidant-Coenzyme/dp/B00E00618C> - take 1 gel twice a day, if you don't feel any benefit, go up to 3 a day and even 4. There are many other vitamins to choose from as my paper describes. You should ensure that you have a regular caloric intake with avoidance of fasting - 3 major meals a day (don't skip breakfast, clichés like it's most the important meal of the day are usually accurate) and healthy snacks in between so that you don't go beyond 3 hours of fasting. I've attached the list of healthy snacks (good for both kids and adults). Try organic cornstarch before bedtime - 1-2 tbs. in water or soft snack like yogurt. This would allow you to get energy from a complex carbohydrate at night (which slowly releases glucose which gives you ATP) when you typically fast and undergo catabolism which is better to stay away from whether you have mito or not. **Dmitriy M. Niyazov, M.D.**

**Q:** Are **sulfonylureas** safe to use with complex I and complex III deficiency mito? My hgb A1c is 5.8 and my average blood sugar level is 99. I still get hypoglycemic. I have a new doctor in the mix and she wants me to take one of these and I feel uncomfortable about this as I feel my sugar is controlled.

**A:** In general sulfonylureas are not contraindicated in mitochondrial disease. Some mitochondrial patients have had trouble tolerating Metformin, which is in a different class of diabetes drugs. In regards to whether or not you need this medicine for your diabetes, I would have to defer to an endocrinologist. You may want to ask her to explain her reasoning as to why she wants you to try this medicine if your numbers are as good as you noted. - **Sumit Parikh, M.D.**

**Q:** Are there any laboratories in the United States that can do pre-implantation genetic diagnosis for **maternally inherited Leigh's syndrome** if I do invitro fertilization??? If so, how do I contact them??? I've already lost my baby to this disease. Please help me.

**A:** Pre-implantation diagnosis is available for known autosomal recessive and autosomal dominant genetic mutations. However, because of problems with heteroplasmy in maternally inherited mutations, evaluating laboratories are unable to determine with a high degree of accuracy whether or not the cells tested for the presence of a maternally inherited mutation are reflective of the overall status of mutation load in the fetus. More simply stated, the laboratories are not sure if the cells of the fetus evaluated accurately reflect the status of the new baby meaning is it affected or not? As such, I am unaware of any preimplantation diagnostic centers that will screen for maternally inherited mtDNA mutations.- Fran D. Kendall, MD

**Q:** My maternal 1st cousin (**Complex IV Mito** with Limb Girdle Dystrophy per exome sequencing) and I were just diagnosed in March 2013 after a lifetime of symptoms. What do you think are the chances of gene or stem cell therapy for me in my lifetime?

**A:** I think the chances of seeing gene or stem cell therapy in our lifetime is extremely high. There are already several clinical trials dealing with gene therapy, including targeting diseased mitochondrial DNA by several researchers at the U of Miami <http://med.miami.edu/news/clinical-trial-uses-gene-therapy-to-target-mutations-in-mitochondria> . And work by Carlos Moraes, Univ of Miami <http://biomed.miami.edu/?p=493&pid=309&m=facultyph&mid=2&item=128> . Also, there are active trials in the UK with mitochondrial replacement in embryos, termed three parent babies. Of course, all gene therapy techniques are going to be met with skepticism and must pass various ethical hurdles to be fully engaged. One of the more promising and wide spectrum gene therapies involves a newly discovered/invented technique called CRISPR, which was first described only two years ago. This involves a highly efficient and rapid inactivation and replacement of a target disease gene with a functional one. For more information, please see Wikipedia or read its potential use in gene therapy in the December 2014 issue of Scientific American, pp 42-46. **William Copeland, PhD**

**Q:** My daughter was diagnosed with **multi-complex mitochondrial disease**. They called it multi-complex because all of her super complexes in her muscle biopsy were abnormal as well as complex 1,3, and 5. She has been having constipation issues. She is prone to dehydration even while being on a 16 hour continuous feed. My question is: Her GI doctor has placed her on mineral oil and on Senna because of constipation. Is it safe to use this with her history of dehydration? If she starts having complications of diarrhea from these meds I am afraid she will get dehydrated. I don't want to go against the GI doctor but I want to get an opinion.

**A:** In general, mineral oil and Senna are relatively mild treatments. Because constipation can be so difficult to treat, it seems reasonable to try these laxatives, and taper back if there is any indication of diarrhea. Of course, monitoring your daughter closely for dehydration sounds like a good idea too given her history. - **Greg Enns, MD, ChB**