Welcome to MitoAction

Dear Mito Warrior,

As you open this information kit for mitochondrial disease, or "Mito," you likely have mixed emotions: Fear of the unknown. Anger at the diagnosis. Relief that you finally have some answers. Frustrated that you may still be waiting for a diagnosis. Overwhelmed with trying to process so much new information as you learn all that you can about mitochondrial disease. No matter where you stand, MitoAction is here for you and your family as you embark on this journey.

You are not alone!

For almost 20 years, MitoAction has served the mitochondrial disease community and has been a partner to those facing the daily challenges of this rare disease. We want you to know that we are here for you every step of the way. We will continue to work tirelessly to offer meaningful resources and support. We will be your voice to help us get closer to the approval of treatments, therapies, and, ultimately a cure.

This kit is the first step in gathering information vital to living your best life with mitochondrial disease and outlines our programs and resources available to you.

- Introduction to the MitoAction team
- Mitochondrial disease FAQs
- Options for support and services
- Information about clinical trials
- Diagnosis and treatment
- How you can Join the Cause

It is our wish that the materials in this kit provide a starting point to help you prioritize which questions to ask, and opens the doors for you to the MitoAction community so we can walk and learn together.

Know that we are here to support you in any way we possibly can, and encourage you to reach out to the MitoAction team whenever you need us!

Kira Mann

SUPPORT • EDUCATE • ADVOCATE

About MitoAction

MitoAction became a reality in 2005 when a group of families affected by mitochondrial disease became empowered to make a positive impact on the larger Mito community. Originally formed as the Mitochondrial Disease Action Committee, MitoAction evolved from a small New England support group to a dynamic, active service organization that helps thousands of patients and families across the United States and the world. Despite the growth of the organization, our goal remains the same: to make a measurable impact in the lives of those who are affected by mitochondrial disease through support, education, advocacy, and the advancement of research.

Since our inception, MitoAction has been a leading resource for the mito community to put their ideas into ACTION. Moms, dads, patients, therapists, physicians, nurses, teachers, researchers – even children – can get involved with MitoAction and make a difference. We believe that by working together on projects that provide support, advocacy, and education, we are simultaneously fulfilling the tremendous needs faced by families living with mito. We are committed to expanding awareness of this rare disease and helping others understand the challenges the mito community faces daily.

Our Mission

MitoAction is a non-profit organization dedicated to improving the quality of life for children, adults, and families living with mitochondrial disease through support, education, outreach, advocacy, clinical research initiatives, and by granting wishes for children affected by mitochondrial disease.

We accomplish this mission through our comprehensive offerings, which include educational materials, live patient events, local and national advocacy efforts, partnerships with the clinical community, and tools to help families manage the care of their loved ones on a daily basis. Examples include:

- The **MyMito platform** transforms how families manage the care of their loved ones and communicate with their entire medical team.
- **Weekly support calls** and our **Mito411** hotline provide participants with a safe and supportive environment to share their experiences, ask questions and connect with others facing the same challenges with mito.
- The **Matthew Harty Camper Fund** sends children with mitochondrial disease to summer camp and grants college scholarships.
- An updated **website** with expanded educational resources.
- Live **Patient Educational Forums and Monthly Expert Series** allow families to learn from leading mito experts and network with others on a similar journey.
- Exciting **MitoPlaydates** allow children to engage and play creatively with other children.
- **MitoSocials** provide opportunities for families to connect with others in their local community.
- **Dalia's Wish** offers once-in-a-lifetime wish trips to families affected by mitochondrial disease... and more!

The programs and services provided by MitoAction continue to be a lifeline for families impacted by mitochondrial disease. Families know that with MitoAction, they will never be alone on this challenging journey.

Meet the Staff

Kira Mann, CEO

Kira serves as CEO of MitoAction and champions the growth of the programs and services offered by MitoAction. Her priority is to ensure that each and every person affected by mitochondrial disease knows they are not alone and that the MitoAction team will be here every step of their journey. Kira is committed to stewarding key funding opportunities, strengthening the organization's business development and governance and working with the community to increase MitoAction's national impact and presence in the areas of awareness, education and advocacy. "I am honored to lead this incredible team who works tirelessly each and every day on behalf of the amazing community we serve. I love hearing from our families, and I welcome you to reach out, share your story and help ensure that MitoAction is doing everything we can to provide the support and services that are most meaningful to you."

Email Kira at kira@mitoaction.org

Stephanie Harry, Patient Support Coordinator

Stephanie's son was diagnosed in 2008 with LCHAD deficiency. She spent her son's early years educating herself through research, journal articles, work groups, and clinicians. She worked alongside her son's dietitian to publish a children's book called "My Special Body" geared toward educating young children with LC-FAODs. She is passionate about education, mentorship, and advocacy. In 2022 Stephanie joined the MitoAction team to support the greater mitochondrial community. "I am so excited to be a part of the MitoAction team! My goal is to always create a safe inquisitive space where people feel loved, listened to and have continued access to meaningful resources. I look forward to connecting with each family and patient, and feel honored to walk this journey with you!"

Email Stephanie at sharry@mitoaction.org

Soozi Scheller, Patient Support Coordinator

Since 2019, Soozi has been supporting families with MitoAction. She originally connected with MitoAction in 2012 when she started having pronounced mito symptoms and called Mito 411 for help.

Soozi is a graduate of UC Berkeley in Conservation and Resource Studies. First a botanist, then a special education teacher, Soozi earned a master's to better support children with disabilities. In 2021, Soozi completed her Biotechnology/Ethics M.T.S. degree at John Paul II Institute in Washington, D.C. She specializes and is published in mother-child health incorporating breakthroughs in understanding the woman's cycle that allow for better diagnosis and treatment in women's health. She is a Creighton Model Fertility Care Practitioner intern and continues her graduate studies at Catholic University of America. Soozi is the mother of 3. Service dogs have also played a positive role in her family "I'm honored to be able to support the families in this community and ensure others can benefit for my experiences as a patient and mom."

Email Soozi at soozi@mitoaction.org

Hilary Romkey, Director of Programs & Events

Hilary serves as the Director of Programs and Special Events for MitoAction. Hilary strives to bring an innovative approach to programming and to bring an enthusiastic energy to the team. She has been in the rare disease world for the last eight years, and prior to that worked for a large hospital system foundation assisting with special events and planned giving.

"I'm passionate about truly connecting with people and I'm excited to learn more about this disease and the individuals affected by it. I look forward to bringing a fresh approach to our programs and serving this inspirational community!"

Email Hilary at hilary@mitoaction.org

Jeannie Freeman, Finance & Operations Manager

After serving as a volunteer for several months, Jeannie officially joined the MitoAction team in January 2018. Although she had never heard of mitochondrial disease until she started working for MitoAction, Jeannie has dedicated herself to learning about this rare disease so she can help MitoAction continue to expand the ways in which we serve the mitochondrial disease community. "I couldn't be happier to be a part of the MitoAction team! truly love all that we do and feel so
fortunate to be a part of something that touches the lives of so many people."

Email Jeannie at jeannie@mitoaction.org

Jenevieve Woods, Communications Intern

Jenevieve, also known as "Peach" joined MitoAction in 2019. She was diagnosed with mitochondrial neuropathy ATP deletion, but despite the challenges she has faced, she continues to inspire the community through her Positive Peach Packages. Jenevieve is also a published author, writing 3 books sharing her journey with a rare metabolic disorder. Her books, *Peach: An Exceptional Teen's Inspiring Journey for Universal Acceptance; Peach: Celebrating Life in the Shadow of Death and My Poems are Yours: The Poetic Soliloquies of Hope and Courage*, are available on Amazon.

In 2015 Jenevieve was diagnosed with mitochondrial disease but that wasn't going to stand in her way. In 2020, she graduated with a degree in psychology and minor in professional writing from La Roche University.

Jenevieve lives everyday to its fullest in Pittsburgh, with her four dogs. "It is an honor to share my journey with the mito community and uplift and provide positivity to others who need to know they are not alone."

Email Jenevieve at jenevieve@mitoaction.org

Join the Cause

MitoAction offers many ways for you to get involved and offer your time and talent to make a difference for the mitochondrial disease community. We hope you find a way that is most meaningful to you to join the cause!

Energy Walk

MitoAction Energy Walks are held in September during Mitochondrial Disease Awareness Week and raise both awareness about mitochondrial disease and funds that allow MitoAction to continue to support the mito community on a daily basis. Energy Walks provide hope, friendship, and support for the community.

There are so many ways to get involved! Host a walk in your local community. Create a team or join one. Walk or run in-person or virtually. Volunteer your time on the day of a walk, or help us prepare by spreading the word.

"There are no words to describe what it feels like to be a patient on that day," said Sheridan Johnston, captain of the Mito "Maineiacs" team. "There's some sort of freedom on that day ... being around people like me. There's a camaraderie that's instantly felt. We build each other up."

To learn more or to host an Energy Walk in your local community, email info@mitoaction.org or visit www.mitoaction.org/energywalk.

Sandra K. Russell Derby Day Benefit for Mito

The Sandra K. Russell Derby Day Benefit for Mito is New England's most exciting Kentucky Derby party. Founded after the passing of a MitoAction Board Member's wife, this high-energy fundraiser supports all of the programs and resources that MitoAction offers for free to the mitochondrial disease community, including sending mito kids to summer camp, offering scholarships for students with mitochondrial disease to attend college and granting once-in-a-lifetime wish trips to families.

So, ladies grab your most fabulous hat, gentlemen tighten up your flashy bow tie, and join us for an incredible evening of fun and excitement while supporting our mito community.

To learn more visit www.mitoaction.org/derbyday.

Host Your Own Awareness or Fundraising Event

Capes for Cal 5K. Cinco de Mito. Cooper's Race. Gareth's Get Up & Go. These are events that people just like you have hosted to raise awareness about mito and funds for MitoAction.

Our Events Guide will walk you through hosting your own event. But, know that the MitoAction team will help you every step of the way, including: setting up registration and fundraising pages, finding a venue, creating flyers, and ordering materials for your event.

Hosting a Restaurant Night is a great way to raise awareness, eat, and have fun. Many restaurants offer "charity nights" in which they will donate a percentage of sales on a specific date to your charity!

For a list of fundraising and awareness ideas or a copy of our Events Guide, email info@mitoaction.org. Or, you can come up with your own ideas. We are open to your suggestions and would love to brainstorm with you.

For more information or to request a copy of the Events Guide, email info@mitoaction.org.

Host A MitoPlaydate or MitoSocial

MitoAction wants to help our families across the country connect with one another to expand the community of support. MitoPlaydates and MitoSocials are low-key gatherings that allow Mito families to meet each other, share stories, and give and receive support in their local community.

MitoPlaydates provide children with Mito an opportunity to connect with other kids, to play creatively, and just have fun! We have an extensive list of adaptive playgrounds across the U.S. that make great sites for these events.

MitoAction will help throughout the entire process and offers a stipend to cover the cost of snacks and activities. If you are interested in hosting a MitoPlaydate or a MitoSocial, email info@mitoaction.org.

For more information on any of the events or to host your own, email info@mitoaction.org.

MitoChampions

Would you like to be a voice for the broader mito community? Help with awareness events and support in your area? Provide feedback to MitoAction to help us serve the mito community to the best of our ability? Then our MitoChampions program IS for you!

Some of the ways to engage as a MitoChampion include:

- One-on-one support
- Raising Awareness
- Fundraising
- Legislative Advocacy
- Education
- Focus Groups
- Hosting Local Events

MitoChampions are pivotal members of our volunteer program and direct contributors to upholding our mission.

To request more information or to become a MitoChampion, visit www.mitoaction.org/mitochampions.

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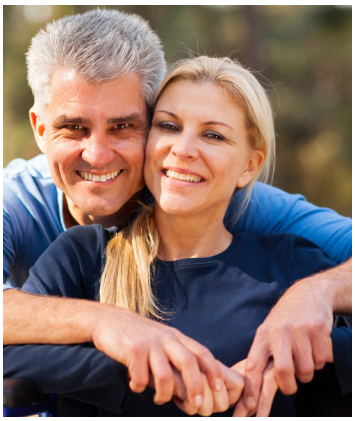
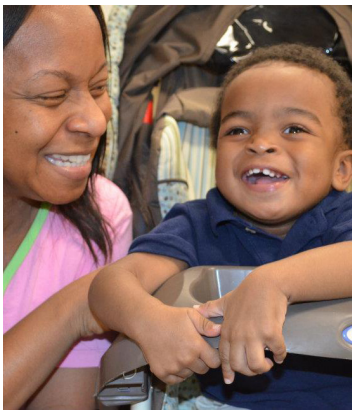
Programs & Resources





Mito411
Mito411 is designed to offer hands-on, live support for families by families. Callers will connect with a volunteer who can relate to the journey of diagnosis and the challenges of living with mitochondrial disease. Volunteers are adults with mitochondrial disease, parents of children with mito, and caregivers. This service is not intended to provide medical advice.

Call us at 1-888-MITO-411 (648-6411) or email mito411@mitoaction.org.

MyMito
MyMito is a comprehensive platform that will support you in managing your day-to-day with mitochondrial disease. Track symptoms, appointments, medications, physical activity, vitals - anything relevant to your care management. Take control of your care journey while providing critical data about living with mitochondrial disease to help clinicians and researchers develop treatment options and a cure!

To sign up visit www.mitoaction.org/mymito.

Weekly Support Groups
MitoAction hosts weekly teleconferences to provide vital support to mitochondrial disease patients, caregivers, and families, no matter where you are on your journey with mitochondrial disease.

Mito Weekly Support Group - Fridays at 12:00 pm EST
FAOD Evening Support Group - 2nd Thursday at 8:15 pm EST
FAOD Afternoon Support Group - 4th Thursday at 1:00 pm EST
Men's Monthly Support Group - Sundays as scheduled

Learn more at www.mitoaction.org/supportcall.

Monthly Mito Expert Series
Our monthly educational webinars feature guest speakers addressing topics important to the mito community, giving patients and families unprecedented access to leading clinical experts. More than 150 presentations have been recorded and posted on the MitoAction website for future reference. All presentations are available on iTunes, Spotify, and Google Podcasts!

Join Genetic Counselor Devin Shuman for our Expert Series, Wondering Wednesdays: Ask the Genetic Counselor to answer your questions and gain a better understanding of genetics in mitochondrial disease.

Visit www.mitoaction.org/expert-series for more information.

Patient Education Forums
These live events held across the country bring the clinical experts to you! Join us to learn about recent developments in mitochondrial disease diagnosis, treatment, and research, and meet other families from your local community.

Learn more at www.mitoaction.org/pefs.

Dalia's Wish
Enjoy the experience of a lifetime as MitoAction sends your family on an unforgettable wish trip through our partnership with Give Kids the World Village in Orlando, FL.

To apply, visit www.mitoaction.org/wishtrips.

Matthew Harty Camper Fund & Scholarship
The Matthew Harty Camper Fund allows kids to just be kids, despite the challenges of a diagnosis with mitochondrial disease. Through this fund, MitoAction sends children with mitochondrial disease to summer camp and awards scholarships to high school graduates pursuing college degrees.

Learn more at www.mitoaction.org/mhcf.

Marcel's Way Family Fund
This fund offers a helping hand through direct financial support, up to $500, to those living with mitochondrial disease. The Marcel's Way Family Fund can alleviate some of the burdens of expenses such as wheelchairs, adaptive equipment, travel to doctors' appointments, and medicines.

To apply, download the application at www.mitoaction.org/marcelsway.

MitoAction Memories
This group is a source of support for parents, caregivers, family members, or anyone who has lost a loved one to mitochondrial disease. We know all too well that grieving is an ongoing process and MitoAction is here to support you every step of the way.

For more information visit www.mitoaction.org/memories.

MitoSocials & MitoPlaydates
These events allow families and children to meet one another, share stories, give and get support, and realize they are not alone on this journey. Mito-Socials and MitoPlaydates are held across the U.S. and are hosted by volunteers with the support of the MitoAction staff. If you are interested in hosting or attending a event in your area, visit www.mitoaction.org/mito-socials or www.mitoaction.org/mito-playdate.

Energy in Action Podcast
Our podcast series, Energy In Action consists of conversations with patients, families, researchers and thought leaders in the mitochondrial disease communities. These podcasts will give you a glimpse into the lives of families affected by mitochondrial disease and the latest in clinical trials, diagnosis, research, and the advancement of therapies.

To listen to the podcast, visit www.mitoaction.org/energyinaction.

Energy 4 Education DVD and School Advocacy
This comprehensive DVD contains six videos: Energy 4 Education, Living with Mitochondrial Disease, How Energy is Made, Faces of Mito, This is My Mito, and My Mitochondria: Making Energy You Need. Play it for teachers, friends, and family. Show it at school assemblies and community meetings.

For additional tools and ideas visit www.mitoaction.org/school-education.

Protocols for Mito Patients
What should you do if you become sick? From dehydration to surgery, fever, or infection, manage these challenges better with clinical protocols that can be customized in the event of a medical emergency or illness. Be sure your clinical team has a copy of the protocols.

Download the protocols at www.mitoaction.org/protocol.

Physicians List
Are you looking for a medical professional familiar with mitochondrial disease? This list can help guide you to a mito specialist in your area.

The list can be found at www.mitoaction.org/doctors.

MitoChampions
Our volunteer leaders are instrumental in raising awareness of mito, providing hope to others affected by the disease and being a voice for the entire mito community.

To become a MitoChampion visit www.mitoaction.org/mitochampions.

Advocacy
Be prepared to face non-medical issues such as disability law, insurance concerns, special education, and even allegations of medical child abuse with information and community resources that can make this journey a little easier. MitoAction empowers the mitochondrial disease community with the tools needed to let their voices be heard for their individual healthcare needs.

More information can be found at www.mitoaction.org/advocacy.

For more detail on all MitoAction's programs and resources
visit www.mitoaction.org

Symptoms

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Mitochondrial diseases are a varied group of disorders characterized by impaired energy production. The symptoms of mitochondrial disease can arise in any organ at any age. Some symptoms are hallmarks of mitochondrial disease and are called “red flag” symptoms.

Neurologic

- Cerebral stroke-like lesions in a nonvascular pattern (brain lesions that do not appear like a regular stroke on imaging)
- Basal ganglia disease (physical dysfunction, such as would occur with Parkinson’s disease)
- Encephalopathy (brain disease) recurrent or with low/ moderate dosing of valproate (a medicine used to treat epilepsy, bipolar disease, and migraines)
- Neurodegeneration (the progressive loss of structure or function of neurons, including death of neurons)
- Epilepsia partialis continua (recurrent epileptic seizures that affect specific areas and recur every few seconds or minutes for extended periods)
- Myoclonus (jerky contraction of groups of muscles)
- Ataxia (loss of control of body movements)
- MRI findings consistent with Leigh Syndrome (in basal ganglia or brain stem)
- Characteristic magnetic resonance spectrometry (MRS) peaks

Cardiovascular

- Hypertrophic cardiomyopathy with rhythm disturbance (thick heart muscle that can lead to irregular heartbeat)

- Unexplained heart block in a child
- Cardiomyopathy with lactic acidosis (build up of lactic acid in the body)
- Dilated cardiomyopathy with muscle weakness
- Wolff-Parkinson-White arrhythmia (a disorder of the heart's electrical system that can cause fast heartbeat, palpitations, shortness of breath, and fainting)

Ophthalmologic

- Retinal (the back of the eye) degeneration with signs of night blindness, color-vision deficits, decreased visual acuity, or pigmentary retinopathy
- Ophthalmoplegia/paresis (weakness or paralysis of eye muscles)
- Fluctuating, dysconjugate eye movements (eyes not moving together)
- Ptosis (droopy upper eyelid)
- Sudden or insidious-onset optic neuropathy/atrophy (damage to the optic nerve)

Gastroenterological

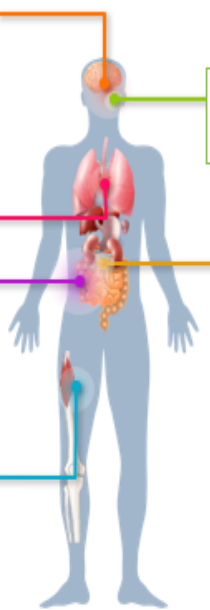
- Unexplained or valproate-induced liver failure
- Severe dysmotility (digestive tract muscles are impaired; food does not move through the system)
- Pseudo-obstructive episodes (problem with gut motility that mimics an obstruction.

Other

- A newborn, infant, or young child with unexplained hypotonia (low muscle tone), weakness, failure to thrive, and a metabolic acidosis (particularly lactic acidosis)
- Exercise intolerance that is not in proportion to weakness
- Hypersensitivity to general anesthesia
- Episodes of acute rhabdomyolysis (death of muscle fibers, which are then released into the blood stream)

Provided by www.mitosoc.org
For more information about symptoms visit www.mitoaction.org/symptoms

Clinical Features of Mitochondrial Myopathies by Organ System



Neurologic
- Attention difficulty
- Memory problems
- Seizures
- Headache
- Noise sensitivity
- Light sensitivity
- Smell sensitivity

Ocular
- Blurry vision
- Redness around eyes

Cardiac/Heart Issues
- Arryhthmia/Irregular heartbeat
- Low/high blood pressure

Gastrointestinal
- Lack of appetite
- Difficulty eating
- Vomiting
- Gagging/cant swallow
- Dehydration
- Nausea
- Stomach cramps

General

Constant/Frequent
- Lack of energy
- Shortness of breath
- Mouth sores
- Fever
- Dizziness/lightheadedness
- Balance/coordination problems
- Congestion
- Coughing
- Dry skin

Occasional
- Kidney stones
- Swollen hands

Musculoskeletal
- Muscle pain
- General pain
- Muscle cramping
- Joint pain
- Muscle weakness

Other
- Infection

Adapted from Pfeffer G, Chinnery PF. *Ann Med.* 2013 Feb;45(1):4-16.

Diagnosis

The field of mitochondrial medicine is relatively new. Having only developed over the past 25 years, mitochondrial disease still lacks specific biomarkers that could simplify a diagnosis. Currently, establishing a diagnosis can be challenging, costly, and at times, invasive. Even though specialists are creating protocols for diagnosing mitochondrial disease, a diagnosis may still take years and involve many specialists. Mitochondrial disease is now known to occur at any age, although the adult disease may be more difficult to diagnosis because it can be more varied, subtle, and have a narrower spectrum of laboratory findings compared to mitochondrial disease that begins in childhood.

Blood and urine studies are often the first step in diagnosing mitochondrial disease. These studies typically include measurements of lactate and pyruvate in plasma, cerebrospinal fluid (CSF), and urine, as well as measuring specific amino and organic acids. Additional tests may be added, including neuroimaging, electromyography (EMG) to measure muscle activity, and nerve conduction studies (NCS). Some of the “Red Flag” symptoms in the brain, such as stroke-like lesions are classic findings in mitochondrial disease, but cannot be used solely for disease confirmation.

Primary mitochondrial diseases (PMD) result from mutations in the nuclear DNA (nDNA) or mitochondrial DNA (mtDNA). Genetic studies of these two sources of DNA have replaced muscle biopsies as the gold standard for diagnosis. Unfortunately, genetic testing is expensive and requires a good deal of evidence that the cause of symptoms is mitochondrial before insurance will cover this level of testing. Some health insurance plans currently do not cover genetic testing for PMD, and patients must rely on other methods of diagnosis. When mitochondrial disease is strongly suspected but genetic studies do not reveal a known mitochondrial disease-causing mutation, patients may still receive a clinical diagnosis of mitochondrial disease.

Clinicians are using muscle and tissue biopsies less frequently for mitochondrial diagnosis because these tests may not be as comprehensive as genetic testing and may not be well tolerated by mitochondrial disease patients. PMD and mitochondrial dysfunction (secondary) cannot be differentiated with laboratory tissue testing alone. Functional tests – evaluations of how mitochondria are functioning in cells - remain important measures of mitochondrial function. In patients with a disease of muscle tissue, certain other neuromuscular diseases can be excluded by a muscle biopsy.

To learn more about mitochondrial disease diagnostics, visit www.mitoaction.org/diagnosis.

Treatment

Clinicians and researchers are working to develop therapies to treat and cure mitochondrial disease. Current treatments and therapies can help reduce symptoms, delay or prevent the progression of the disease. Even though a cure for mitochondrial disease has not been discovered, many clinical trials are underway to evaluate new therapies.

Physicians specializing in metabolic diseases have found that every child and adult is biochemically different, meaning that no two people will respond to a particular treatment in a specific way, even if they have the same disease. Therefore, treatment is individualized for each patient and type of mitochondrial disease.

Mitochondrial patients may become ill more quickly and more severely than other people because of a lower cellular reserve of energy. Cellular stresses, such as illness, fatigue, or poor nutrition, may lead to cell injury and associated worsening of baseline symptoms or the onset of new symptoms.

Exercise

Research has shown that both endurance (such as running) and resistance (such as weight lifting) exercise can benefit patients with mitochondrial disease. Some benefits include an increase in mitochondrial health, antioxidant and muscle mitochondrial enzyme activity, oxygen uptake, and muscle strength, as well as improved clinical symptoms and a decrease in resting and post-exercise blood lactate levels.

The majority of research has shown exercise that is slowly increased can be safe for patients with mitochondrial diseases. Exercise should begin with short duration and low intensity. Exercise intolerance is common with mitochondrial disease, but even patients who have a difficult time exercising should still be

encouraged to exercise beginning at their current level of function. Patients should consult their physician before beginning to exercise as cardiac or other evaluations may be needed. Physicians may recommend supervised progressive exercise aimed at improving function.

Treatment during illness

- Carry an emergency care plan that explains the disorder and management recommendations.
- Wear a Medic Alert bracelet or similar device.
- Take precautions to prevent prolonged fasting, including IV hydration for prolonged vomiting or other GI issues or fasting prior to procedures.
- IV hydration and/or lipids may be necessary for acute decompensation (organ failure from functional overload).
- Certain drugs or treatments should be used with caution. For the most updated list and more specific details on the safety of drug use in patients with a primary mitochondrial disease, visit www.mitoaction.org/medicationsafety.

Vitamins and supplements prescribed typically include:

- Coenzyme Q10 - ubiquinol preferred
- Alpha lipoic acid
- Riboflavin, and possibly other B vitamins
- Arginine - for stroke-like events
- Folinic acid - only routine for documented CSF deficiencies and diseases known to cause deficiency and considered with central nervous system manifestations
- L-carnitine - for carnitine deficient patients only
- Vitamin C - for intercurrent illness supplement

Diet therapy, as prescribed by your doctor along with a registered dietitian, may be recommended.

Important: A physician should always guide specific treatments. Patients should not take any supplements or try any treatment unless prescribed by a doctor.

Energy Well Spent

Energy is required for life. Mitochondria are the body's energy factories and are vital for optimal body functioning. Mitochondria reside in every cell in the body except for red blood cells.

Normal functioning mitochondria make energy and help allocate that energy to each cell. Our cells then work in concert to complete the jobs our body needs done. In a sense, our body is one big energy factory and the mitochondria are the workers. Rest, foods, nutritional supplements, vitamins, and hydration all provide the building blocks necessary to make the fuel our body needs.

One way for individuals with mitochondrial disease or dysfunction to conserve energy is by resting. Sleep helps recharge our batteries, and pacing activities during the day helps keep extreme energy draining at bay and builds up a buffer to regenerate energy. Staying as healthy as possible by limiting exposure to germs is also important, as is good preventative care.

Another important way to conserve energy is to keep both physical and emotional stress within limits as much as possible. Life brings stress and there is no way to avoid it all. Pure joy at a wedding or birthday party can be an energy drain, but people with mitochondrial disease should live life and not avoid the good stressors. Plan accordingly with extra rest, good hydration and nutrition to help rebalance your energy.

Exercise can be good for mitochondria, but activities well beyond your baseline will drain your energy bucket and cause negative symptoms such as pain, fatigue, and even signs of organ dysfunction if severe.

The most common energy drains include:

- Physical exertion, including daily activities and extras, such as sports

- Intense moods, such as stress, anger, anxiety, and depression
- Hyperactivity
- Extreme temperatures
- Infections

Respecting these energy drains can help to maximize energy conservation and use.

Your MitoACTION Plan: Know your Baseline

We all have a unique baseline of how we make and use energy. This baseline changes over time but these changes occur more dramatically for children with mitochondrial disease, especially when very young. Your baseline is specific for you, and changes from that baseline are typically predictable after you discover your energy drains and ways to restore energy reserves.

The Big 5 Baseline Features

- Skin Color
- Basic Vital Signs (heart rate, respiratory rate and pattern, blood pressure and temperature)
- Overall Energy and Alertness
- Gastrointestinal Function
- Behavior and Appearance

Turn these Big 5 Baseline Features into a simple checklist. By tracking these 5 features twice daily, typically morning and night, you will become well attuned to yourself or your child and learn patterns that indicate when you or your child is having a “good” day or a “bad” day. You will learn what patterns are reassuring and which ones are worrisome. And you will have the information at your fingertips to provide to healthcare providers if medical attention is required. In essence, tracking the Big 5 Baseline Features becomes the key to understanding yourself or your child and knowing when to intervene.

Sign-up for the MyMito platform to track your manage your care, symptoms, medications and more at www.mitoaction.org/mymito.

Have an ACTION Plan

“Every action requires an equal and opposite reaction.” The goal is to keep the body’s energy bucket as full as possible, despite common energy drains. Plan ahead for big activities and be creative when thinking about ways to conserve energy while still living life. The MitoAction team is behind you as you take ACTION to live a full life with mitochondrial disease!

Clinical Trials

Clinical trials are a key component of clinical research and are at the heart of all medical advances. A clinical trial or study adds to medical knowledge by seeking to answer a scientific or medical question about the safety or potential benefit of an intervention, such as a medication, device, teaching concept, or behavioral change.

Many clinical trials are conducted to assess the safety and efficacy of new or investigational drugs, devices, or procedures. Typically, researchers first test new therapies or procedures in the laboratory and in animals. The treatments that prove to be safe and show promise are moved into clinical trials, often requiring multiple phases (Phases I – III) to move the drug or therapy toward approval by the Food and Drug Administration (FDA).

A volunteer's participation in a clinical trial helps researchers to ultimately uncover better ways to treat, prevent, diagnose, and understand human disease. This participation is critical to the advancement of clinical trials and, ultimately, therapy development.

The National Institutes of Health (NIH) identify the following types of clinical trials:

- Treatment: Test new treatments or devices, new combinations of drugs, or new approaches to surgery or radiation therapy. Treatment trials are often categorized by phases I through III.
- Natural History: Provide information about how health and disease progress over time.
- Prevention: Evaluate the effectiveness of ways to reduce the risk of developing a disease or preventing a disease from returning.
- Diagnostic: Develop better tests or procedures to identify/diagnose a particular disease or condition.
- Screening: Assess new ways of detecting disease earlier in healthy people.
- Quality of life (or supportive care): Evaluate measures to improve comfort of and quality of life for people with chronic illnesses through better therapies or psychosocial interventions.

Commonly Used Terms

Randomized: The process that determines which protocol in the study (e.g., treatment, placebo, or one of two treatments) the patient will follow.

Double-blind: Neither the patient, the treating physician, nor any other staff knows which treatment the patient is receiving.

Placebo-controlled: Some patients receive the study drug or treatment and some patients receive a placebo, a harmless substance that has no effect and is used as a control.

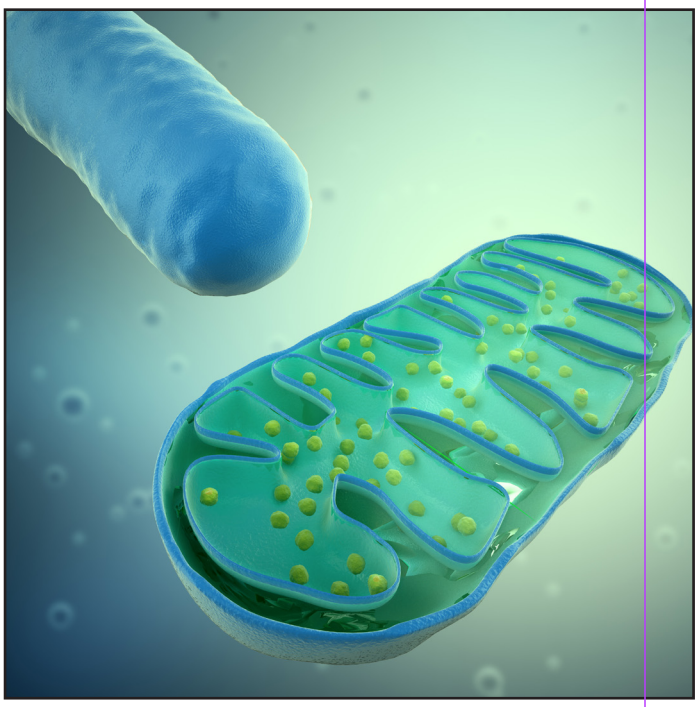
Placebo crossover: Study includes a point whereby participants change study arms, although the timing of that change and whether drug or placebo is received remains blind to all. Some may take placebo for 4 weeks, have a 2-week wash-out period with no drug or placebo, and then switch to taking the study treatment for 4 weeks, for example. Others in the same study would begin with the study drug for 4 weeks, 2-week wash-out and then cross over to take the placebo for 4 weeks.

Safeguards: Many checks and balances are in place to ensure safety.

- New drug applications (NDAs) are submitted to the FDA, requiring one or more Phase II trials. FDA oversight ensures maximal safety.
- An Institutional Review Board (IRB) within the hospital or facility places further safeguards on the study and monitors the ethical aspects and safety profile of the study on a regular basis.
- The Data Safety Monitoring Board (DSMB) comprises independent experts in the field who have no part in the actual study, but who are able to look at the unblinded progress of the trial and recommend changes in the protocol or even an early discontinuation of the trial if warranted. Unintentional toxicity or data revealing clear benefit of the therapy are reasons to alter the study course.

To learn more about specific trials in mitochondrial disease,
visit www.mitoaction.org/clinicaltrials

About Mito: FAQs



Mitochondrial disease is an inherited, chronic illness that can be present at birth or develop later in life. “Mito” is progressive and can cause physical, developmental, and cognitive disabilities. Symptoms can be mild, such as tiredness or weakness, or they can be severe, such as poor growth, loss of muscle coordination, muscle weakness and pain, seizures, vision and/or hearing loss, gastrointestinal issues, learning disabilities, and organ failure. Approximately 1 in 4,000 people have mito. There is no cure, but there are treatments that can help with the symptoms.

What are Mitochondria?

- Mitochondria are tiny organelles found in every cell in the body except red blood cells. The number of mitochondria in a cell varies by tissue and cell type with higher numbers per cell found in high energy-requiring organs, such as the liver, heart, brain, muscles, pancreas, eyes, ears, kidney, and GI tract.
- Mitochondria are known as the “powerhouse of the cell.”
- Mitochondria are responsible for creating more than 90 percent of cellular energy which is necessary for the body to sustain life and support growth.
- Mitochondria turn nutrients into cellular energy in the respiratory chain cycle.
- Mitochondria have their own independent genome (mitochondrial DNA or mtDNA) that was likely derived from early bacteria.
- Mitochondrial failure causes cell injury that leads to cell death. When multiple organ cells die, organs begin to fail.

What is Mitochondrial Disease?

- Mitochondrial disease is a chronic, genetic disorder that occurs when the mitochondria of the cell fail to produce enough energy for cell or organ function.
- Many forms of mitochondrial disease are known, arising from defects in both the mtDNA and the cell’s nuclear DNA (nDNA).
- Mitochondrial disease can be inherited in a number of ways.
- Mitochondrial disease often presents very differently from individual to individual.
- One individual in a family or many individuals affected over a number of generations may be affected.

What are the Symptoms of Mitochondrial Disease?

The severity of mitochondrial disease symptoms is different from person to person. The most common symptoms are:

- Poor growth and failure to thrive (in children)
- Loss of muscle coordination, muscle weakness and pain, low tone, exercise intolerance
- Neurological problems, seizures
- Autism, autistic spectrum, autism-like features
- Visual and/or hearing problems
- Developmental delays, learning disabilities
- Movement disorders
- Heart, liver or kidney disease
- Gastrointestinal disorders, including severe constipation, diarrhea, swallowing difficulty, repeated vomiting, cramping, reflux
- Diabetes
- Increased risk of infection
- Neurological issues, including difficult to treat seizures, migraines, and stroke or stroke like events
- Thyroid and/or adrenal dysfunction
- Autonomic dysfunction (may affect the functioning of the heart, bladder, intestines, sweat glands, pupils, and blood vessels
- Respiratory issues
- Lactic acidosis (the buildup of lactate in the body, which results in an excessively low pH in the bloodstream)
- Neuropsychological changes characterized by confusion, disorientation, dementia, and memory loss

Detailed information about symptoms can be found at www.mitoaction.org/symptoms

How common are mitochondrial diseases?

- Infants, children, and adults may develop mitochondrial disorders. Experts in mitochondrial medicine describe a spectrum of disease, ranging from mild to severe. 1 in 4,000 people are estimated to have a genetically confirmed primary mitochondrial disease, yet many remain undiagnosed.
- In adults, many diseases of aging have been found to have defects of mitochondrial function, including, but not limited to, diabetes, Parkinson's disease, Huntington's disease, atherosclerotic heart disease, stroke, Alzheimer's disease, amyotrophic lateral sclerosis (ALS), autoimmune disorders, environmental toxicities, and cancer.

What causes mitochondrial disease?

- For many patients, mitochondrial disease is an inherited genetic condition. Mutations can also be spontaneous as well as be induced.
- A patient may be found to have a de novo variant, or new mutation, meaning that the mutation arose in this patient early in development and was not passed down from a parent or previous generations.

- An uncertain percentage of patients acquire symptoms due to other factors, including mitochondrial toxins.

It is important to determine which type of mitochondrial disease inheritance is present in order to predict the risk of recurrence for future children. The types of mitochondrial disease inheritance include:

Nuclear DNA (nDNA) inheritance. nDNA is contained in the nucleus of the cell. This type of inheritance is also called autosomal inheritance.

- If the gene trait is recessive (one gene needed from each parent to have the disease), often no other family members appear to be affected. Two recessive mutations, one from each parent, are needed to express the disease. If parents both share the same recessive gene for a particular type of mitochondrial disease, 25% of children will get both mutated genes and have the disease, 25% will get no mutated genes and be healthy, and 50% will get a single mutation and be considered a "carrier," like their parents, also be healthy, but could pass the mutation to their offspring.
- If the gene trait is dominant (a gene from either parent can express disease), the disease often occurs in other family members. There is a 50 percent chance of the trait occurring in other siblings/offspring.

Mitochondrial DNA (mtDNA) inheritance. mtDNA is contained in the mitochondria of the cell.

- There is a 100 percent chance of the trait occurring in other siblings, since all mitochondria are inherited from the mother, although symptoms might be either more or less severe due to heteroplasmy (the percent of mutated cells). Higher rates of heteroplasmy are typically associated with more severe disease.

Combination of mtDNA and nDNA defects:

- The relationship between nDNA and mtDNA and their correlation in mitochondrial formation is a new area of study. MtDNA and nDNA communicate with each other. Researchers believe that such interactions may regulate the expression of particular sets of genes. This communication may explain how mitochondria are involved in cellular processes not related to energy generation, such as cell growth and death.

Random occurrences:

- Diseases specifically from deletions of large parts of the mtDNA molecule are usually sporadic without affecting other family members.
- Medicines or other toxic substances can trigger mitochondrial disease.

How is mitochondrial disease diagnosed?

- No reliable and consistent means of diagnosis currently exist. The road to diagnosis is often personalized based on symptoms. Clinicians are working to create diagnostic and treatment standards for mitochondrial medicine.
- Diagnosis usually is made by DNA testing. Although it is no longer the primary diagnosis method, a muscle biopsy could be an option.

How is mitochondrial disease treated?
The goals of treatment are to improve symptoms and slow progression of the disease. Patients are advised to:

- Use vitamin and supplement therapy
- Conserve energy
- Pace activities
- Avoid exposure to extreme temperatures
- Avoid exposure to illness
- Ensure adequate nutrition and hydration

Misdiagnosis

- Lack of understanding of the disease and misinterpretation of symptoms can lead to misdiagnosis.
- Further progression of symptoms can occur if the symptoms are missed and opportunities for treatment and support are not recognized.

What are the challenges of living with mitochondrial disease?

- Mitochondrial disease can affect multiple organs, multiple family members, and multiple generations.
- Lack of awareness and understanding of the disease can delay treatment and diagnosis.
- Families are continuously forced to expend energy to explain their disease, advocate for themselves, and fight for services.
- Mitochondrial disease is often an "invisible disease." On a good day, a patient may look fine and healthy, with more energy and appear rested. But on a bad day, patients can appear tired or even significantly ill. Repeated bad days may lead to decompensation and patients may have difficulty returning to baseline.
- Mitochondrial disease is unpredictable. Symptoms can vary day to day or even hour to hour.
- Mitochondrial disease is difficult to diagnose. Difficulties establishing a diagnosis interfere with a patient's ability to obtain adequate recognition and appropriate medical care.
- An individual can become symptomatic at any time in life despite the fact that mitochondrial disease is inherited.

To connect with others facing the challenges of mitochondrial disease, visit the MitoAction closed Facebook group or join our weekly support teleconferences.

What is the prognosis for someone with mitochondrial disease?

- The prognosis is variable. Some people live a normal life and are minimally affected; others can be severely compromised with the disease.
- The progression of mitochondrial disease is unpredictable and different for each person.

For more specific details about mitochondrial disease visit www.mitoaction.org