MDA Muscular Dystrophy Association

Mitochondrial Disease

Mitochondria are tiny organelles found in nearly every cell in the body. Often referred to as the cell's "powerhouse," they are responsible for creating cellular energy in the form of adenosine triphosphate (ATP).

Mitochondria are necessary to **sustain life and support growth** in the body, and their failure causes cell injury and cell death due to the creation of reactive oxygen species (ROS).

Mitochondrial disease is a chronic, genetic disorder that occurs when defects in mitochondria lead to a failure to produce enough energy for cell or organ function, or cause mitochondrial dysfunction leading to disruption of normal processes.

Infants, children, and adults may develop mitochondrial disorders. There are many forms of mitochondrial disease and they vary by symptom and severity from individual to individual, even within the same family.

In cases of maternally-inherited mitochondrial disease, each person can have a different mixture of healthy and defective mitochondria, with a unique distribution in the body, which is why each instance of mitochondrial disease is characterized by a **spectrum of abnormalities.**

In many cases, **mitochondrial disease is a multi-system disorder** affecting more than one type of cell, tissue or organ.

Mitochondrial disease may be sporadic, occurring in individuals who do not have a family history of the disease, or it may be familial. It can be inherited in a number of ways.

Because muscle and nerve cells have especially high energy needs, muscular and neurological problems are common features of mitochondrial disease. Mitochondrial diseases that cause prominent muscular problems are called mitochondrial myopathies, while mitochondrial diseases that cause both prominent muscular and neurological problems are called **mitochondrial encephalomyopathies.**

There are **no cures** for mitochondrial diseases, but **medications and therapy can help** manage some symptoms and potentially slow the course of the disease.

What are the Signs and Symptoms of Mitochondrial Disease?

Nervous System

- Absent reflexes
- Ataxia
- Fainting
- Migraines
- Neuropathic pain
- Seizures
- Strokes
- Temperature instability

Cognition

- Autism spectrum disorder (ASD)
- Behavioral issues
- Confusion
- Learning disability
- Memory loss

Sensory/ Perception

- Strabismus
- Retinitis pigmentosa
- Impaired vision
- Ophthalmoplegia
- Hearing loss
- Optic atrophy
- Ptosis

Skeleton and Muscle

- Exercise intolerance
- Hypotonia
- Muscle cramps
- Weakness
- Myoclonus
- Slurred Speech

Gastrointestinal

- Constipation
- Diarrhea
- Reflux
- Gastroparesis
- Difficulty swallowing
- Irritable bowel syndrome

Heart

- Arrhythmias
- Cardiomyopathy

Lungs

- Breathing difficulties

Adrenal and Thyroid

- Adrenal dysfunction
- Thyroid dysfunction

Systemic

- Failure to gain weight
- Fatigue
- Infection
- Short stature

Kidneys/Liver/Pancreas

- Diabetes
- Myoglobinuria
- Kidney, liver, and/or pancreas failure

To learn more about Mitochondrial Disease, visit MDA.org or contact the MDA Resource Center at 1-833-ASK-MDA1 (275-6321) or ResourceCenter@mdausa.org.

Common Subtypes and Clinical Features of Mitochondrial Disease

Kearns-Sayre syndrome (KSS)

Onset: Typically before age 20

Features: Progressive external ophthalmoplegia (PEO) and pigmentary retinopathy, a “salt-and-pepper” pigmentation in the retina that can affect vision. Other common symptoms include cardiomyopathy, conduction block (a type of cardiac arrhythmia), ataxia, short stature, neuropathy, diabetes mellitus, and deafness.

Leigh syndrome

Onset: Infancy or early childhood

Features: Brain abnormalities that can result in abnormal muscle tone, movement disorders, ataxia, seizures, impaired vision and hearing, developmental delays, and respiratory problems.

Mitochondrial DNA depletion syndromes (MDDS)

Onset: Infancy or early childhood

Features: A myopathic form of Mitochondrial DNA depletion syndromes (MDDS) is characterized by weakness that eventually affects the respiratory muscles. Some forms of MDDS, such as Alpers-Huttenlocher syndrome, are marked by brain abnormalities and progressive liver disease.

Mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes (MELAS)

Onset: Childhood to early adulthood

Features: The hallmarks of MELAS are encephalomyopathy with seizures and/or dementia, lactic acidosis (a buildup of lactic acid in the body), and recurrent stroke-like episodes. These episodes are not typical strokes, which are interruptions in the brain’s blood supply that cause sudden neurological symptoms. However, the episodes can produce stroke-like symptoms in the short term (such as temporary vision loss, difficulty speaking, or difficulty understanding speech, hemiplegia) and lead to progressive brain injury due to the recurrent nature of the disease. In addition, symptoms may include migraine headaches, short stature, learning disabilities, gastrointestinal issues, diabetes mellitus, hearing loss, cardiomyopathy, kidney problems, neuropathy and myopathy.

Mitochondrial neurogastrointestinal encephalomyopathy (MNGIE)

Onset: Usually before age 20

Features: This disorder is characterized by PEO, ptosis, limb weakness, and gastrointestinal (digestive) problems, including vomiting, chronic diarrhea, and abdominal pain. Another common symptom is peripheral neuropathy (a malfunction of the nerves that can lead to sensory impairment and muscle weakness).

Common Subtypes and Clinical Features of Mitochondrial Disease

Myoclonus epilepsy with ragged red fibers (MERRF)

Onset: Late childhood to adolescence

Features: The most prominent symptoms of MERRF are myoclonus, seizures, ataxia, and muscle weakness. The disease also can cause hearing impairment and short stature.

Neuropathy, ataxia, and retinitis pigmentosa (NARP)

Onset: Infancy to adulthood

Features: In addition to the core symptoms for which it is named, NARP can involve developmental delay, seizures, and dementia.

Pearson syndrome

Onset: Infancy

Features: This syndrome involves severe anemia and malfunction of the pancreas. Children who have the disease usually go on to develop Kearns-Sayre syndrome.

Progressive external ophthalmoplegia (PEO)

Onset: Adolescence or early adulthood

Features: PEO is often a symptom of mitochondrial disease. In some people, it is a chronic, slowly progressive condition associated with an inability to move the eyes and general weakness and exercise intolerance.

Thymidine Kinase 2 Deficiency (TK2d)

Onset: Infancy to adulthood (most common in childhood)

Features: TK2d is a mitochondrial DNA maintenance disorder and mitochondrial DNA depletion syndrome (MDDS) disorder that primarily affects skeletal muscle. It is characterized by progressive muscle weakness (myopathy), difficulty walking, respiratory muscle involvement, and fatigue. Early-onset forms often lead to rapid progression and respiratory failure, while later-onset cases tend to progress more slowly. Other symptoms may include feeding difficulties, ptosis (drooping eyelids), and difficulty swallowing.

How is Mitochondrial Disease treated?

The goal of treatment in mitochondrial diseases is to alleviate symptoms and preserve or improve functioning, mobility and strength. Treatment must be tailored to the individual by his or her physician and may include treatment of symptoms with medications, surveillance for potential new symptoms with appropriate testing and referrals to specialists, therapies, and support from the community.

- **Physical and Occupational therapy** can help improve independence, daily living, and work skills.
- **Surgery** can be used to remove cataracts or to correct ptosis
- Supportive aids such as **railings, braces, walkers or wheelchairs** may help those who experience problems with muscle weakness, fatigue, or impaired balance/ coordination
- Respiratory support, such as from **non-invasive ventilation, occasional assisted ventilation or permanent support from a ventilator**, can help those with breathing problems.
- A **pacemaker** can be used to stimulate a normal heartbeat in individuals who experience arrhythmia.
- **Speech therapy** can help individuals who experience slurred speech.
- **Anticonvulsant and anti-epileptic drugs** may be effective in treating and helping prevent migraines and seizures.
- **Hearing aids and cochlear implants** can help with hearing loss or deafness.
- Dietary supplements including **creatine, alpha lipolia acid, and coenzyme Q10** are aimed at fixing or bypassing defective mitochondria. These supplements often are combined into a “cocktail.” Evidence from clinical trials will be needed to determine whether any or all of these supplements are effective.*
- An **individualized education program (IEP)** at school can help children with developmental or learning problems.
- In November 2025, the US FDA approved **KYGEVVI® (doxecitine and doxribtimine)**, the first therapy for both children and adults with TK2d. Clinical trial data showed that in patients whose symptoms began at age 12 or younger, treatment reduced the risk of death by more than 90%, led to at least 75% of patients regaining at least one previously lost motor skill, and allowed many to reduce or discontinue ventilatory support.*

*Please talk to your medical provider before taking any medication or supplement.

MDA Glossary

Adenosine triphosphate (ATP)
An energy molecule, derived from sugars and fats, manufactured by proteins in the mitochondrion; it is the primary energy source of cells

Ataxia
The inability to maintain balance and coordination

Cardiac arrhythmia
Abnormal heartbeat

Cardiomyopathy
A condition in which the heart muscle is weakened, making it harder for the heart to pump blood to the body

Encephalomyopathy
A disorder characterized by the combined involvement of the brain and skeletal muscle, leading to both neurological and muscular symptoms.

Gastroparesis
Also known as delayed gastric emptying; a condition that affects the ability of the stomach to empty its contents into the small intestine, even though there is no blockage.

Hypotonia
Poor muscle tone

Mitochondria
Organelles found in the nucleus of nearly every cell in the body; Responsible for creating cellular energy

Mutation
A flaw in the DNA code

Myoclonus
Muscle jerks

Myoglobinuria
A breakdown of muscle after exercise that causes leakage of a protein called myoglobin from the muscles into the urine; it stresses the kidney's ability to filter waste from the blood and can cause kidney damage

Neuropathic pain
Pain caused by damage in the sensory nervous system. The pain is often described as abnormal sensations (dysesthesia) or pain caused by normal touch or other stimuli that is not normally painful

Ophthalmoplegia
A condition associated with inability to move the eyes

Optic atrophy
Degeneration and death of the optic nerve that carries vision-information to the brain

MDA Glossary (continued)

Peripheral neuropathy
A malfunction of the nerves that can lead to sensory impairment and muscle weakness

Ptosis
Drooping of the eyelids

Retinitis pigmentosa
Degeneration of the retina in the eye, with resulting loss of vision

Strabismus
A vision condition sometimes referred to as cross-eyed, in which a person cannot align both eyes simultaneously under normal conditions

Syndrome
A condition characterized by an associated group of symptoms

This resource was developed with the expertise and knowledge of Amy Goldstein, MD.