

Myths & Facts About Mitochondrial Cytopathies

By **Sumit Parikh, M.D. & Bruce H. Cohen, M.D.**

Myth A diagnosis of mitochondrial disease must include an acronym reference (MELAS, MERRF, NARP, LHON).

Fact The majority of people with mitochondrial disorders do not have such a syndrome. Mitochondrial syndromes named by acronym were among the first described disorders. The nomenclature for mitochondrial diseases has since evolved, but is probably not in a final form. The current accepted list of mitochondrial disorders includes disorders with acronymic descriptions, a name based on a person that described the disease, a name based on a specific genetic mutation, a name based on a microscopic description of tissue or a name based on the deficient enzyme. These labels do not, in and of themselves, predict prognosis or alter treatment.

Myth Mitochondrial diseases are maternally inherited.

Fact The majority of mitochondrial diseases are due to mutations in nuclear DNA (the “regular” DNA contained in the nucleus of the cell). The current thinking is that the majority of persons with mitochondrial diseases have inherited the disorder as a consequence of autosomal recessive inheritance or one of more complex inheritance patterns. Only mitochondrial disorders caused by mutations in the mitochondrial DNA are maternally inherited. However, mitochondrial DNA contains the genetic code for only a small number of the proteins in the mitochondria. Secondary mitochondrial disorders may also account for a large percentage of affected individuals, where the mitochondria becomes poorly functional as a consequence of another disease process (including other chromosomal disorders), toxin or viral exposure. Finally there may be inherited genetic mutations that in and of themselves are not pathologic until there is another trigger (an epigenetic factor).

Myth Mitochondrial disease is a childhood disease.

Fact Although many disorders present in infancy or childhood, the onset of symptoms may occur at any age.

Myth An individual with mitochondrial disease has mental retardation, growth problems and/or seizures.

Fact Only some individuals have these developmental problems. Patients can have varying signs and symptoms, ranging from extremely mild to severe, involving a single or multitude of body systems, which can occur at any age. The brain, muscles, heart, liver, nerves, eyes, ears and kidneys are the organs and tissues most affected. These disorders can be static or progressive. Most individuals have waxing and waning severity of their symptoms. Members of the same family with the same disorder can have vastly different symptoms.

Myth Since mitochondrial diseases are incurable, nothing can be done for these patients.

Fact Even though these disorders are chronic and incurable, treatment is available. Rapid symptom treatment and prevention of metabolic crises at times of stress may limit morbidity and onset of further handicap. Avoidance of certain medications and stressors that worsen symptoms is also helpful. As is the case with treatments for many other incurable diseases such as diabetes and emphysema, some medications and supplements may improve the symptoms related to mitochondrial diseases.

Myth Patients with mitochondrial disease all have elevated lactic acid levels in their blood.

Fact Although elevated lactic acid levels are often seen in those with mitochondrial disease, this is not always the case. Lactic acidosis may occur only at times of metabolic decompensation and in other disorders may never be present. High levels of lactic acid can also be found in other disorders. An elevated lactic acid level, in the context of other symptoms, is suggestive of a mitochondrial problem and further investigation may be warranted. Other biochemical markers of mitochondrial dysfunction in blood, urine and spinal fluid are routinely considered in the diagnostic evaluation.

Myth A muscle biopsy is the gold standard for the diagnosis of mitochondrial disease.

Fact The muscle biopsy is a powerful diagnostic tool but should not be considered a “gold standard.” There are several laboratory components to a biopsy, including microscopic evaluation, enzyme testing, and genetic testing. Although all labs in the USA that offer muscle biopsy have met strict laboratory guidelines, there is no standard approach that is agreed upon by these labs for enzyme testing. A muscle biopsy with full analysis costs well over \$10,000 and poses both surgical and anesthetic risks. Some patients may have a definitive diagnosis based on clinical symptoms and a positive genetic mutation found on a blood test, in which case a muscle biopsy is not necessary. In other patients, the combination of clinical findings and non-invasive testing offers strong enough evidence of mitochondrial disease. Since biopsy results do not necessarily alter prognosis or treatment, some specialists and families choose to treat the patient without the biopsy.

Myth A muscle biopsy is a muscle biopsy no matter where and how it is done.

Fact As stated above, the muscle removed at the time of biopsy can be tested in many ways. When the muscle is removed, it must be handled correctly so that all important testing is performed accordingly. Enzyme testing can be done on either the ground up muscle, or on mitochondria extracted from that muscle. Testing in extracted mitochondria is performed in only a few laboratories since a larger sample of muscle is taken and the testing is done immediately. This procedure is known as a “fresh biopsy.” If the biopsy is performed at a medical center without the ability to extract the mitochondria and test it immediately, it is called a “frozen biopsy,” since the muscle is quickly cooled and stored at –80 degrees Celsius for testing at an outside facility. There remains considerable debate as to the advantages of testing the fresh mitochondria versus frozen ground up muscle though there is some evidence indicating that a “fresh biopsy” has better sensitivity and specificity. Muscle is also routinely processed for light and electron microscopy to further evaluate the mitochondria and must be processed appropriately for such testing. Certain laboratories offer limited but valuable genetic testing in muscle.

For appointments contact:

216.444.5559 or
800.223.2273 x45559

Cleveland Clinic

Pediatric Neurology, S71
9500 Euclid Ave.
Cleveland, OH 44195

For additional information please
contact the United Mitochondrial
Disease Foundation (www.umdf.org)
or the Mitochondrial Medicine Society
(www.mitosoc.org)