What is MELAS?

Mitochondrial Encephalomyopathy, Lactic Acidosis, and Stroke-like Episodes (more commonly known as MELAS syndrome), is a rare disorder that affects many of the body's systems, particularly the brain and nervous system (encephalo-) and muscles (myopathy).

MELAS syndrome affects boys and girls equally and all ethnic groups equally. Onset of the condition generally occurs at a young age, with approximately 75 percent of cases beginning before the age of 20 years and most before age 40.

Stroke-like episodes and mitochondrial myopathy characterise MELAS syndrome. Mitochondrial myopathies cause muscular and neurological problems. Most people with MELAS also have a buildup of lactic acid in their bodies (a condition called lactic acidosis). This increased level of acidity in the blood can lead to vomiting, abdominal pain, extreme tiredness (fatigue), muscle weakness, and difficulty breathing.

Features of MELAS

The typical features of MELAS syndrome are ones that make up the name of the disorder i.e. mitochondrial encephalomyopathy (muscle problems), lactic acidosis, and stroke-like episodes, with the main symptoms being headaches and seizures. Early symptoms of MELAS may include muscle weakness and pain, recurring headaches, loss of appetite, difficulty breathing, exercise intolerance and seizures. Less commonly, people with MELAS may experience involuntary muscle spasms, impaired muscle coordination, hearing loss, heart and kidney problems, diabetes, and hormonal imbalances.

The distinguishing feature in MELAS syndrome is the recurrence of stroke-like episodes. Migraines occur in the majority of affected individuals and are often severe during the acute stage of a stroke. Individuals with MELAS may also have psychiatric conditions such as depressive disorders, cognitive impairments, anxiety disorder or personality change. People with MELAS may also have episodes of confusion and hallucinations often due to a fever and/or headache.

Stroke-like episodes involve temporary muscle weakness on one side of the body, altered consciousness, vision abnormalities, seizures, and severe headaches resembling migraines. Repeated stroke-like episodes can progressively damage the brain, leading to vision loss, problems with movement, and a loss of intellectual function (e.g. dementia). If there is a history of developmental delays, learning disabilities or attention deficit disorder then this is typically discovered before the first stroke has been experienced.

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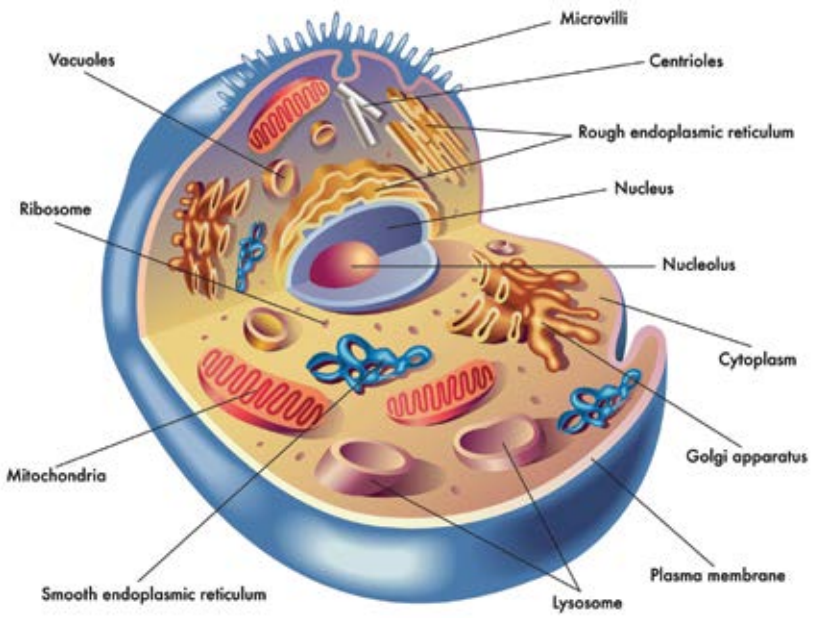
Genetics of MELAS

MELAS is caused by a defect in one of several mitochondrial genes. Mitochondrial (mt) genes are found in the DNA of cellular structures called mitochondria, which convert the energy from food into a form that cells can use. The genes that are not working correctly can be in any of these mitochondrial genes called MT-ND1, MT-ND5, MT-TH, MT-TL1, and MT-TV. Both normal and mutated mtDNA can exist in the same cell, which is a situation known as heteroplasmy.

Symptoms may not appear until the mutation affects a significant proportion of mtDNA. The uneven distribution of normal and mutant mtDNA in different tissues can affect different organs in members of the same family. This can result in a variety of symptoms in affected family members.



Mitochondria are tiny structures located within nearly all cells of the body. They are the parts of the cell that are primarily responsible for creating energy. They do this by generating adenosine triphosphate (ATP), which is the essential "fuel" that drives all of the body's functions. For this reason, mitochondria are often described as the "powerhouse" of the cell.

Mutations in the mtDNA gene MT-TL1 cause more than 80 percent of all cases of MELAS. These mutations impair the ability of mitochondria to make proteins, use oxygen, and produce energy. Researchers have not determined how changes in mtDNA lead to the specific signs and symptoms of MELAS. They continue to investigate the effects of mitochondrial gene mutations in different tissues, particularly in the brain.

Children can only inherit this disorder from their mother. This is because egg cells contribute the mitochondria to the developing embryo, and sperm do not. The condition can appear in every generation of a family and can affect both males and females, but fathers do not pass traits associated with changes in mtDNA to their children. In most cases, people with MELAS inherit an altered mitochondrial gene from their mother. Less commonly, the disorder results from a new mutation in a mitochondrial gene and occurs in people with no family history of MELAS which is now able to be passed on.

Diagnosis of MELAS

The diagnosis of MELAS is usually determined by clinical examination. However, confirmation of the diagnosis usually requires molecular, genetic testing and a muscle or brain biopsy. The muscle biopsy shows characteristic ragged fibers for MELAS syndrome and a brain biopsy shows the stroke-like changes.

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The clinical diagnosis of MELAS is based on the following features:

- Stroke-like symptoms, typically before the age of 40
- Encephalopathy with seizures and/or dementia
- Mitochondrial myopathy, evidenced by lactic acidosis and/or ragged red fibers on muscle biopsy.

To confirm the diagnosis, two of the following are also required:

- Normal early psychomotor development
- Recurrent headache
- Recurrent vomiting

Management

There is no known treatment for MELAS syndrome, however, patients are managed according to what areas of the body are affected at a particular time. Sensorineural hearing loss has been treated with cochlear implantations; Anti-convulsant drugs are used to help prevent and control seizures associated with MELAS syndrome (it is important to note that Valproic acid should not be used as an anticonvulsant);

The above diagram is sourced from: http://www.gohmd.org/mitochondrial-function.html

Therapies are sometimes used to increase energy production by mitochondria and slow down the effects of the condition.

Diabetes mellitus is managed by dietary modification, oral hypoglycemic agents or insulin therapy, Migraine headaches and cardiac manifestations are treated in the usual manner with pain relief medication or preventive medications. The use of L-arginine, a dietry supplement, has been reported to improve the symptoms of disease during the acute stroke-like episode.

Antioxidants and vitamins have also been used, however, consistent success hasn't been reported. Therapies are sometimes used to increase energy production by the mitochondria and slow down the effects of the condition. Coenzyme q10 and L-carnitine have been beneficial in some patients.

Individuals with MELAS should also receive standard childhood vaccinations such as the flu vaccine and pneumococcal vaccine. This is because feverish illnesses may make the condition worse. In general, for patients with mitochondrial myopathies, moderate treadmill training may be beneficial for maintaining muscles strength and endurance.

Genetic counselling is available to families who have had a diagnosis of MELAS. This service provides information, helps families understand inheritance patterns and what this means in their family, as well as enabling people to make more informed family-planning decisions.

Agents to avoid: Mitochondrial toxins including: aminoglycoside antibiotics, linezolid, cigarettes and alcohol; Valproic acid for seizure treatment; dichloroacetate (DCA) due to increased risk for peripheral neuropathy.

Pregnancy management: Affected or at-risk pregnant women should be monitored for diabetes mellitus and respiratory insufficiency. This may require therapeutic interventions. ®