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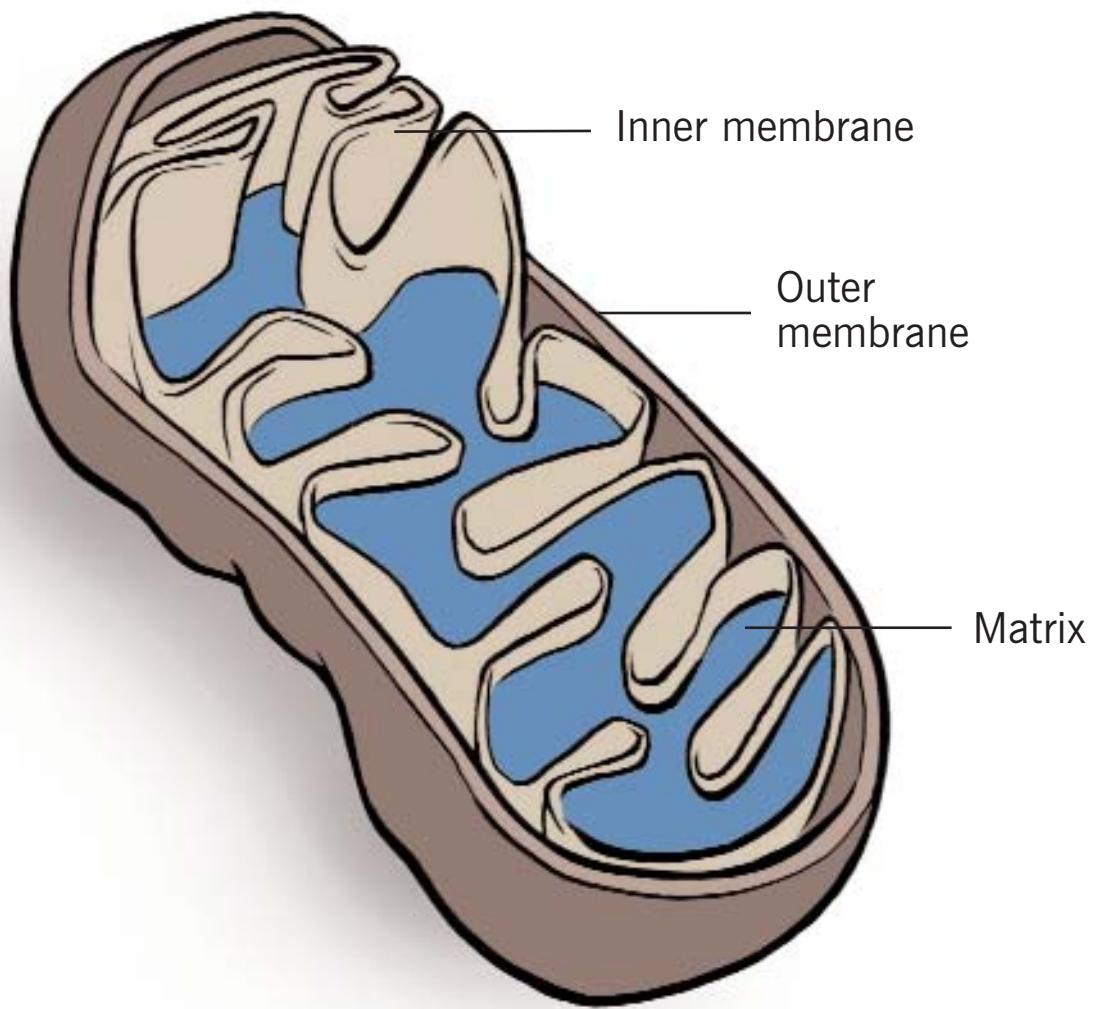
A guide to mitochondrial disease
for patients and parents

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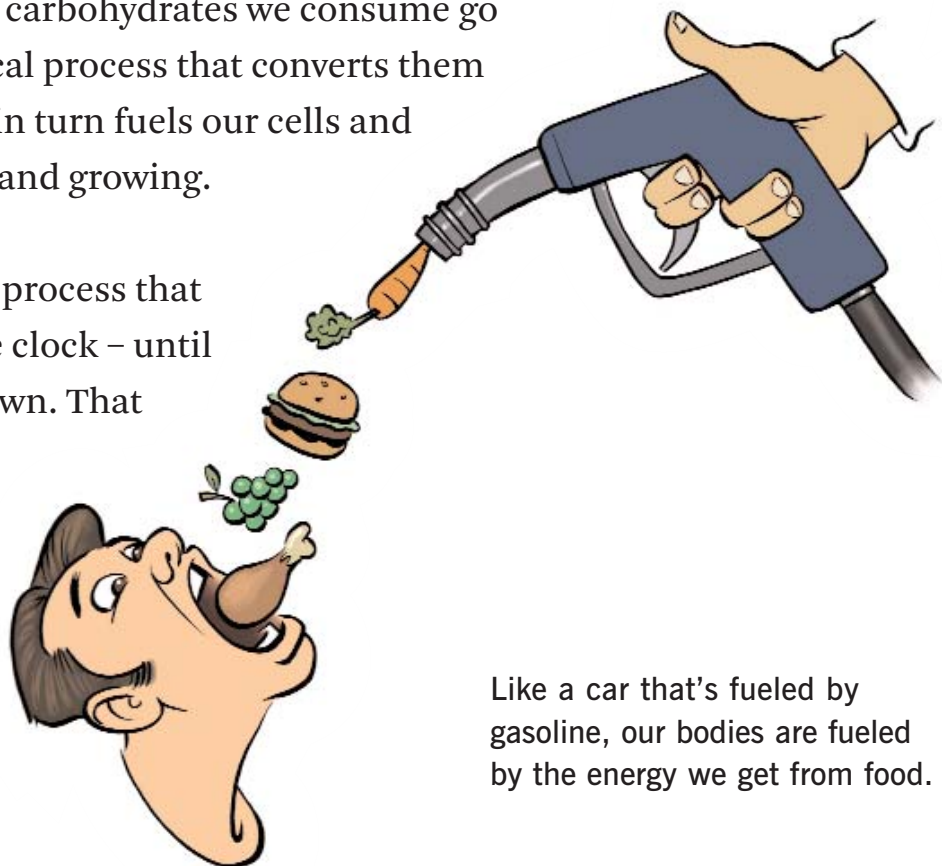
Inside the mitochondrion

Mitochondrial Disease

Like a car that stalls and comes to a stop, certain diseases can make the body feel like it has “run out of gas,” too. But while it’s easy to get a car going by filling up the tank, getting the body running again is a lot more complicated.

Our bodies are fueled by oxygen and the nutrients we get from food. The protein, fats, and carbohydrates we consume go through a chemical process that converts them to energy, which in turn fuels our cells and keeps us moving and growing.

It’s an automatic process that works around the clock – until there’s a breakdown. That breakdown and the problems that come with it are known as mitochondrial disease.

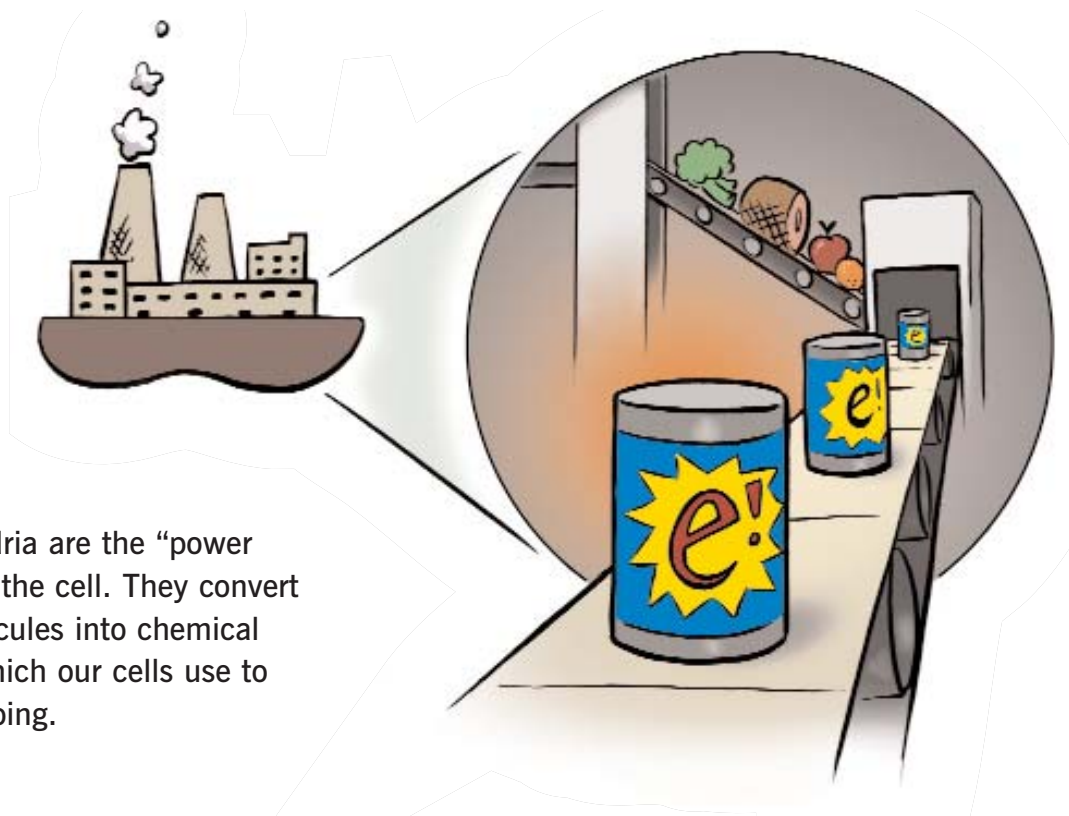


Like a car that’s fueled by gasoline, our bodies are fueled by the energy we get from food.

At Peak Production

For most of us, eating is easy; it's the part where our bodies convert the food to energy that's a lot more complex. Fortunately, the mitochondria do all that work for us.

- Each of us is born with trillions of cells, and each cell comes with several thousand mitochondria—all of which we initially inherited from our mothers.
- Mitochondria are the “power plants” or batteries of the cell. They are living, breathing production factories whose job is to convert food molecules into chemical energy. Our cells use that energy to keep us going.



Mitochondria are the “power plants” of the cell. They convert food molecules into chemical energy, which our cells use to keep us going.

- The number of mitochondria in a cell depends on how much energy that cell needs to do its job.



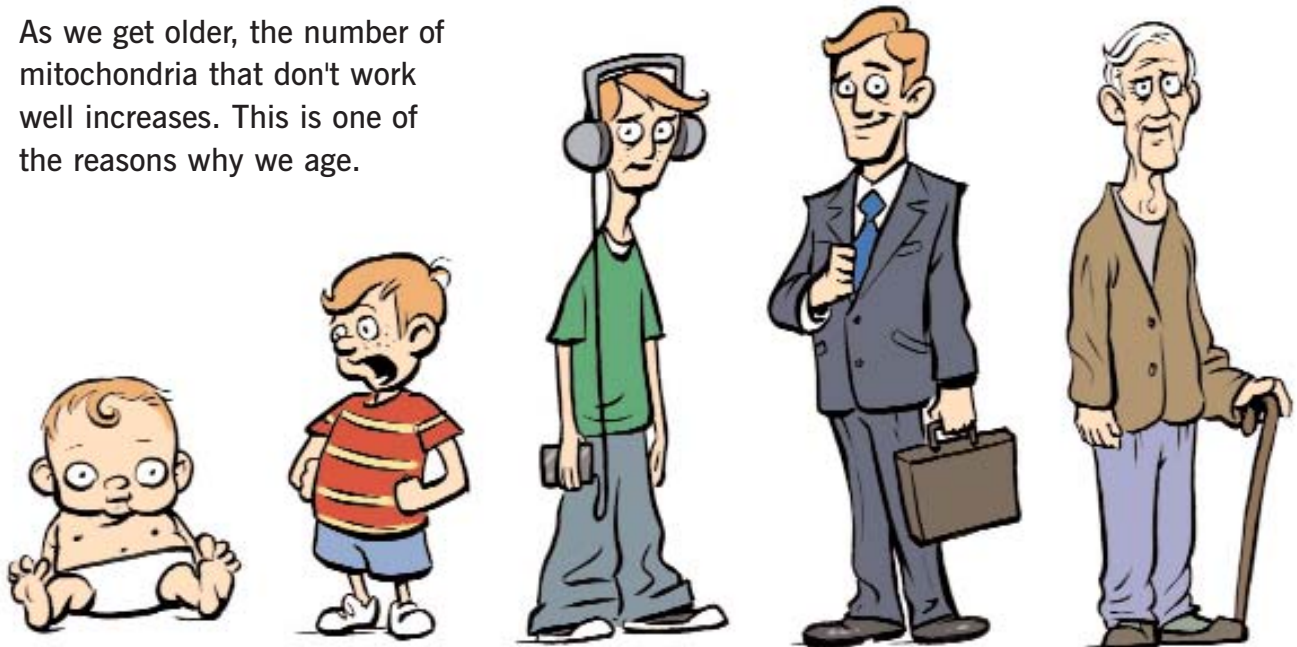
Cells in the brain or nervous system need a lot more mitochondria to function than the skin cells do, just as a semi needs more gas in its tank than a MINI Cooper does.

Our cells use energy to keep our bodies going. The bigger the job a cell has to do, the more energy it needs to get it done.

A Production Breakdown

When there are so many mitochondria at work, not all of them can be top performers. In fact, at birth, a very small number of our mitochondria may not work well, but as we get older that number increases. This is one of the reasons we age.

As we get older, the number of mitochondria that don't work well increases. This is one of the reasons why we age.



Certain diseases can also increase the number of unhealthy mitochondria over a person's lifetime. They include:

- Diabetes
- Huntington's disease
- Alzheimer's disease
- Amyotrophic lateral sclerosis (ALS)

However, some people are born with or develop too many unhealthy mitochondria, cannot make enough mitochondria, or are unable to keep some or all of their mitochondria running at full speed.

Having too many unhealthy mitochondria, or not making enough, keeps the cell from generating enough energy to work properly. The cell may even die. Having too many low-functioning mitochondria results in mitochondrial disease.

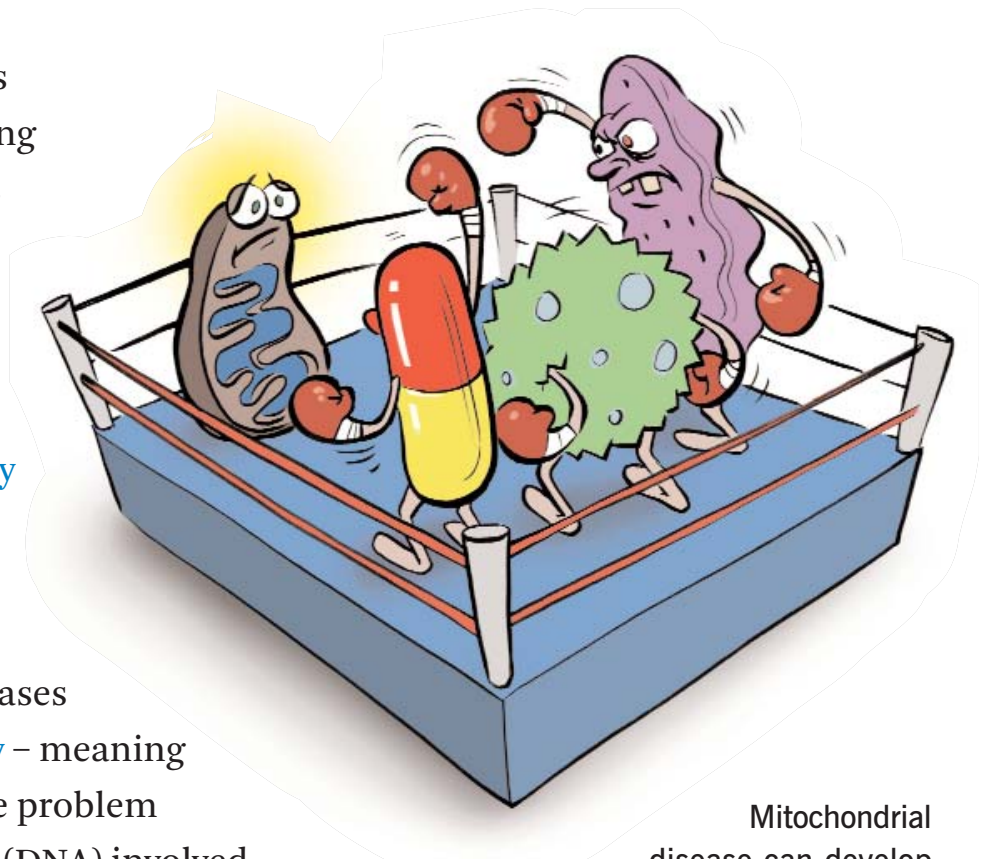
Examining the Causes

In a large percentage of patients, unhealthy mitochondria can develop when they are damaged by a number of things, including:

- Other diseases and disorders that affect the body (several listed on the previous page)
- Viruses and toxins (poisons), including certain medicines

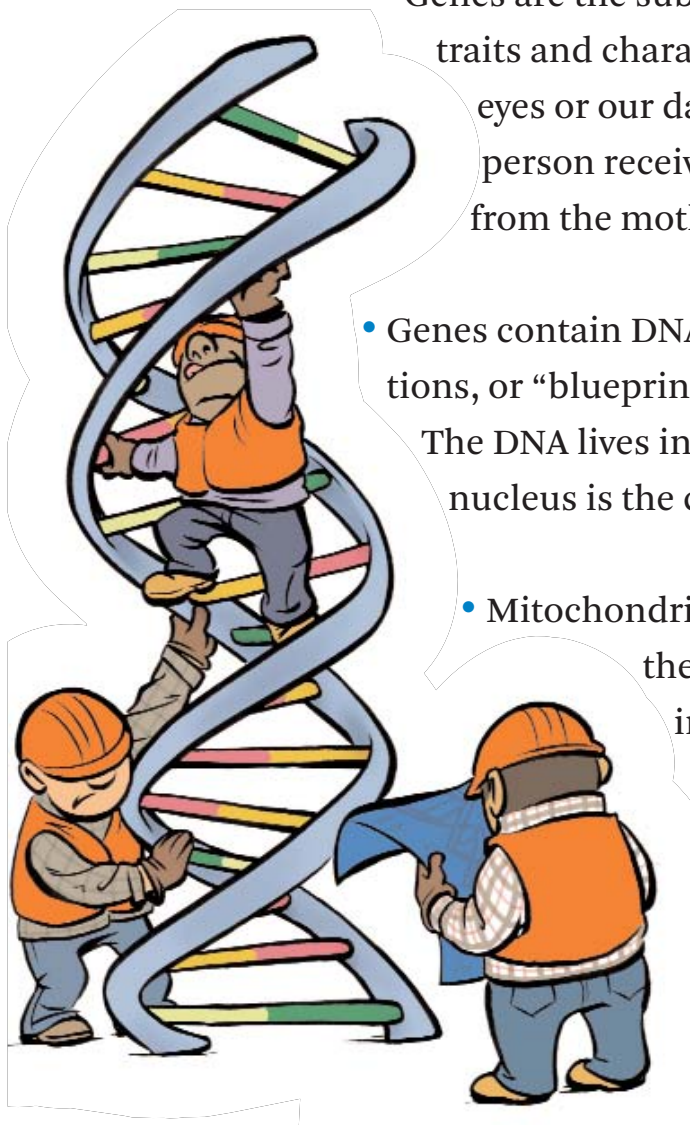
In these circumstances, the mitochondrial disease is **secondary** to that other problem.

Mitochondrial diseases can also be **primary** – meaning genetic – in that the problem is in the blueprints (DNA) involved in building mitochondria or providing the tools to keep them running.



Mitochondrial disease can develop when the mitochondria are damaged by diseases, viruses, and toxins.

While some genetic diseases are inherited, meaning that they are passed down from parent to child through DNA, some changes in the DNA can occur spontaneously in the child and do not exist in the parents. These changes in the child's DNA occur very early in the pregnancy (typically the first two weeks).



- Genes are the substances that give us our physical traits and characteristics, like our mother's brown eyes or our dad's ability to roll his tongue. Each person receives two copies of each gene: one from the mother and one from the father.
- Genes contain DNA, which hold the genetic instructions, or "blueprints," for building a human being. The DNA lives in the cell's nucleus (nDNA). The nucleus is the control center of the cell.
- Mitochondria are unique because they contain their own DNA (mtDNA for short), inherited from only the person's mother. This is in contrast to nDNA, which is inherited from both parents.
- More than 80% of primary mitochondrial disease is caused by nDNA mutations (changes).
- Less than 20% of primary mitochondrial disease is caused by mtDNA mutations.

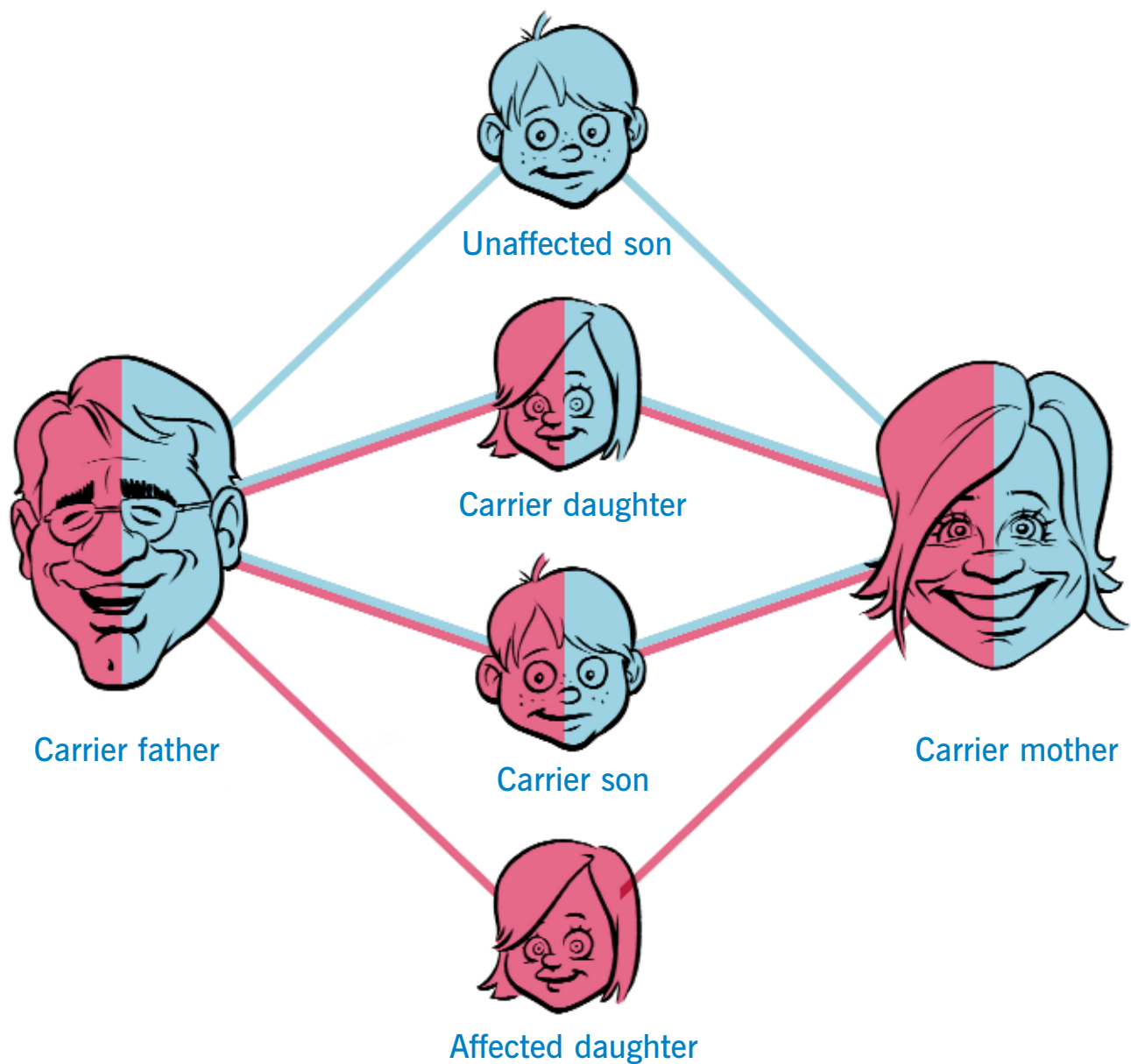
If mitochondrial disease is inherited, it is important to find out which type of inheritance it is. This can predict the risk of the disease being inherited by future children or the risk of the child's siblings, parents, uncles, and aunts of having and passing on the disease.

When inherited, the types of mitochondrial disease inheritance include:

nDNA inheritance (also called autosomal inheritance):

- If the gene is recessive (one gene from each parent), there is a 25% chance that each child will inherit the disease.

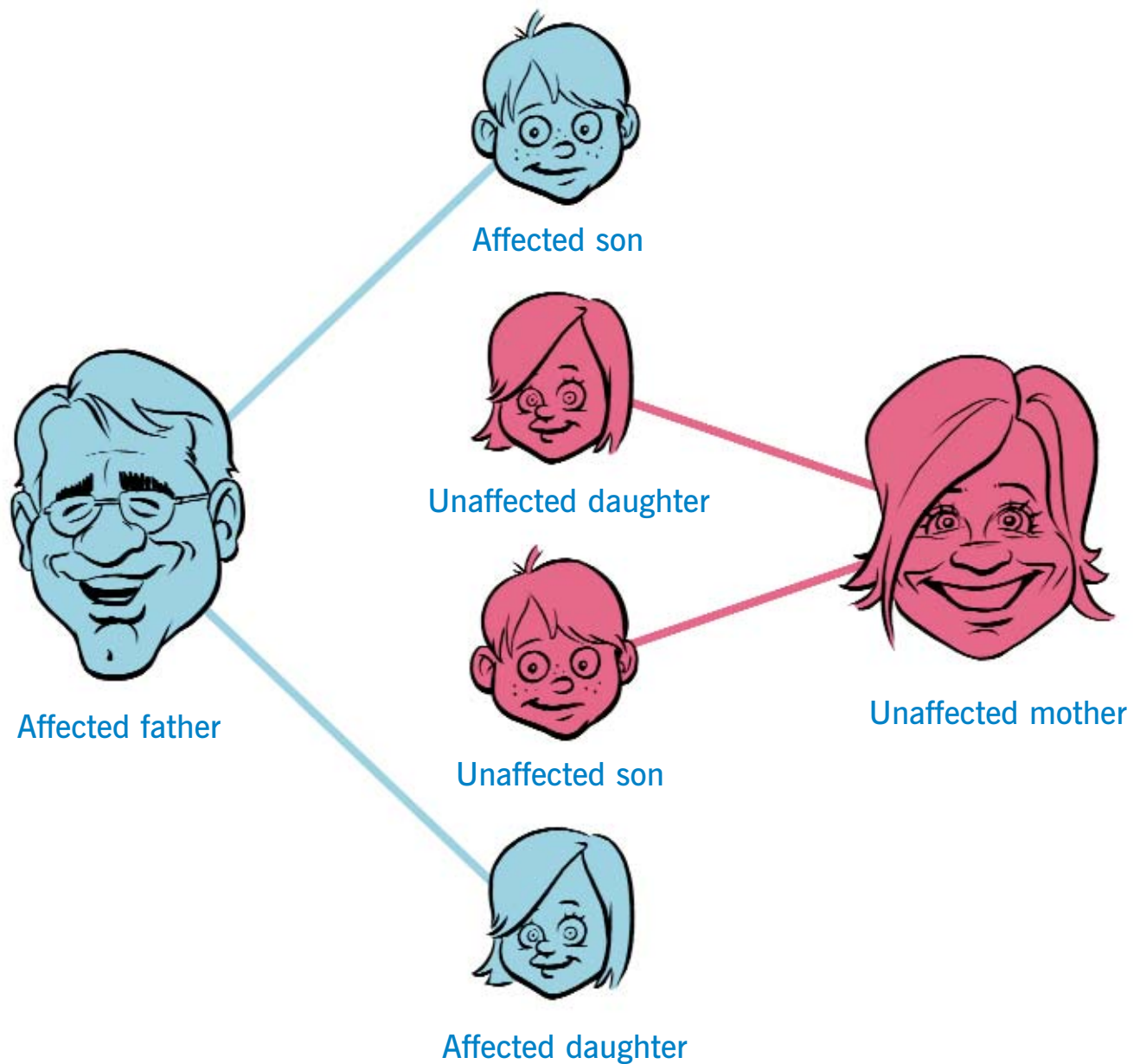
Autosomal Recessive Inheritance



Autosomal Dominant Inheritance

- If the gene is dominant (a gene from either parent), there is a 50% chance that each child will inherit the disease.

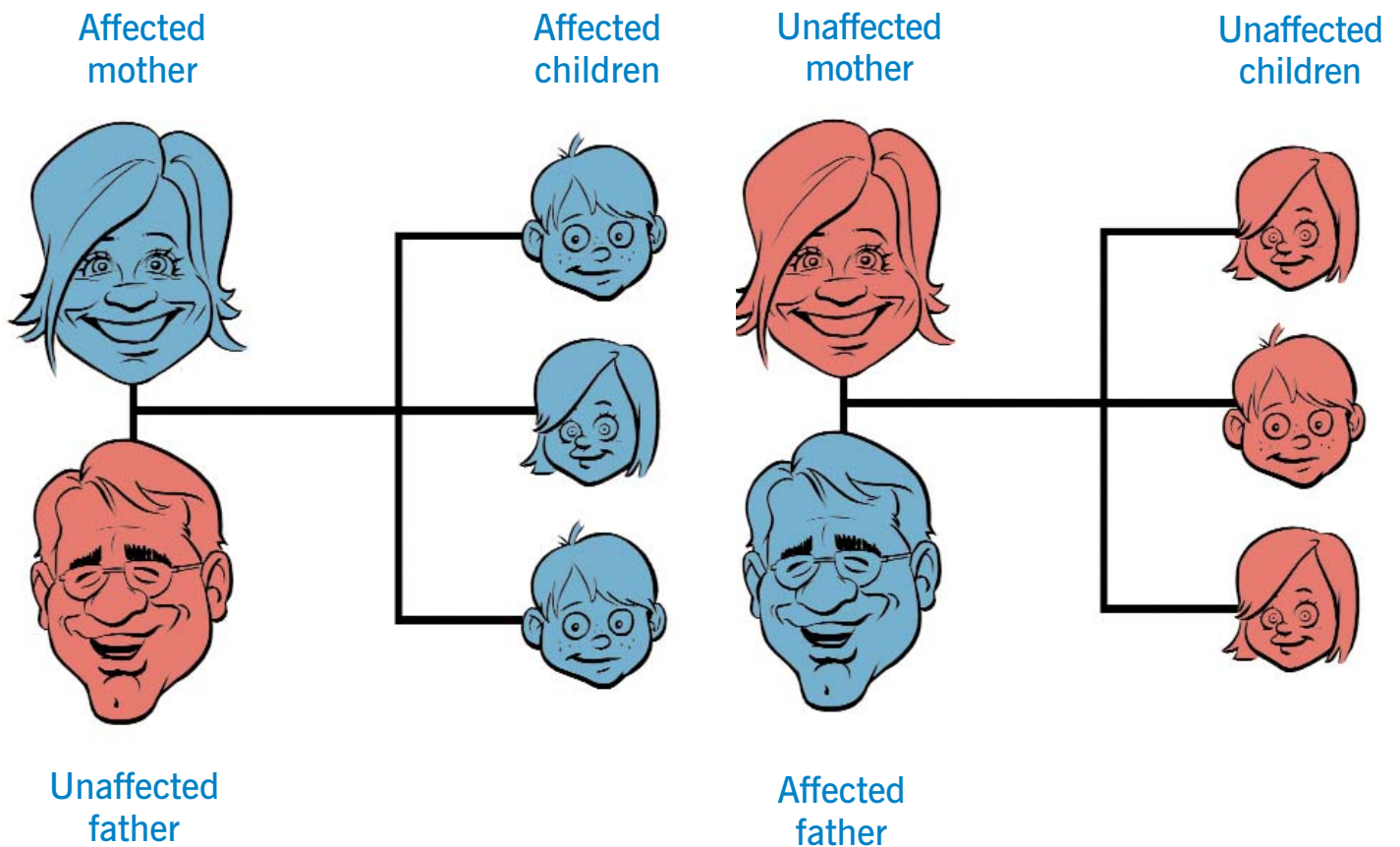
Autosomal Dominant Inheritance



mtDNA inheritance:

- mtDNA are maternally inherited, so if the problem is here, there is a 100% chance that each child will inherit the disease, although symptoms might be markedly different and either more or less severe. But, remember that mtDNA mutations only cause 20% or less of primary mitochondrial disease since most of the blueprints involved in building them come from regular DNA.

Mitochondrial Inheritance



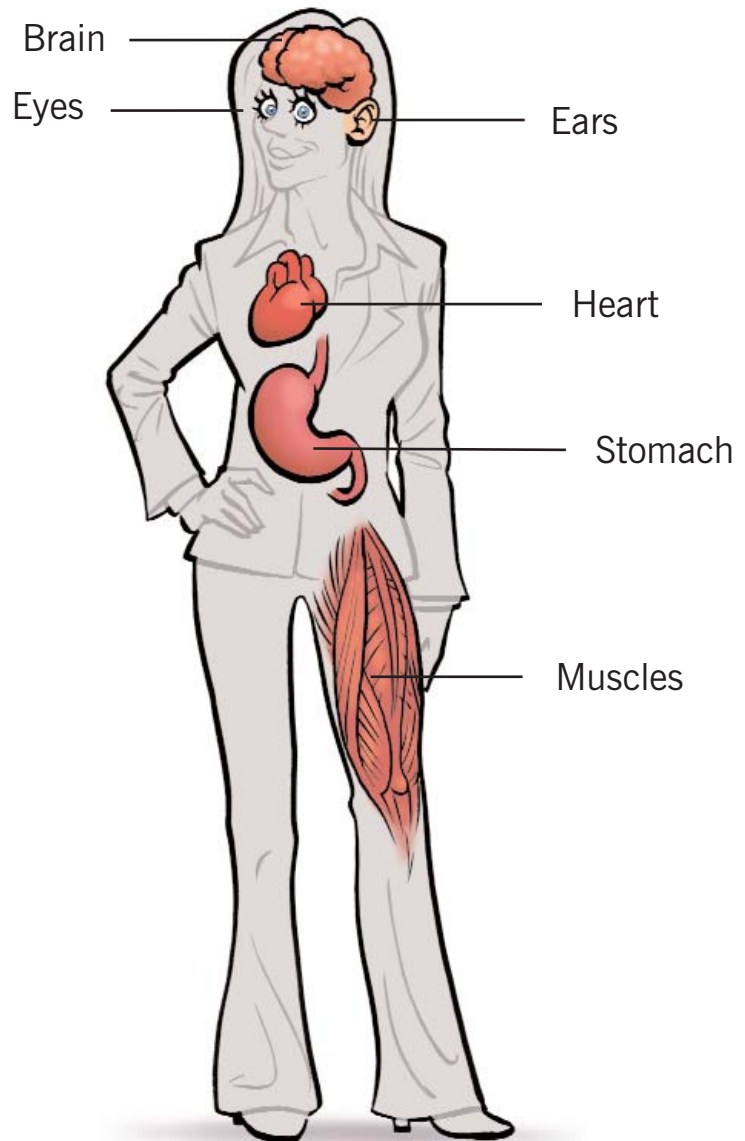
Combination of mtDNA and nDNA defects:

- The complete relationship between nDNA and mtDNA and their correlation in mitochondrial formation isn't known.

Looking at the Symptoms

Because mitochondria are in nearly every cell in the body, mitochondrial disease can affect one or all organs, including the following:

- Brain
- Nerves (including the nerves to the stomach and intestines)
- Muscles
- Kidneys
- Heart
- Liver
- Eyes
- Ears
- Pancreas



Mitochondrial disease can affect one or all organs.

In some patients, only one organ is affected, while in other patients many of the organs are involved.

Depending on which cells of the body are affected, symptoms might include:

- Poor growth
- Loss of muscle coordination, muscle weakness
- Visual and/or hearing problems
- Developmental delays, learning disabilities
- Intellectual disability
- Heart, liver, or kidney disease
- Gastrointestinal disorders, severe constipation
- Respiratory disorders
- Diabetes
- Neurological problems, seizures
- Thyroid dysfunction
- Dementia (mental disorder characterized by confusion, disorientation, and memory loss)



The type of symptoms a person has depends on which cells of the body are affected.

Getting to the Diagnosis

Because mitochondrial disease can affect so many different parts of the body, resulting in many different symptoms, it can be difficult to diagnose.

More Invasive Tests

To diagnose the condition, the doctor will start with a series of examinations and tests that may include the following:

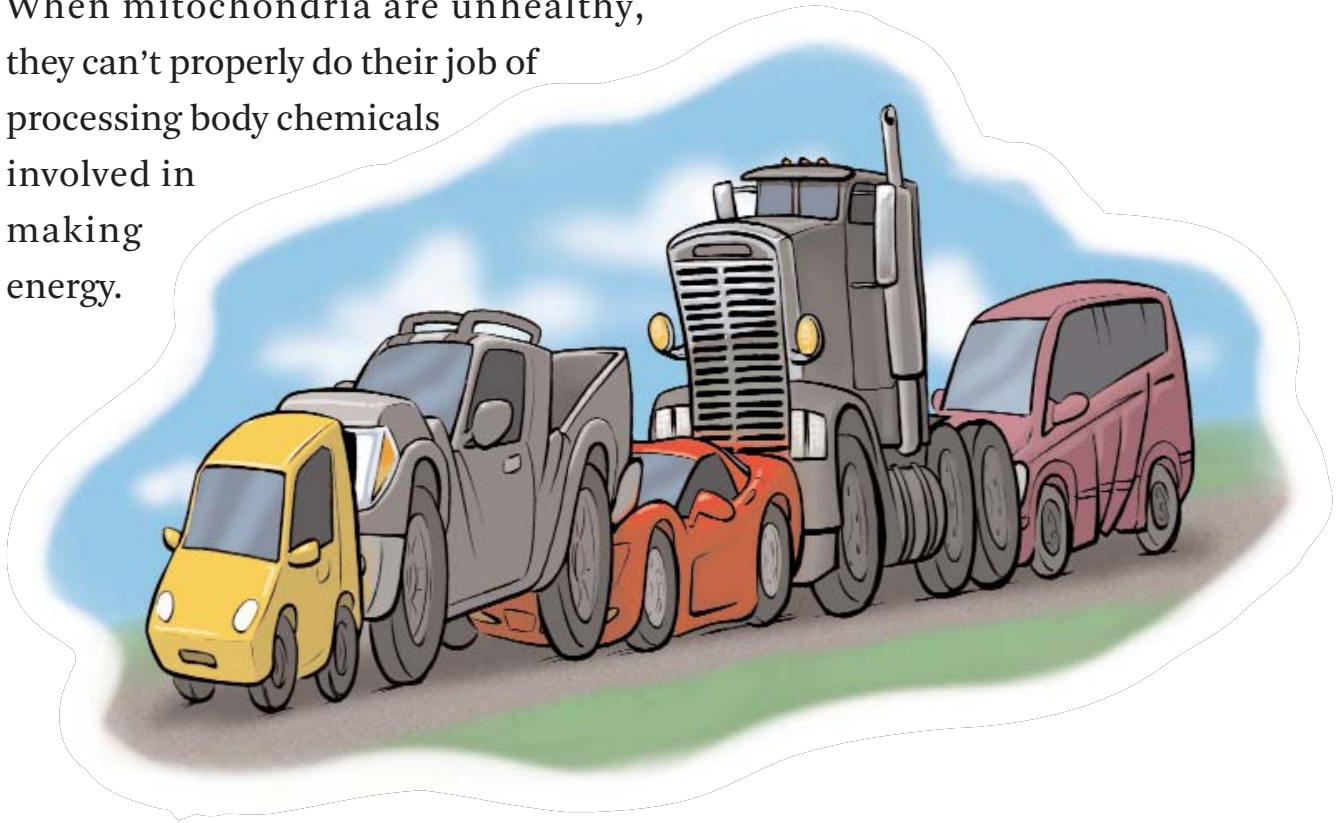
- Evaluating a patient's family history
- A complete physical examination
- A neurological examination
- A metabolic examination that involves testing the blood and urine, and, if needed, doing a cerebral spinal fluid test (spinal tap)
- Genetic DNA tests in blood
- Other tests, depending on the patient's symptoms and the areas of the body that are affected, might include:
 - Magnetic resonance imaging (MRI) or spectroscopy (MRS) for neurological symptoms
 - Retinal exam or electroretinogram (ERG) for vision symptoms
 - Electrocardiogram (EKG) or echocardiogram for symptoms of heart disease
 - Audiogram or Auditory-Brainstem Evoked Responses (ABER) for hearing symptoms
 - Blood test to detect thyroid dysfunction if the patient has thyroid problems

More Invasive Tests

If the first series of tests to diagnose mitochondrial disease doesn't provide any useful results, more tests may be needed. Your doctor may want to test chemical markers in the body's fluid and tissues. This procedure, called biochemical testing, looks for changes in the body's chemistry. Some of these tests, such as tissue analysis, may be invasive (meaning that they involve making a puncture or incision on a part of the body).

Testing Body Fluids

When mitochondria are unhealthy, they can't properly do their job of processing body chemicals involved in making energy.



When mitochondria can't process chemicals properly, some of the chemicals hit a roadblock that causes a pileup, spilling them into blood, urine, and spinal fluid.

Instead of continuing into the mitochondria for processing, some of the chemicals essentially hit a roadblock, resulting in a pileup. This chemical accumulation spills over and can be measured in the blood, urine, and spinal fluid.

These chemicals include:

- Lactate
- Pyruvate
- Alanine
- Products of the Krebs cycle (also called the citric acid cycle)

Testing the Tissue: Skin Biopsy

A skin biopsy is a procedure in which the doctor removes a small sample of skin to have it tested. The skin sample may be removed with a punch biopsy, a type of biopsy that uses an instrument similar to a pencil with a sharp, round, hollow opening where the eraser should be.

During the biopsy:

- The doctor will clean the biopsy site.
- He or she will then numb the skin with an anesthetic spray, cream, or injection.
- Next, the doctor will remove two small (3 mm) pieces of skin.
- A nurse may apply pressure to the area to stop the bleeding.
- The doctor will then close the incision, using adhesive strips that look like small pieces of tape.

The entire biopsy procedure lasts about 15 minutes.

After the biopsy:

- You will need to stay in the treatment area for a short time for observation.
- You may have some soreness around the biopsied area for one to two weeks.
- Ask your doctor when you should come back for a follow-up visit.
- You may have a small scar at the biopsy site.

Testing the skin sample:

The skin sample is sent to a lab and the mitochondria are examined with an electron microscope. Because skin tissue is different from muscle, brain, heart, and liver tissue, the test results are not always helpful in diagnosing a disease.

Testing the Tissue: Muscle Biopsy

A muscle biopsy is a surgical procedure in which small samples of muscle tissue are removed for testing. Because a muscle biopsy is an invasive, expensive test that requires the use of general anesthesia for children, you and your doctor may want to compare the risks and costs of the test with any benefits that could result from a diagnosis.

Before the biopsy:

- You (or your child) will be given general anesthesia. This will make you very relaxed and you will then be sedated (in a sleep-like state) for the procedure.

During the biopsy:

- The surgeon will clean the biopsy site.
- He or she will then make a small incision (1- to 2-inch cut), usually in the top of the thigh, and remove up to three one-cubic centimeter samples from the muscle.
- The doctor will close the incision, usually with stitches.

The entire biopsy procedure lasts about 30 minutes.

After the biopsy:

- You will stay in the treatment area for a short time for observation.
- There will be some muscle soreness (similar to a pulled muscle or a muscle strain) around the biopsied area for one to two weeks.
- Your doctor may prescribe medication to relieve pain for a few days after the procedure.
- Keep the incision area as clean and as dry as possible. The doctor will tell you when the stitches should be removed.
- Ask your doctor when you should come back for a follow-up visit.
- You may have a 1- to 2-inch scar from the biopsy.

Testing the muscle sample:

Muscle removed for biopsy can be tested in many ways. Muscle is studied under the microscope to see how the mitochondria appear. Some of the enzymes that work in the mitochondria can also be measured.

While these test results can show signs of mitochondrial disease or that the mitochondria are not healthy, this only confirms that there is a problem, and not necessarily what the problem is.

Muscle should also be sent for specialized genetic which cannot be performed accurately in blood.

Treating the Problem

There is no cure for mitochondrial disease, but treatment can help reduce symptoms, or delay or prevent the progression of the disease.

However, each person needs a treatment that is individually tailored to him or her. Because people are “**biochemically different**,” no two people will respond to a treatment in the exact way, even if they have the same condition.

Treatments for mitochondrial disease may include:

- Screening test to see if any other body systems are affected
- Special medical precautions when sick or needing medical procedures or surgeries
- Physical, speech and occupational therapy
- Vitamins and supplements, including:
 - Coenzyme Q10
 - B complex vitamins: thiamine (B₁), riboflavin (B₂), niacin (B₃), B₆, folate, B₁₂, biotin, pantothenic acid
- Increasing the doses of these supplements during illness
- **Diet changes** prescribed by a doctor along with a registered dietitian

Moving Forward

Once a person has been diagnosed with a specific mitochondrial disease, work on treating it can begin. However, there is no way to predict how the disease will affect a person in the long run. It might progress quickly or slowly, even over decades. It might also appear stable for years.

Your doctor can help you figure out what course your condition might take and provide you with the proper treatment.

Mitochondrial Disease Organizations

United Mitochondrial Disease Foundation (UMDF)

8085 Saltsburg Road, Suite 201

Pittsburgh, PA 15239

Phone: 1.888.317.UMDF (8633)

E-mail: info@umdf.org

www.umdf.org

Mitochondrial Medicine Society (MMS)

www.mitosoc.org

Organic Acidemia Association

9040 Duluth Street

Golden Valley, MN 55427

Phone: 763.559.1797 (Central Time)

Fax: 866.539.4060 (Toll-free)

E-mail: mkstagni@gmail.com

www.oaanews.org

Fatty Oxidation Disorder Support Group

PO Box 54

Okemos, MI 48805-0054

Phone: 517.381.1940 (8 am-8 pm EST)

Fax: 866.290.4060 (Toll-free)

E-mail: deb@fodsupport.org

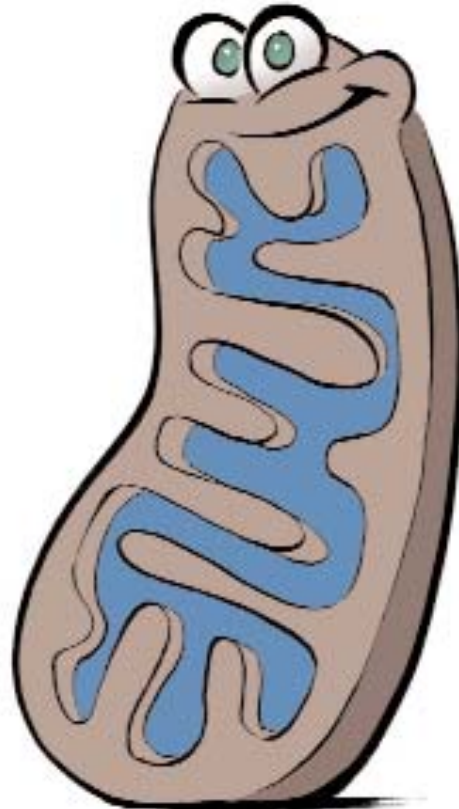
www.FODsupport.org

Cleveland Clinic

Neurological Institute

Pediatric Neurology & Neurosurgery

<http://my.clevelandclinic.org/departments/neurological>



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This information is not intended to replace the medical advice of your doctor or health care provider. Please consult your health care provider for advice about a specific medical condition.



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Produced by the Cleveland Clinic Center for Consumer Health Information

Illustrations by Joe Bluhm, www.joebluhm.com

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