

Facts About **Genetics** and Neuromuscular Diseases

MDA[®] Muscular
Dystrophy
Association
Fighting Muscle Disease

Dear Friends:

Most of the neuromuscular disorders in the Muscular Dystrophy Association's program are genetic, and MDA's worldwide research program has discovered the genetic causes and inheritance patterns of dozens of these diseases. Building on these recent findings, MDA-supported investigators are exploring a world of potential treatments.

"Facts about Genetics and Neuromuscular Diseases" gives an up-to-date review of genetics information relating to neuromuscular diseases.

This booklet describes what a genetic disorder is and explains how genetic testing and counseling can help people understand how disorders that may affect themselves or their children are inherited. It also gives examples of the major patterns of inheritance, with specific neuromuscular diseases as examples. Finally, it looks at mitochondrial inheritance, an aspect of genetics whose importance is becoming increasingly appreciated.

If you have a neuromuscular disease, or would like to know more about a particular disease in MDA's program, ask at your local MDA office for the booklet covering that disorder.

You also can find out more about MDA's services and other programs, keep current on new research, and get information on medical and disability issues by reading other MDA publications, visiting www.mda.org or calling (800) 572-1717.



What Is a Genetic Disorder?

A genetic disorder is a condition that's caused by a change, called a mutation, in a gene. A disease-causing mutation generally interferes with the body's production of a particular protein.

What is a gene?

Genes, made of the chemical known as DNA (deoxyribonucleic acid), are strings of chemicals that form a "rough draft" of the recipes (often called codes) for the thousands of proteins our bodies use to build cellular structures and carry out the functions of our cells.

DNA is stored on strands called chromosomes, located mostly in the nucleus of each cell in the body.

How do genes lead to proteins?

The final copies of the protein recipes are actually carried in RNA (ribonucleic acid), a very close chemical cousin of DNA. The cell converts DNA to RNA in its nucleus. Each RNA recipe then leaves the cell's nucleus and becomes the instruction manual for the manufacturing of a protein outside the nucleus.

How do mutations in genes lead to problems in proteins?

A mutation in the DNA for any protein can become a mutation (error) in the RNA recipe and then an error in the protein made from those RNA instructions. Some mutations are worse than others for the cell. Some mutations lead to production of a slightly abnormal protein, while others lead to a very abnormal protein or to the complete absence of a particular protein.

How do protein problems affect people?

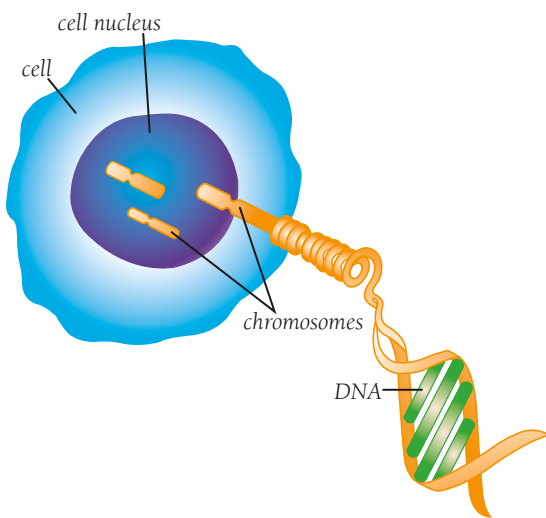
The effects of a mutation in DNA in a person depend on many factors, among them exactly how the mutation affects the final protein (whether the protein is made at all and, if so, how close to normal it is), and how crucial that protein is in the body.

For example, some mutations in the gene for the protein dystrophin lead to relatively mild muscle weakness, while others lead to very severe weakness, depending on how much dystrophin is produced and how close it is to normal dystrophin. The mutations leading to severe weakness ultimately threaten life because dystrophin is needed for cardiac and respiratory muscle functions.

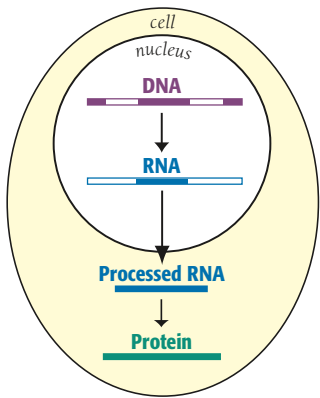
All this may seem like a lot of explanation, but it's the basis for how you and the professionals you consult can make decisions about any genetic disorder that may be in your family.

What do proteins do?

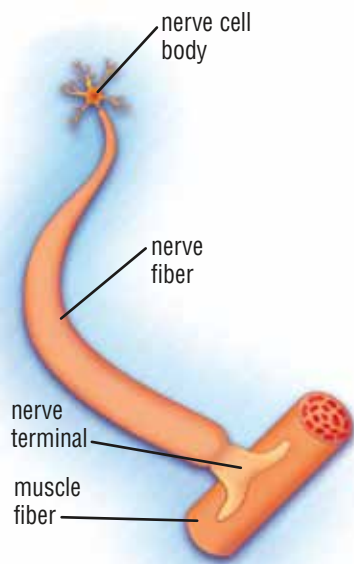
The functions of proteins include such things as sending or receiving signals to or from other cells, breaking down large molecules into smaller ones, combining smaller molecules to make larger ones, and producing energy for all cellular activities. These activities ultimately result in functions like muscle contraction, digestion and metabolism of food, and regulation of blood pressure and temperature, as well as seeing, hearing, thinking and feeling.



Genes are made of DNA, which is stored on chromosomes in each cell nucleus.



A cell converts each gene (DNA sequence) into RNA in the nucleus. A fully processed copy of the gene's RNA moves out of the nucleus, where a protein is made from this RNA "recipe."



Proteins in nerve cells affect the way the cell receives and transmits signals, including those it sends to muscle fibers. Muscle fiber proteins affect muscle contraction and protect fibers from contraction-related damage.

What about the proteins in MDA-covered disorders?

The proteins involved in the genetic disorders that MDA covers are normally present in nerve cells or muscle cells. Proteins in nerve cells affect the way a nerve cell receives signals from other cells or transmits signals to other cells, including muscle cells.

Proteins in muscle cells affect the functions of the muscle cell, such as contraction (the action that moves muscles), the way in which the muscle cell receives signals from a nerve cell or the various mechanisms by which a muscle cell protects itself from the stresses of its own workload.

When genes for these nerve and muscle proteins are mutated, loss of or abnormalities in these proteins cause genetic neuromuscular disorders.

What is genetic testing?

Genetic testing usually means the direct examination of the DNA in a gene associated with a particular disorder. (It can sometimes mean RNA or the protein product of the DNA and RNA.) The examination is usually made in order to enhance the understanding of symptoms (for example, to confirm a diagnosis of a muscular dystrophy), or to predict the occurrence of a genetic disorder in which symptoms haven't yet appeared.

What kind of sample is needed for genetic testing?

Usually, only a blood sample is needed, but occasionally other tissues are used for the testing.

Why should I get a genetic test?

Just a few years ago, genetic testing was mainly undertaken when people were thinking about starting or adding to a family and wanted more precise information about inheritance risks than they

already had; or to confirm a physician's clinical diagnosis and add to information about the probable course and severity of a disease.

However, as of 2007, there are many experimental treatments for neuromuscular diseases in development that require precise knowledge of a person's genetic mutation.

For example, there are compounds in development that are designed to make cells ignore a type of mutation known as a "premature stop codon," which arrests the synthesis of a protein before the genetic instructions are completely processed. And there are others that are targeted to block a cell's ability to "read" specific, error-containing instructions.

When genetic testing was thought to be largely predictive and to have no therapeutic value, many medical centers discouraged testing of children before the appearance of symptoms, for fear of stigmatizing them or jeopardizing insurance coverage.

However, those ideas are being re-examined in light of new knowledge. It's likely that newborns will be screened for an increasing number of genetic disorders in the coming years, as treatments become available, and that the barriers to DNA testing of children will be lowered. Treatments for genetic disorders will almost certainly be more successful if they're started early in life.

Where can I get a genetic test?

You can ask about genetic testing at your MDA clinic. In some cases, the testing can be done at the same institution where the clinic is held. But in most cases, the blood sample will be sent to an outside laboratory. Athena Diagnostics (www.athenadiagnostics.com), for example, is a large commercial laboratory in Worcester, Mass., that can perform DNA testing for a number of MDA's diseases. You also can check www.genetests.org for a laboratory near you.



Some treatments being developed for neuromuscular diseases will require precise knowledge of a patient's genetic mutation.



Genetic counselors and physicians can help people make decisions about genetic testing and childbearing.

How much does genetic testing cost?

If you're part of a study, there's usually no cost for DNA testing. In some cases, an MDA clinic may have set aside funds specifically for genetic testing. And in some instances, insurance will cover the test. If, however, you have to pay for genetic testing, costs range from about \$250 to almost \$4,000, depending on the specific test and the laboratory.

What's the downside of genetic testing?

In the United States, fears about being discriminated against when applying for health insurance are not without basis. Even fears about discrimination by employers, although less likely, are not out of the question, although privacy regulations generally prohibit this kind of information from being accessed by most potential employers.

Prenatal testing almost always causes anguish for parents if the results show the baby has a disease-causing mutation. Sometimes the test results can't tell the family how seriously the child is likely to be affected, making the choice of whether or not to continue the pregnancy even more difficult. Some parents would rather just take their chances than have to face this type of decision.

Testing that reveals a young child's genetic destiny may affect relationships within the family or may cause parents more sadness than they would have experienced had events simply unfolded, especially if no treatment for the disease in question is available. A positive genetic test that reveals a child is a carrier of a disease (see page 6) may be unsettling, especially if the child is young and the implications for his or her future children are uncertain.

In addition, the results of one person's tests have implications for the genetic status of relatives, whether or not they have volunteered to be tested themselves. For

example, if an autosomal recessive disease (see page 6) is diagnosed by genetic testing, it usually means that both the patient's parents are carriers and that the patient's siblings are also at risk.

Last but not least, the results of a DNA test are not always easy to interpret. Some types of tests only reveal the presence or absence of a disease-causing mutation in a certain percentage of cases, leaving the person who gets a negative result (no mutation found) uncertain about the future. In other cases, mutations may be found whose significance is uncertain. Or a mutation may be a known risk factor for a disease, but the degree of risk may be hard to estimate. On occasion, actual errors are made in the testing process.

Can someone give me guidance?

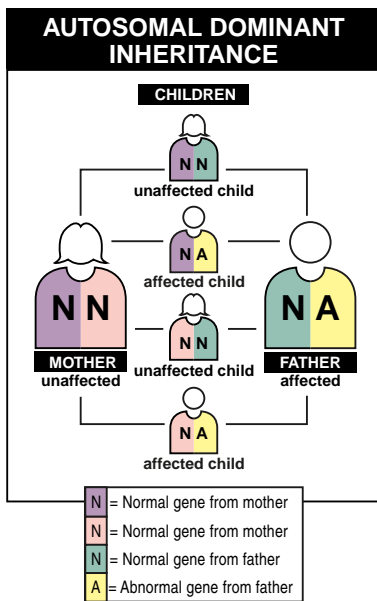
The best way to make the right decision about genetic testing and make sure you get the right test and understand the results is to work with a certified genetic counselor.

Genetic counselors have graduate degrees that reflect extensive knowledge of both biology and counseling principles. They can guide you through the testing process.

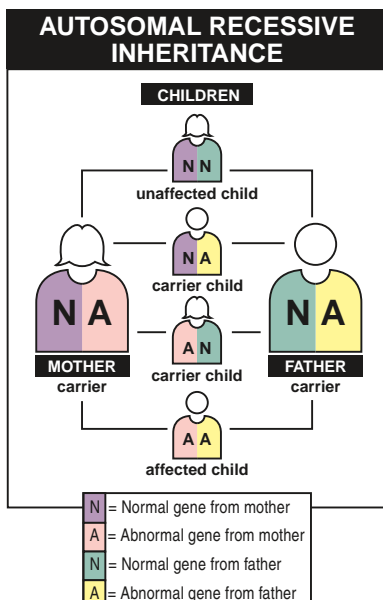
Almost all major medical centers now have genetic counselors on staff, and your MDA clinic physician can refer you to one.

How are genetic disorders inherited?

Long before the advent of genetic testing or even complete understanding of DNA and RNA, astute observers noticed that genetic traits, including many disorders, were passed from one generation to another in somewhat predictable patterns. These came to be known as autosomal dominant, autosomal recessive, X-linked recessive and X-linked dominant patterns of inheritance.



Diseases inherited in an autosomal dominant pattern require only one genetic mutation to cause symptoms.



Diseases inherited in an autosomal recessive pattern require two genetic mutations (one from each parent) to cause symptoms.

To understand heredity, you have to know a little about human chromosomes and how they work.

Chromosomes come in pairs in the cell's nucleus. Humans have 46 chromosomes in each cell nucleus, which are actually 23 pairs of chromosomes. For 22 of these pairs, numbered chromosome 1 through chromosome 22, the chromosomes are the same; that is, they carry genes for the same traits. One chromosome comes from a person's mother, the other from his father.

The 23rd pair is an exception and determines gender. The 23rd chromosomal pair differs according to whether you're a male or a female. Males have an X and a Y chromosome, while females have two Xs for this 23rd pair of chromosomes. Every female gets one X chromosome from her mother and one X from her father. Every male gets an X chromosome from his mother and a Y from his father.

Y chromosomes are unique to males and, in fact, determine maleness. If a man passes to his child an X chromosome from this 23rd pair, it will be a girl; if he donates a Y, it will be a boy.

Autosomal dominant conditions require only one mutation to show themselves. When specialists use the term autosomal dominant, they mean that the genetic mutation is on an autosome, one of the chromosomes that's not an X or a Y. They also mean that the condition caused by the mutation can occur even if only one of the two paired autosomes carries the mutation. It's a way of saying that the mutated gene is dominant over the normal gene.

In autosomal dominant disorders, the chance of having an affected child is 50 percent with each conception.

Autosomal recessive conditions require two mutations to show themselves. When they use the term autosomal recessive,

they mean that the disorder is again located on chromosomes that aren't Xs or Ys. However, when a disorder is recessive, it takes two mutated genes to cause a visible disorder in a person.

The word "recessive" comes from the idea that, when only one gene mutation exists, it may remain undetected ("recede" into the background) for several generations in a family — until someone has a child with another person who also has a mutation in that same autosomal gene. Then, the two recessive genes can come together in a child and produce the signs and symptoms of a genetic disorder.

You can think of recessive genes as "weaker" than "dominant" genes, in that it takes two of them to cause a problem.

People with one gene mutation for disorders that require two to produce the disorder are said to be carriers of the disorder. Carriers are usually protected from showing symptoms of a genetic disease by the presence of a normal corresponding gene on the other chromosome of each chromosome pair.

Sometimes, biochemical or other electrical testing, or certain conditions (for example, vigorous exercise or fasting) will reveal subtle cellular abnormalities in carriers of various genetic conditions.

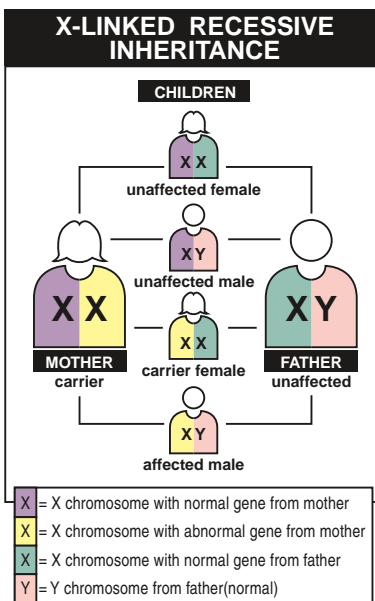
In autosomal recessive disorders, the chance of having an affected child is 25 percent with each conception.

X-linked disorders affect males and females differently. Another important inheritance pattern is the X-linked pattern. X-linked disorders come from mutations in genes on the X chromosome.

X-linked disorders affect males more severely than they do females. The reason is that females have two X chromosomes, while males have only one. If there's a mutation in an X-chromosome gene, the



Duchenne muscular dystrophy is an X-linked disease and mostly affects boys. Female carriers usually don't have symptoms.



Diseases inherited in an X-linked recessive pattern mostly affect males because a second X chromosome usually protects females from showing symptoms.

female has a second, “backup” X chromosome that almost always carries a normal version of the gene and can usually compensate for the mutated gene. The male, on the other hand, has no such backup; he has a Y chromosome paired with his sole X.

In reality, females sometimes have disease symptoms in X-linked conditions despite the presence of a backup X chromosome. In some X-linked disorders, females routinely show symptoms of the disease, although they’re rarely as serious (or lethal) as those in the males.

Some experts prefer the term X-linked recessive for the type of X-linked disorder in which females rarely show symptoms and X-linked dominant for the type in which females routinely show at least some disease symptoms.

Females with mild or no disease symptoms who have one mutated gene on an X chromosome and a normal version of the gene on the other X chromosome are called carriers of an X-linked disorder.

In X-linked recessive disorders, when the mother is a carrier, the chance of having an affected child is 50 percent for each male child. If the father has the mutation and is able to sire children, boys won’t be affected because they receive only a Y chromosome from him. Girls receive his X chromosome and will be carriers.

Can inheritance diagrams predict what my family will look like?

No. Many of us have seen diagrams like those on pages 6 through 7 during our school years or perhaps in medical offices. Unfortunately, these diagrams very often lead to misunderstandings.

The diagrams are mathematical calculations of the odds that one gene or the other in a pair of genes will be passed on to a child during any particular conception.

These are the same kinds of calculations one would make if asked to predict the chances of a coin landing as heads or tails. With each coin toss (assuming the coin isn’t weighted and the conditions are otherwise impartial), the chances that the coin will land in one position or the other are 50 percent.

In reality, if you were to toss a coin six times, you might come up with any number of combinations: All your tosses might be heads, or five could be heads with one tails, or four might be tails with two heads.

In fact, every coin toss was a new set of odds: 50 percent heads, 50 percent tails. The second coin toss wasn’t the least bit influenced by the first, nor the third by the first two, nor the sixth by the previous five.

So it is with the conception of children. If the odds of passing on a certain gene (say a gene on the X chromosome that carries a mutation versus a gene on the other X chromosome that doesn’t) are 50 percent for each conception, they remain 50 percent no matter how many children you have.

Don’t be misled by an orderly diagram that shows one out of two children getting each gene so that a family of four children has two children with and two children without the gene in question.

Like the coin toss where six tosses turned up six heads, you could have six children who all inherit the gene, or none who inherit the gene.

What happens in actual families?

In real life, it’s impossible to predict which genes will be passed on to which children at each conception. This kind of prediction would be the same as trying to predict the outcome of any particular coin toss. Even though the overall odds are 50 percent

heads and 50 percent tails, you can get six heads in a row.

This pamphlet offers some examples of what could happen in actual situations.

The type of diagram seen on pages 11, 12 and 13 is called a family tree or pedigree. Geneticists and genetic counselors may construct a pedigree or tree as you give your family history, or you may see these in books or on Web sites.

How can a disease be genetic if no one else in the family has it?

This is a question often asked by people who have received a diagnosis of a genetic disorder or who have had a child with such a diagnosis. “But, doctor,” they often say, “There’s no history of anything like this in our family, so how can it be genetic?” This is a very understandable source of confusion.

Very often, a genetic (or hereditary) disorder occurs in a family where no one else has been known to have it.

One way for this to happen is the mechanism of recessive inheritance (see page 6). In recessive disorders, it takes two mutated genes to cause disease symptoms. A single genetic mutation may have been present and passed down in a family for generations but only now has a child inherited a second mutation from the other side of the family and so developed the disease.

A similar mechanism occurs with X-linked disorders (see page 7). The family may have carried a mutation on the X chromosome in females for generations, but until someone gives birth to a male child with this mutation, the genetic disorder remains only a potential, not an actual, disease. (Females rarely have significant symptoms in X-linked disorders.)

Another way for a child to develop a dominant or X-linked disease that’s never

been seen in the family follows this scenario: One or more of the father’s sperm cells or one or more of the mother’s egg cells develops a mutation. Such a mutation would never be detected by standard medical tests or even by DNA tests, which generally sample the blood cells. However, if this particular sperm or egg is used to conceive a child, he or she will be born with the mutation.

Until recently, when parents who didn’t have a genetic disorder and tested as “noncarriers” gave birth to a child with a genetic disorder, they were reassured that the mutation was a one-time event in a single sperm or egg cell, and that it would be almost impossible for it to happen again.

Unfortunately, especially in the case of Duchenne dystrophy, this proved to be false reassurance. We now know that sometimes more than one egg cell can be affected by a mutation that isn’t in the mother’s blood cells and doesn’t show up on standard carrier tests. Such mothers can give birth to more children with Duchenne dystrophy because subsequent egg cells with the Duchenne mutation can be used to conceive a child.

In a sense, these mothers actually are carriers — but carriers only in some of their cells. They can be thought of as “partial” carriers. Another term is mosaic carrier. It’s very hard to estimate the precise risk of passing on the disorder in these cases.

It’s very likely that this kind of situation occurs in other neuromuscular genetic disorders, although most haven’t been as well studied as Duchenne dystrophy. For example, more than one sperm or egg cell could pass on a dominant mutation to more than one of a parent’s children. Or, in a recessive disorder like spinal muscular atrophy, a child could inherit one mutation from a parent who’s a full carrier, and then acquire a second genetic mutation



This mother and son have myotonic dystrophy, which is dominantly inherited. By contrast, in recessive or X-linked disorders, parents who are unaffected carriers can give birth to affected children.

from the other parent, a mosaic carrier. Standard carrier testing wouldn't pick up any problem in the latter parent.

In practical terms, the most important message of recent research is that a genetic test that looks only at blood cells and shows that a parent is not a carrier can't be completely relied upon with regard to the risk of having another affected child. The mutation may be present in cells that weren't tested, and if those include some of the sperm or egg cells, there's a risk that more than one affected child could be born.

A geneticist or genetic counselor can help you make informed decisions regarding childbearing if you've already had a child with a genetic disorder. The recurrence risk is different in different disorders.

Are there genes outside the cell's nucleus?

Yes. There's actually another small set of genes that we all possess, inside our cells but outside the cell nucleus. The cell nucleus is where most of our genes reside on the 23 pairs of chromosomes already discussed.

The additional genes, which make up less than 1 percent of a cell's DNA, are the

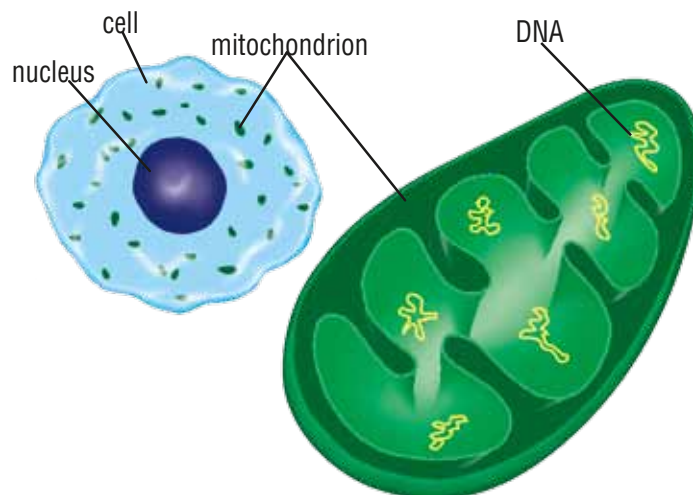
mitochondrial genes, and they exist as circular strands of DNA inside mitochondria, the "energy factories" of cells. (The singular for mitochondria is mitochondrion.)

What are genes doing inside the mitochondria?

There are 37 genes, mostly involved in energy production, inside the mitochondria. Scientists believe that mitochondria were once independent organisms resembling today's bacteria, and that when they became part of human and animal cells, they kept their own genes. These genes, arranged on structures that are like the nuclear chromosomes but are ring-like in shape, carry the recipes for 13 proteins needed for mitochondrial functions. They also carry codes for 24 specialized RNA molecules that are needed to assist in the production of other mitochondrial proteins. For reasons that will become clear, it's important to know that mitochondria also use proteins made by genes in the cell's nucleus. These proteins are "imported" into the mitochondria.

Can disease-causing mutations occur in mitochondrial genes?

Yes. Disease-causing mutations can occur in the mitochondrial genes. The disorders are often, as one would predict, associ-



Each mitochondrion has its own DNA (genes) but also is affected by genes from the cell's nucleus.

ated with energy deficits in cells with high energy requirements, such as nerve and muscle cells. The disorders as a whole are called mitochondrial disorders. Mitochondrial disorders affecting muscle are known as mitochondrial myopathies.

How are mitochondrial mutations inherited?

Mitochondrial DNA inheritance comes only through the mother and is therefore completely different from nuclear (from the nucleus) DNA inheritance. The rules for recessive, dominant and X-linked inheritance don't apply at all.

An embryo receives its mitochondria from the mother's egg cell, not the father's sperm cell, at conception. (Research suggests that sperm mitochondria are eliminated by the egg cell.)

Mutations can exist in some of the mitochondria in a person's cells and never cause much, if any, trouble. (In fact, one theory of aging says that it's caused by an accumulation of mutations in mitochondrial DNA.) The normal mitochondria are usually enough to produce the needed energy for the body. But once a person has a certain percentage of mutated mitochondria (perhaps 30 percent or so), the energy deficits become crucial and a mitochondrial disorder can result.

Mothers can pass on mitochondrial mutations to their children, but fathers can't, so mitochondrial DNA inheritance follows a pattern called maternal inheritance. The severity of the child's disorder depends on how many normal versus abnormal mitochondria the child receives from the mother.

Mitochondrial DNA mutations can also occur during development of an embryo. Not all mitochondrial mutations are inherited. Some occur as an embryo is developing in the womb. Researchers have found that embryonic mitochondrial mutations generally occur after sperm or egg cells

have formed in the affected embryo, so, as far as has been observed, these mutations are not passed on to the next generation.

Does DNA from the cell's nucleus affect the mitochondria?

Yes. DNA from the nucleus also affects mitochondrial function, so some mitochondrial disorders are inherited according to the same rules as are other genetic disorders.

Most mitochondrial proteins aren't made in the mitochondria but come from genes in the cell's nucleus. These nuclear proteins are later imported into the mitochondria, where they too help with energy production.

As you may have guessed, mutations also can occur in these nuclear genes that affect mitochondria. So, that's another way to get a "mitochondrial disorder" — but one that's not caused by mutated mitochondrial DNA.

Nuclear DNA that affects mitochondrial function is inherited according to the autosomal and X-linked patterns described on pages 5 to 7.

For family planning, it's important to know exactly what kind of DNA mutation exists in a family with a mitochondrial disorder — whether it's a mitochondrial DNA mutation or a nuclear DNA mutation. As you can see, these have very different patterns of inheritance and implications for the family.



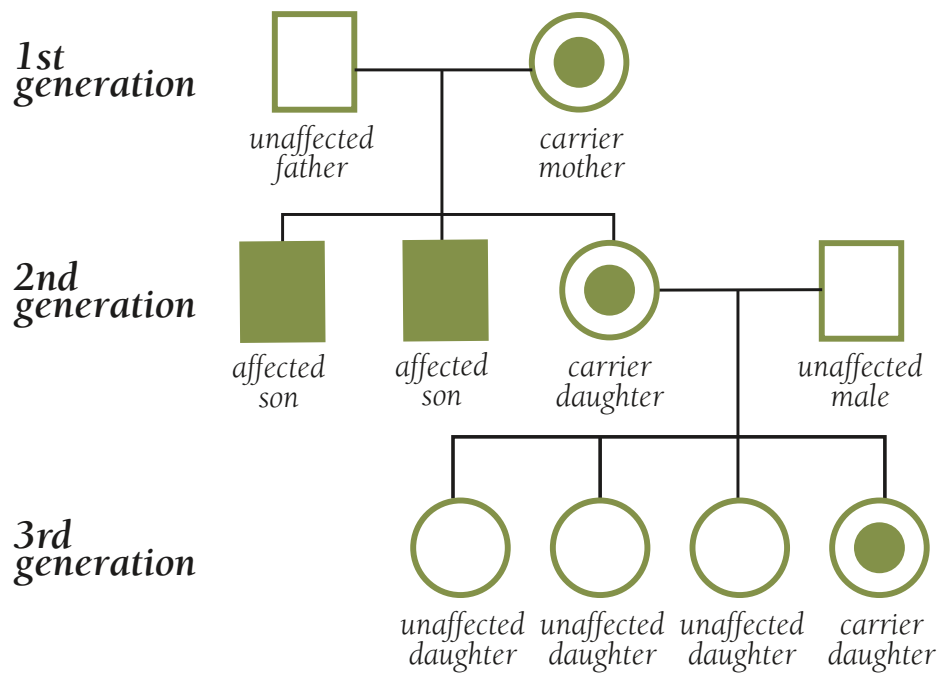
Mothers can pass flawed mitochondrial genes to their children, but fathers can't.

What May Happen in a Family with Duchenne MD

In this hypothetical family, all three children in the second generation got the X chromosome with the flawed gene.

Duchenne muscular dystrophy (DMD) is an X-linked disorder in which females rarely show symptoms but can be carriers. The mother in this family is a carrier. The parents have two sons with DMD, each of whom received an X chromosome with a DMD mutation from their mother.

They also have a daughter who received an X chromosome with a DMD mutation; she, like her mother, is a carrier. The daughter has married a man with no DMD mutation, and they've had four daughters. Three of the daughters didn't get the DMD mutation from their mother, but one did. She's also a carrier.

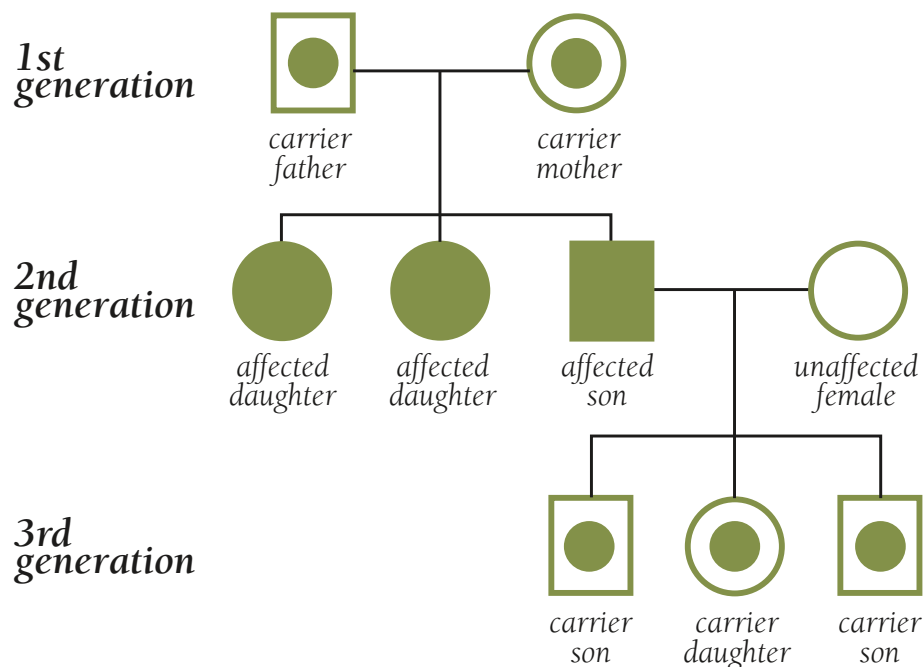


What May Happen in a Family with Spinal Muscular Atrophy

Recessive genes came together in all three children in the second generation of this hypothetical family, making it inevitable that the third generation would be carriers.

Spinal muscular atrophy (SMA) is an autosomal recessive disorder carried on chromosome 5. In this family, the father and mother are both carriers of a mutation on chromosome 5. They have no symptoms of the disease, since it takes two such mutations in a recessive disorder to cause symptoms. They had two daughters and one son, all of whom inherited a chromosome 5 with an

SMA-causing mutation from each parent. They all have the disorder. One affected son married an unaffected woman. Their children are all unaffected carriers of SMA, having inherited one chromosome 5 with a mutation from their father and one without this mutation from their mother. All of the children of this man had to inherit a chromosome 5 SMA mutation, because they had to get one chromosome 5 from their father and both of his chromosome 5s have this mutation. They couldn't have inherited this kind of mutation from their mother because she's not a carrier.

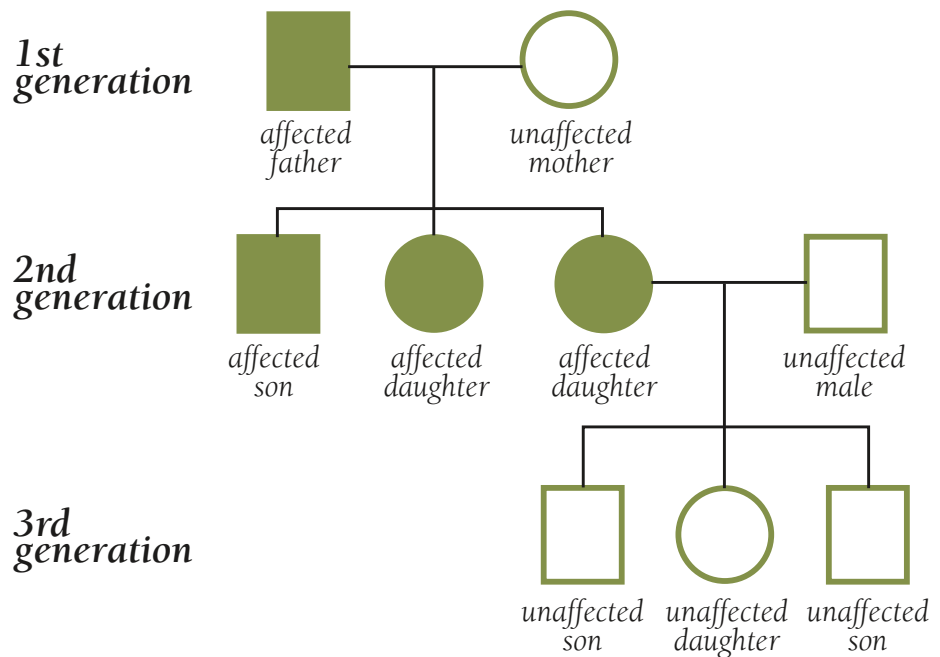


What May Happen in a Family with Myotonic MD

The third generation escaped the disease in this hypothetical family, but the son and both daughters in the second generation got the disease-causing mutation.

Myotonic muscular dystrophy (MMD) is an autosomal dominant disorder carried on chromosome 19 or chromosome 3. In this family, the father has the mutation on one of his chromosome 19s. His square is colored in because he has the symptoms of MMD, as would be expected in a dominant disorder. Since he has one chromosome 19 with the MMD mutation and another that doesn't

have it, he can pass either one to his children. He married an unaffected woman. Unfortunately, all three of their children — one son and two daughters — inherited from their father a chromosome 19 with an MMD mutation. Even one mutation was enough to cause the disease in all three. One of the affected daughters married an unaffected man. By luck, neither their two sons nor their daughter inherited a chromosome 19 with an MMD mutation from their affected mother. The father's chromosome 19s are both normal.



MDA Is Here to Help You

The Muscular Dystrophy Association offers a vast array of services to help you and your family deal with neuromuscular disease. The staff at your local MDA office is there to assist you in many ways. The Association's services include:

- nationwide network of clinics staffed by top neuromuscular disease specialists
- MDA summer camps for kids with neuromuscular diseases
- help with locating durable medical equipment through its national equipment program
- financial assistance with repairs or modifications to all types of durable medical equipment
- annual occupational, physical, respiratory or speech therapy consultations
- annual flu shots
- support groups for those affected, spouses, parents or other caregivers
- online support services through the e-community *myMDA* and through *myMuscleTeam*, a program that helps recruit and coordinate in-home help

MDA's public health education program helps you stay abreast of research news, medical findings and disability information through magazines, publications, educational speakers, seminars, videos and newsletters.

MDA's website at www.mda.org contains thousands of pages of valuable information, including disease specifics, research findings, clinical trials and past magazine articles.

Everyone registered with MDA automatically receives *Quest*, MDA's award-winning quarterly magazine. *Quest* publishes detailed articles about research findings, medical and day-to-day care, helpful products and devices, social and family issues, and much more. Other MDA publications can be found at www.mda.org/publications; many booklets are available in Spanish. Ask your local office for "MDA Services for the Individual, Family and Community" and for help with obtaining copies of other publications.

If you want to learn about the genetics of your particular neuromuscular disorder, you'll need to consult a specialist. Your MDA clinic physician can refer you to a geneticist or genetic counselor for testing and information.

If you have any questions about muscular dystrophy and neuromuscular disease, someone at MDA will help you find the answer. To reach your local MDA office, call (800) 572-1717.



On the cover: Alexis "Lexye," center, has spinal muscular atrophy (SMA). Pictured here with her parents and her twin siblings, Jory and Aaron.



MDA's website, mda.org, is constantly updated with the latest research news and information about the diseases in its program. Follow MDA on Facebook, Twitter and YouTube.



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MDA's Purpose and Programs

The Muscular Dystrophy Association fights neuromuscular diseases through an unparalleled worldwide research effort. The following diseases are included in MDA's program:

Muscular Dystrophies

Myotonic dystrophy (*Steinert disease*)
Duchenne muscular dystrophy
Becker muscular dystrophy
Limb-girdle muscular dystrophy
Facioscapulohumeral muscular dystrophy
Congenital muscular dystrophy
Oculopharyngeal muscular dystrophy
Distal muscular dystrophy
Emery-Dreifuss muscular dystrophy

Motor Neuron Diseases

Amyotrophic lateral sclerosis (*ALS*)
Infantile progressive spinal muscular atrophy
(*Type 1, Werdnig-Hoffmann disease*)
Intermediate spinal muscular atrophy
(*Type 2*)
Juvenile spinal muscular atrophy
(*Type 3, Kugelberg-Welander disease*)
Adult spinal muscular atrophy (*Type 4*)
Spinal-bulbar muscular atrophy
(*Kennedy disease*)

Inflammatory Myopathies

Polymyositis
Dermatomyositis
Inclusion-body myositis

Diseases of Neuromuscular Junction

Myasthenia gravis
Lambert-Eaton (myasthenic) syndrome
Congenital myasthenic syndromes

Diseases of Peripheral Nerve

Charcot-Marie-Tooth disease
Friedreich's ataxia
Dejerine-Sottas disease

Metabolic Diseases of Muscle

Phosphorylase deficiency (*McArdle disease*)
Acid maltase deficiency (*Pompe disease*)
Phosphofructokinase deficiency
(*Tarui disease*)
Debrancher enzyme deficiency
(*Cori or Forbes disease*)
Mitochondrial myopathy
Carnitine deficiency
Carnitine palmityl transferase deficiency
Phosphoglycerate kinase deficiency
Phosphoglycerate mutase deficiency
Lactate dehydrogenase deficiency
Myoadenylate deaminase deficiency

Myopathies Due to Endocrine Abnormalities

Hyperthyroid myopathy
Hypothyroid myopathy

Other Myopathies

Myotonia congenita
Paramyotonia congenita
Central core disease
Nemaline myopathy
Myotubular myopathy
Periodic paralysis