



## **FACIOSCAPULOHUMERAL MUSCULAR DYSTROPHY**

This fact sheet is provided to help you understand the current evidence for diagnosing and managing facioscapulohumeral muscular dystrophy (FSHD).

The American Academy of Neurology (AAN) is the world's largest association of neurologists and neuroscience professionals. Neurologists are doctors who identify and treat diseases of the brain and nervous system, including neuromuscular disorders. The American Association of Neuromuscular & Electrodiagnostic Medicine (AANEM) is an association of neurologists, doctors of physical medicine and rehabilitation (PMR), and other health care professionals. PMR doctors specialize in rehabilitation. The AAN is dedicated to promoting the highest quality patient-centered neurologic care. The AANEM is dedicated to advancing the care of patients with muscle and nerve disorders.

Experts from the AAN and AANEM carefully reviewed the available scientific studies on diagnosing and managing FSHD. The following information is based on evidence from those studies and other key information. The information summarizes the main findings of the 2015 AAN and AANEM guideline on FSHD.

To read the full 2015 guideline, visit [AAN.com/guidelines](http://AAN.com/guidelines).

FSHD is a muscle disease with two genetic causes. People with either genetic cause show similar signs and symptoms. In the majority of cases, genetic testing can confirm an FSHD diagnosis. Doctors should know about and help manage related health problems.

### **What is FSHD?**

FSHD is one of the most common forms of muscular dystrophy (MD). MD is a group of several different genetic diseases. These cause muscle wasting (damage) and weakness. Depending on the MD type, different muscles of the body can be affected. These may include the muscles that control breathing, swallowing, and heart function. The muscle weakness is progressive. This means the muscle damage gets worse and spreads over time to involve other muscles. Muscle weakness can make it difficult to move or to lift objects. It also affects posture, or the ability to hold the body upright.

In FSHD, symptoms typically develop during the teenage years. However, symptoms can begin at any age from infancy to later adulthood. Both males and females can be affected. In general, FSHD targets the muscles of the face, shoulder blades, upper arms, and lower legs. It causes muscles to weaken. The weakness spreads slowly. It often is asymmetric, meaning it spreads unevenly through the two sides of the body. The weakness becomes more severe over time.

FSHD is divided into two types based on the genetic cause. Type 1 accounts for 95 percent—or more than nine in ten—people with FSHD. Type 2 affects only 5 percent—or fewer than one in twenty—people with FSHD. More is known about type 1 than type 2.

- FSHD types 1 and 2 have different genetic causes. However, the two types generally cause the same symptoms. Weakness of the face muscles can occur. This leads to difficulty opening or closing the eyes, or moving the lips. Weakness also can develop in the shoulders and upper arms. This causes the shoulder blades to stick out more than normal (scapular winging). The person can have trouble lifting objects overhead. Finally, weakness of the muscles of the lower leg can develop. This can lead to falls and foot drop. Foot drop happens when the person cannot keep the foot up when lifting it while walking.

Other common symptoms include:

- Weakening of the muscles of the abdomen (muscles of the rib cage and belly) and back—this may lead to a large curve in the lower spine and difficulty doing a sit-up
- Lower-leg weakness—this typically develops later in the disease and can lead to foot drop
- Greater weakness on one side of the body than the other—this does not occur as often in other forms of MD
- Pain of the muscles or joints—pain usually results from joints that are not aligned. This causes them to pull too much on muscles and tendons

Less common symptoms include:

- Abnormal changes in the blood vessels of the retinas (part of the eye)—happens more often in early-onset FSHD and, in rare cases, can lead to vision loss (a condition called Coats disease)
- Breathing (respiratory) problems—rare but can be very serious
- Hip and upper-leg weakness—can cause the person to waddle when walking
- Moderate to severe hearing loss in both ears with or without muscle weakness in young children

About one-third—or more than three in every ten—people with the genetic FSHD diagnosis do not have signs or symptoms found by clinical exam alone.

## What causes FSHD?

FSHD is a genetic disorder. The disorder is caused by changes or errors in a person's DNA or in specific genes. Genes are a part of the cells of the body. DNA contains the genes and the material that regulates genes. Everyone is born with a set of genes from both of their parents. The genes contain a program that tells the cells what to do.

Changes or errors in DNA or in specific genes are known as mutations. They interfere with the cells' ability to build proteins that help muscles develop or function. Different mutations affect different proteins. In FSHD, the patient has one or more mutations in his or her DNA. Changes in the DNA can turn on a gene that normally is inactive. In FSHD, the *DUX4* gene is turned on in muscle. This results in muscle weakness. Most often, this change in the DNA is passed on from the parents. Each family affected by FSHD passes on the same size of mutation. However, sometimes the mutation cannot be traced to either parent. In about 30 percent of cases, there will be no family history of FSHD. In these cases, the mutation happens unexpectedly in the person's genetic code.

Currently, there are two types of genetic mutations related to FSHD. Each of these mutations causes a type of FSHD (1 or 2). In FSHD type 1, the size of the mutation is one factor that can affect:

- How severely the disease will affect the person
- How early in life symptoms will occur
- What types of complications to expect

## How is FSHD diagnosed?

FSHD can be difficult to diagnose for these reasons:

- Most health care providers have little experience diagnosing and treating people with these disorders
- It can be confused with other neuromuscular disorders (such as other muscular dystrophies or polymyositis)—this may lead to the wrong diagnosis and, sometimes, to unnecessary treatment
- Genetic testing for FSHD type 2 is not widely available at this time

For an accurate diagnosis, it is important for doctors to obtain key information. They can start with:

- Detailed knowledge of the person's symptoms, including where he or she has muscle weakness
- Details from personal and family health history
- Information from a complete physical examination, including:
  - Signs of facial weakness
  - Signs of muscle weakness in the arms and legs
  - Signs of scapular winging
  - Signs of excessive curvature (curving) of the lower or upper back (lordosis or scoliosis)
  - Signs of hearing loss (in children)
  - Signs of breathing/respiratory problems (trouble breathing)
  - Signs of foot drop
  - Signs of difficulty in physical education (gym) class with sit-ups, pull-ups, rope climbing
  - Signs of difficulty flexing (tightening) or extending (straightening out) the arm at the elbow

## Initial Testing

For diagnosis, the person's symptoms and exam results are important. Additional information may be needed to confirm that a muscle disease is causing the weakness. Depending on the person's situation, the doctor may order some of the following:

- Results from blood tests for creatine kinase—an enzyme that leaks from damaged muscle and is found in high levels in some people with these diseases
- Results from an electromyogram, or EMG—measures the electrical activity in the muscles
- Results from nerve conduction velocity, or NCV—measures how fast signals move from one part of a nerve to another
- Findings from a muscle biopsy—a procedure that involves removing a piece of muscle tissue for study
- Retinal (eye) exams—this checks for damaged blood vessels in the retinas
- Results from breathing tests of pulmonary (lung) function—this checks whether the amount of air entering or exiting the lungs is reduced
- Findings from a cardiac echocardiogram—a procedure that involves looking at ultrasound images of the heart

## Genetic Testing

Genetic testing can be helpful for confirming the accuracy of an FSHD diagnosis. A genetic test is a blood test to confirm a change or error in the gene that causes these diseases and their symptoms. Genetic testing can confirm the diagnosis in many patients with FSHD type 1. The genetic testing looks for the contraction (shortening) of part of the DNA. This DNA portion is in identical lengths called D4Z4 repeats. When a person has fewer than 11 repeats, FSHD type 1 can occur. At this time, there are limited options for commercial testing for FSHD type 2.

Genetic testing starts with testing for FSHD type 1. This tests for a D4Z4 contraction. There is moderate evidence\* (for evidence levels, see key shown below table) that this test likely can confirm an FSHD diagnosis.

If the patient tests positive for the D4Z4 contraction, the doctor may order further testing for more information (depending on the person's signs and symptoms).

If the patient tests negative for the D4Z4 contraction, the doctor will test for FSHD type 2 or other myopathies. Although these cases are rare, they are important to diagnose. Research on FSHD type 2 is increasing. At this time, there is one commercial lab in the Netherlands that can test for FSHD type 2.

The decision to test often depends on the person's personal and family history. Some patients have a family member with an FSHD diagnosis. If the family member's diagnosis was confirmed by genetic testing, the patient may not need to be tested.

## Disease Severity

Two factors can point to the severity of a person's FSHD disease course:

- Age at disease onset
- The size of the contraction or mutation of the D4Z4 repeats (from 1 to 10 repeats)

Moderate evidence\* shows that a smaller D4Z4 repeat can be linked to:

- More severe disease
- Younger age at onset
- Need for wheelchair at younger age

Having an accurate diagnosis is very important for directing treatment. It also helps in planning major life decisions. These include:

- Education and career choices
- Family planning
- Housing to meet the person's health needs
- Long-term care planning
- Financial and estate planning
- Peer relationships and other social interaction in childhood (for example, limited facial expression can lead to misunderstanding on the part of others)

## How is FSHD treated and managed?

Currently, there is no cure for FSHD. However, therapies are available to help with complications. These are used to:

- Help with daily living activities and mobility
- Improve functioning and quality of life
- Lower the risk of associated complications and early death

FSHD complications require many types of care, including:

- Monitoring for and treatment of breathing problems
- Testing for retinal (eye) problems in patients whose disease course is more severe
- Testing for hearing loss in children and some adults
- Working with physical therapists to manage pain of the muscles, other soft tissues, and joints
- Use of orthotics—devices that help with movement such as ankle-foot orthotics to help with walking
- Orthopedic therapy or surgery, especially to lock the shoulder blades or to treat injuries from falls
- Physical and occupational therapy, including exercise to maintain range of motion, prevent weakness from lack of muscle use, and improve cardiorespiratory status (function of heart and lungs)

Therapies are available to help with muscle symptoms. Symptoms include pain and problems with mobility. Some of these therapies have been studied for how well they work:

- Drug therapies
  - Strong evidence\* shows albuterol does not help improve muscle strength. There is not enough information to show if it helps treat pain or tiredness.
  - Moderate evidence\* shows the myostatin inhibitor MYO-029 probably does not help improve muscle strength, lung function, or quality of life.
  - There is not enough information to show if prednisone or diltiazem help improve muscle strength.

Note: The US Food and Drug Administration has not approved any drugs that have been shown to slow, stop, or reverse muscle weakness in FSHD.

- Shoulder blade surgery
  - Low evidence\* suggests this surgery helps with shoulder range of motion and pain.
- Exercise
  - Moderate evidence\* shows that strength training probably does not help improve muscle strength much.
  - There is very low evidence\* that aerobic exercise is helpful.

Certain multispecialty clinics may be helpful for managing care. Families can look for clinics focused on evaluating and treating people with muscle diseases. Ask your doctor about clinics near you. Or contact:

- FSH Society at [FSHSociety.org](http://FSHSociety.org)
- Muscular Dystrophy Association (MDA) at [MDAUSA.org](http://MDAUSA.org)

The table below presents the guideline recommendations.

**Table: FSHD Recommendations for Clinicians**

<b>Category and Recommendation</b>		<b>Strength of Recommendation**</b>
<b>Diagnosis</b>		
Clinicians caring for people who may have FSHD type 1	Order genetic testing to confirm FSHD type 1 diagnosis in people with unusual patterns of signs and symptoms and no first-degree relatives with the disease	Moderate
<b>Factors That Can Predict Disease Severity</b>		
Clinicians caring for people with FSHD	Look for certain information from genetic test results (large D4Z4 deletion sizes) that may point to more significant disability at an earlier age	Moderate
<b>Monitoring for Complications: Breathing (Pulmonary)</b>		
Clinicians caring for people with FSHD	Order baseline pulmonary (breathing) function testing for all patients with FSHD. Monitor regularly if patient has abnormal test results or any combination of severe weakness near the lungs or chest, kyphoscoliosis, wheelchair dependence, or related conditions that affect breathing	Moderate
Clinicians caring for people with FSHD and 1) poor results from pulmonary function tests or 2) symptoms of extreme daytime tiredness or poor sleep	Refer patients for pulmonary or sleep medicine consultation for possible nighttime sleep monitoring or nighttime breathing machine in order to improve quality of life	Moderate
Clinicians caring for patients with FSHD who do not get regular pulmonary function testing	Order testing before any surgery requiring general anesthesia (such testing may uncover hidden breathing problems)	Moderate
<b>Monitoring for Complications: Cardiac (Heart) Abnormalities</b>		
Clinicians caring for patients with FSHD	Refer for cardiac (heart) evaluation if the patient has clear signs or symptoms of heart disease (shortness of breath, chest pain, palpitations). Routine screening is not needed in patients with no clear signs or symptoms	Weak
<b>Monitoring for Complications: Retinal Vascular Disease (Eye Disease)</b>		
Clinicians caring for patients with FSHD and certain genetic signs (large deletions)	Refer the patient to an experienced ophthalmologist (eye doctor) for dilated indirect ophthalmoscopy (an eye test to examine the retina). Eye doctor should use presence of disease on first screening in order to determine how often to follow up with the patient	Moderate
<b>Monitoring for Complications: Hearing Loss</b>		
Clinicians caring for young children with FSHD	Screen at diagnosis and yearly afterward until the children start school (hearing loss not always present at diagnosis and can be progressive)	Moderate
<b>Monitoring for Complications: Pain</b>		
Clinicians caring for patients with FSHD	Ask regularly about pain. May refer for physical therapy as a helpful first step. If pain continues, may prescribe nonsteroidal anti-inflammatory drugs for acute (short-term) pain and antidepressants and epilepsy drugs for chronic (long-term) pain	Moderate
<b>Treatment: Pharmaceutical Drugs</b>		
Clinicians caring for patients with FSHD	Should not prescribe albuterol, corticosteroid, or diltiazem for improving strength	Moderate
<b>Treatment: Scapular Surgical Fixation (Surgery to Lock Shoulder Blade)</b>		
Clinicians caring for patients with FSHD	Might offer surgical scapular fixation (surgery to lock the shoulder blade) to certain patients after careful consideration of arm muscle problems, potential gain in range of motion, rate of disease progression, and potential for poor outcomes from surgery and long periods of bracing	Weak

<b>Treatment: Aerobic Exercise</b>		
Clinicians caring for patients with FSHD	Might encourage patients to do low-intensity aerobic exercise program (program might be developed with help of physical therapist). Might use guidelines for physical activities for people with disabilities from US Department of Health and Human Services <sup>1</sup>	Weak
Clinicians caring for patients with FSHD who are interested in strength training	May refer patients to physical therapists to develop safe exercise program using appropriate weights and resistance and is tailored to the patient's abilities	Weak

<sup>1</sup> US Department of Health and Human Services Office of Disease Prevention and Health Promotion. Additional Considerations for Some Adults. In: Physical Activity Guidelines for Americans; chap 7. <http://www.health.gov/paguidelines/guidelines/chapter7.aspx>. Published September 2008. Accessed October 1, 2012

\*After the experts review all of the published research studies, they describe the strength of the evidence supporting each recommendation:

*Strong evidence* = Future studies very unlikely to change the conclusion

*Moderate evidence* = Future studies unlikely to change the conclusion

*Low evidence* = Future studies likely to change the conclusion

*Very low evidence* = Future studies very likely to change the conclusion

\*\*Key to Recommendation Levels:

*Strong recommendation* = In *almost all* circumstances, *almost all* patients would want the course of action described in the recommendation to be followed

*Moderate recommendation* = In *most* circumstances, *most* patients would want the course of action described in the recommendation to be followed

*Weak recommendation* = In *some* circumstances, *some* patients would want the course of action described in the recommendation to be followed

*No recommendation made* = The balance of the benefits, harms, and costs is unknown

Note: When they write recommendations, the experts consider:

- The evidence
- The balance of potential benefit and potential harm of a diagnostic test or therapy
- The cost and availability of the test or therapy
- The patient's values and preferences

The Child Neurology Society, the FSH Society, and the MDA reviewed the content of this fact sheet. Some information on disease background was provided by the FSH Society at [FSHSociety.org](http://FSHSociety.org) and the MDA at [MDAUSA.org](http://MDAUSA.org).

## This guideline was endorsed by the FSH Society and the MDA.

This statement is provided as an educational service of the American Academy of Neurology and the American Association of Neuromuscular & Electrodiagnostic Medicine. It is based on an assessment of current scientific and clinical information. It is not intended to include all possible proper methods of care for a particular neurologic problem or all legitimate criteria for choosing to use a specific procedure. Neither is it intended to exclude any reasonable alternative methodologies. The AAN and the AANEM recognize that specific patient care decisions are the prerogative of the patient and the physician caring for the patient, based on all of the circumstances involved.

### Study Funding

Funding for this publication was made possible (in part) by grant DD10-1012 from the Centers for Disease Control and Prevention. The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention. The remaining funding was provided by the American Academy of Neurology.

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