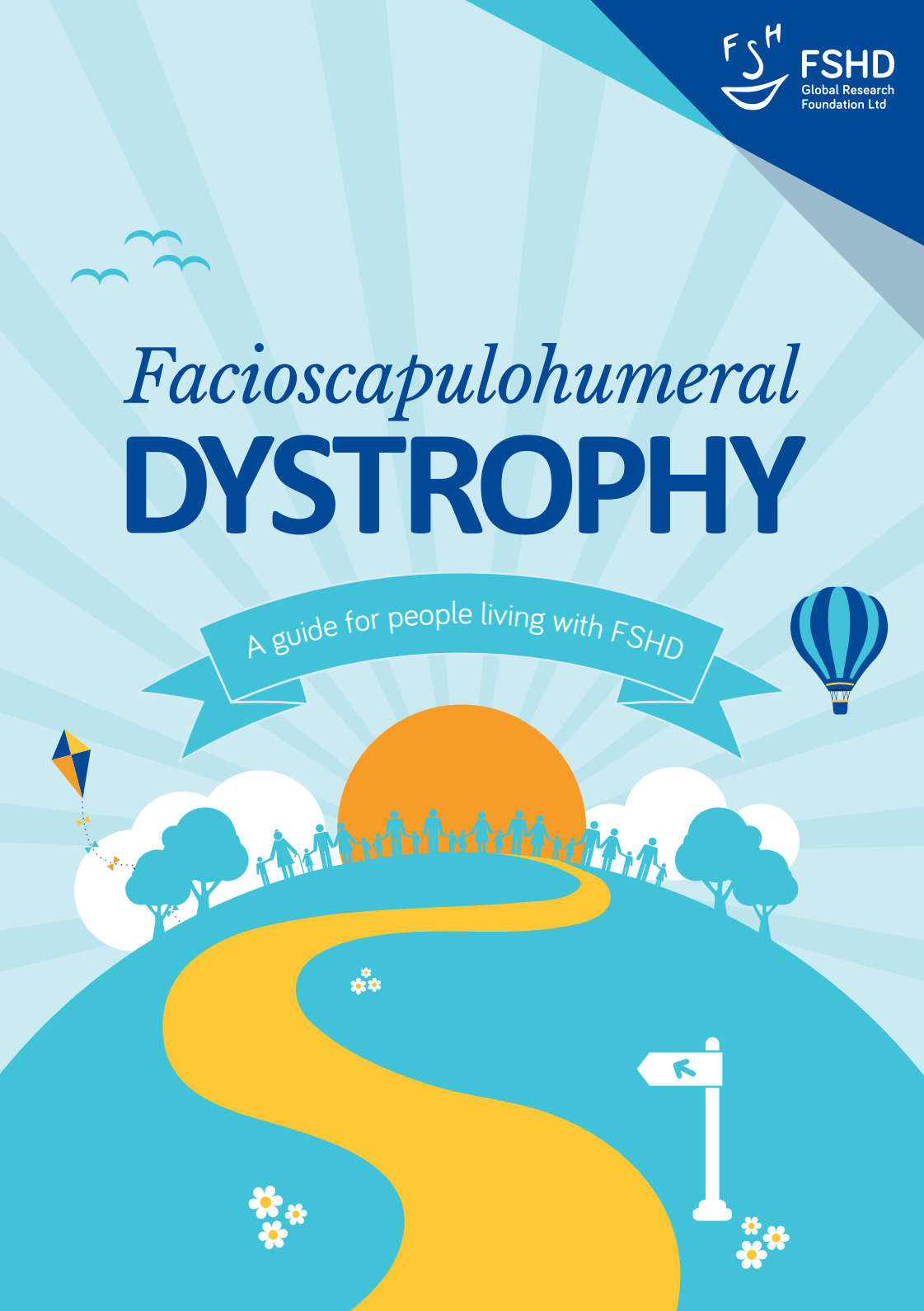
FSHD
Global Research
Foundation Ltd

Facioscapulohumeral DYSTROPHY

A guide for people living with FSHD



Facioscapulohumeral muscular dystrophy is a progressive muscle wasting condition for which there is no treatment and no cure.

The sentence above is probably one that people diagnosed with FSHD have heard multiple times from multiple sources and, while it is factually correct, it does not reflect the array of management options available or give credit to the people who live full and happy lives in spite of the challenges FSHD gives them.

This booklet has been developed for people with FSHD and their families. FSHD Global Research Foundation hopes that it will help you navigate the healthcare system, gain access to professionals who can help you manage the symptoms associated with FSHD and give you tools for dealing with health care encounters. To view the full published consensus paper visit: http://www.nmd-journal.com/article/S0960-8966(16)30096-7/abstract

The FSHD Global Research Foundation is an Australian based charity, committed to finding treatments and an ultimate cure for FSHD as quickly as possible. In September 2015 the Foundation brought together a group of leading global experts on FSHD to develop the first clinical consensus on the diagnosis and management of FSHD.

This booklet covers the care that you should expect from your healthcare team, steps for diagnosis and understanding test results, guidance on communicating with health professionals and some handy tools that may help make appointments more productive.

The Foundation has also prepared a suite of materials for healthcare providers. These are available to download from our website www.fshdglobal.org

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Understanding FSHD

Signs and symptoms

Facioscapulohumeral dystrophy (FSHD) is a type of neuromuscular condition called a muscular dystrophy. There are more than 30 muscular dystrophies currently known and FSHD is thought to be one of the most common affecting both adults and children.

The key feature of all muscular dystrophies is progressive skeletal muscle weakness. FSHD is named for the pattern of muscle weakness that is typical for this condition. That is weakness in the facial (facio), shoulder and back (scapula), and upper arm (humeral) muscles. However, while this is the typical pattern, most people with FSHD have weakness in other areas as well with the hips, trunk and lower limb commonly affected.

The age when people notice symptoms varies greatly. Most people notice something by the age of 20, but symptoms can start in children or infants, or as late as middle age.

Initially the muscle weakness may only affect one side, so one arm or one leg, for example.

The slow onset and asymmetric pattern can lead people to attribute the symptoms to sports injuries or strains.

Symptoms vary between people however there are some common ones:

- Inability to pucker lips, whistle or use a straw
- Chronic fatigue
- Eyes that don't close fully during sleep
- Difficulty with such exercises as sit-ups and pull-ups
- Shoulder blades that "wing" out
- Difficulty raising arm(s) above shoulder height
- Foot drop inability to keep the foot up when walking
- Weak lower abdominal muscles, protruding abdomen
- Curved spine (lordosis)
- Episodes of aching, discomfort or burning pain in muscles
- Severe pain from changes in posture and strain on remaining muscles

Genetic mechanism of FSHD

FSHD is arguably one of the most complex genetic conditions currently known. FSHD involves a convoluted and complicated interplay between genes and proteins in the muscle cell. While a massive amount of progress has occurred resulting in an improved understanding of the genetic mechanism for FSHD, we are still trying to completely understand how the genetic mutation causes the range of symptoms experienced by people with FSHD. Here we have outlined the mechanism for FSHD Type 1 and FSHD Type 2. At the moment there are researchers investigating an FSHD Type 3 and it is likely that more subtypes of FSHD will be identified as our knowledge of FSHD improves.

FSHD Type 1

FSHD is caused by mutations that actually increase the expression of a toxic protein.

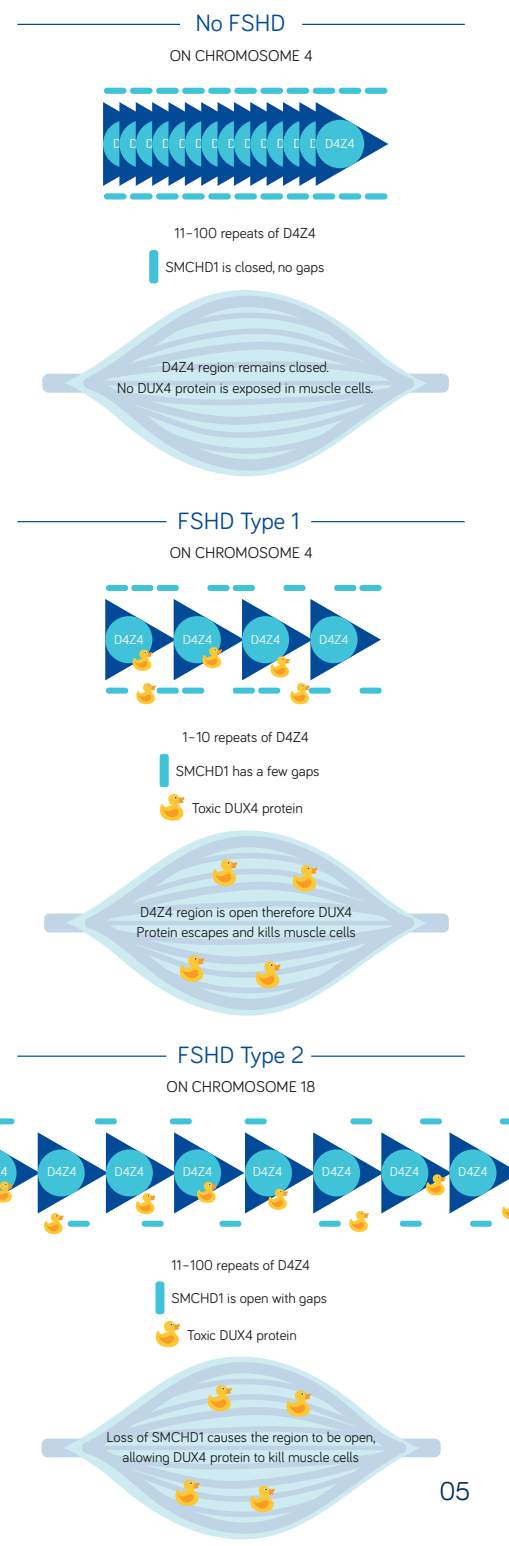
Nearly all cases of FSHD are associated with a mutation on chromosome 4. Chromosome 4 contains a series of repeated pieces of DNA, called D4Z4 units (array). People without FSHD Type 1 have 11-100 D4Z4 repeat array. In people with FSHD Type 1 (95% of cases) the D4Z4 array is shortened to 1-10 units.

The D4Z4 units act like a lock for this region of the genome. With fewer repeats, a gene embedded in this region called DUX4 is expressed. DUX4 kills muscle cells. The unwanted production of the DUX4 protein, sets in motion a cascade of events that leads to loss of muscle function. The exact mechanisms are still being studied, however it appears that DUX4 expression causes muscle cell death. This loss of cells causes muscles to waste away. DUX4 may also damage the normal muscle regeneration pathways preventing muscles from repairing any damage experienced through normal daily activities. DUX4 is also thought to provoke an immune response further inflicting damage on the muscles. Increased susceptibility of muscles to free radical damage, termed “oxidative stress”, may also play a role. As we learn more about the role of DUX4 the exact mechanisms for FSHD will become clearer.

FSHD Type 2

FSHD Type 2 was characterised when a large family was found with FSHD symptoms indistinguishable from FSHD1, but without the contraction of the D4Z4 domain on chromosome 4. People with FSHD Type 2 (5% of cases) have more than 11 D4Z4 units like people without FSHD.

The defect in FSHD Type 2 was found to be in a gene called Structural Maintenance of Chromosomes Hinge Domain Containing 1 (SMCHD1). This gene makes a protein that acts as a lock on regions of the genome. In people without FSHD, SMCHD1 protein keeps regions like the D4Z4 region (where the DUX4 gene is found) closed. Mutations in the SMCHD1 gene lead to reduced amounts of the protein being produced, meaning areas of the genome are less well locked. In FSHD Type 2, failure to lock the D4Z4 domain allows expression of DUX4 and hence leads to the same types of damage to muscle cells as seen in FSHD Type 1. Mutations in SMCHD1 lead to a smaller amount of this protein being produced. Less protein means less repression on regions of the genome that are usually closed. This includes the D4Z4 region causing DUX4 to be expressed where it is able to cause the same types of damage to muscle cells observed in FSHD Type 1.



Finding answers: diagnosing FSHD

For many people with FSHD the journey from first noticing something is wrong to getting a definitive diagnosis is long. Often people face years of questions and many people are misdiagnosed with other conditions such as chronic fatigue syndrome or multiple sclerosis, or are told there is nothing wrong with them.

Here we describe the pathway to getting a diagnosis.

Diagnosing FSHD: what are the steps?

The diagnosis of FSHD is more than just getting a simple blood test. There are a number of steps that you will need to take to get to the answers you want. Your doctor will be able to help you through all of this. The Foundation can provide you with information and help link you with clinicians and people who have been diagnosed. Outside the Foundation, there are a number of other groups around Australia who can give you help and support such as the Muscular Dystrophy Associations and the Genetics Alliance.

Step 1.
Finding the right health professional

If you think you have FSHD you should ask for a referral to a neurologist. It can be challenging to find a neurologist in your area. However, your GP should be able to help you find one. A neurologist with experience in neuromuscular disorders will probably be the most helpful for you. You could also consider seeking out a clinical geneticist who will have experience in diagnosing genetic conditions.

Most importantly, if you suspect you have FSHD then ask specifically to be tested for it. Genetic tests need a target gene to test for. If you do not mention FSHD then you may end up being tested for mutations in genes involved in other neuromuscular disorders.

A genetic counsellor will also be able to help you understand the diagnostic process and be able to give you support.

Step 2.
Stepping through the process

Diagnosis of FSHD may involve a combination of physical examination to assess muscle weakness, blood, neurological and imaging investigations to confirm a muscular disorder and rule out other causes of weakness, and molecular investigations to determine whether a disease-causing genetic change is present.

There are a number of ways to confirm the diagnosis of FSHD. The simplest is through a blood test where your genetics can be assessed. The only test that can diagnose FSHD and rule out other causes of muscle weakness is a genetic test.

Progressing straight to a genetic test may be appropriate for some people such as those with typical symptom pattern and family history of FSHD. For many people it makes more sense clinically to perform some other tests before going to genetic testing.

If you have the typical pattern of symptoms expected of FSHD and a first degree relative (a person's parent, sibling or child) with genetically confirmed FSHD then proceeding to a genetic test is probably unnecessary. Family history and evidence of symptoms is sufficient to confirm an FSHD diagnosis. However, you may wish to be part of a natural history study to help improve the understanding of FSHD. Contact the Foundation for more information.

Step 3.
Genetic testing for FSHD

If you decide to go ahead with genetic testing there are a number of options and things to consider.

Cost

The cost of getting the test done will depend on where you do it. The test will be provided free of charge if you are being seen in a public hospital. However, some facilities may not offer this, and there may be a charge for getting the test done. You should ask your care provider what the costs are before agreeing to the test.

You may be concerned that getting a diagnosis of FSHD will affect your health insurance premiums. This is not the case and premiums will be unaffected by an FSHD diagnosis. What may be affected are things like life insurance policies.

FSHD testing: the technical information

At the moment it is most common for people who are displaying symptoms associated with FSHD to be tested for contraction of the D4Z4 region on chromosome 4. How contracted this region is may tell you how severe your symptoms are likely to be with a smaller number of D4Z4 repeats associated with more severe symptoms. However, this is not a perfect measure of disease severity, so at the moment it is not possible to tell someone exactly how their condition is going to progress by measuring the size of the contraction.

Measuring the contraction of the D4Z4 region is done by cutting up the DNA at specific points inside the area and performing what is called 'Southern Blot' analysis. This technique allows you to measure how many D4Z4 repeats a person has. Less than 10-11 repeats is considered a definitive diagnosis of FSHD.

Testing of FSHD Type 2 is more complex because there are a number of genetic factors that cause the symptoms. At the moment the DNA sequence is read using a method called next generation sequencing. This is a high throughput technique that is very effective. However, it may not cover the entire genomic region that needs to be covered to pick up mutations. Some disease-causing mutations may sit well outside what would normally be sequenced and would therefore be missed. At the moment, testing for FSHD Type 2 has limited availability in Australia.

If you are interested in being tested for FSHD, please contact the Foundation at admin@fshdglobal.org for more information.

All genetic tests for FSHD that are being used at the moment have limitations. There is a chance that your test result will come back negative for FSHD when in fact you do have the disease-causing mutation.

Step 4.
Getting the result

Getting a test result back is only the start of a journey for someone with FSHD. You should have access to a clinical geneticist and genetic counsellor to support you regardless of the test result. These health professionals are highly trained and are there to help you and your family process the diagnostic result.

A positive test

Getting a positive test result means you have a confirmed diagnosis of FSHD. Your specialist should provide you with significant support over this time to help you understand what this means for you and to connect you with other health professionals and services that you may need as your condition progresses.

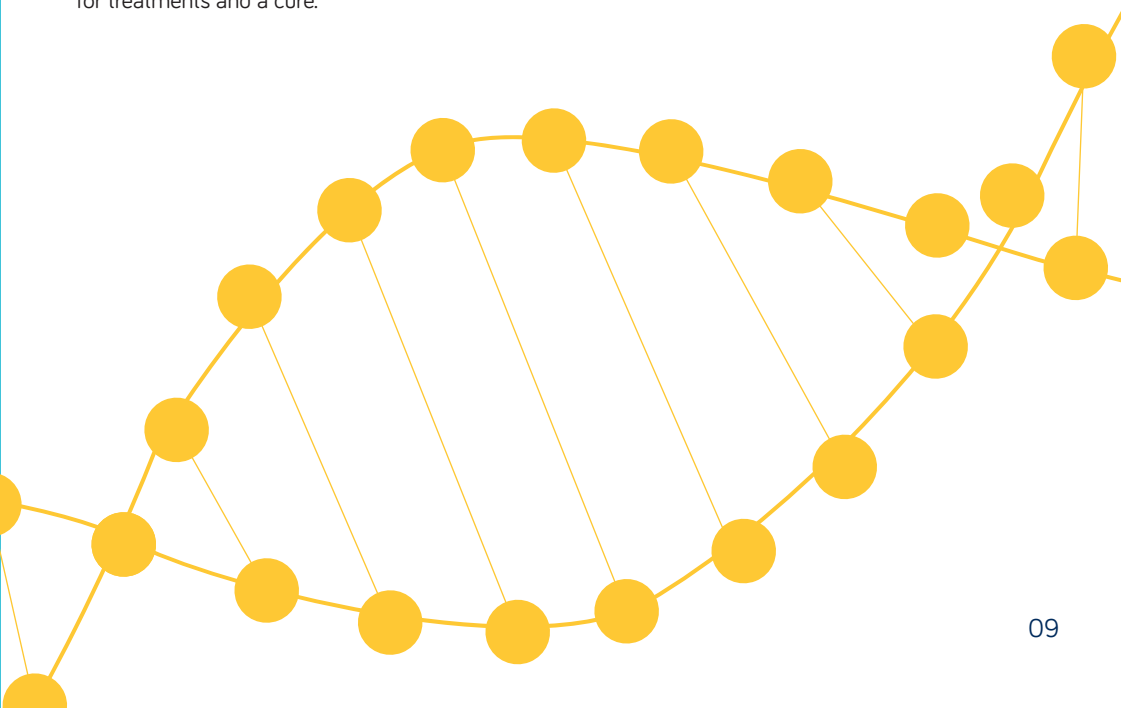
The Foundation offers support to people with FSHD and their families. We have a welcoming community and support network should you wish to meet others with FSHD and follow our quest for treatments and a cure.

A negative test

A negative test may be met with mixed emotions. For people with symptoms this means their journey to find a diagnosis continues. This can be frustrating.

It's important to note that the tests that are currently available are not perfect. A negative test does not necessarily mean you do not have FSHD. If your symptoms continue to progress in the absence of any other explanation you may want to consider repeating the test.

Misdiagnosis is a common issue experienced by people with FSHD. We have received reports from members of our community who have received misdiagnoses of multiple sclerosis, other forms of muscular dystrophy or fibromyalgia, or simply been told that there is nothing wrong.



After the diagnosis: what should your care team look like?

FSHD is a complex condition and you should have the support of a multidisciplinary team to help support you through the challenges of living with FSHD.

The diagram opposite shows what your care team should look like.

If you do not live in an area that has a dedicated neuromuscular clinic then this will probably look different. The point is, you should have access to all the health professionals listed in the diagram and these health professionals need to have experience in neuromuscular conditions, or in the management of degenerative conditions. Professionals without this experience may be less able to provide effective help for you.

It is important to note that you are at the top of the pyramid. You are the most important person in a care team and you should be included in all decision making and in discussion on care plans.

Neuromuscular clinic

Who:
Neurologist specialising in neuromuscular disorders. Geneticist, nurse, physiotherapist, orthotist, surgeon, sleep/respiratory physician, occupational therapist, social worker.

What:
Development of care plans and referrals.

When:
Review yearly.

Primary care

Who:
General practitioner.

What:
Facilitation of care plans and referrals. Point of contact for other issues such as mental health or for further care planning.

When:
As often as needed.

Other support network

Who:
Government and non-government support - income, work, caring, FSHD Global Research Foundation.

What:
Co-ordinate support for all social and economics aspects.

When:
As often as needed.

Getting the most out of healthcare

The problem below is a common occurrence for people with rare diseases. Often the expert in the room is the person with the condition and not the health professional to whom they have gone to for help.

This is not particularly surprising. Neuromuscular conditions affect a small percentage of the population and as such many health professionals will not have received a great deal of training in them. If you think about the work that a GP has done, they see hundreds of patients all with different healthcare needs. GPs are required to be the first point of contact for people with the healthcare system and know enough about a lot of conditions that they are able to assess, treat and refer. FSHD is one of thousands of conditions that GPs may encounter and they simply can't be an expert on all of them.

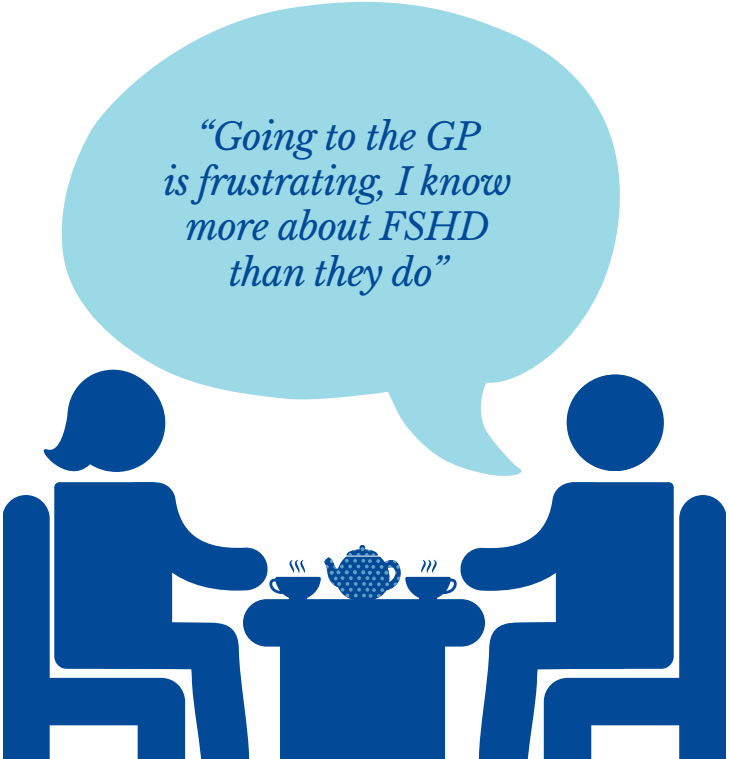
This does not mean that there is no point going to a GP, or that they can't provide any help.

Your GP is there to help enact the care plans set out by you and your neurologist. They can advocate for you, refer you to other health professionals, help you through other health problems, assist you in managing your pain and give you access to medicare benefits.

The Foundation has prepared fact sheets for managing FSHD in primary care. It may be helpful to print these out to give to your GP, or tell them about our website so they can look themselves.

These fact sheets give an overview of FSHD and outline some important practice points.

Visit https://fshdglobal.org/managing-your-health/ to find out more.



Tips for visiting your GP

Getting the most out of an appointment with your GP is all about planning ahead.

Decide on one or two issues

People with complex conditions such as FSHD often have a lot of things they want to get through in an appointment. However, it may help to focus on the one or two issues that are most important. Are you seeking a referral to a particular service or is there a symptom that you are having a particular problem with? Do you want to be genetically tested for FSHD?

Plan ahead with appointment times

Some issues can't be dealt with in the usual 10 minute appointment time. This is especially true if you are discussing complex issues such as managing your mental health or redesigning a pain management plan. If you think it might be a long appointment, it's probably a good idea to book a double slot.

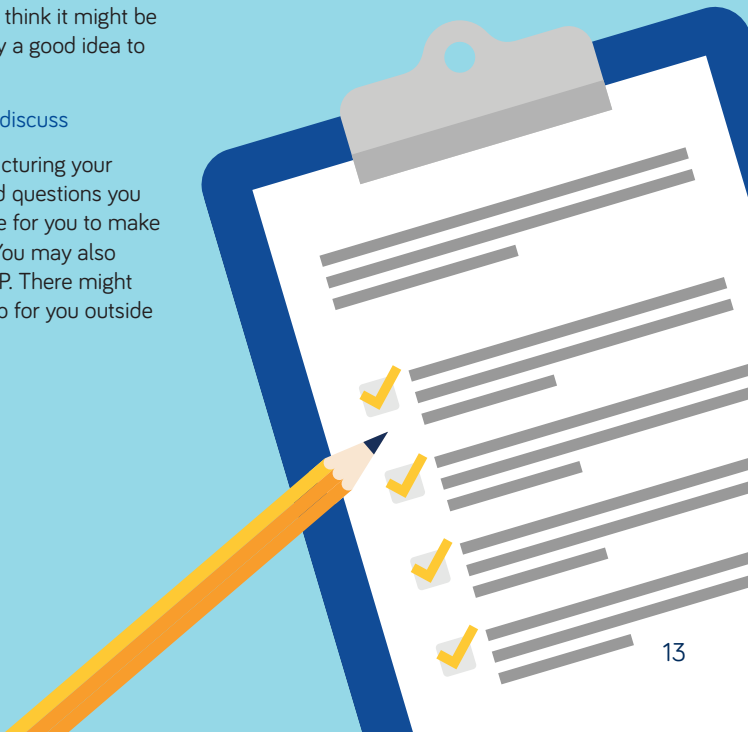
Make a list of what you want to discuss

This can be really helpful in structuring your appointment. List the issues and questions you have for the GP and leave space for you to make notes during the appointment. You may also want to make a copy for your GP. There might be things that they can follow up for you outside your appointment.

Take someone with you

Taking a person you trust along with you can be very helpful. It takes the pressure off you having to remember everything and they can also help get your point across.

If there is something you do not understand or agree with, tell your GP. You are the most important person in the consulting room and you are the one who has the issue being treated. You need to understand the treatment plan, agree with the treatment plan, and know what you need to do to effectively follow the plan. If there is something you don't understand then ask your GP to explain it. If there is something you disagree with don't be afraid to question. There may be other options that you can explore.



Options for management

There is a misconception that because there are no approved drug treatments for FSHD, then there is nothing you can do.

While it is true that at the moment there has been no treatment that has been shown to stop progression or reverse damage caused by FSHD, there are many treatment techniques used that are applicable to FSHD and may provide some help and improve quality of life.

It's important to note that many of the therapies listed have little empirical evidence supporting their use in FSHD. This just means that studies have not been done on these treatments. Because FSHD is so variable it is difficult to predict what treatments may work for you. An individualised plan developed in collaboration with a health professional you trust will help you decide on the best treatments.

It's important that you consult your health professional before you embark on any treatment strategy.

The FSHD Global website has a forum to help people find suitably qualified professionals in their area. You might want to consider joining the forum to connect with people in your area who know what you are going through and who can help you find the care you need.

Physiotherapy

There are many different techniques and types of physiotherapy. They won't all work for everyone and you may have to engage in some trial and error to find a practitioner and a technique that works for you.

It's important that you find a practitioner who has some experience in neuromuscular conditions, or degenerative conditions. This is because much physiotherapy is focussed on recovery. With FSHD, as with many chronic degenerative conditions, recovery is not the goal. Maintenance of condition, improving or maintaining balance and supporting fitness is the aim of therapy.

It may be helpful to speak about your goals and your physical limitations before you start on treatment planning with your physiotherapist. This may help avoid frustration.

Finding a practitioner who is suitably trained and experienced may be challenging. If you are currently seeing a neurologist ask for a referral to a physiotherapist, or for some suggestions.

You can also ask your GP, nurse or other care worker if they know anyone in your area who is trained to work on neuromuscular disease.

Hydrotherapy

There are no trials looking at the benefits of hydrotherapy for FSHD. However, hydrotherapy does assist mobility and can be an efficient means of exercising. Many physiotherapists will offer hydrotherapy sessions.

Massage

Massage may be effective for managing pain and help with stretched and strained muscles.

Speak to your health professional about massage, they may be able to refer you to a good therapist in your area, or direct you to therapists who may be covered by your health insurance.

Exercise

There have been a number of studies into exercise for FSHD. Unfortunately, these studies were short with a small population and it is therefore difficult to extrapolate the results to a recommendation for treatment. However, a recent review concluded that the evidence suggested exercise for FSHD is not harmful. There are more groups around the world performing studies on exercise for FSHD so hopefully in the future we will have some more concrete evidence.

Exercise does have a number of benefits so the lack of evidence should not deter you from speaking with your health professional about designing an exercise program. There are a few considerations you should take into account while planning an exercise program.

There are two types of exercise: aerobic and resistance. Aerobic exercises include activities like running, cycling and swimming. They temporarily elevate heart rate and breathing rate.

Resistance exercise includes activities such as lifting weights. They build strength in the muscles.

While aerobic exercise has not been associated with negative effects, there are a couple of concerns with resistance exercises that may leave people prone to injury. The first is the differences in strength in different muscle groups. For example, let's say your bicep muscle in your arm does not have any significant weakness, but the muscles surrounding the bicep do.

Then weight training your arms may lead to overuse or stretch injury in the weaker muscle. The second concern is fatigue. For people with significant weakness simply performing activities of daily living may be exercise enough. Further stressing the muscles with weight training may result in overuse injuries.

If you would like to engage in a resistance training program it is best to do it with direction and support from a physiotherapist with experience in neuromuscular disease and an exercise physiologist also with neuromuscular disease experience.

Aerobic exercise like swimming, using a stationary bike and walking will improve your overall fitness with less risk of injury.

Before embarking on any exercise program please consult your health professional.

Surgical management

There are a number of options for surgical management of FSHD that are mainly concerned with fusing bones. The basis of these surgical methods is to help treat the instability created when muscles weaken.

One of the most common ones is scapular fixation. The scapular is also called the shoulder blade and sits on the back. Often in FSHD progressive weakness in the muscles that hold the scapular against the back and attached to the arm leads to winging and eventually an inability to lift arms. During the procedure the scapular is attached to the rib bones that lie underneath it.

This can improve the function of the shoulder.

There are other surgical techniques that may provide some help. However, surgery does not always result in significant improvement and it's important that you have considered all the risks and benefits with your health professional before deciding on a surgical treatment strategy.

Respiratory support

Other muscular dystrophies are associated with breathing difficulties because eventually the progressive weakness spreads to the muscles that control breathing. This is not a common complication of FSHD. However regular monitoring of breathing function is recommended, especially as you may not realise you have poor breathing function.

Difficulty breathing means there is not enough oxygen getting to your tissues. This can exacerbate the negative effect of FSHD on your muscles.

Breathing problems during sleep is also not a common complication of FSHD, but it can happen. Symptoms include disturbed sleep, morning headaches, daytime fatigue and sleepiness. It is relatively simple to diagnose and treat night time breathing problems. Some people may respond well to position therapy to help you sleep in a position that limits any obstruction to breathing. Non-invasive ventilation is also an option.

Orthotics, walkers, crutches and the chair

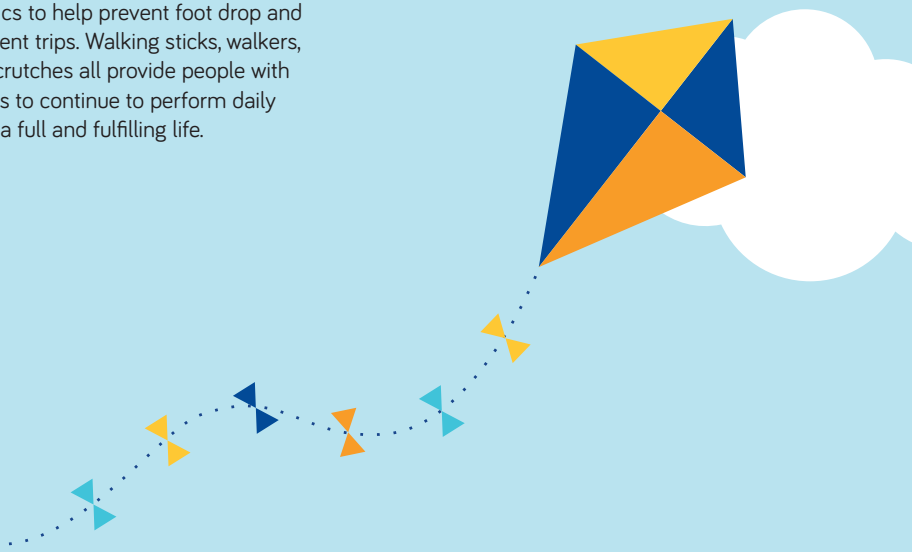
When many people think about muscular dystrophy they think about people confined to a wheelchair. While it is true that many people with FSHD do use a wheelchair for mobility the idea that they are confined to it is misleading. Some people may have lost the ability to walk and therefore need the chair to get from A to B. Others may use a chair for long distances to prevent fatigue. Some people may have significant foot drop and therefore use the chair because it allows them to get around while preventing falls and fractures that might see them completely reliant on the chair.

Far from being trapped many people who use a chair actually report that the wheelchair gives them more freedom to go about their daily tasks.

A wheelchair is not the only mobility aid available. There are many other forms of mobility aid, and they are improving all the time. Some examples include orthotics to help prevent foot drop and therefore prevent trips. Walking sticks, walkers, scooters and crutches all provide people with FSHD a means to continue to perform daily tasks and live a full and fulfilling life.

Bone health

Low bone density is a risk with FSHD. Weakened muscles and reduced ability to do weight bearing exercise can lead to reduced bone density and osteoporosis. Reduced bone density may make you more vulnerable to fractures. A bad fracture can seriously affect your mobility and reduce your quality of life. You should ask your GP about being screened for osteoporosis and for low levels of vitamin D. There are effective treatments available if you are found to be vitamin D deficient or have osteoporosis. There are some excellent resources available if you want to know how to prevent and treat osteoporosis. To learn more visit http://www.nps.org.au/conditions/hormones-metabolism-and-nutritional-problems/bone-disorders-and-calcium-metabolism/osteoporosis



More resources

The Foundation is committed to advancing global medical research, education and collaboration to improve quality of life and ultimately find a cure for Facioscapulohumeral Dystrophy. Through transparency, accountability, good governance and pure passion we aim to achieve results as quickly as possible.

About the Foundation

The FSHD Global Research Foundation focusses on finding treatments and a cure for the debilitating disease Facioscapulohumeral Muscular Dystrophy (FSHD). In doing so, we fund world-class medical research, awareness and education. We are also committed to complete transparency and accountability in our operations.

The Foundation was established in 2007 by Bill Moss AO, a well known Australian businessman and philanthropist who has FSHD. Since then, we have been addressing the chronic lack of medical funding and awareness of FSHD, both in Australia and globally. Over the past 9 years, the Foundation has committed $8.3 million to fund 40 ongoing medical research grants in 9 countries; the USA, Canada, the Netherlands, Italy, France, Belgium, Spain, New Zealand and Australia.

The FSHD Global Research Foundation does not operate like an average not-for-profit. We allocate 100% of all cash tax deductible donations to current and future medical research grants. We are also transparent in doing so, offering all donors via the 'FSHD – Find the Cure' mobile app the opportunity to track exactly which research programs their money has been allocated and the latest milestones of those programs.

The main sources of our funding for FSHD research are individuals afflicted by FSHD, their friends, supporters, as well as corporate sponsors. All funds donated are invested through careful consideration, guided by our Scientific Advisory Boards, Board of Directors and International Research Committees, ensuring FSHD Global remains a leader in discovering the world's best science.

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