FSHD Global Research Foundation Ltd

Clinical consensus on

Facioscapulohumeral DYSTROPHY

A resource for primary care

Primary care practice points

Diagnosis of FSHD involves clinical and genetic investigations

Consider referral to a clinical genetics service for people with a family history of FSHD or who are displaying symptoms consistent with FSHD.

Management of FSHD is complex and involves a multidisciplinary team

Consider referral to a variety of health professionals including physiotherapy, occupational therapy and exercise physiology.

FSHD is associated with poor bone density

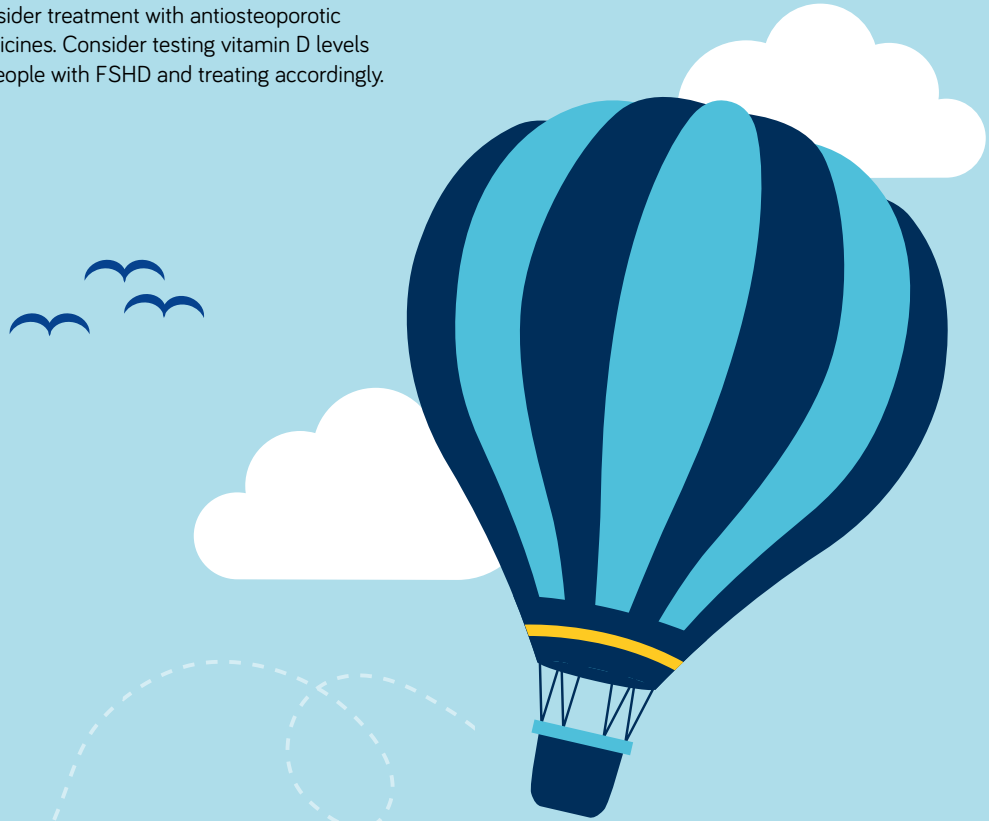
Consider treatment with antiosteoporotic medicines. Consider testing vitamin D levels of people with FSHD and treating accordingly.

Pain is a common presentation of FSHD

Consider options for pain management including pharmacological and nonpharmacological methods including referral to pain management specialist.

People with FSHD may experience respiratory insufficiency through muscle weakness or obstruction

Consider referral to a respiratory/sleep physician for assessment and management of sleep-disordered breathing with mechanical support.



Facioscapulohumeral muscular dystrophy (FSHD) is an autosomal dominant muscular dystrophy that affects an estimated 3,500 people in Australia (prevalence 1217: 100,000).

While FSHD is considered a rare disease it is likely that you, or someone in your practice has encountered someone with FSHD or with a family history of FSHD.

At the moment there is no approved treatments for FSHD and no cure. However, this does not mean that there is nothing that can be done to help people with FSHD maintain quality of life.

This resource is for health professionals working in primary care. As the main point of contact for the health system you are vitally important to people with FSHD. This resource may help you by providing up to date information on the condition and the latest thinking about what works for people with FSHD.

For more information on this resource, please contact the FSHD Global Research Foundation: admin@fshdglobal.org, (02) 8007 7037, fshdglobal.org

FSHD: symptoms & prognosis

FSHD, like all the muscular dystrophies, is associated with progressive muscle weakness and loss of function.

The condition is named for the typical pattern of muscle weakness observed in FSHD: face, shoulder and upper limb. However, for many people with FSHD, the effect is not limited to these areas. Many people experience weakness in the trunk and lower limbs.

In addition, while the cardinal sign of FSHD is facial weakness leading to an inability to express emotions, some people may not exhibit any facial weakness.

FSHD can manifest at any point in a person's life from infancy through to late adulthood, and the severity and rate of deterioration is highly heterogeneous. FSHD that manifests in infants and children is usually particularly severe. The reason for the highly variable presentation of FSHD is not currently known.

Most people with FSHD will require mobility aids to complete activities of daily living. However, the rate of progression is highly variable. Some people may be reliant on mobility aids soon after diagnosis while others may not require support for many years after the first symptoms are noticed.

Unfortunately for people with FSHD this means that there is no prognosis that can be given at diagnosis. Vigilance is required to ensure that problems with walking are identified early to prevent falls and further loss of mobility.

FSHD: genetic cause and diagnostic pathway

There are two sub-types of FSHD that are genetically distinct, but clinically indistinguishable.

FSHD Type 1, which accounts for over 95% of cases, is caused by mutations on chromosome 4. This mutation is a contraction of a D4Z4 repeat region. People without FSHD have between 11 and 100, people with FSHD have less than 11. These regions act like genetic silencing elements in regions of the genome where expression of genes is undesirable. In FSHD, the contraction of the D4Z4 region leads to the production of RNA for a protein called DUX4. The presence of a poly-adenylation signal in the permissive allele allows the RNA to be translated into DUX4 protein. This protein is normally expressed during development. However, when expressed in mature muscle tissue it causes a cascade of epigenetic changes in muscle cell expression which leads to cell death and eventual loss of muscle function. The exact mechanism for DUX4 mediated damage is still to be elucidated.

FSHD Type 2, around 5% of cases, is associated with mutations in a gene called the Structural Maintenance of Chromosomes Hinge Domain Containing 1 (SMCHD1). This gene acts as a transcriptional silencer preventing expression from the D4Z4 domain. Mutations in this gene cause a reduction in protein and a resultant reduction in inhibition that is independent of the number of repeats. The resultant pathology is caused by DUX4 expression and is therefore clinically identical.

FSHD Type 1 and Type 2 testing are available in Australia, although FSHD Type 2 testing is more limited. You will need to refer any people who you suspect have FSHD to the relevant clinical genetics service to receive testing and genetic counselling.

Figure 1. Example of a clinical diagnosis pathway modified from Tawil et. al. 2015

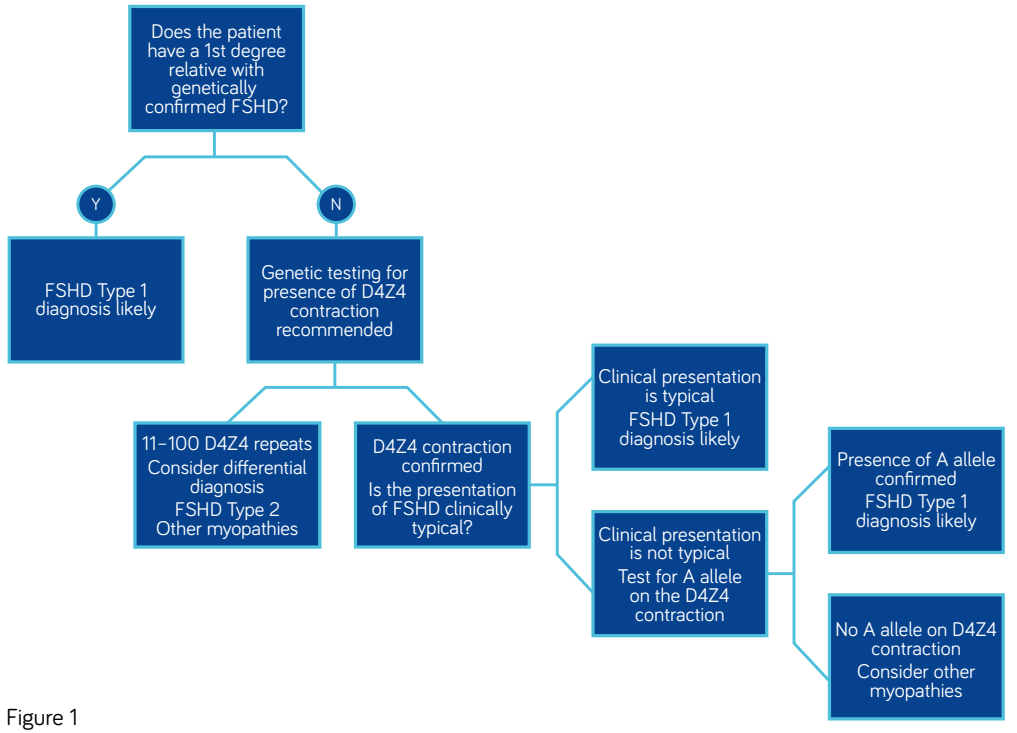


Figure 1

Management of FSHD

While there are no treatments for FSHD an effective rehabilitation program may help people with FSHD maintain quality of life.

To date, there have been no dietary interventions that significantly modify disease progression for FSHD. However, studies have generally been small and of short duration so this may change in the future.

Physiotherapy can be helpful for people with FSHD, particularly in identifying poor condition in muscles that are not effective and devising treatment strategies to help maintain function. It is important that the physiotherapist you refer people with FSHD to has experience in neuromuscular conditions. Most physiotherapy is based around a recovery model which is inappropriate for people with progressive degenerative conditions. People with FSHD report frustration and high levels of dissatisfaction with physiotherapy providers who do not have experience with progressive conditions.

Exercise may be helpful for people with FSHD for a number of reasons. Exercise may assist with maintaining a healthy weight, maintaining condition in unaffected muscles and preventing decline in function. Exercise may also be helpful to counteract fatigue and pain, but may also exacerbate these symptoms of FSHD so care must be taken when designing an exercise program. Exercise prescriptions can be complicated with FSHD due to asymmetric muscle weakness and variability in age of onset, progression and compensatory mechanisms.

It is advisable that people with FSHD receive professional assistance with developing an exercise program ideally from an exercise expert with experience in neuromuscular or other degenerative conditions.

Exercise programs should be started soon after diagnosis and designed around the goals of the person with FSHD such as maintaining independence or preventing falls. Current thinking is that moderate aerobic exercise (eg. stationary bike for up to 30 minutes three times a week) is not harmful and may be beneficial. Other elements of exercise programs may include balance training, transfers endurance. Vigorous exercise that causes fatigue and longer lasting muscle soreness should be avoided. Homebased exercise programs can offer a lot of benefits so long as they are accompanied by regular review and modification.

A recent study found that combining exercise with cognitive behaviour therapy was more effective than exercise alone in helping people with FSHD maintain levels of physical activity and help combat fatigue.

Hydrotherapy may be a useful strategy for general fitness and for managing pain. Exercises such as pilates and yoga may also be beneficial to assist with balance and flexibility

The use of mobility aids should be considered to maintain mobility as well as orthotics to help correct poor mechanics. Both can help prevent injury and ensure people with FSHD maintain their independence. Many people with FSHD will have access to specialist rehabilitation physicians and orthoptists if they are regularly seen in a neuromuscular clinic. If not, then referral should be considered for people who are experiencing problems with moving around and falls or near falls.

Respiratory insufficiency due to weakness of the respiratory muscles occurs in about one in ten people with FSHD. Regular monitoring of respiratory function is recommended for all people with FSHD. Sleep-disordered breathing due to upper airway obstruction may also occur in people with FSHD. Consider referral to a respiratory/sleep physician for assessment.

Low bone density is an expected comorbidity of inherited myopathies although the exact prevalence and severity of the problem is currently unknown. The Foundation funded a clinical trial to look at this in 2015 (ClinicalTrials.gov identifier NCT02413190), the results of which should be released in the first half of 2017. In the absence of data regarding the prevalence and severity of osteoporosis in FSHD it is recommended that you screen people with FSHD according to the guidelines available for the general population and treat any evidence of reduced bone density according to prescribing guidelines.

Hearing loss and retinal vasculopathy affects a minority of people with FSHD. Prevalence estimates for audiometric abnormalities are estimated at around 15%. However, most hearing abnormalities are asymptomatic. Children affected by FSHD, particularly those with large D4Z4 deletions may have symptomatic hearing loss. Consider referral to an audiologist for monitoring. About a quarter of people with FSHD have peripheral retinal vascular abnormalities. However, a small minority of people will have vision abnormalities.

Medicare care plans. People with FSHD should be eligible for treatment under GP management plan and team care arrangements. Other referral pathways you may want to consider include psychology for assessment and treatment of mental health issues, but also for pain and fatigue management. A recent study found that exercise sessions combined with cognitive behavioural therapy increased physical activity and reduced fatigue in people with FSHD.

People with FSHD face a myriad of challenges that include long delays in diagnosis, lack of clarity on prognosis and the need to constantly cope with a body that changes often suddenly and without warning. However, there are a great deal of options for people with FSHD and as their primary point of contact with the healthcare system you are vitally important to them.

More resources

References: Tawil, R., Mah, J.K., Baker, S., Wagner, K.R., Ryan, M.M., The Sydney Workshop Participants., Clinical practice considerations in facioscapulohumeral muscular dystrophy Sydney, Australia, 21 September 2015. Neuromuscular Disorders 2016; 26: 462 - 471

Tawil R., Kissel, J.T., Heatwole, C., Pandya, S., Gronseth, G., Benatar, M., Evidence-based guideline summary: Evaluation, diagnosis and management of facioscapulohumeral dystrophy. Neurology 2015; 85:357-364

About the Foundation

The FSHD Global Research Foundation focuses 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.

The FSHD Global Research 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.

FSHD
Global Research
Foundation Ltd

FSHD Global Research Foundation

www.fshdglobal.org
Email: admin@fshdglobal.org
Phone: (02) 8007 7037