



Diagnostic tests

An overview of different diagnostic and genetic tests.

For most people affected by a muscle-wasting condition, the pathway to diagnosis starts with a visit to their General Practitioner (GP). Maybe somebody notices that their child falls over more than his or her friends, or an adult finds they can no longer walk very far without tiring. The GP may carry out some initial tests to explain the symptoms, but since these conditions are often difficult to diagnose, the individual will usually be referred to a specialist – typically a neurologist with a specialist interest in neuromuscular conditions – for further investigation and diagnosis.

The specialist will use a range of tools and tests to reach a clinical diagnosis that best explains the symptoms and test results, and this will be used as the basis for genetic testing. This factsheet describes some of the more common diagnostic tests and looks in more detail at genetic testing.

Blood tests

People with a suspected neuromuscular condition are likely to have their blood tested for creatine kinase (CK) levels (also called the CPK test). CK is a protein – more specifically, an enzyme – that is normally found in muscle but can leak into the blood following muscle damage. The test measures the level of CK in the blood and clinicians can use this as a measure of muscle damage.

Although raised levels of CK in the blood point towards muscle damage, the test is not specific for damage caused by neuromuscular conditions. A particularly hard session in the gym can also lead to increased CK levels, so the test result cannot provide an accurate diagnosis by itself.

Magnetic Resonance Imaging (MRI)

MRI is a fast and non-invasive technique that can produce images of the inside of our bodies. Unlike an X-ray, which only shows our bones, MRI images can show the structure of different types of tissue such as muscle, fat and bone (see Figure 1). An MRI scan can highlight which muscles are affected by a condition and can help a surgeon choose the most suitable muscle on which to perform a biopsy.

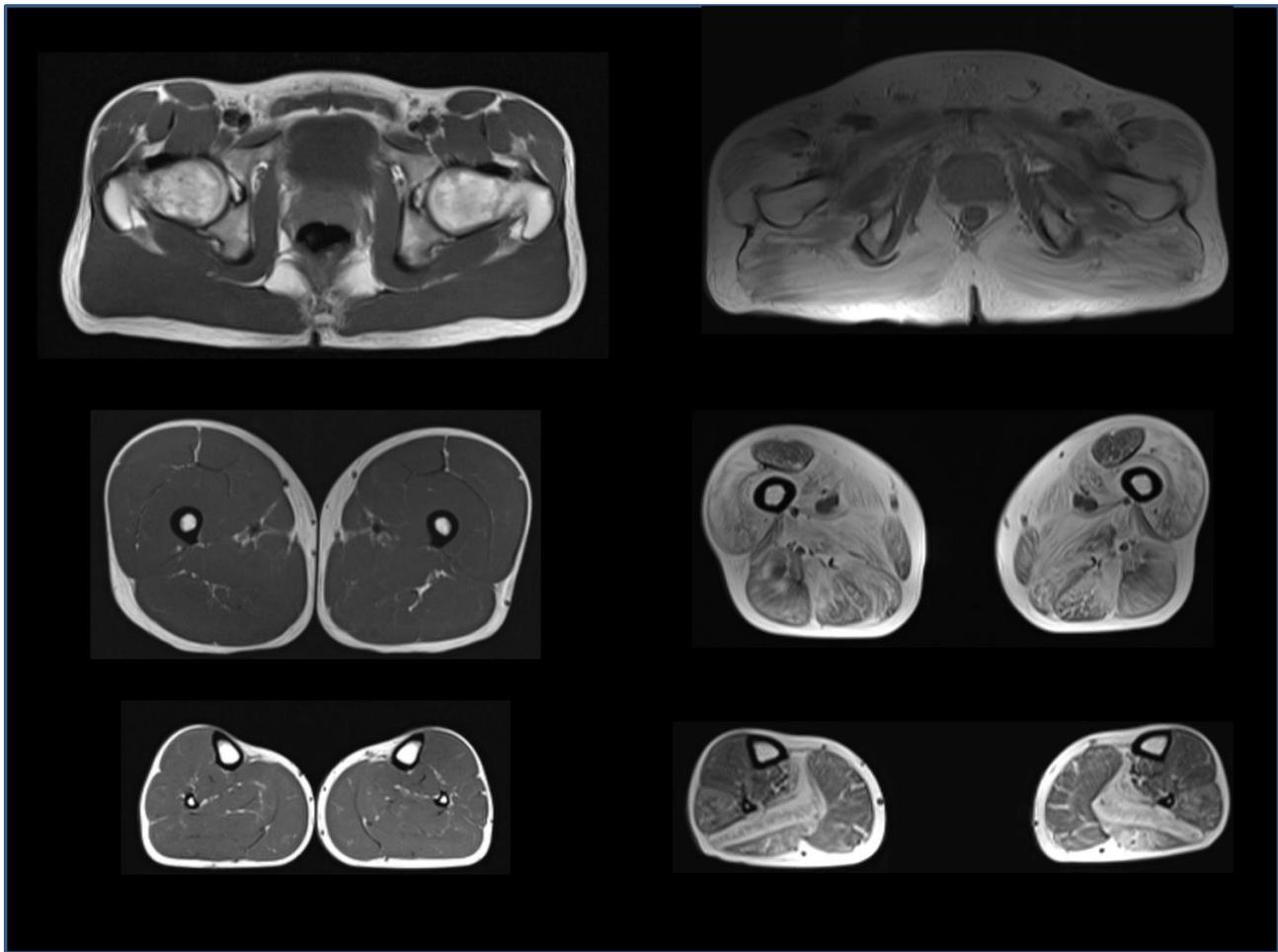


Figure 1: Example of an MRI image of muscle

Muscles of the pelvis (top), the thighs (middle) and lower legs (bottom). The left-hand images are from a healthy person and the right-hand images are from someone with an RYR1-associated myopathy. While muscle appears as a dark grey colour, fat appears as white. Most of the muscle in the RYR1 patient has been replaced by fat.

Muscle biopsy

A muscle biopsy is a small piece of muscle removed through a small cut or with a hollow needle, usually from the leg or arm. The tissue sample enables clinicians to examine the muscle structure in detail under a microscope.

Using dyes to stain specific proteins, a clinician can also identify proteins that are missing from the muscle. In some cases this may provide a diagnosis, for example, the lack of dystrophin in Duchenne muscular dystrophy. However in other conditions, where several genes may play a role in the biological pathway that produces the protein, genetic testing will be required to identify the precise cause of the condition. (For more information, please read our factsheet on muscle biopsies).



Functional test of muscles and nerves

The clinician may also use other tests like electromyography (EMG) or tests of nerve function. These tests examine electrical activity in nerves and muscles. By comparing when someone is at rest and when the muscles are contracting, clinicians can pinpoint the location of underlying problems – either in the muscles themselves, or in the nerves carrying signals to the muscles.

Genetic testing

Although careful assessment of the symptoms and the results of clinical tests can enable clinicians to reach a diagnosis, genetic testing can often provide a more precise diagnosis.

Genetic tests are usually performed on a blood sample. The tests aim to identify which faulty gene is causing a condition and the precise nature of the genetic fault, in other words, the mutation. There are several different types of mutation, which are named for their effect on the DNA. For instance, a 'deletion mutation' is caused when some of the DNA is deleted and 'duplications' occur when part of the DNA is repeated.

The clinical diagnosis suggests which gene (or genes) should be tested but often it does not point towards a single gene. For example, the early symptoms of some cases of limb girdle muscular dystrophy can be hard to distinguish from other conditions like Becker muscular dystrophy.

Some neuromuscular conditions can be caused by mutations in any one of several genes. For example, over 20 different genes are associated with limb girdle muscular dystrophy. In these cases, the gene that is most likely to cause the condition and symptoms observed is tested first. If no mutation is found, the next most likely gene will be tested, and so on. In this case a diagnosis can take some time, depending on how many genes need to be tested.

Occasionally, if a genetic test is not available through the diagnostic service, samples are sent to laboratories where the DNA is analysed as part of ongoing research.

Sometimes, a clinical diagnosis points clearly in the direction of a single gene. A clinical diagnosis of Duchenne muscular dystrophy points to the dystrophin gene and testing then focuses on identifying the mutation in that gene. In these cases, testing initially looks for the most common mutations (for example, deletions in Duchenne muscular dystrophy) and gradually works towards rarer mutations.

Despite recent advances in identifying mutations that can cause neuromuscular conditions, clinicians will sometimes test all the known genes and still fail to identify the mutation causing the condition. Currently, about 50 percent of people with congenital muscular dystrophy do not receive a genetic diagnosis.

Why is a genetic diagnosis important?

A precise genetic diagnosis allows clinicians to give their patients better information about how the condition will progress during their lifetime. This can help individuals and families



to prepare in advance to manage their condition and to make informed family planning decisions.

Some clinical trials require prospective participants to have a genetic diagnosis. This might be because the therapy being tested targets the underlying genetic cause of the condition. For example, exon skipping therapies for Duchenne muscular dystrophy are mutation-specific. This means that when these therapies are made available, they will potentially benefit only people with certain mutations.

Other related publications

- ▶ Inheritance
- ▶ Muscle biopsies
- ▶ Genetic counselling and family planning

We're here for you at the point of diagnosis and at every stage thereafter, and can:

- ▶ give you accurate and up-to-date information about your or your child's muscle-wasting condition, and let you know of progress in research
- ▶ give you tips and advice about day-to-day life, written by people who know exactly what it's like to live with a muscle-wasting condition
- ▶ put you in touch with other families living with the same muscle-wasting condition, who can tell you about their experiences
- ▶ tell you about – and help you get – the services, equipment and support you're entitled to.

If you have feedback about this factsheet or would like to request any references used to produce it, please email info@musculardystrophyuk.org.

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Here for you

The friendly staff in the care and support team at the Muscular Dystrophy UK's London office are available on **0800 652 6352** or **info@musculardystrophyuk.org** from 8.30am to 6pm Monday to Friday to offer free information and emotional support.

If they can't help you, they are more than happy to signpost you to specialist services close to you, or to other people who can help.

www.musculardystrophyuk.org