# MUSCULAR DYSTROPHY JK OUR MUSCLES MATTER

# **Myotonic dystrophy**

### **Overview**

Myotonic dystrophy is a genetic condition that causes progressive muscle weakness and wasting. It typically affects muscles of movement and commonly the electrical conduction system of the heart, breathing muscles, swallowing muscles, bowels, lens of the eye and brain.

The age when symptoms start varies a lot and can be any time from birth to old age. In general, the later the condition starts, the milder it will be.

There are two types of myotonic dystrophy. Type I tends to be more severe and more common in the UK than type 2. This information will refer to only myotonic dystrophy type I apart from the section specific to myotonic dystrophy type 2.

### **Symptoms**

Myotonic dystrophy type I (DMI) can affect affect people in a number of ways.

### **Muscles of movement**

There are two problems that may affect muscles of movement or 'skeletal muscle'.

The first is a gradual weakening of certain muscles, over time, caused by a 'muscular dystrophy'. The muscles in the face, eyelids, jaw and neck are commonly affected. The muscles in the forearm that enable us to grip objects are often affected early on. The muscles around the ankles are also commonly affected, causing 'foot drop', which cause people to catch their toes and trip. The large, weight-bearing muscles of the legs and thighs are usually affected much later.

The rate of deterioration in muscle strength is typically slow over many years. Some people never have significant muscle weakness. Some people, who are more severely affected, may need a wheelchair, but many people with myotonic dystrophy do not.

The second problem affecting skeletal muscles is an electrical problem, called 'myotonia'. Myotonia causes muscle stiffness (difficulty relaxing the muscle), which especially affects the hands and jaw. This can be helped with medication supplied by your specialist but usually does not need treatment.

### Heart

The wiring or 'conduction system' of the heart is often affected and this can lead to attacks of dizziness or even blackouts. Sometimes a pacemaker or other device may be recommended. The mechanical system which pumps the heart may be affected but usually it does not cause a problem that needs treatment.

### Lungs

The pumping of air in and out of the lungs, or 'ventilation', may be affected. This may cause daytime sleepiness and increase the risk of chest infections, especially after a general anaesthetic. Pneumonia is very common and requires prompt treatment. You should stay up-to-date with your immunisations, including the flu and pneumococcal vaccines.

# Gastrointestinal (GI) tract

Because the swallowing muscles are affected, swallowing can often lead to coughing and spluttering when eating or drinking. This can be dangerous. If food or drink goes into the lungs rather than the stomach, this leads to 'aspiration pneumonia', which is a severe chest infection. The lower bowels are also typically affected by irritable bowel syndromelike symptoms, with a mixture of constipation, crampy abdominal pain and diarrhoea.

# Lens of the eye

It is very common for cataracts to form across the lens of the eye in people with myotonic dystrophy, but they usually cause few symptoms because they appear so slowly. However, early onset cataracts can be easily treated.

### **Brain**

The brain can be affected in many ways and excessive daytime sleepiness is one of the most common consequences. Reduced motivation can also be a common problem.

Children with myotonic dystrophy may have learning difficulties, even if they have no muscle problems.

# Myotonic dystrophy type 2 (DM2)

An important recent advance is the recognition of a second, milder condition with features resembling myotonic dystrophy type 1 (DM1). In this condition, weakness tends to occur in muscles close to joints (proximal muscles), such as those in the neck, fingers, elbows and hips. Facial weakness and myotonia (difficulty relaxing the muscle) is often mild or absent. Cataracts and heart problems can occur but are usually less severe than in DM1.

### Causes

Myotonic dystrophy is caused by a specific genetic change (mutation) within the DMPK gene on chromosome 19.

Our DNA is made up of lots of individual building blocks represented by the letters A,C,T and G. The DMPK gene contains lots of Cs,Ts and Gs repeated over and over like this:

CTGCTGCTGCTGCTGCTGCTGCTGCTGCTG...

The CTG 'triplet' in the DMPK gene is usually repeated between five and 34 times in a healthy person. However, in someone with myotonic dystrophy type I, the CTG triplet is unstable and is repeated more than this.

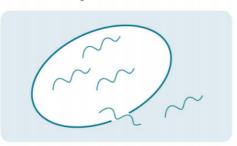
The number of CTG repeats in the DMPK gene generally correlates with the severity of myotonic dystrophy type 1 and the age of onset. For example, individuals with 50 to 100 repeats are usually mildly-affected and symptoms may not arise until adulthood. In contrast, individuals with thousands of repeats are likely to have the severe, congenital (present from birth) form of the condition. The number of CTG repeats, and hence the severity of the condition, usually increases from generation to generation.

Recent scientific advances have shown that too many CTG repeats leads to abnormal RNA production in the cells of people with myotonic dystrophy type 1. When a gene is expressed (or active), RNA copies of the gene are produced in the cell nucleus. This RNA acts as a messenger that travels out of the nucleus and then instructs the cell's machinery to make proteins.

In myotonic dystrophy type 1, this RNA production process is disrupted. Too many CTG repeats in the DMPK gene cause the resulting RNA to have an unusual shape (see figure below). It becomes trapped in clumps in the nucleus and affects the function of important proteins that regulate other genes. It is the disruption of these other genes that is thought to cause the body-wide symptoms of myotonic dystrophy type 1.

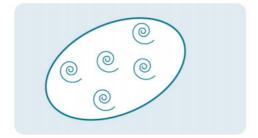


DMPK RNA message leaves nucleus = normal cell functioning



### Myotonic dystrophy cell

Trapped DMPK RNA forms clumps in nucleus = disrupted cell functioning



# How is myotonic type I (DMI) dystrophy inherited?

The condition follows a 'dominant' inheritance pattern, which means that children of a person with the condition have a 50 percent chance of inheriting it. Men and women are equally likely to be affected and to pass on the condition, but children of women with the condition are likely to be more severely affected. In general, though not always, the condition tends to be more severe with each generation OR in each younger generation. Please also see our factsheet on congenital myotonic dystrophy for more information on the most severe form of myotonic dystrophy.

Very few cases of myotonic dystrophy occur 'out of the blue' with no evidence of family history. Almost always, one parent is affected, often very mildly. Some parents (or grandparents) may carry a very slight genetic change that will never cause any symptoms and may not be diagnosed. Careful study of the whole family often shows more members with the condition than would appear likely at first.

# What causes Myotonic dystrophy type 2 (DM2) or PROMM (proximal myotonic myopathy)?

This condition was initially called proximal myotonic myopathy (PROMM) because affected individuals had clinical signs of myotonic dystrophy but did not have the increased number of CTG repeats in the DMPK gene. It was later discovered that these individuals instead had a similar genetic fault in a different gene. This led to the condition being renamed as myotonic dystrophy type 2 (DM2).

People with myotonic dystrophy type 2 have a genetic fault (mutation) in the CNBP gene (also called the ZNF9 gene) on chromosome 3. Although this gene is quite different from the DMPK gene that is mutated in myotonic dystrophy type 1, it contains a very similar, repeated section of DNA made up of lots of C's, T's and G's:

CCTGCCTGCCTGCCTGCCTGCCTGCCTG...

The number of CCTG repeats in the CNBP gene is increased in people with myotonic dystrophy type 2. This is thought to disrupt RNA production in the cell, in a similar way to myotonic dystrophy type 1 (see figure above). Clumps of CNBP RNA build up in the cell nucleus and interrupt the activities of important proteins and genes. Exactly how this leads to symptoms is not well understood, but researchers are looking into this.

In contrast with type 1, the number of CCTG repeats does not relate to the age of onset or severity of myotonic dystrophy type 2. In addition, type 2 does not tend to get worse with each generation.

However both types are dominantly inherited. This means that children of an affected person have a 50 percent chance of inheriting it.

Clinicians and scientists are still learning about myotonic dystrophy type 2, but it is probably uncommon and accounts for only a small proportion of people in the UK thought to have a myotonic dystrophy

### **Treatment**

Although there is currently no cure for myotonic dystrophy, there are ways to help manage the condition.

Since many doctors are unfamiliar with the condition (because it is so rare), it is essential that people who have myotonic dystrophy are aware of the problems and complications they may face and share this information with their health professionals. Some of these are mentioned on pages 1 and 2. They do not always all occur, and many people have few symptoms, but it is still important to be aware of them.

Some specialist centres now recommend an active monitoring process of people with myotonic dystrophy type 1 so that the effects of the condition can be found and managed before they become a severe problem.

### What are the risks with anesthetics?

Operations and anaesthetics can be risky, even for people mildly affected. It is very important that surgeons and anaesthetists know that a person has myotonic dystrophy before any surgery is planned. Problems only usually occur when doctors are unaware of the condition.

It is also helpful to carry a myotonic dystrophy alert card, and a care plan, both of which contain information to alert emergency and other healthcare professionals to the specific issues that affect people living with myotonic dystrophy. These are available for free from Muscular Dystrophy UK – call the freephone helpline on 0800 652 6352 or email <a href="mailto:info@musculardystrophyuk.org">info@musculardystrophyuk.org</a> to order one.

## Related health issues

Many people can develop heart problems, which are commonly treatable but can be serious if ignored. Speak to your neurologist or GP about having an annual electrocardiogram (ECG). This can be performed by a cardiologist.

Some people who have myotonic dystrophy may have more trouble with other body systems than they do with their muscles. For example, excessive daytime sleepiness, swallowing difficulties and a range of bowel symptoms may appear unrelated, but they may all be connected to myotonic dystrophy. They may be helped by specific drugs. It is important that people with myotonic dystrophy make sure that whoever treats them is aware they have the condition and knows the wide range of associated problems.

# Things to think about during a pregnancy

People with the condition need careful management if planning a pregnancy: not only is there a risk of a baby being severely affected, but sometimes serious problems during pregnancy and delivery may also affect the individual.

If an individual is concerned their baby may be affected, it is possible to test a pregnancy. Your GP can refer to local clinical genetics departments for more information and testing. Please see our genetic counselling and family planning factsheet for more information.

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If you have feedback about this factsheet or want to request references, please email info@musculardystrophyuk.org.

### 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.

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