What is Myotonic Dystrophy Type 2?

Myotonic dystrophy type 2 (DM2) also known as Proximal Myotonic Myopathy (PROMM) is a multisystem condition which usually presents in adulthood with muscle stiffness, mild myotonia (delayed muscle relaxation), proximal muscle weakness (weakness in the muscles closest to the torso), myalgia (muscle pain), heart issues, insulin resistance/diabetes and cataracts in some people.

The abbreviation 'DM' comes from the latin name of dystrophia myotonica.

DM2 is a rare multisystem condition which is clinically similar to but distinct from myotonic dystrophy type 1. The exact prevalence is unknown but is reported to be between 2 – 14 per 100,000 people.

DM2 presents itself with great variability. People who have the genetic mutation known to cause DM2 can be asymptomatic, mildly affected or physically disabled.

If you have a clinical diagnosis of myotonic dystrophy type 1 but the genetic test could not confirm this then you may benefit from having the now known genetic test for DM2.

Myotonia (Myo from Greek; muscle, and Tonus from Latin; tension) is a symptom of a few neuromuscular disorders characterized by delayed relaxation (prolonged contraction) of the skeletal muscles after voluntary contraction or electrical stimulation.

Features of Myotonic Dystrophy

Myotonic dystrophy type 2 (DM2) is an inherited condition which affects many different types of tissue or body functions and is characterized by myotonia (involuntary muscle contraction with delayed relaxation). Other muscle dysfunction includes fatigue, weakness, pain and stiffness.

People also experience seemingly unrelated issues in other areas of the body including: cardiac conduction defects, cataracts in both eyes which generally occur earlier than the common, age-associated cataracts, and a specific set of endocrine changes including insulin insensitivity/diabetes mellitus, hypogammaglobulinemia (an immune disorder characterized by a reduced ability to fight infections) and testicular failure.

Typically the first symptoms are experienced in the third decade as fluctuating or episodic muscle pain and weakness of the neck flexors (front muscles that assist with nodding and turning the head) and finger flexors (presenting as finger weakness) .

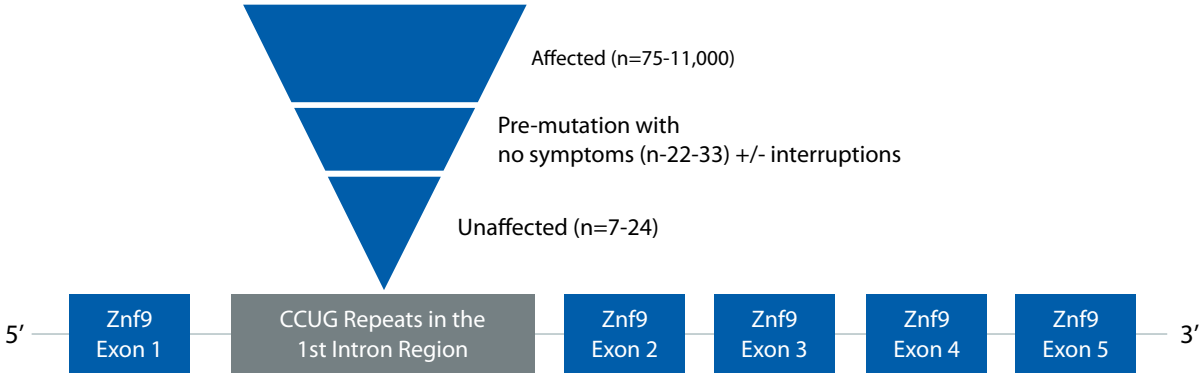
Flexors – these muscles are attached to bone and when they contract they cause a bend. For example pulling the hand to the shoulder bending at the elbow.

Extensors – these are the opposite muscles and when these contract they straighten the limb.

Over time the weakness also begins to occur in the elbow extensors and the hip flexors and extensors (See above). This results in weakness in the thighs. Facial weakness and weakness of the ankle dorsiflexors are less common. This makes standing and lifting the head difficult. A link to deafness in some cases has been described.

The myotonia which is present in almost all individuals with DM2 only rarely causes severe symptoms. Although the condition is progressive this progression is slow and life expectancy is only reduced in cases when there is severe cardiac involvement. Fainting, near fainting or dizzy spells are the usual

The figure below presents a visual explanation of the cause of DM2.



symptoms of conduction block, and these should never be ignored. Such problems can be fatal.

People with DM2 share some similarities to that of people with DM1. Key differences include the absence of congenital (present at birth) defects in any affected family members in DM2 which does occur with DM1. Unlike DM1 there is hardly any cognitive impairment, excessive sleepiness, ptosis (eyelid droop), muscle wasting, dysphagia (swallowing difficulties) or respiratory insufficiency (when the lungs cannot inhale or exhale enough to meet the body's requirements).

If you have DM1 or DM2 there is information about managing these symptoms on the MDA USA website: http://www.mda.org/disease/myotonic-muscular-dystrophy/medical-management/adult-mmd1-mmd2-juvenile-mmd1 and also on the Myotonic Dystrophy Foundation's website: http://www.myotonic.org/

Cause of Myotonic Dystrophy

DM2 is caused by a defect in a gene called Cellular nucleic acid-binding protein (CNBP) which was previously called zinc finger protein 9 (Znf9). This gene is located on chromosome 3.

How the CCTG repeat expansion causes the symptoms experienced by people with DM2 remains unclear.

The error is caused when part of this gene which has a repeating pattern expands beyond a certain size, called a "repeat expansion". There are normally 3 ranges of repeat numbers. This is shown in the diagram above. The normal range is between 7 and 24 repeats. And the expanded and affected range which is from 75 – 11,000 repeats.

How the CCTG repeat expansion causes the symptoms experienced by people with DM2 remains unclear. The faulty protein seems to interfere with proteins in the cell and also affect how other gene proteins function which could explain the multisystem nature of the condition.

Inheritance of Myotonic Dystrophy

DM2 is inherited in an autosomal dominant manner which means that only one copy of the abnormally long and defective gene is needed to cause the disease. Each child of an affected parent has a 50% chance of inheriting the condition.

Genetic counseling is available via Genetic Health Service NZ to families who have had a diagnosis of DM2. This service provides information, helps families understand inheritance patterns and what this means in their family, as well as enabling

The above diagram is sourced from: http://www.myotonic.org/what-dm/disease-mechanism

people to make more informed family-planning decisions.

Diagnosis of Myotonic Dsytrophy

Because of DM2 presents itself with such variability the condition can be suspected clinically, but can only be confirmed genetically. Myotonic dystrophy type 2 should be suspected in individuals with the following:

- **Muscle weakness** in neck and fingers
- **Myotonia** (sustained muscle contraction) that can manifest as grip myotonia (the inability to release a tightened fist quickly).
- **Early onset, bilateral cataracts**
- **Cardiac conduction defects or progressive cardiomyopathy**
- **Hypogammaglobulinemia**, defined as low gamma protein fraction on serum protein electrophoresis or low immunoglobulin G or immunoglobulin M content on immunoprotein electrophoresis
- **Insulin insensitivity**
- **Primary gonadal failure** in males, as evidenced by low serum testosterone concentration, elevated serum Follicle stimulating hormone concentration, oligospermia, and infertility
- **Elevated creatine kinase concentrations** which does not exceed four times the upper limit of the normal range
- **Elevated specific liver enzymes** particularly gammaglutamyltransferase

Myotonia is typically mild and rarely requires treatment.

Management of Myotonic Dystrophy

Treatment guidelines for DM2 have been published and are available on the MDA NZ website.

There is no cure and treatment focuses on the symptoms that are presenting in each person. A multidisciplinary approach is needed and may include; a neurologist, an ophthalmologist and a cardiologist. An occupational therapist, or physiotherapist can help determine the need for ankle-foot orthoses, wheelchairs, or other assistive devices which may be of assistance as the disease progresses.

Routine physical activity appears to be beneficial for maintaining muscle strength and endurance in persons with DM2, and as an aid to control musculoskeletal pain.

Myotonia is typically mild and rarely requires treatment, though use of mexilitene, which is very effective in controlling some forms of myotonia, has helped control muscle pain in some individuals with DM2.

The effectiveness of medications in pain management varies, since no one medication has been consistently effective please discuss pain management with your neurologist. Some people find warm baths, heating pads or massage to be helpful.

Routine physical activity appears to be beneficial for maintaining muscle strength and endurance ...

Establishment of regular routine measures/surveillance of cardiac function is recommended. Consultation with a cardiologist is strongly recommended for individuals with cardiac symptoms or ECG evidence of arrhythmia (a problem with the rate or rhythm of the heartbeat) because fatal arrhythmias can occur prior to the onset of other symptoms.

Cataracts can be removed if they impair vision.

Testosterone replacement therapy can be beneficial in males with symptomatic hypogonadism (reduction or absence of hormone secretion or other physiological activity of the gonads). R