Myotonic Dystrophy

A multi-systemic disorder.

What is myotonic dystrophy?

Myotonic Dystrophy (DM) is an inherited disorder. It is abbreviated as DM as the Latin name for this condition is *'Dystrophia Myotonica'.* In DM, a defective gene causes a multitude of symptoms including progressive muscle weakness accompanied by myotonia, which is the delayed relaxation of muscles after contraction. It is a multi-systemic disorder, meaning that it affect tissues and organs throughout the body.

Primarily the muscles of the face, neck, hands, forearms and feet are affected, although DM can have a wide range of different effects on different individuals.

DM is a rare condition that affects both males and females. Age of onset is variable from birth through to old age.

Speech therapy and audiological assessment is beneficial.

What are the features of myotonic dystrophy?

Body system	Possible Effects
Skeletal muscles	• Muscle weakness (myopathy) • Muscle stiffness and trouble relaxing a muscle (myotonia) • Muscle wasting that gets worse over time (atrophy) • Severe muscle weakness and delayed development in newborns and infants
Cardiac system	• Heart rhythm problems (arrhythmias) • Enlarged heart muscle • Low blood pressure • Sudden death
Respiratory system	• Breathing problems in newborns • Frequent lung infections • Aspiration of food or fluids into airways • Inability to breathe in enough oxygen • Sleep apnea
Gastrointestinal (GI) system	• Difficulty swallowing • Pain and bloating after meals • Constipation, diarrhea, irritable bowel syndrome, gastrointestinal reflux • Gallstones • Enlarged colon
Brain and central nervous system (CNS)	• Difficulty with thinking and problem-solving • Emotional and behaviour problems • Excessive daytime sleepiness • Nerve damage in feet and hands
Reproductive system	• Small testes, low sperm count, low testosterone • Higher risk of miscarriage and stillbirth; early menopause • Problems with pregnancy and delivery • Newborn complications
Hormones	• Insulin resistance • Premature frontal balding in men
Immune system	• Lower levels of antibodies in bloodstream
Tumors	• Higher risk of benign skin tumor (pilomatrixoma)
Vision	• Cataracts • Damage to the retina • Drooping eyelids (ptosis)

Congenital myotonic dystrophy

Congenital myotonic dystrophy is a severe form of DM that is present at birth, and tends to occur in individuals with mothers with DM1. In many instances, the mother's condition is so mild that having a baby with congenital myotonic dystrophy is the first indication that the mother has DM. Congenital myotonic dystrophy affects boys and girls equally.

Babies with congenital myotonic dystrophy have severe muscle weakness and hypotonia (loss of muscle tone). This includes weakness of the face and children characteristically have a 'tented' upper-lip. Babies are also often born with clubfeet – a curvature of the feet and lower legs. Surgical correction is necessary to enable the child to walk. The muscles that control breathing and swallowing are also involved. These problems can be life-threatening and need early intervention and intensive care to improve the chance of survival. This may include the use of artificial ventilation and a feeding tube inserted into the stomach.

As the child gets older it may become apparent that the muscles used for speech are often affected and hearing can also be impaired. Speech therapy and audiological assessment is beneficial. Weakness of the eye muscles can result in strabismus, a condition where the eyes do not work together. This can be corrected with surgery. Congenital myotonic dystrophy may also result in learning disabilities and special education is often necessary.

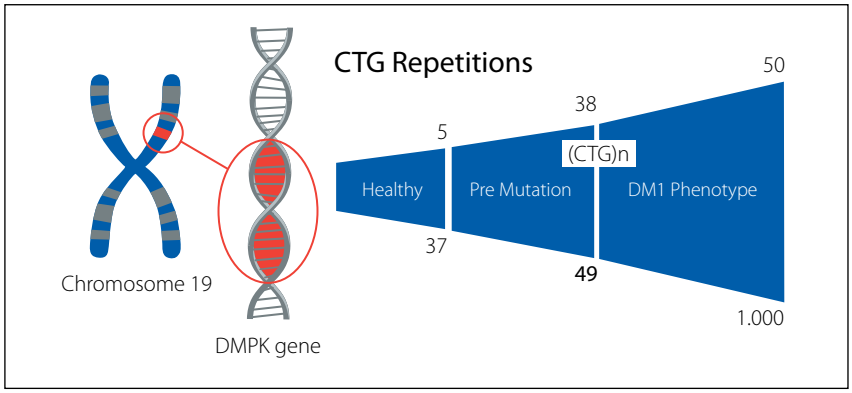
Myotonia is not present in babies with congenital myotonic dystrophy, however he or she may develop myotonia as well as the same clinical signs of DM1 later in life.

What causes myotonic dystrophy?

Humans have 46 chromosomes made up of genes. Each chromosome, which is a tightly coiled chain of DNA (deoxyribose nucleic acid) contains millions of chemicals called bases. The four bases are adenine, thymine, cytosine and guanine (A, T, C and G), which pair together in sets of three to form coded messages. These messages are instructions for producing proteins that make the body function. Many disorders are a result of a mutation to these bases.

DM1 is caused by an abnormality in the DMPK gene on chromosome 19. Affected individuals have an increased number of copies of a portion of this gene called CTG trinucleotide (A sequence of three nucleotides repeated a number of times within a gene). The greater the number of repeated copies, the more likely the condition will be severe and the onset will be earlier.

DM1 is inherited as an autosomal dominant genetic trait. This occurs when only one copy of an abnormal gene is necessary for the appearance of the disease. The abnormal gene can be inherited from either parent or can be a result of a new mutation



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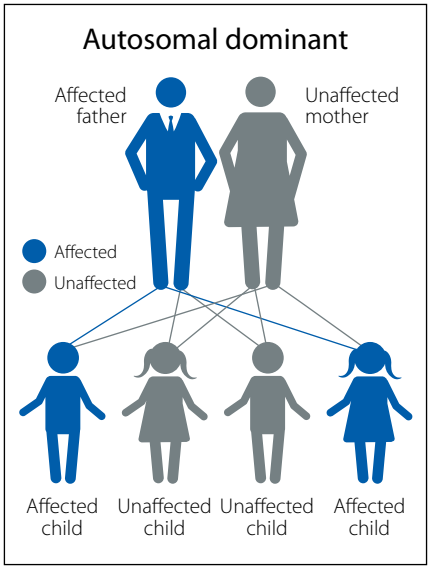


(gene change) in the affected individual. The risk of passing on the abnormal gene from an affected parent to offspring is 50%.

One distinctive genetic mechanism in DM1, is a process called 'anticipation'. The number of repeats of the CTG trinucleotide increases with each affected generation, particularly when passed on by the mother thereby causing the condition to be more severe and occur at an earlier age in the next generation.

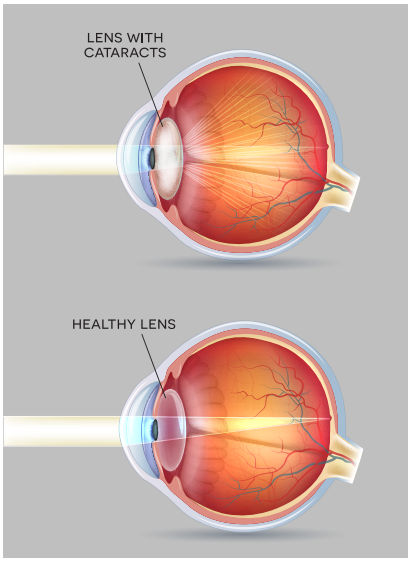
It is currently unknown how the gene changes affect multiple biological systems, however it appears that the problem lies in RNA, which is a copied version of DNA for processing genes into proteins. When the expanded sequence in the DNA is copied, there is an over-accumulation of RNA which traps the information inside the centre of the cell. This blocks several other types of RNA and disrupts the protein-manufacturing process for the genes which control several bodily processes.

Diagnosis of myotonic dystrophy

Diagnosis sometimes occurs as a result of a member of the family being diagnosed with myotonic dystrophy and genetic testing being subsequently offered to others at risk in the family.

In other circumstances diagnosis usually commences after key early symptoms of DM are identified:

- 'Grip Test' - affected individuals will not be able to open and close their hand rapidly and will have a characteristic grip



Heart problems can be monitored and checked using an electrocardiogram (ECG), which measures the beating patterns of the heart.

- Blood Testing – elevated levels of creatine phosphokinase (CPK) are indicative of muscle problems
- Electromyography (EMG) – observes the electrical activity of muscles and its consistency with activity typical of DM individuals
- DNA Testing – can identify the presence of the expanded DMPK gene in the individual with DM

Soon after a diagnosis of DM in the family, it is essential that genetic counselling is arranged, for one or both of two issues. The first is the probability of Mum, Dad or siblings having the disorder, and the second is whether testing for DM in pregnancy can be offered and with what degree of accuracy. Genetic counselling provides information about possible diagnostic tests.

Genetic services for families with DM are available and a referral can be made by the MDA.

Management of myotonic dystrophy

Treatment focuses on the prevention and management of symptoms which vary according to severity.

The use of hand or ankle supports, foot orthotics, walking sticks or wheelchairs, pain management, diabetes mellitus management (insulin therapy), removal of cataracts if vision is impaired, and hormone replacement therapy for males with testicular atrophy. Sleep patterns can be improved with medication and breathing can be helped with a portable ventilator. A speech language therapist can help people to swallow more safely as well as educate about understanding the consistencies of food and liquids so that they can be swallowed more easily.

Importantly, heart problems can be monitored and checked using an electrocardiogram (ECG), which measures the beating patterns of the heart. Severe problems can be corrected with the insertion of a pacemaker.

It is also important to have an annual measurement of serum glucose concentrations, have an eye test every 2 years and have a good nutritional diet and enjoy exercise.