Charcot-Marie-Tooth disease (CMT)

Summary

- Charcot-Marie-Tooth disease (CMT) is the umbrella term for a range of inherited genetic conditions affecting the peripheral nervous system (the nerves stretching from the spinal cord to the muscles).
- Symptoms include progressive weakness and muscle wasting of the legs and arms.
- The ways people are affected can vary widely. Questions about your individual case are best discussed with your treating doctor, who is familiar with your details.

Charcot-Marie-Tooth disease (CMT) is an umbrella term for a range of certain inherited genetic conditions that affect the peripheral nervous system. The peripheral nervous system controls your ability to move and feel parts of your body, such as your hands and feet.

Conditions of the peripheral nerves – the nerves stretching from the spinal cord to the muscles – are known as ‘neuropathies’.

Peripheral nervous system

Nerve tissue outside the brain and spinal cord is known as the peripheral nervous system. This system causes body movements by contracting and relaxing the muscles under instruction from the brain. The peripheral nervous system also relays sensory information from the sense organs of the skin, tendons and muscles back to the spinal cord. (The spinal cord and the brain make up the central nervous system.)

The building block of the nervous system is the nerve cell, or neuron. Neurons from the brain or spinal cord send electrical impulses down nerve fibres from the spinal cord to the muscles. The nerve fibres, which are like fibres in an electrical cable, are called ‘axons’. Axons are protected by an insulating material called myelin. Each axon is covered in a sheath of myelin, which keeps the axon healthy and helps electrical impulses travel quickly down nerve fibres.

CMT either interferes with the production of proteins that make up the myelin sheath, or else affects the structure or function of the axon. Neuropathies that affect myelin are known as ‘demyelinating’ neuropathies. Those that affect primarily the nerve fibres are called ‘axonal’ neuropathies. The result of both is that affected nerves cannot work properly to control movement or sensation.

Symptoms of Charcot-Marie-Tooth disease

For people with CMT, the nerves of the arms and legs work less well than usual. This happens gradually and leads to wasting of the muscles that are served by those nerves. The muscles of the feet, legs and hands are often most affected. Over time, they become weaker and harder to control.

The effects of CMT disease can vary widely. Some people may be only slightly affected – for example, high-sided shoes may be enough to deal with weakness of the legs and feet. Other people may need walking aids like sticks. Some people may need to use a wheelchair.

The onset of symptoms usually occurs in childhood or during the teenage years. The legs are most commonly affected first.

Symptoms of CMT are progressive and can include:

- weakness in the muscles of the hands and feet
- ankle weakness, with ‘rolling-over’ – this is a common early symptom. Later, the person loses the ability to bend their foot upward

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• handgrip is affected – it may become difficult to do things like open screw-top jars or turn taps
• high foot arches (this is known as ‘pes cavus’) and clawed toes
• high-stepping gait and ‘slapping’ of the feet on the floor while walking
• muscle wasting in the legs and arms
• poor balance and occasional falls
• loss of sensation, such as reduced ability to feel pain in the feet and hands
• scoliosis (abnormal sideways curvature of the spine) in some cases.

**CMT is a common inherited condition**

CMT is the most common inherited condition affecting the peripheral nervous system. Around one in 2,500 Australians are thought to be affected. CMT takes its name from the three doctors who first recognised the disorder – Jean-Marie Charcot and Pierre Marie from France and Howard Henry Tooth from the United Kingdom. Other names for CMT include peroneal muscular atrophy, hereditary motor and sensory neuropathy types I, II and X, and progressive neuopathic muscular atrophy. At this stage, there is no cure for CMT.

**Causes of CMT**

Most inherited conditions can only be passed on by one or two patterns of inheritance. However, CMT can be inherited via most known patterns of inheritance and is the most common inherited condition of the peripheral nervous system.

Patterns of inheritance for CMT include:

- **autosomal dominant** – if the condition is inherited in an autosomal dominant pattern, the child only has to inherit one copy of the altered gene to have the condition. Therefore, if either parent has CMT there is a 50 per cent chance that the child may also develop the condition
- **autosomal recessive** – a condition that means the individual must have two copies of the altered gene to have the condition. Therefore, individuals with CMT have two copies of the altered gene, one inherited from each parent. If someone carries one copy of the altered gene of an autosomal recessive condition they are known as a carrier. They carry the CMT gene but have no symptoms
- **X-linked** – the altered gene is carried on the X-chromosome, which is involved in determining the baby’s sex. Each child, male or female, of a mother carrying the CMT type X-linked gene has a 50 per cent chance of inheriting the condition. Males are more affected than females. Females may be carriers without showing any obvious effects. All daughters of an affected man would inherit the gene, but none of his sons. (There is no ‘male-to-male transmission’ in these families.)

The causes of the various types of CMT include:

- CMT Type 1A – a duplicated gene on chromosome 17
- CMT Type 1B – a genetic change on chromosome 1
- CMT Type 1C – a genetic change on chromosome 16
- CMT Type X-linked – a genetic change on the X chromosome
- CMT Type 2A – a genetic change on chromosome 1
- CMT Type 2B – a genetic change on chromosome 3
- CMT Type 2C – a genetic change on chromosome 12
- CMT Type 2D – a genetic change on chromosome 7.

Recently, a number of ‘new’ genes have been discovered, which cause some less common forms of CMT.

**Diagnosis of CMT**

CMT is diagnosed using a number of tests including:

- **physical examination** – strength testing and assessment of reflexes and sensation. Common findings in CMT are loss of the muscle stretch reflexes (especially the ankle jerk reflex), and weakness with lifting the feet (ankle dorsiflexion) and bringing the thumb upwards (thumb abduction)
- **nerve conduction tests** – used to measure the strength and speed of nerve signals in the peripheral nervous system.
system to determine which form of CMT is present. (Different types of CMT affect different aspects of the nervous system.) For example, nerve responses are much smaller than usual in axonal CMT, and the speed at which nerves are able to send signals is much slower in demyelinating forms of CMT.

- **genetic tests** – to identify the altered gene. For example, CMT Type 1A can be diagnosed using a relatively routine test called a chromosome microarray.
- **biopsy** – small samples of tissue are removed and examined in a laboratory. Either nerve or muscle tissue (or both) may be examined. This is not commonly done and is usually unnecessary if a genetic alteration is found.

**Genetic counselling and CMT**

If you or a family member have been diagnosed with CMT, or if CMT runs in your family, it may be helpful to speak to a genetic counsellor.

Genetic counsellors are health professionals qualified in both counselling and genetics. Genetic counsellors provide emotional support and information for people and families affected by genetic conditions. They can help you to understand CMT and what causes it, how it is inherited, and what a diagnosis means for your child’s health, lifestyle and plans for the future, and for your family. They can also provide information about genetic testing for you and your family.

Genetic counsellors are trained to provide information and support that is sensitive to your family circumstances, culture and beliefs.

**Victorian Clinical Genetics Services (VCGS)** provides genetic consultation, counselling, testing and diagnostic services for children, adults, families, and prospective parents.

**Treatment for CMT**

There is no cure for CMT, but treatment can help manage some of the symptoms. Options can include:

- leg and ankle braces or orthotics
- specially designed orthopaedic shoes
- thumb splints
- physical therapy
- muscle strength training
- regular stretching
- regular, moderate exercise involving low impact activities such as swimming or cycling
- occupational therapy
- orthopaedic surgery to correct deformities.

**Support for people and families with CMT**

The **Genetic Support Network of Victoria (GSNV)** is connected with a wide range of support groups throughout Victoria and Australia and can connect you with other individuals and families affected by CMT.

**Where to get help**

- Your **GP (doctor)**
- **Genetic Support Network Victoria** Tel. (03) 8341 6315
- **Charcot-Marie-Tooth Association of Australia (CMTAA)** Tel. (02) 9767 5105
- **Neurology Department, Royal Children’s Hospital** Tel. (03) 9345 5661
- **Victorian Clinical Genetics Services** Tel. 1300 118 247
- **Genetic Support Network of Victoria (GSNV)** Tel. (03) 8341 6315

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