

Charcot-Marie-Tooth disease

Charcot-Marie-Tooth disease (CMT) is an umbrella term for a range of certain inherited genetic disorders that affect the peripheral nervous system. The peripheral nervous system controls our ability to move and feel parts of our body, such as hands and feet. Disorders of the peripheral nerves – the nerves stretching from the spinal cord to the muscles – are known as ‘neuropathies’.

A range of effects

In patients 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 Charcot-Marie-Tooth 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.

A common inherited disease

CMT is the most common inherited disease 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, 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 neuropathic muscular atrophy. There is no cure for CMT.

Symptoms

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
- 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.

Peripheral nervous system explained

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.

Inheritance patterns

Most inherited disorders 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 disorder of the peripheral nervous system.

Patterns of inheritance for CMT include:

- **Autosomal dominant** – the parent has one abnormal gene and one normal gene in the pair. Each child of this parent has a 50 per cent chance of inheriting the abnormal gene and a 50 per cent chance of developing CMT.
- **Autosomal recessive** – the child can only inherit the disorder if both parents are carriers (carriers show no signs of CMT), and both pass on the abnormal gene. The child has CMT but neither parent has any symptoms at all.
- **X-linked** – the abnormal 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 disorder. 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.)

A range of causes

The causes of the various types of CMT include:

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

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

Diagnosis

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 jerks), and weakness with lifting the feet (ankle dorsiflexion) and bringing the thumb upwards (thumb abduction).
- **Nerve conduction tests** – used to determine which form of CMT is present; nerve responses are much smaller in axonal CMT, while conduction of impulses down nerves is much slower in demyelinating forms of CMT.
- **Genetic tests** – to identify the abnormal gene.

- **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 abnormality is found.

Treatment

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.

Where to get help

- Your doctor
- Genetic Support Network Victoria Tel. (03) 8341 6315
- Charcot-Marie-Tooth Association Australia Tel. (02) 9767 5105
- Neurology Department, Royal Children's Hospital Tel. (03) 9345 5661

Things to remember

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

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Genetic Health Services Victoria

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