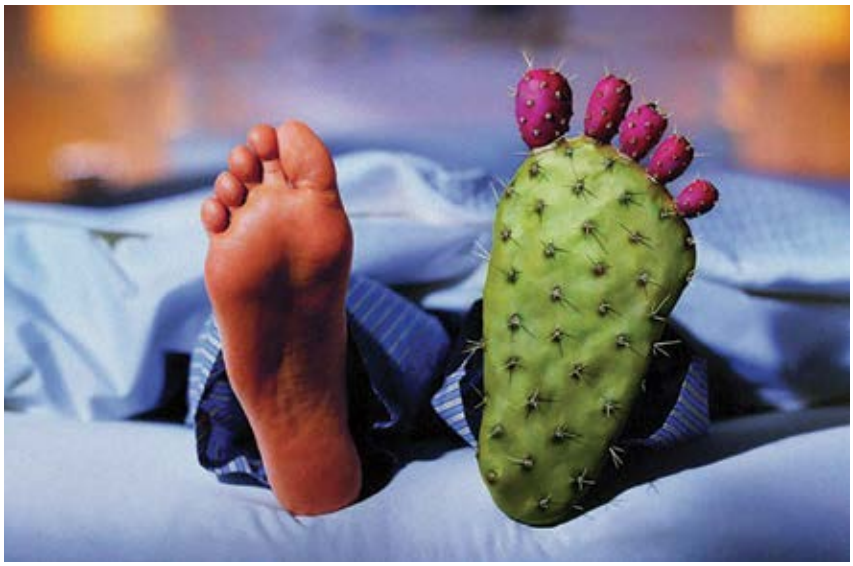
Charcot-Marie-Tooth disease

Understanding our most common condition.



What is Charcot-Marie-Tooth disease?

Charcot-Marie-Tooth disease (CMT), also known as hereditary motor and sensory neuropathy (HMSN), comprises a family of genetic conditions that mainly affect the motor and sensory nerves, which run from the spinal cord down the arms and legs.

CMT is named after the three physicians who first described it in 1886, Jean-Marie Charcot, Pierre Marie, and Howard Henry Tooth. CMT is a relatively common rare disorder affecting both males and females from childhood or adulthood depending on the type. It's estimated that CMT affects 1 in approximately 2,500 people.

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What causes CMT?

CMT is caused by alterations in genes that produce proteins involved in the structure and function of either the peripheral nerve cell (axon), or the myelin sheath that wraps around the axon to insulate it and in normal circumstances allows the signals to travel faster and better.

What are the different types of Charcot-Marie-Tooth Disease?

There are many forms of CMT. Due to the increase in knowledge of the various genetic causes of CMT, the way the different types are described and classified is being re-thought. The most common form is CMT is called CMT1A and is caused by a duplication of a gene called PMP22. It's inherited in an autosomal dominant way, meaning that a child with CMT1A will have one parent with the condition. CMT1A affects the myelin sheath surrounding the nerve. There are other forms of CMT1 and what they all have in common is that they affect the structure and function of the myelin sheath.

Symptoms of CMT1A usually become apparent during childhood. Children with this condition are often slow runners, develop high arches, hammer toes and often require orthotics (braces) for ankle support as the ankles weaken and become prone to sprains. Later, often ten years or more after the onset of foot and leg problems, varying degrees of hand weakness can occur resulting in problems holding pens, grasping, performing fine motor tasks such as doing up buttons or zippers. Problems with balance because of ankle weakness and loss

of proprioception are common, although most people remain mobile throughout life, and life expectancy is normal.

CMT2 is caused by abnormal genes involved in the structure and function of **axons** and is divided into subtypes on the basis of which gene is involved. The clinical picture is similar to CMT1 with distal weakness, muscle atrophy, sensory loss and foot deformities, but is often more variable between and even within families. Some types of CMT2 also cause deafness or eye problems.

Other features of CMT include:

- The loss of nerve function is often accompanied by tingling and burning sensations in the hands and feet. This usually causes little more than mild discomfort, but some people experience severe neuropathic pain and require medication to control it.
- Loss of nerve function in the extremities can also result in sensory loss. The sense of touch is diminished, as is the ability to perceive changes in temperature, and patients may unknowingly injure themselves. They can be unaware of having developed ulcers of the feet or of cuts or burns on the hands. Sensory loss in CMT patients may also be associated with dry skin and hair loss in the affected areas.
- Many patients are extremely sensitive to the cold or even to temperatures a few degrees lower than normal. CMT results in the loss of insulating muscle mass, which, combined with reduced muscular activity and circulation, can leave patients with chronically cold hands and feet. Impairment of the normal circulatory process can also result in swelling (oedema) of the feet and ankles.
- Deep-tendon reflexes, such as the knee jerk reaction, are lost in many patients, and is of diagnostic importance. Some people with CMT also have tremor (usually of the hands) and the combination of tremor and CMT is sometimes referred to as Roussy-Levy Syndrome.
- Scoliosis or mild curvature of the spine can also occur, often in puberty and tends to be most common in people with early onset of gait abnormalities. Hip dysplasia also affects a small number of CMT patients at an early age.

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Diagnosis of Charcot-Marie-Tooth disease

Diagnosis of CMT begins with a standard patient history, family history, and neurological examination. People will be asked about the nature and duration of their symptoms and whether other family members have the disease. During the neurological examination a physician will look for characteristic features of the disease, and will then order diagnostic testing, which may include the following.

Electrodiagnostic Testing

Electrodiagnostic testing usually includes a nerve conduction velocity test (NCV), which measures the strength and speed of electrical signals moving down the peripheral nerves. Delayed responses are a sign of demyelination, and small responses are a sign of axonal involvement – some types of CMT show mixed both axonal and demyelinating signs. An electromyography (EMG) is another type of electrodiagnostic test, which measures the electrical signal's strength in the muscles of the arms or legs.

DNA Studies

These molecular genetic tests, usually performed on white blood cells extracted from a blood sample are available to test for some of the common genetic causes of CMT, including PMP22 duplications and deletions, MPZ and GJB1. A positive genetic test can provide definitive diagnosis and provide useful information for family planning, hence genetic counselling is highly recommended. However, a negative result does not rule out CMT as many forms are not yet able to be tested by single-gene DNA testing. Neuromuscular gene panels are increasingly being used once the common causes have been excluded.

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Management of Charcot-Marie-Tooth disease

CMT is managed symptomatically via a number of therapies depending on the needs of the individual.

These include:

- **Podiatry:** for the care and monitoring of foot problems.
- **Orthotics** for the manufacture and fitting of braces and customised footwear.
- **Orthopaedic surgery** to traighten toes, lengthen heel cords or lower arches;
- **Physiotherapy and occupational therapy** to design exercise programmes to strengthen muscles or learn about energy conservation, as well as provide assistive devices and equipment to be able to continue day to day activities as independently as possible.
- **Dietitian visits or dietary advice** to maintain a healthy, balanced diet and weight.
- **Regular medicines reviews:** some medications should be avoided by people with CMT, as they are contra-indicated and can seriously worsen the condition or cause severe side-effects. The full list of medications to be avoided by people with CMT is available on the MDANZ website or can be obtained by contacting MDANZ. ®