Charcot-Marie-Tooth disease (CMT)

What is Charcot-Marie-Tooth disease?

Charcot-Marie-Tooth disease (CMT) is also commonly referred to as hereditary motor and sensory neuropathy (HMSN). This is an accurate term as it refers to the two primary features of this condition, i.e. the condition is hereditary and affects the motor and sensory peripheral nerves. CMT therefore is used to describe a group of conditions that give rise to weakness and wasting of the muscles below the knees and often those of the hands. Many affected people also have loss of feeling in the hands and feet, and this is the ‘sensory’ component. The term neuropathy refers to the fact that it is the peripheral nerves (which connect the spinal cord to the muscles, joints and skin, carrying messages in both directions), which do not function normally. As the name implies, these are inherited disorders.

CMT is also referred to as peroneal muscular atrophy, because the peroneal muscles on the outer side of the calves are particularly affected. Other names include Dejerine-Sottas disease and hereditary hypertrophic neuropathy. The term CMT is now the favoured term and is most commonly used in the literature.

What causes Charcot-Marie-Tooth disease?

There are two main types of CMT – type 1 and type 2. They are classified according to exactly which part of the nerve is affected. If you think of a nerve as being a little like an electrical cable, the part of the nerve called the axon is like the metal wire that conducts the electrical signal. Around the axon is a protective myelin sheath that is like the plastic insulation you would find around an electrical cable. In CMT type 1 it is the myelin sheath that is affected and in type 2 it is the axon itself that is affected. This damage makes it more difficult for the nerve to conduct the electrical signal from the brain to the muscle resulting in muscle weakness and loss of sensation. These two main types are further divided into different subtypes, depending on how they are inherited and the gene that is involved.

There have been major advances in the last two decades with the identification of the causative genes for CMT. To date there have been more than 45 genes identified in which mutations are known to cause CMT. Researchers have not yet identified all the genes linked to CMT and so not everyone who is suspected of having the condition is currently able to have a genetic diagnosis. Currently, patients with CMT are more likely to be given a genetic diagnosis if they have CMT type 1 rather than CMT type 2.

CMT type 1 and type 2 are further classified by the way they are inherited. Some forms are inherited in an autosomal dominant manner – that is you need only one copy of the mutated gene to show symptoms – and some in an autosomal recessive manner, where you need to have two copies of the mutated gene to show symptoms. One form of CMT – CMT X1 – has a slightly different type of inheritance called X-linked inheritance. These conditions are determined by genes which are carried on one of the chromosomes which control the sex of a child. You might wish to read more about this in more detail in our Inheritance factsheet.

The most common form of CMT type 1 – CMT 1A - is usually caused by the duplication of a gene on chromosome
number 17. This gene carries the instructions for a protein found in myelin called peripheral myelin protein 22 (PMP-22). Affected individuals have an extra copy of PMP-22 (three copies instead of the usual two) because they have an extra copy of a small part of chromosome 17 containing the PMP-22 gene. Although this mutation, commonly called the chromosome 17 duplication, is usually inherited in an autosomal dominant manner (that is you only need to inherit one copy of the mutated gene in order to develop symptoms), it has been found in some individuals with healthy parents (and thus represents a new mutation). More rarely, patients with CMT1A have a change in, rather than a duplication of, the PMP-22 gene.

There are many other sub-types of CMT involving a large number of other genes and it is important for patients with CMT to know which genes are currently available for testing in the UK. Testing for the chromosome 17 duplication referred to above, which causes most cases of CMT 1A, is widely available in most regional genetic laboratories. Testing for all other less common genes is not routinely available but testing may be available on a research basis and new sophisticated techniques to identify mutations in genes are currently being introduced which will make genetic testing in CMT much easier. If you would like to find out more about a specific sub-type of CMT, then please contact us on 020 7803 4800 or info@muscular-dystrophy.org.

Is there a treatment or cure?

There is no specific treatment at present for the underlying genetic defect in CMT even in those patients in whom a genetic diagnosis has been made, although there are many groups researching this area. The first trial of a treatment in CMT (Vitamin C in CMT1A) has been completed although it unfortunately showed that vitamin C had no beneficial effect in CMT1A.

The lack of a specific treatment does not mean that patients with CMT cannot be treated or helped in many other ways. It is very important that problems patients experience, such as foot problems, are addressed appropriately and this may greatly improve a patient’s quality of life. Accurate genetic diagnosis and genetic counselling is the other area of management in which there has been rapid development in recent years.

One of the most common problems in CMT is difficulty in getting well-fitting shoes because of the arched feet. It is important to wear shoes with good support, and arch supports or other devices within the shoes may be needed. In people who have quite a lot of weakness of the leg muscles, splints are often very helpful to reduce the tendency of the foot to drop. New types of splints are continually being developed and patients should discuss the options with their physiotherapist. Ideally, children and teenagers with CMT should be seen annually by a neurologist or a paediatrician to ensure that severe problems with the feet do not develop. Surgery may be helpful for very highly arched feet, either to reduce the arch and the curling of the toes which often goes with it, or to fuse together some of the foot bones. After procedures of this sort, and any other operation, it is essential to minimise periods spent in bed, as increased difficulties in walking are often noticed afterwards. Just as rest may enhance difficulty in walking, active exercise and maintaining fitness help to maintain mobility. Surgery is not usually needed for scoliosis but may have to be considered in the very few cases in which this is severe. In those with a lot of numbness of the feet, it is important to take great care of the feet, washing and drying them carefully, and inspecting the skin for small ulcers. The inside of the shoes should be shaken out to remove small stones etc., and the insides felt for irregularities that could damage the skin.

Accurate genetic counselling is one of the mainstays of management and typically involves detailed assessment, including blood and electrical tests of close relatives. Despite the major advances in understanding the genetic abnormalities in CMT, the electrical studies remain the initial and most important tool in the diagnosis of most patients. In CMT 1A, affected children will show the typical electrical abnormality from about the age of five years. Once a genetic diagnosis is made in a patient with CMT, the blood test can then be used to diagnose other affected members of a family. Occasionally members of a family with CMT, without signs of the disease or electrical abnormalities, request a genetic test to see if they are likely to develop the disease in the future (predictive testing). This is usually not done in unaffected children, the preference being to wait until they are adult and can make their own decision about testing.

What is the prognosis?

The first evidence of CMT is usually in the first 10 years of life but sometimes may not be until very much later, even into middle-age. Usually the first symptom is slight difficulty in walking because of problems with picking up the feet, and this may well be noted by parents first. Many people, particularly those with CMT type 1, have high arched feet (referred to as pes cavus) and this may be obvious from a very early age. It tends to become particularly noticeable at the time of the growth spurt associated with puberty. Weakness of the hands occurs in some people, but this does not usually cause symptoms until after the age of 20.

Patients can experience numbness of the feet and hands (usually noticed in the feet first) which is not often
troublesome, but the tendency to have cold feet is frequent. Very rarely the numbness can be severe, and it is then easy for affected individuals to injure themselves without knowing it; painless ulcers of the feet may develop as a result of poorly-fitting shoes, or burns on the hand from hot cups etc. Nerve pain is not a common feature of CMT but pain from secondary effects on the joints or muscles is not uncommon. The reflexes (such as the knee jerk) are commonly lost. This does not cause any trouble for the individual, but is often noted early on by doctors. A few people with CMT 1 have shakiness of the hands (tremor) and the combination of tremor and CMT is sometimes referred to as the Roussy-Levy Syndrome. Mild curvature of the spine (scoliosis) occurs in some people and tends to be more severe in those with early onset of limb problems.

The types of CMT which run through the generations in families are not usually severely disabling disorders and are very slowly progressive. It is unusual for people with CMT to lose the ability to walk, although some people – especially when older – need a stick or other walking aids. It is important to stress that the disorder often varies enormously in severity, even in members of the same family, and 10 to 20 percent of affected individuals have no symptoms at all but are found to have evidence of the condition on examination, or on using electrical tests.

Other related publications

This factsheet is to be used alongside the following publications:

- Inheritance
- Adult Self-Management Pack
- An introductory guide for families with a child newly diagnosed with a neuromuscular condition
- Inclusive Education Guide
- Wheelchair Provision for Children and Adults with Muscular Dystrophy and other Neuromuscular conditions

References


The friendly staff in the care and support team at the Muscular Dystrophy Campaign’s London office are available from 8.30am to 6pm Monday to Friday to offer free information and emotional support. If they can’t help you, they are more than happy to signpost you to specialist services close to you, or to people who can help.

Contact our Freephone helpline on 0800 652 6352 or info@muscular-dystrophy.org

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