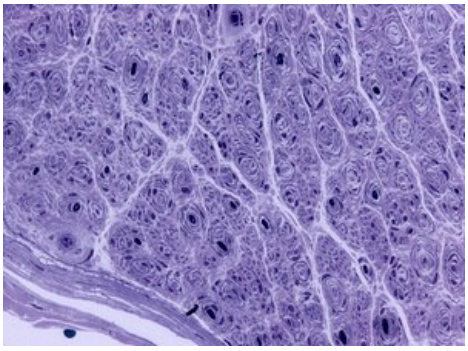
Charcot-Marie-Tooth Syndrome

This is a large group of genetic neuropathies. Sometimes referred to as **CMT**. Degenerative changes affect both the **motor** and **sensory** components. The changes are most pronounced on the lower limb, especially on the feet. It is one of the most common **hereditary neuropathies**.

CMT classification

CMT is divided into five basic groups:

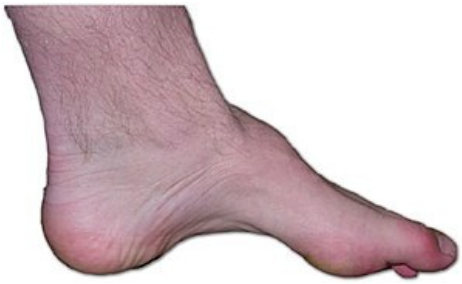
- CMT1 - is autosomal dominantly inherited. It is further divided into 6 subtypes (CMT1A to CMT1F)
- CMT2 - is autosomal dominantly inherited. It contains 11 subtypes, designated CMT2A – L, while subtype B is then further subdivided (B, B1, B2).
- CMT3 - is autosomal recessively inherited. Extremely rare form. It has no further division.
- CMT4 - is autosomal recessively inherited. Extremely rare form. Contains 8 types of CMT4A-J, with diversified group B (B1, B2)
- CMTX - has gonosomal inheritance. There are 5 subtypes marked with numbers, ie CMTX1–5



"Onion bulb formations" in nerve biopsy

Genetic nature of CMT

Recent studies list 39 different genes whose mutations cause some form of CMT.



Manifestation of CMT syndrome

Probably the most common mutation that causes the first type of CMT, **CMT1A** (and also **CMT1E**) is a mutation in the **PMP22** (http://omim.org/entry/601097) gene, the product is a protein called **peripheral myelin protein 22**. It is a transmembrane protein contained mainly in the membrane of Schwann cells, it passes through the membrane 4 times and is incorporated into the structure of myelin. Dozens of gene sites are known in which a point mutation causes CMT.

A less common mutation is a mutation in the gene for the so-called **MPZ** (http://omim.org/entry/159440) protein, ie **myelin protein zero**. It is one of the most important proteins in the **formation and maintenance** of the myelin sheath. It is a transmembrane protein, also part of the Schwann cell membrane, which passes through the membrane only once. It belongs to the immunoglobulin family, has extracellular, transmembrane and intracellular domains. It forms a homotetramer and its function is that the two homotetramers combine when the individual leaves of the Schwann cell membrane fold together due to their extracellular domains. This keeps the structure of the myelin sheath firm. Mutations in the MPZ gene cause CMT1B and CMT2J.

- CMT1C is caused by a mutation in the **LITAF** (http://omim.org/entry/603795) gene, a *lipopolysaccharide-induced tumor necrosis factor-alpha factor*. According to the latest research, it is associated with obesity and insulin resistance.
- CMT1D and CMT4E are caused by a mutation in the **EGR2** (http://omim.org/entry/129010) gene, *early growth response protein 2*.
- CMT1F and CMT2E cause mutations in the **NEFL** (http://omim.org/entry/162280) gene, a *neurofilament light polypeptide*.
- The mutation in the mitofusin 2 gene is responsible for CMT2A.
- CMT3, termed **Dejerine-Sottas syndrome**, is associated with the PMP22, MPZ, EGR2 and PRX (*periaxin*) genes.

Other types of CMT are caused by mutations in many other genes (if identified). Probably the latest discovery is the clarification of the cause of CMTX5, which is the gene for **PRPS1** (http://omim.org/entry/311850), ie *phosphoribosyl pyrophosphate synthetase 1*.

Links

External links

- **Databáze OMIM**
  - gen PMP22 (http://omim.org/entry/601097)
  - gen MPZ (http://omim.org/entry/159440)
  - gen LITAF (http://omim.org/entry/603795)

    - gen EGR2 (http://omim.org/entry/129010)
    - gen NEFL (http://omim.org/entry/162280)
    - gen MFN1 (http://omim.org/entry/608506)
    - gen MFN2 (http://omim.org/entry/608507)
    - gen PRPS1 (http://omim.org/entry/311850)

- Other:
    - Wikipedia – PMP22 (https://en.wikipedia.org/wiki/PMP22)
    - Wikipedia – Charcot–Marie–Tooth disease (https://en.wikipedia.org/wiki/Charcot%E2%80%93Marie%E2%80%93Tooth_disease)
    - Wikipedia – LITAF (https://en.wikipedia.org/wiki/LITAF)
    - Wikipedia – EGR2 (https://en.wikipedia.org/wiki/EGR2)
    - Wikipedia – NEFLW (https://en.wikipedia.org/wiki/NEFLW)
    - Dejerine-Sottas disease (https://en.wikipedia.org/wiki/Dejerine-Sottas_disease)

References

- ws:Charcotův-Marieův-Toothův syndrom
- SANDERS, Charles, et al. *Peripheral Myelin Protein 22* [online]. Sander's lab, [cit. 2011-04-15]. <http://structbio.vanderbilt.edu/sanders/Research_Julia_Ver_1/Research.html>.
- TRIGGS, William J., et al. *A 57-Year-Old Woman with Numbness and Weakness of the Feet and Legs* [online]. NEJM, [cit. 2011-04-15]. <http://www.nejm.org/action/cookieAbsent>.
- HEE-JIN, Kim, et al. *Mutations in PRPS1* [online]. [cit. 2011-04-15]. <https://www.ncbi.nlm.nih.gov/pubmed/17701900>.
- LITAF (https://www.ncbi.nlm.nih.gov/pubmed?term=LITAF)

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