

Anaesthesia recommendations for **Charcot-Marie-Tooth disease**

Disease name: Charcot-Marie-Tooth disease

ICD 10: G60.0

Synonyms: -

Disease summary: Hereditary motor and sensory neuropathy. Includes: Charcot-Marie-Tooth, Déjerine-Sottas, hereditary motor and sensory neuropathy (however this term includes several entities different from Charcot-Marie-Tooth with heterogeneous inheritance), hypertrophic neuropathy of infancy, peroneal muscular atrophy (axonal type) (hypertrophic type), Roussy-Lévy syndrome.

Charcot-Marie-Tooth (CMT) disease is the most prevalent peripheral inherited neuropathy (1/2,500 to 10,000; 2.8/10,000 in Spain), and the mean age at onset is 16 years (range from 2 to 50 years, but presentation in the early infancy and as late as the 80s has been reported). Patients present with motor and sensory polyneuropathic semiology (distal lower limb weakness and atrophy, gait abnormalities and frequent falls) and pes cavus. Apart from the motor nerve related deficits, most patients suffer a slight sensory loss in hands and feet. The treatment of the disease is supportive. Life expectancy is not shortened – except in some forms of Déjerine-Sottas and severe forms of CMT – but disabilities are the rule.

Guidelines for differential diagnosis of neuropathies in children and adolescents have been recently released (see Korinthenberg et al.).

Gene therapies and others are now under development (see general references).

A clinical synopsis of the most prevalent forms CMT 1 and 2 is shown in Tables 1 and 2.

Charcot-Marie-Tooth disease (CMT) is a sensorineural peripheral polyneuropathy. Affecting approximately 1 in 2,500 individuals, CMT is the most common inherited disorder of the peripheral nervous system. Autosomal dominant, autosomal recessive, and X-linked forms have been recognised.

The slow increase in physical disability in adulthood may well be explained by decreased reserves and compensatory mechanisms together with progression of skeletal deformations due to muscle weakness. However, this classic concept is controversial, as it can be related to CMT1A only: progression of axonal loss definitely occurs in most if not all CMT types and is a cause of progressive wasting and weakness in many patients. A summary of overall clinical features is depicted in Table 3.

Sometimes CMT disease is associated with moderate to severe chronic extremity pain, which is usually related to bone, joint and muscle involvement, and rarely neuropathic.

CMT is more frequently an autosomal dominant disease (but there is genetic heterogeneity, and more than 30 pathogenic genes have been implicated, X-linked and autosomal recessive forms, even mitochondrial DNA mutations showing a CMT-like phenotype have been reported). The most common syndrome is CMT1A, which accounts for 55 % of all CMT cases and 66.8 % of CMT1 cases, and which is usually caused by an duplication of or mutation in the gene encoding peripheral myelin protein-22 on chromosome 17p12, containing the PMP22 gene (causing excessive gene dosage, and overproduction of PMP22 and its accumulation in Schwann cells that is a proposed mechanism resulting in programmed cell death, the ultimate mechanism of CMT development remaining unknown), but the percentages can vary according to different series reported and geographic origin. The 1970s classification from Dyck is valid, but molecular genetics has changed the nosology (see Berciano J, et al. for complete information):

a) type I (CMT1, demyelinating or hypertrophic) with AD or AR inheritance; b) type II (CMT2, neuronal or axonal) with AD or AR inheritance; c) type III (CMT3, usually with de novo heterozygous gene mutations, AR uncommon) reserved for Déjérine-Sottas disease or patients with severe forms of hypomyelinating CMT; d) X-linked forms, and e) complex forms (e.g. associated with pyramidal involvement, optic atrophy, deafness, occurring in several CMT types; pigmentary degeneration of the retina suggest mitochondrial disease). See Table 4.

Diagnostic: lineage of affected ancestors, and/or (in the case of negative family survey), onset during childhood; prolonged and slowly progressive clinical course; presence of pes cavus, and – unlike in acquired neuropathies – absence of positive sensory symptoms (paraesthesias or dysaesthesias) despite a clear semiology of sensory deficit. An electrophysiologic examination should follow (CMT1 and CMT2 classification depends on the cut-off value 38m/s by convention, for the upper limb motor nerves conduction velocity, both median and ulnar nerves), and, in selected cases, neuropathologic criteria (nerve biopsy). Finally, genetic testing specifically targeted (molecular diagnosis).

Medicine is in progress



Perhaps new knowledge

Every patient is unique

Perhaps the diagnosis is wrong



Find more information on the disease, its centres of reference and patient organisations on Orphanet: www.orpha.net

Typical surgery

Orthopaedic procedures are common: Soft tissue, osteotomies and arthrodesis (both isolated or combined), i.e. multiple tendinous transposition in foot deformities, and scoliosis. Nerve biopsy. A case of diaphragmatic plication has been reported.

Type of anaesthesia

Case reports or case series are the source of information.

Intravenous sedation can be used in selected procedures, with the precautions suggested for general anaesthesia.

General anaesthesia is usually selected: Balanced (halogenated agents) and total intravenous (propofol based) anaesthesia have been safely used, with or without muscle relaxation. Neuromuscular monitoring should be used.

Total intravenous anaesthesia propofol based without neuromuscular block can be chosen depending on the surgical procedure.

Sometimes extremely difficult cases present for surgery as if the nerve involvement is of both upper and lower extremities and thoracic nerves. A case was published by Kim et al. of a patient that, in addition, showed several previous surgeries including extensive spine surgery. General anaesthesia was used and monitored muscle relaxation reversed with pyridostigmine/glycopyrrolate. The same occurs in a case report of supraventricular tachycardia ablation under general anaesthesia in a patient with CMT and Kearns-Sayre mitochondrial myopathy.

It has been recommended to avoid succinylcholine, but it has been extensively used with no problems. No malignant hyperthermia developed after this drug, but hyperkalaemia could appear due to the existence of pathologic muscle fibres.

Neuraxial blocks have been successfully performed (epidural, spinal and combined spinal-epidural anaesthesia).

In a few cases, ultrasound-guided nerve blocks for post-operative analgesia have been used, without long lasting neurologic complications. Muscle response to neurostimulation can be abnormal (low). Moreover, ultrasound findings can reveal an abnormal sonoanatomy thus precluding nerve block. Giant nerve appearance is a form of presentation, in a patient previously diagnosed or not of CMT. In a case report, the peripheral nerve block was successful with no sequelae.

In a short case series, Schmitt et al. showed adequate analgesic effect of peripherally inserted catheters under nerve stimulator guidance (7 out of 17 were inserted with difficulties, several attempts, high electrical current).

Necessary additional pre-operative testing (beside standard care)

Patients need to be closely evaluated. In a few cases, restrictive pulmonary impairment has been described in association with phrenic nerve dysfunction, diaphragm dysfunction, or thoracic cage abnormalities. Central sleep apnoea may be associated with diaphragm

dysfunction and hypercapnia, whereas obstructive sleep apnoea has been reported as possibly due to a pharyngeal neuropathy. Restless legs and periodic limb movement during sleep are found in some patients with CMT2. Vocal cord dysfunction, possibly due to laryngeal nerve involvement, is found in association with some CMT types, and there are some risks of progression to bilateral paralysis and aspiration.

Patients should be assessed for the presence of autonomic denervation as it is common.

Assessment for other co-morbidities should be undertaken as the presence of diabetes mellitus can lead to further deterioration in neuropathy.

Particular preparation for airway management

None reported.

Particular preparation for transfusion or administration of blood products

None reported.

Particular preparation for anticoagulation

None reported.

Particular precautions for positioning, transportation and mobilisation

Cautious positioning and protection of pressure points (padding) is recommended because nerve compression may aggravate the neuropathy. Difficulties are sometimes possible due to anatomical or postsurgical deformities. In addition, positioning should be careful to prevent haemodynamic instability.

Interactions of chronic disease and anaesthesia medications

Drugs for neuropathy (restless legs syndrome) or chronic pain.

Some patients can be under psychoactive drug therapy due to psychiatric symptoms (i.e. depression, anxiety).

In a few cases, spinal cord stimulation has been used to treat chronic limb pain.

Anaesthetic procedure

In a case series, thiopental dose required for induction in CMT was less than in control patients, and was related to the severity of the neuropathy.

Theoretically, nitrous oxide use could cause neurotoxicity through its inhibition of methionine synthase in patients with CMT, and it is quoted as 'moderate to significant' risk of potential toxicity and worsening neuropathy in people with CMT by the CMT Association (USA), CMT Association of Australia, CMT International (Canada) and CMT United Kingdom. Nevertheless, a systematic review (11 studies, 41 exposures) observed no neurologic worsening, with the authors quoting the drug as safe in adults and children.

Response to non-depolarising neuromuscular blocking agents can be unpredictable, but information is controversial.

Safe sugammadex neuromuscular block reversal has been reported.

Patients severely affected (as the kyphoscoliotic ones) can develop respiratory insufficiency after neuraxial anaesthesia (higher than expected sensory and motor block level).

A combination of anaesthetic procedures has been safely used. Alzaben et al reported on a young 17 year old male patient under a lower limb orthopaedic surgery which was carried out under general total iv anaesthesia (dexmedetomidine-propofol) combined with caudal block (bupivacaine-dexmedetomidine). In thoracic surgery, balanced anaesthesia (propofol, remifentanil infusion, lidocaine bolus, rocuronium and sevoflurane maintenance) plus skin incisions infiltration with bupivacaine was useful. Iv morphine and paracetamol were used in the post-operative period. Separated alternated one lung ventilation with volume controlled ventilation was used (bilateral sympathectomy procedure). Sugammadex reverted neuromuscular block completely.

Particular or additional monitoring

Neuromuscular block monitoring is recommended. Monitoring at the ulnar nerve-adductor pollicis brevis is recommended as lower limbs are often severely denervated. However sometimes monitoring can be difficult especially if upper limbs are affected, too.

Possible complications

Probably this disease is not especially associated with hyperkalaemic response after succinylcholine, but it has been recommended to avoid it.

Response to non-depolarising neuromuscular blocking agents can be quite variable, prolonged and attenuated responses have both been described.

Lung aspiration due to vocal cord paresis has been described.

If associated pulmonary diseases present, post-operative ventilatory assistance (i.e. BiPAP or CPAP) should be considered. This includes patients under spinal anaesthesia.

Post-operative care

Care should be taken regarding possible disautonomy and lower urinary tract dysfunction (male and female).

See before for ventilatory support. Respiratory insufficiency could develop (because of several factors: muscle weakness, diaphragm paresis, infections, insufficient cough reflex, etc.), and several forms of respiratory support would be needed.

Disease-related acute problems and effect on anaesthesia and recovery

Respiratory insufficiency can develop after surgery. The cause may be multifactorial. Patients whose respiratory system is affected (thoracic muscles and diaphragm) can be at risk of this complication, and this should be taken into account to minimise other factors (drugs, type of surgery, surgical approaches).

Ambulatory anaesthesia

In this setting, avoiding neuromuscular blocking agents might be recommended.

Obstetrical anaesthesia

In a study (Medical Birth Registry of Norway, n=108), women with CMT had a higher occurrence of presentation anomalies and bleeding post partum; the rate of operative delivery was twice that of the reference group), and forceps was used three times as often in the CMT group. The majority of CMT Caesarean sections were emergency sections.

Epidural or combined spinal-epidural anaesthesia for labour and caesarean delivery can be chosen. Most published cases showed no symptoms or functional status worsening.

If neuraxial blocks cannot be used, as in a case of CMT and HELLP syndrome with low platelet count, general anaesthesia needs to be performed. In the cited case, a modified rapid sequence induction with remifentanil infusion, propofol and rocuronium 1.2 mg/kg was chosen. Forty-five minutes afterwards, adequate recovery was observed without reversal drugs.

The availability of sugammadex permits the use of aminosteroid neuromuscular blocking agents, mainly rocuronium, for emergent Caesarean sections using rapid sequence induction of anaesthesia.

Spinal anaesthesia has been used for Caesarean section (both scheduled and emergency), as has been epidural anaesthesia.

Table 1. Charcot-Marie-Tooth disease, type 1A, chromosome 17p12 (gene locus PMP22)

<p>INHERITANCE</p> <ul style="list-style-type: none">- Autosomal dominant
<p>SKELETAL</p> <p>Spine</p> <ul style="list-style-type: none">- Kyphoscoliosis may occur <p>Hands</p> <ul style="list-style-type: none">- Claw hand deformities (in severe cases) <p>Feet</p> <ul style="list-style-type: none">- Pes cavus- Hammer toes- Foot deformities
<p>NEUROLOGIC</p> <p>Peripheral Nervous System</p> <ul style="list-style-type: none">- Distal limb muscle weakness due to peripheral neuropathy- Distal limb muscle atrophy due to peripheral neuropathy- 'Steppage' gait- Foot drop- Cold-induced muscle cramps- Distal sensory impairment- Hyporeflexia- Areflexia- Decreased motor nerve conduction velocity (NCV) (less than 38 m/s)- Hypertrophic nerve changes- 'Onion bulb' formations seen on nerve biopsy- Segmental demyelination/remyelination seen on nerve biopsy- Decreased number of myelinated fibers- Myelin outfoldings (in some patients)
<p>MISCELLANEOUS</p> <ul style="list-style-type: none">- Onset in first or second decade- Usually begins in feet and legs (peroneal distribution)- Upper limb involvement usually occurs later- Slowly progressive- Insidious onset- Variable severity- Allelic disorders with overlapping phenotypes include Dejerine-Sottas syndrome (DSS, 145900), hereditary neuropathy with liability to pressure palsies (HNPP, 162500), and CMT with deafness (118300)
<p>MOLECULAR BASIS</p> <ul style="list-style-type: none">- Caused by mutation in the peripheral myelin protein-22 gene (PMP22, 601097.0001)

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Table 2. Charcot Marie Tooth disease, type 1B, chromosome 1q23.3, autosomal dominant (gene locus MPZ)

<p>INHERITANCE - Autosomal dominant</p> <p>HEAD & NECK Eyes - Tonically dilated pupils (in some patients) - Adie pupil</p> <p>SKELETAL Spine - Kyphoscoliosis may occur Hands - Claw hand deformities (in severe cases) Feet - Pes cavus - Hammer toes - Foot deformities</p> <p>NEUROLOGIC Peripheral Nervous System - Distal limb muscle weakness due to peripheral neuropathy - Distal limb muscle atrophy due to peripheral neuropathy - 'Steppage' gait - Foot drop - Cold-induced muscle cramps - Distal sensory impairment - Hyporeflexia - Areflexia - Decreased motor nerve conduction velocity (NCV) (less than 38 m/s) - Hypertrophic nerve changes - 'Onion bulb' formations seen on nerve biopsy - Segmental demyelination/remyelination seen on nerve biopsy - Decreased number of myelinated fibers - Myelin outfoldings may occur in a subset of patients</p> <p>MISCELLANEOUS - Onset in first or second decade - Usually begins in feet and legs (peroneal distribution) - Upper limb involvement usually occurs later - Slowly progressive - Insidious onset - Variable severity - Allelic disorders with overlapping phenotypes include Dejerine-Sottas syndrome (DSS, 145900), congenital hypomyelination (CHN, 605253), and some forms of axonal CMT2 (see 607677)</p> <p>MOLECULAR BASIS - Caused by mutation in the myelin protein zero gene (MPZ, 159440.0001)</p>

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Table 3. Clinical features of CMT disease

In general, CMT disease is characterised by an insidious onset and slowly progressive weakness and atrophy of the distal limb muscles usually beginning in the legs and feet (especially in the peroneal compartment). As a result, patients frequently trip while walking, have foot drop, and steppage gait. As both motor and sensory nerve function are affected in CMT, other features include impaired sensation and absent or hypoactive deep tendon reflexes. Weakness in the intrinsic hand muscles may occur later. The onset of CMT is typically in the first or second decade of life, although it may be detected in infancy. Variation in clinical presentation is wide, ranging from patients with severe distal atrophy and marked hand and foot deformity to individuals whose only finding is pes cavus and minimal distal muscle weakness.

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Table 4. Classification of CMT disease

Basis: electrophysiologic properties and histopathology.

1. Primary peripheral demyelinating (type 1, or HMSNI) and primary peripheral axonal (type 2, or HMSNII) neuropathies.

The demyelinating neuropathies classified as CMT type 1 are characterised by severely reduced motor NCVs (less than 38 m/s) and segmental demyelination and remyelination with onion bulb formations on nerve biopsy.

The axonal neuropathies classified as CMT type 2 are characterised by normal or mildly reduced NCVs and chronic axonal degeneration and regeneration on nerve biopsy. Distal hereditary motor neuropathy (dHMN), or spinal CMT, is characterised by exclusive motor involvement and sparing of sensory nerves.

McAlpine (1989) proposed that the forms of CMT with very slow nerve conduction be given the gene symbol CMT1A and CMT1B, CMT1A being the gene on chromosome 17 and CMT1B being the gene on chromosome 1. CMT2 was the proposed symbol for the autosomal locus responsible for the moderately slow nerve conduction form of the disease (axonal).

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References

Inheritance related:

<https://www.omim.org/entry/118220?search=%22charcot%20marie%20tooth%22&highlight=%22charcot%20marie%20tooth%22>

Anesthesia related:

1. Barbary JB, Remérand F, Brilhault J, Laffon M, Fusciardi J. Ultrasound-guided nerve blocks in the Charcot–Marie–Tooth disease and Friedreich’s ataxia. *Br J Anaesth*.2012;108(6):1042-3.10.1093/bja/aes160
2. Skaribas IM, Washburn SN. Successful treatment of charcot-marie-tooth chronic pain with spinal cord stimulation: A case study. *Neuromodulation*. 2010;13:224-8. DOI 10.1111/j.1525-1403.2009.00272.x
3. Errando CL. Anestesia en el paciente con enfermedades neuromusculares para cirugía torácica [Anesthesia in patients with neuromuscular diseases for thoracic surgery]. In: Granell Gil M, editor. *Actualización sobre Anestesiología y Reanimación en Cirugía Torácica [Update on Anesthesia and Critical Care in Thoracic Surgery]*, 4th ed. Madrid: Ergón; 2012. pp. 3-7
4. Pasternak JJ, Lanier WL. Diseases of the autonomic and peripheral nervous systems. In: Stoelting R, Dierdorf S, editors. *Stoelting’s anesthesia, coexisting disease*. Philadelphia, PA: Elsevier Saunders; 2012:264-273
5. Gálvez-Cañellas JL, Errando CL, Martínez-Torrente F, Mayor F, Zasadowski M, Villanueva Y, Soria-Bretones C. Anaesthesia and orphan disease: Difficult monitoring of neuromuscular blockade in a patient with severe Charcot-Marie-Tooth disease type I. *Eur J Anaesthesiol* 2013;30:770-80
6. Aceto P. Cisatracurium-induced neuromuscular block during total intravenous anaesthesia in a patient with Charcot-Marie-Tooth disease. *Eur J Anaesthesiol* 2010;27:670–672
7. Brock M, Guinn C, Jones M. Anesthetic management of an obstetric patient with Charcot-Marie-Tooth disease: A case study. *AANA J* 2009;77:335-7
8. Bui AH, Marco AP. Peripheral nerve blockade in a patient with Charcot-Marie-Tooth disease. *Can J Anesth* 2008;55:718-9
9. Dhir S, Balasubramanian S, Ross D. Ultrasound-guided peripheral regional blockade in patients with Charcot-Marie-Tooth disease: A review of three cases. *Can J Anesth* 2008; 55:515-20
10. Fernandez Perez AB, Quesada Garcia C, Rodriguez Gonzalez O, Besada Estevez JC. [Obstetric epidural analgesia, a safe choice in a patient with Charcot-Marie-Tooth disease]. *Rev Esp Anesthesiol Reanim* 2011;58:255-6
11. Freire Vila E, Criado Alonso MJ, Barjacoba Perez L, Chamadoira B, Taboada Ben MR. [General anesthesia with laryngeal mask and remifentanyl for remodelling and corrective osteosynthesis of neuropathic foot in a case of type I Charcot-Marie-Tooth disease]. *Rev Esp Anesthesiol Reanim* 2000;47:178-9
12. Garcia-Ferreira J, Hernandez-Palazon J. Response to cisatracurium in patient with Charcot-Marie-Tooth disease. *Eur J Anaesthesiol* 2005;22:160-1
13. Greenwood JJ, Scott WE. Charcot-Marie-Tooth disease: Peripartum management of two contrasting clinical cases. *Int J Obstet Anesth* 2007;16:149-54
14. Hashimoto T, Morita M, Hamaguchi S, Kitajima T. [Anesthetic management for pancreaticoduodenectomy in a patient with Charcot-Marie-Tooth disease and liver cirrhosis]. *Masui* 2009;58:1313-5
15. Isbister GK, Burns J, Prior F, Ouvrier RA. Safety of nitrous oxide administration in patients with Charcot-Marie-Tooth disease. *J Neurol Sci* 2008;268:160-2
16. Kapur S, Kumar S, Eagland K. Anesthetic management of a parturient with neurofibromatosis 1 and Charcot-Marie-Tooth disease. *J Clin Anesth* 2007;19:405-6
17. Kotani N, Hirota K, Anzawa N, Takamura K, Sakai T, Matsuki A. Motor and sensory disability has a strong relationship to induction dose of thiopental in patients with the hypertropic variety of Charcot-Marie-Tooth syndrome. *Anesth Analg* 1996;82:182-6
18. Kuczkowski KM, Fernandez CL, Drobniak L, Chandra S. Anesthesia for cesarean section in a parturient with Charcot-Marie-Tooth disease: unresolved controversies. *Arch Gynecol Obstet* 2010;282:347-8
19. Niiyama Y, Kanaya N, Namiki A. [Anesthetic management for laparoscopic surgery in a patient with Charcot-Marie-Tooth disease]. *Masui* 2003;52:524-6

20. Pasha TM, Knowles A. Anaesthetic management of a patient with Charcot-Marie-Tooth disease for staged diaphragmatic plication. *Br J Anaesth* 2013;110:1061-3
21. Pelaez Romero R, Alonso Chico A, Villamandos BQ, Garcia de Lucas E. [Subarachnoid anesthesia for an emergency cesarean section in Charcot-Marie-Tooth disease]. *Rev Esp Anesthesiol Reanim* 2003;50:106-7
22. Schmitt HJ, Munster T. Mivacurium-induced neuromuscular block in adult patients suffering from Charcot-Marie-Tooth disease. *Can J Anesth* 2006;53:984-8
23. Shankar V, Markan S, Gandhi SD, Iqbal Z, Novalija J, Nicolosi AC, Pagel PS. Perioperative implications of charcot-marie-tooth disease during coronary artery bypass graft surgery. *J Cardiothorac Vasc Anesth* 2007;21:567-9
24. Soto Mesa D, Bermejo Alvarez MA, Rubio Marauri P, Garcia Menendez MJ. [Anesthetic considerations in Charcot-Marie-Tooth disease]. *Rev Esp Anesthesiol Reanim* 2011;58: 256-8
25. Sugai K, Sugai Y. [Epidural anesthesia for a patient with Charcot-Marie-Tooth disease, bronchial asthma and hypothyroidism]. *Masui* 1989;38:688-91
26. Sugino S, Yamazaki Y, Nawa Y, Sato K, Sonoda H, Namiki A. [Anesthetic management for a patient with Charcot-Marie-Tooth disease using propofol and nitrous oxide]. *Masui* 2002;51:1016-9
27. Tanaka S, Tsuchida H, Namiki A. [Epidural anesthesia for a patient with Charcot-Marie-Tooth disease, mitral valve prolapse syndrome and IInd degree AV block]. *Masui* 1994; 43:931-3
28. Valles Torres J, Martinez-Ubieto J, Colas Rodriguez A, Abengoechea Beisty JM. [General anesthesia with a laryngeal mask in a patient with long-standing Charcot-Marie-Tooth disease]. *Rev Esp Anesthesiol Reanim* 2009;56:194-5.

General:

29. <http://omim.org/entry/606482>, <http://omim.org/entry/118220>
30. <http://emedicine.medscape.com/article/1173484-overview#aw2aab6b3>
31. <http://neuromuscular.wustl.edu/time/hmsn.html>
32. Berciano J, Sevilla T, Casasnovas C, Sivera R, Vilchez JJ, Infante J, Ramón C, Pelayo-Negro AL, Illa I, Programme 3 (Neuromuscular Diseases), and Centro de Investigación Biomédica en Red de Enfermedades Neurodegenerativas (CIBERNED), Instituto de Salud Carlos III. Guidelines for molecular diagnosis of Charcot-Marie-Tooth disease. *Neurologia* 2012;27:169-78
33. Verhamme C, van Schaik IN, Koelman JHTM, de Haan RJ, de Visser M. The natural history of Charcot-Marie-Tooth type 1A in adults: a 5-year follow-up study. *Brain* 2009; 132: 3252-62
34. Kang JH, Kim HJ, Lee ER. Electrophysiological evaluation of chronic inflammatory demyelinating polyneuropathy and Charcot-Marie-Tooth Type 1: Dispersion and correlation analysis. *J Phys Ther Sci* 2013;25: 1265-8
35. Aboussouan LS, Lewis RA, Shy ME. Disorders of pulmonary function, sleep, and the upper airway in Charcot-Marie-Tooth disease. *Lung* 2007;185:1-7
36. Colomban C, Micallef J, Lefebvre MN, Dubourg O, Gonnaud PM, Stojkovic T, Jouve E, Blin O, Pouget J, Attarian S. Clinical spectrum and gender differences in a large cohort of Charcot-Marie-Tooth type 1A patients. *J Neurol Sci* 2013; DOI 10.1016/j.jns.2013.10.029
37. Dziejwas R, Waldmann N, Bontert M, Hor H, Muller T, Okegwo A, Ringelstein EB, Young P. Increased prevalence of obstructive sleep apnoea in patients with Charcot-Marie-Tooth disease: a case control study. *J Neurol Neurosurg Psychiatr* 2008;79:829-31
38. Eklund E, Svensson E, Hager-Ross C. Hand function and disability of the arm, shoulder and hand in Charcot-Marie-Tooth disease. *Disabil Rehab* 2009;31:1955-62
39. Hoff JM, Gilhus NE, Daltveit AK. Pregnancies and deliveries in patients with Charcot-Marie-Tooth disease. *Neurology* 2005;64:459-62
40. Krhut J, Mazanec R, Seeman P, Mann-Gow T, Zvara P. Lower urinary tract functions in a series of Charcot-Marie-Tooth neuropathy patients. *Acta Neurol Scand* 2013. DOI 10.1111/ane.12176
41. Sivera R, Sevilla T, Vilchez JJ, Martinez-Rubio D, Chumillas MJ, Vazquez JF, Muelas N, Bataller L, Millan JM, Palau F, Espinos C. Charcot-Marie-Tooth disease: Genetic and clinical spectrum in a Spanish clinical series. *Neurology* 2013;81:1617-25. DOI 10.1212/WNL.0b013e3182a9f56a
42. Steiner I, Gotkine M, Steiner-Birmanns B, Biran I, Silverstein S, Abeliovich D, Argov Z, Wirguin I. Increased severity over generations of Charcot-Marie-Tooth disease type 1A. *J Neurol* 2008;255:813-9

43. Ursino G, Alberti MA, Grandis M, Reni L, Pareyson D, Bellone E, Gemelli C, Sabatelli M, Pisciotta C, Luigetti M, Santoro L, Massollo L, Schenone A. Influence of comorbidities on the phenotype of patients affected by Charcot-Marie-Tooth neuropathy type 1A. *Neuromusc Disord* 2013;23:902-6
44. Kang JH, Kim HJ, Lee ER. Electrophysiological Evaluation of Chronic Inflammatory Demyelinating Polyneuropathy and Charcot-Marie-Tooth Type 1: Dispersion and Correlation Analysis. *J Phys Ther Sci* 2013;25:1265-68
45. Pons Odena M, Piqueras Marimbardo I, Colomer Oferil J, Segura Matute S, Palomeque Rico A. [Respiratory disease and diaphragm paralysis in Charcot-Marie-Tooth disease]. *An Pediatr (Barc)* 2010;72:267-71
46. Taniguchi JB, Elui VM, Osorio FL, Hallak JE, Crippa JA, Machado-de-Sousa JP, Kebbe LM, Lourenco CM, Scarel-Caminaga RM, Marques W, Jr. Quality of life in patients with Charcot-Marie-Tooth disease type 1A. *Arq Neuro-psiquiatr* 2013;71:392-6
47. Vallat JM, Mathis S, Funalot B. The various Charcot-Marie-Tooth diseases. *Curr Opin Neurol* 2013;26 473-80
48. Fiacchino F, Grandi L, Ciano C, Sghirlanzoni A. Unrecognized Charcot-Marie-Tooth disease: diagnostic difficulties in the assessment of recovery from paralysis. *Anesth Analg.* 1995 Jul;81(1):199-201.

References included in the 2021 update

General:

1. Bird TD. Charcot-Marie-Tooth (CMT) Hereditary Neuropathy Overview. In: *GeneReviews*, edited by M. P. Adam, H. H. Ardinger, R. A. Pagon, S. E. Wallace, L. J. H. Bean, K. W. Gripp, et al. University of Washington, Seattle. 1993.
2. Korinthenberg R, Trollmann R, Plecko B, Stettner GM, Blankenburg M, Weis J, et al. Differential diagnosis of acquired and hereditary neuropathies in children and adolescents-Consensus-Based Practice Guidelines. *Children (Basel)* 2021;8(8). DOI: 10.3390/children8080687.
3. Sun H, Shen XR, Fang ZB, Jiang ZZ, Wei XJ, Wang ZY, et al. Next-generation sequencing technologies and neurogenetic diseases. *Life (Basel)* 2021; 11(4). DOI: 10.3390/life11040361.
4. Miniou P, Fontes M. Therapeutic development in Charcot Marie Tooth Type 1 Disease. *Int J Mol Sci* 2021;22(13). DOI: 10.3390/ijms22136755.
5. Rossor AM, Shy ME, Reilly MM. Are we prepared for clinical trials in Charcot-Marie-Tooth disease? *Brain Res* 2020; 1729: 146625. DOI: 10.1016/j.brainres.2019.146625.
6. Sahenk Z, Ozes B. Gene therapy to promote regeneration in Charcot-Marie-Tooth disease. *Brain Res* 2020; 1727: 146533. DOI: 10.1016/j.brainres.2019.146533.
7. Nagappa M, Sharma S, Taly AB. Charcot Marie Tooth. In: *StatPearls*, StatPearls Publishing, 2022.
8. Stavrou M, Sargiannidou I, Georgiou E, Kagiava A, Kleopa KA. Emerging therapies for Charcot-Marie-Tooth inherited neuropathies. *Int J Mol Sci* 2021; 22(11). DOI: 10.3390/ijms22116048.

Anesthesia related:

1. Alvarez N, Gonzalez A. Anaesthesia and orphan diseases: anaesthetic management of a patient with X-linked Charcot-Marie-Tooth disease type 1. *Eur J Anaesthesiol* 2018; 35(7):544-547. DOI: 10.1097/EJA.0000000000000743.
2. Alzaben KR, Samarah OQ, Obeidat SS, Halhouli O, Al Kharabsheh M. Anesthesia for Charcot-Marie-Tooth Disease: Case Report. *Middle East J Anaesthesiol* 2016; 23(5): 587-590.
3. Darquennes K, De Jonghe P, Daems D, De Backer W, Verbraecken J. Intermittent positive airway pressure by nasal mask as a treatment for respiratory insufficiency in a patient with Charcot-Marie-Tooth disease. *Acta Clin Belg* 2006; 61(4): 176-181. DOI: 10.1179/acb.2006.030.
4. Del-Rio-Vellosillo M, Garcia-Medina JJ, Martin-Gil-Parra R. Anaesthetic management of a patient with Charcot-Marie-Tooth disease for staged diaphragmatic plication. *Br J Anaesth* 2014;112(2): 390. DOI: 10.1093/bja/aet572.
5. del-Rio-Vellosillo M, Martin-Gil-Parra R, Garcia-Medina JJ. Anesthetic considerations for Cesarean section in a parturient with Charcot-Marie-Tooth disease and HELLP syndrome. *J Clin Anesth* 2014; 26(3): 251-252. DOI: 10.1016/j.jclinane.2014.01.005.

6. Falyar CR. To block or not to block: Role of ultrasonography in guiding an anesthetic plan for a patient with Charcot-Marie-Tooth disease. *AANA J* 2019 Vol. 87 Issue 2 Pages 110-113
7. Ginz HF, Ummenhofer WC, Erb T, Urwyler A. [The hereditary motor-sensory neuropathy Charcot-Marie-Tooth disease: anesthesiologic management--case report with literature review]. *Anaesthesist* 2001;50:767–771. DOI: 10.1007/s001010100203
8. Heller JA, Marn RY. Laparoscopic appendectomy in a pediatric patient with type 1 Charcot-Marie-Tooth disease. *J Clin Anesth* 2015; 27: 680-681. DOI: 10.1016/j.jclinane.2015.07.021
9. Kim JW, Kim G, Kim TW, Han W, Maeng JH, Jeong CY, et al. Anesthesia in a patient with Charcot-Marie-Tooth disease with pneumothorax: a case report. *J Int Med Res* 2019;47: 5896–5902. DOI: 10.1213/XAA.0000000000001488
10. hshita N, Oka S, Tsuji K, Yoshida H, Morita S, Momota Y, et al. Anesthetic management of a patient with Charcot-Marie-Tooth disease. *Anesth Prog* 2016; 63:80-83. DOI: 10.2344/15-00010R1.1
11. Pehlivanov B, Matev M. [Pregnancy and Delivery in a Patient with Charcot-Marie-Tooth Disease]. *Akush Ginekol (Sofia)* 2016; 55:34-35
12. Schmitt HJ, Huberth S, Huber H, Munster T. Catheter-based distal sciatic nerve block in patients with Charcot-Marie-Tooth disease. *BMC Anesthesiol* 2014; 4:8. DOI: 10.1186/1471-2253-14–18
13. Shiraishi T, Masumoto K, Nakamura M, Hidano G. Enlarged brachial plexus nerve found during ultrasound-guided peripheral nerve block diagnosed as Charcot-Marie-Tooth disease: A case report. *Local Reg Anesth* 2020; 13: 141-146. DOI: 10.2147/lra.s270189
14. Smith JD, Minkin P, Lindsey S, Bovino B. Anesthetic and surgical management of a bilateral mandible fracture in a patient with Charcot-Marie-Tooth disease: A case report. *J Oral Maxillofac Surg* 2015; 73(10): 1917 e1–6
15. Warncke KA, Marshall JM. A patient with Kearns Sayre syndrome and Charcot-Marie-Tooth for supraventricular tachycardia ablation: A case report. *A A Pract* 2021;15:e01488. DOI: 10.1213/XAA.0000000000001488.

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