U.S. National Library of Medicine
National Center for Biotechnology Information

NLM Citation: Kim JW, Kim HJ. Charcot-Marie-Tooth Neuropathy X Type 5 – RETIRED CHAPTER, FOR HISTORICAL REFERENCE ONLY. 2008 Aug 26 [Updated 2013 Jun 6]. In: Adam MP, Feldman J, Mirzaa GM, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2024.
Bookshelf URL: https://www.ncbi.nlm.nih.gov/books/

Charcot-Marie-Tooth Neuropathy X Type 5 – RETIRED CHAPTER, FOR HISTORICAL REFERENCE ONLY

Synonyms: CMTX5, Rosenberg-Chutorian Syndrome

Jong-Won Kim, MD, PhD[1] and Hee-Jin Kim, MD, PhD[1]

Created: August 26, 2008; Updated: June 6, 2013.

Summary

NOTE: THIS PUBLICATION HAS BEEN RETIRED. THIS ARCHIVAL VERSION IS FOR HISTORICAL REFERENCE ONLY, AND THE INFORMATION MAY BE OUT OF DATE.

Clinical characteristics

X-linked Charcot-Marie-Tooth neuropathy type 5 (CMTX5), part of the spectrum of *PRPS1*-related disorders, is characterized by peripheral neuropathy, early-onset (prelingual) bilateral profound sensorineural hearing loss, and optic neuropathy. The onset of peripheral neuropathy is between ages five and 12 years. The lower extremities are affected earlier and more severely than upper extremities. Initial manifestations often include foot drop or gait disturbance. Onset of visual impairment is between ages seven and 20 years. Intellect and life span are normal. Carrier females do not have findings of CMTX5.

Diagnosis/testing

Diagnosis is based on clinical findings, family history consistent with X-linked inheritance, and identification of a pathogenic variant in *PRPS1*, the only gene in which pathogenic variants are known to cause CMTX5.

Management

Treatment of manifestations: Peripheral neuropathy, hearing loss, and visual impairment are managed in a routine manner.

Surveillance: Regular neurologic and ophthalmologic evaluations to monitor symptom development and disease progression.

Agents/circumstances to avoid: Medications known to cause acquired peripheral neuropathy.

Author Affiliation: 1 Department of Laboratory Medicine & Genetics Samsung Medical Center Sungkyunkwan University School of Medicine, Seoul, Republic of Korea; Email: kimjw@skku.edu; Email: heejinkim@skku.edu.

Evaluation of relatives at risk: It is appropriate to evaluate at-risk males at birth with detailed audiometry to assure early diagnosis and treatment of hearing loss.

Genetic counseling

CMTX5 is inherited in an X-linked manner. Carrier women have a 50% chance of transmitting the *PRPS1* pathogenic variant in each pregnancy. Males who inherit the pathogenic variant will be affected; females who inherit the pathogenic variant will be carriers and typically will not be affected. Males pass the pathogenic variant to all of their daughters and none of their sons. Carrier testing for at-risk family members and prenatal testing for a pregnancy at increased risk are possible if the pathogenic variant has been identified in the family.

Diagnosis

Clinical Diagnosis

X-linked Charcot-Marie-Tooth neuropathy type 5 (CMTX5), part of the spectrum of *PRPS1*-related disorders, is characterized by the following:

Peripheral neuropathy

- Motor nerve conduction velocities (NCVs) of affected males reveal delayed distal latencies and decreased amplitudes with relatively normal velocities (median motor NCV ≥38 m/s), consistent with an axonal neuropathy.
- Compound motor/sensory action potentials are not induced.
- Needle electromyography (EMG) reveals polyphasic potentials with a prolonged duration and reduced recruitment pattern.

Early-onset sensorineural hearing loss

- Pure tone audiograms demonstrate bilateral profound sensorineural hearing loss.
- Auditory brain stem response waveforms may not be obtained.
- Temporal bone computed tomography reveals no abnormal findings.

Optic neuropathy

- Fundoscopic examination shows bilateral optic disc pallor, indicating optic atrophy.
- Visual evoked potentials demonstrate delayed latency and decreased amplitudes of P100.
- Electroretinogram is normal.

Testing

Phosphoribosylpyrophosphate synthetase (PRS) enzyme activity can be analyzed in fibroblasts, lymphoblasts, and erythrocytes [Torres et al 1996].

PRS enzyme activity in three individuals with CMTX5 was decreased compared to controls [Kim et al 2007].

Note: Because it is difficult to assay PRS1 enzyme activity separately from that of the other two isoforms (PRS2 and PRS3), decrease in PRS enzyme activity is assumed to reflect decreased activity of PRS1, not PRS2 or PRS3.

Serum uric acid concentrations measured in three individuals with CMTX5 of Korean descent and two of European descent (originally reported as having Rosenberg-Chutorian syndrome) were within the normal range [Kim et al 2007].

Molecular Genetic Testing

Gene. *PRPS1*, encoding phosphoribosyl pyrophosphate synthetase I, is the only gene in which pathogenic variants are known to cause CMTX5.

Table 1. Molecular Genetic Testing Used in CMTX5

Gene [1]	Method	Variants Detected [2]	Variant Detection Frequency by Method [3]
PRPS1	Sequence analysis [4]	Sequence variants	100% [5, 6]
	Deletion/duplication analysis [7]	Exon/whole-gene deletions or duplications	Unknown [8]

1. See Table A. Genes and Databases for chromosome locus and protein.
2. See Molecular Genetics for information on variants.
3. The ability of the test method used to detect a pathogenic variant that is present in the indicated gene
4. Sequence analysis detects variants that are benign, likely benign, of uncertain significance, likely pathogenic, or pathogenic. Variants may include small intragenic deletions/insertions and missense, nonsense, and splice site variants; typically, exon or whole-gene deletions/duplications are not detected. For issues to consider in interpretation of sequence analysis results, click here.
5. Two families reported to date [Kim et al 2007]
6. Sequence analysis of genomic DNA cannot detect deletion of one or more exons or the entire X-linked gene in a heterozygous female.
7. Testing that identifies deletions/duplications not readily detectable by sequence analysis of the coding and flanking intronic regions of genomic DNA. Methods used may include a range of techniques such as quantitative PCR, long-range PCR, multiplex ligation-dependent probe amplification (MLPA), and chromosomal microarray (CMA) that includes this gene/chromosome segment.
8. No deletions or duplications of *PRPS1* have been reported to cause Charcot-Marie-Tooth neuropathy X type 5.

Testing Strategy

To confirm/establish the diagnosis in a proband, identification of a pathogenic variant in *PRPS1* is necessary.

Carrier testing for at-risk relatives requires prior identification of the pathogenic variant in the family.

Note: (1) Carriers are heterozygotes for this X-linked disorder and are not known to be at risk of developing clinical findings related to the disorder. (2) Identification of female carriers requires either (a) prior identification of the pathogenic variant in an affected male relative or, (b) if an affected male is not available for testing, molecular genetic testing first by sequence analysis and then, if no pathogenic variant is identified, by deletion/duplication analysis.

Prenatal diagnosis and preimplantation genetic testing for at-risk pregnancies require prior identification of the pathogenic variant in the family.

Clinical Characteristics

Clinical Description

The symptom triad of CMTX5 is peripheral neuropathy, sensorineural hearing loss, and optic neuropathy.

The age at onset of symptoms of peripheral neuropathy ranges from five to 12 years. The initial manifestation is often foot drop or gait disturbance. Deep tendon reflexes are usually absent. Motor signs predominate, but impairment of sensory function may accompany motor dysfunction or develop during disease progression. Lower extremities are affected earlier and more severely than upper extremities.

Typically, boys with CMTX5 have early-onset (prelingual) sensorineural hearing loss.

The age at onset of visual impairment ranged from seven to 20 years.

Affected individuals have normal intellect.

Both peripheral neuropathy and optic neuropathy progress with time. With advancing disease, affected individuals may become dependent on crutches or a wheelchair. There is no evidence that life span is shortened in individuals with CMTX5 [Rosenberg & Chutorian 1967, Kim et al 2007].

Carrier females do not have findings of CMTX5.

Sural nerve biopsy demonstrates demyelination and axonal loss. Electron microscopic examination reveals onion bulb formation [Kim et al 2007].

Genotype-Phenotype Correlations

Across the four disease phenotypes included as *PRPS1*-related disorders, only pathogenic missense variants have been reported to date. No correlation between specific *PRPS1* pathogenic missense variants and phenotype is known.

Penetrance

Penetrance is complete for CMTX5.

Prevalence

Prevalence has not been estimated. Two families with CMTX5 have been identified worldwide [Rosenberg & Chutorian 1967, Kim et al 2007].

CMTX5 appears to be very rare; however, it may be underdiagnosed as a result of under-recognition by physicians.

Genetically Related (Allelic) Disorders

The spectrum of *PRPS1*-related disorders includes four phenotypes, CMTX5, PRS superactivity, Arts syndrome, and DFNX1 (DFN2) nonsyndromic hearing loss and deafness (see Table 2).

Table 2. Major Clinical Findings in *PRPS1*-Related Disorders by Phenotype

Phenotype		Gouty Arthritis [1]	Peripheral Neuropathy	ID	SNHL	Other
PRS superactivity	Infantile onset	+	-	±	±	Hypotonia; ataxia
	Late-juvenile/ early-adult onset	+	-	-	-	-
CMTX5		-	+	-	Early onset	Optic atrophy
Arts syndrome		-	-	+	Profound congenital	Hypotonia; ataxia; optic atrophy;↑ risk of infection
DFNX1 (DFN2) nonsyndromic hearing loss and deafness		-	-	-	Postlingual progressive, severe to profound / congenital	-

± = variably present ; ID = intellectual disability; SNHL = sensorineural hearing loss
1. Associated with hyperuricemia, hyperuricosuria

Phosphoribosylpyrophosphate synthetase (PRS) superactivity is characterized by hyperuricemia and hyperuricosuria and is divided into a severe phenotype with infantile or early-childhood onset and a milder

phenotype with late-juvenile or early-adult onset. Variable combinations of sensorineural hearing loss, hypotonia, and ataxia observed in the severe type are not usually present in the mild type. In the mild type, uric acid crystalluria or a urinary stone is commonly the first clinical finding, followed later by gouty arthritis if serum urate concentration is not controlled.

Arts syndrome is characterized by profound congenital sensorineural hearing impairment, early-onset hypotonia, delayed motor development, mild to moderate intellectual disability, ataxia, and increased risk of infection, all of which (with the exception of optic atrophy) present before age two years. Signs of peripheral neuropathy develop during early childhood. Twelve of 15 boys from the two Dutch families reported with Arts syndrome died before age six years of complications of infection. Carrier females can show late-onset (age >20 years) hearing impairment and other findings.

DFNX1 (DFN2) nonsyndromic hearing loss and deafness. Individuals with DFNX1 nonsyndromic hearing loss and deafness (DFN2) have postlingual progressive nonsyndromic hearing loss, although in one family congenital profound nonsyndromic hearing loss was reported [Liu et al 2010]. Affected individuals have normal intellect.

Differential Diagnosis

Peripheral neuropathy. See Charcot-Marie-Tooth Hereditary Neuropathy Overview.

X-linked Charcot-Marie-Tooth disease (CMTX). CMTX5 is clearly distinguishable from the five other forms of X-linked Charcot-Marie-Tooth disease [Kim et al 2005] (see Charcot-Marie-Tooth Neuropathy X Type 1):

- **CMTX type 1** is characterized by a moderate to severe motor and sensory neuropathy in affected males and usually mild to no symptoms in carrier females. Sensorineural deafness and central nervous system symptoms also occur in some families. The gene in which mutation is causative is *GJB1* (*Cx32*).
- **CMTX2** with intellectual disability maps to Xp22.2 [Ionasescu et al 1991, Ionasescu et al 1992].
- **CMTX3** with spasticity and pyramidal tract signs maps to Xq26 [Ionasescu et al 1991, Ionasescu et al 1992, Huttner et al 2006].
- **CMTX4** (Cowchock syndrome) with deafness and intellectual disability resulting from mutation in *AIFM1* [Cowchock et al 1985, Priest et al 1995, Rinaldi et al 2012].
- **CMTX6,** resulting from mutation in *PDK3.* Males have childhood onset of a slowly progressive motor and sensory neuropathy that is largely axonal (variable mild conduction slowing) with steppage gait and absent tendon reflexes. Carrier females may have a mild sensory motor axonal neuropathy [Kennerson et al 2013].

Sensorineural hearing loss. It is important to suspect CMTX5 when boys with early-onset sensorineural hearing loss develop gait disturbance and visual disturbance.

See Deafness and Hereditary Hearing Loss Overview.

Management

Evaluations Following Initial Diagnosis

To establish the extent of disease and needs in an individual diagnosed with CMTX5, the following evaluations are recommended:

- Neurologic examination
- Pure tone audiograms, auditory brain stem response test
- Evaluation of visual acuity, fundoscopic examination

- Consultation with a clinical geneticist and/or genetic counselor

Treatment of Manifestations

Peripheral neuropathy. See Charcot-Marie-Tooth Hereditary Neuropathy Overview, Management.

Sensorineural hearing loss. See Deafness and Hereditary Hearing Loss Overview, Management.

Optic atrophy. Use of routine low-vision aids as needed is appropriate.

Prevention of Secondary Complications

Daily heel cord stretching exercises are desirable to prevent Achilles' tendon shortening from peripheral neuropathy, which can occur in individuals with CMTX5.

Surveillance

Individuals should be evaluated regularly by a team comprising otologists, ophthalmologists, neurologists, physiatrists, and physical and occupational therapists to determine neurologic status and functional disability. While profound hearing loss begins during infancy, optic neuropathy and peripheral neuropathy in CMTX5 vary in age of onset of manifestations and progression. Thus, regular ophthalmologic and neurologic exams are warranted to monitor symptom development and progression.

Agents/Circumstances to Avoid

Obesity makes walking more difficult.

Medications that are toxic or potentially toxic to persons with CMT comprise a spectrum of risk ranging from definite high risk to negligible risk. See the Charcot-Marie-Tooth Association website (pdf) for an up-to-date list.

Evaluation of Relatives at Risk

It is appropriate to evaluate at-risk males at birth with detailed audiometry to assure early diagnosis and treatment of hearing loss.

See Genetic Counseling for issues related to testing of at-risk relatives for genetic counseling purposes.

Therapies Under Investigation

Dietary *S*-adenosylmethionine (SAM) supplementation could theoretically alleviate some of the symptoms of Arts syndrome by providing an oral source of purine nucleotide precursor that is not PRPP dependent. Furthermore, SAM is known to cross the blood-brain barrier. An adult with HPRT deficiency is reported to have benefitted neurologically from SAM administration without untoward side effects [Glick 2006].

An open-label clinical trial of SAM in two Australian brothers (ages 14 and 13 in 2010) with Arts syndrome is continuing [J Christodoulou et al, unpublished data; approved by the ethics and drug committees, Children's Hospital at Westmead, Sydney, Australia]. Oral SAM supplementation is presently set at 30 mg/kg/day. The boys appear to have had significant benefit from this therapy based on decreased number of hospitalizations and stabilization of nocturnal BIPAP requirements; however, slight deterioration in their vision has been noted.

Mildly affected carrier females from families with Arts syndrome may also benefit from SAM supplementation in their diet, although this remains to be tested. Whether treatment with SAM supplementation would benefit individuals with allelic disorders (PRS superactivity, Charcot-Marie-Tooth neuropathy X type 5) remains to be investigated.

Search ClinicalTrials.gov in the US and EU Clinical Trials Register in Europe for access to information on clinical studies for a wide range of diseases and conditions.

Genetic Counseling

Genetic counseling is the process of providing individuals and families with information on the nature, mode(s) of inheritance, and implications of genetic disorders to help them make informed medical and personal decisions. The following section deals with genetic risk assessment and the use of family history and genetic testing to clarify genetic status for family members; it is not meant to address all personal, cultural, or ethical issues that may arise or to substitute for consultation with a genetics professional. —ED.

Mode of Inheritance

CMTX5 is inherited in an X-linked manner.

Risk to Family Members

Parents of a male proband

- In a family with more than one affected individual, the mother of an affected male is likely to be an obligate carrier:
  - A mother who is a carrier may have a *de novo* pathogenic variant or may have inherited the pathogenic variant from either her mother or her father.
  - The father of an affected male will not have the disease nor will he be a carrier of the pathogenic variant.
- When an affected male is the only affected individual in the family; several possibilities regarding his mother's carrier status need to be considered:
  - He has a *de novo* pathogenic variant in *PRPS1*, in which case his mother is not a carrier. The frequency of *de novo* pathogenic variants is not known.
  - His mother has a *de novo* pathogenic variant in *PRPS1*, either (a) as a "germline variant" (i.e., present at the time of her conception and therefore in every cell of her body) or (b) as "germline mosaicism" (i.e., present in some of her germ cells only).
  - His mother has a pathogenic variant that she inherited from a maternal female ancestor.

Sibs of the proband

- The risk to the sibs of a proband depends on the genetic status of the parents:
  - If the mother has a pathogenic variant, the chance of transmitting the *PRPS1* pathogenic variant in each pregnancy is 50%. Male sibs who inherit the variant will be affected; female sibs who inherit the variant will be carriers and typically will not be affected.
  - If the pathogenic variant cannot be detected in the DNA of the mother of the only affected male in the family, the risk to sibs is low but greater than that of the general population because of the possibility of germline mosaicism.
- No instances of germline mosaicism have been reported, but it remains a possibility.

Offspring of a male proband. Males pass the pathogenic variant to all of their daughters and none of their sons.

Other family members of the proband. If the mother of a proband also has a pathogenic variant, her female family members may be at risk of being carriers and her male family members may be at risk of being affected depending on their genetic relationship to the proband.

Carrier Detection

Carrier testing is possible if the pathogenic variant has been identified in the family.

Related Genetic Counseling Issues

See Management, Evaluation of Relatives at Risk for information on evaluating at-risk relatives for the purpose of early diagnosis and treatment.

Family planning

- The optimal time for determination of genetic risk, clarification of carrier status, and discussion of the availability of prenatal/preimplantation genetic testing is before pregnancy.
- It is appropriate to offer genetic counseling (including discussion of potential risks to offspring and reproductive options) to young adults who are affected, are carriers, or are at risk of being carriers.

Prenatal Testing and Preimplantation Genetic Testing

Once the pathogenic variant has been identified in an affected family member, prenatal testing for a pregnancy at increased risk and preimplantation genetic testing are possible.

Resources

GeneReviews staff has selected the following disease-specific and/or umbrella support organizations and/or registries for the benefit of individuals with this disorder and their families. GeneReviews is not responsible for the information provided by other organizations. For information on selection criteria, click here.

- **Association CMT France**
  France
  Phone: 820 077 540; 2 47 27 96 41
  www.cmt-france.org
- **Charcot-Marie-Tooth Association (CMTA)**
  Phone: 800-606-2682 (toll-free); 610-427-2971
  Email: info@cmtausa.org
  www.cmtausa.org
- **Charcot-Marie-Tooth Association of Australia**
  Concord Hospital
  Building 51
  Concord New South Wales 2139
  Australia
  Phone: 02 9767 5105
  Fax: 02 9767 5167
  Email: cmtaa@email.cs.nsw.gov.au
  Charcot-Marie-Tooth Association of Australia
- **European Charcot-Marie-Tooth Consortium**
  Department of Molecular Genetics
  University of Antwerp
  Antwerp Antwerpen B-2610
  Belgium

Fax: 03 2651002
Email: gisele.smeyers@ua.ac.be

- **Hereditary Neuropathy Foundation**
  Phone: 855-435-7268 (toll-free); 212-722-8396
  Fax: 917-591-2758
  Email: info@hnf-cure.org
  www.hnf-cure.org
- **Medical Home Portal**
  Charcot-Marie-Tooth Disease (Hereditary Motor Sensory Neuropathy)
- **TREAT-NMD**
  Institute of Translational and Clinical Research
  University of Newcastle upon Tyne
  International Centre for Life
  Newcastle upon Tyne NE1 3BZ
  United Kingdom
  Phone: 44 (0)191 241 8617
  Fax: 44 (0)191 241 8770
  Email: info@treat-nmd.eu
  Charcot-Marie-Tooth Disease
- **Association Francaise contre les Myopathies (AFM)**
  1 Rue de l'International
  BP59
  Evry cedex 91002
  France
  Phone: +33 01 69 47 28 28
  Email: dmc@afm.genethon.fr
  www.afm-telethon.fr
- **European Neuromuscular Centre (ENMC)**
  Netherlands
  Phone: 31 35 5480481
  Email: enmc@enmc.org
  www.enmc.org
- **Muscular Dystrophy Association (MDA) - USA**
  Phone: 833-275-6321
  www.mda.org
- **Muscular Dystrophy UK**
  United Kingdom
  Phone: 0800 652 6352
  www.musculardystrophyuk.org
- **RDCRN Patient Contact Registry: Inherited Neuropathies Consortium**
  Patient Contact Registry

Molecular Genetics

Information in the Molecular Genetics and OMIM tables may differ from that elsewhere in the GeneReview: tables may contain more recent information. —ED.

Table A. Charcot-Marie-Tooth Neuropathy X Type 5: Genes and Databases

Locus Name	Gene	Chromosome Locus	Protein	Locus-Specific Databases	HGMD	ClinVar
CMTX5	*PRPS1*	Xq22.3	Ribose-phosphate pyrophosphokinase 1	IPN Mutations, PRPS1 PRPS1 @ LOVD	PRPS1	PRPS1

Data are compiled from the following standard references: gene from HGNC; chromosome locus from OMIM; protein from UniProt. For a description of databases (Locus Specific, HGMD, ClinVar) to which links are provided, click here.

Table B. OMIM Entries for Charcot-Marie-Tooth Neuropathy X Type 5 (View All in OMIM)

311070	CHARCOT-MARIE-TOOTH DISEASE, X-LINKED RECESSIVE, 5; CMTX5
311850	PHOSPHORIBOSYLPYROPHOSPHATE SYNTHETASE I; PRPS1

Gene structure. *PRPS1* is located on the chromosome band Xq21.32-q24 and spans 23 kb with seven exons. Two other PRPS genes have been identified: *PRPS2* (OMIM 311860) maps to chromosome Xp22 and *PRPS3* (or *PRPS1L1*; OMIM 611566) maps to chromosome 7 and appears to be transcribed only in testis [Becker 2001]. For a detailed summary of gene and protein information, see Table A, **Gene**.

Benign variants. Kim et al [2007] described their observation of a synonymous variant, c.447G>A, with an allele frequency of 1.1%, while resequencing *PRPS1* in control chromosomes of Korean descent. See Table 3.

Pathogenic variants. Two missense variants of *PRPS1* have been reported in individuals with CMTX5. The p.Glu43Asp variant was reported in a Korean family with CMTX5 [Kim et al 2007]. The p.Met115Thr variant was detected in an affected family of European descent, originally reported as having Rosenberg-Chutorian syndrome [Rosenberg & Chutorian 1967, Kim et al 2007]. See Table 3.

Table 3. *PRPS1* Variants Discussed in This *GeneReview*

Variant Classification	DNA Nucleotide Change	Predicted Protein Change (Alias [1])	Reference Sequences
Benign	c.447G>A [2]	(Pro149Pro)	NM_002764.3 NP_002755.1
Pathogenic	c.129A>C	p.Glu43Asp	
	c.344T>C	p.Met115Thr	

Variants listed in the table have been provided by the authors. *GeneReviews* staff have not independently verified the classification of variants.
GeneReviews follows the standard naming conventions of the Human Genome Variation Society (varnomen.hgvs.org). See Quick Reference for an explanation of nomenclature.
1. Variant designation that does not conform to current naming conventions
2. Observed with an allele frequency of 1.1% (2/185) in control chromosomes of Korean descent [Kim et al 2007]

Normal gene product. *PRPS1* encodes a 318-amino acid protein, the PRPS1 (phosphoribosyl pyrophosphate synthetase 1) enzyme. The enzyme catalyzes the phosphoribosylation of ribose 5-phosphate to 5-phosphoribosyl-1-pyrophosphate, which is necessary for the *de novo* and salvage pathways of purine and pyrimidine biosynthesis.

Abnormal gene product. Four loss-of-function pathogenic missense variants have been reported in *PRPS1*: two in CMTX5 (Table 3), and two in Arts syndrome. The PRS enzyme activity was shown to be decreased in cells of affected males [de Brouwer et al 2007, Kim et al 2007].

Chapter Notes

Revision History

- 8 June 2023 (ma) Chapter retired: covered in Phosphoribosylpyrophosphate Synthetase Deficiency
- 6 June 2013 (me) Comprehensive update posted live
- 18 January 2011 (cd) Revision: additions to therapies under investigation
- 23 September 2010 (cd) Revision: prenatal testing available clinically
- 10 June 2010 (cd) Revision: edits to agents and circumstances to avoid
- 26 August 2008 (cg) Review posted live
- 3 June 2008 (jwk) Original submission

References

Literature Cited

Becker MA. Phosphoribosylpyrophosphate synthetase and the regulation of phosphoribosylpyrophosphate production in human cells. Prog Nucleic Acid Res Mol Biol. 2001;69:115–48. PubMed PMID: 11550793.

Cowchock FS, Duckett SW, Streletz LJ, Graziani LJ, Jackson LG. X-linked motor-sensory neuropathy type-II with deafness and mental retardation: a new disorder. Am J Med Genet. 1985;20:307–15. PubMed PMID: 3856385.

de Brouwer AP, Williams KL, Duley JA, van Kuilenburg AB, Nabuurs SB, Egmont-Petersen M, Lugtenberg D, Zoetekouw L, Banning MJ, Roeffen M, Hamel BC, Weaving L, Ouvrier RA, Donald JA, Wevers RA, Christodoulou J, van Bokhoven H. Arts syndrome is caused by loss-of-function mutations in PRPS1. Am J Hum Genet. 2007;81:507–18. PubMed PMID: 17701896.

Glick N. Dramatic reduction in self-injury in Lesch-Nyhan disease following S-adenosylmethionine administration. J Inherit Metab Dis. 2006;29:687.

Huttner IG, Kennerson ML, Reddel SW, Radovanovic D, Nicholson GA. Proof of genetic heterogeneity in X-linked Charcot-Marie-Tooth disease. Neurology. 2006;67:2016–21. PubMed PMID: 17159110.

Ionasescu VV, Trofatter J, Haines JL, Summers AM, Ionasescu R, Searby C. Heterogeneity in X-linked recessive Charcot-Marie-Tooth neuropathy. Am J Hum Genet. 1991;48:1075–83. PubMed PMID: 1674639.

Ionasescu VV, Trofatter J, Haines JL, Summers AM, Ionasescu R, Searby C. X-linked recessive Charcot-Marie-Tooth neuropathy: clinical and genetic study. Muscle Nerve. 1992;15:368–73. PubMed PMID: 1557086.

Kennerson ML, Yiu EM, Chuang DT, Kidambi A, Tso SC, Ly C, Chaudhry R, Drew AP, Rance G, Delatycki MB, Züchner S, Ryan MM, Nicholson GA. A new locus for X-linked dominant Charcot-Marie-Tooth disease (CMTX6) is caused by mutations in the pyruvate dehydrogenase kinase isoenzyme 3 (PDK3) gene. Hum Mol Genet. 2013;22:1404–16. PubMed PMID: 23297365.

Kim HJ, Hong SH, Ki CS, Kim BJ, Shim JS, Cho SH, Park JH, Kim JW. A novel locus for X-linked recessive CMT with deafness and optic neuropathy maps to Xq21.32-q24. Neurology. 2005;64:1964–7. PubMed PMID: 15955956.

Kim HJ, Sohn KM, Shy ME, Krajewski KM, Hwang M, Park JH, Jang SY, Won HH, Choi BO, Hong SH, Kim BJ, Suh YL, Ki CS, Lee SY, Kim SH, Kim JW. Mutations in PRPS1, which encodes the phosphoribosyl pyrophosphate synthetase enzyme critical for nucleotide biosynthesis, cause hereditary peripheral

neuropathy with hearing loss and optic neuropathy (cmtx5). Am J Hum Genet. 2007;81:552–8. PubMed PMID: 17701900.

Liu X, Han D, Li J, Han B, Ouyang X, Cheng J, Li X, Jin Z, Wang Y, Bitner-Glindzicz M, Kong X, Xu H, Kantardzhieva A, Eavey RD, Seidman CE, Seidman JG, Du LL, Chen ZY, Dai P, Teng M, Yan D, Yuan H. Loss-of-function mutations in the PRPS1 gene cause a type of nonsyndromic X-linked sensorineural deafness, DFN2. Am J Hum Genet. 2010;86:65–71. PubMed PMID: 20021999.

Priest JM, Fischbeck KH, Nouri N, Keats BJ. A locus for axonal motor-sensory neuropathy with deafness and mental retardation maps to Xq24-q26. Genomics. 1995;29:409–12. PubMed PMID: 8666389.

Rinaldi C, Grunseich C, Sevrioukova IF, Schindler A, Horkayne-Szakaly I, Lamperti C, Landouré G, Kennerson ML, Burnett BG, Bönnemann C, Biesecker LG, Ghezzi D, Zeviani M, Fischbeck KH. Cowchock syndrome is associated with a mutation in apoptosis-inducing factor. Am J Hum Genet. 2012;91:1095–102. PubMed PMID: 23217327.

Rosenberg RN, Chutorian A. Familial opticoacoustic nerve degeneration and polyneuropathy. Neurology. 1967;17:827–32. PubMed PMID: 6069085.

Torres RJ, Mateos FA, Puig JG, Becker MA. Determination of phosphoribosylpyrophosphate synthetase activity in human cells by a non-isotopic, one step method. Clin Chim Acta. 1996;245:105–12. PubMed PMID: 8646809.

License