

Congenital Myasthenic Syndrome Panel (Test #412)

Brief Description of Clinical Features: Congenital myasthenic syndromes (CMS) are disorders of the neuromuscular junction resulting from abnormalities of presynaptic, synaptic, or post synaptic proteins. CMS are characterized by fatiguable weakness affecting limb, ocular, facial, and bulbar muscles. Neonates present with feeding problems, choking, feeble cry, and muscle weakness. Patients presenting in later childhood are seen with abnormal exercise-induced fatigue and difficulty running. Most patients present prior to 2 years of age although rare exceptions are reported (*eg. Croxen et al. Neurol 59:162-168, 2002*). Symptoms are extremely variable, and are in some case induced by febrile illness, infection, or excitement (*eg. Byring et al. Neuromuscul Disord 12:548-553, 2002*). Life threatening respiratory crises may occur in affected neonates or older children. CMS may be differentiated from myasthenia gravis, an acquired autoimmune disorder, by earlier age at onset and by negative serology tests for anti-acetylcholine receptor (AChR) and anti-MuSk antibodies.

Genetics: Abnormalities of proteins involved with neuromuscular transmission underlie CMS, limb girdle CMS, Pena-Shokeir syndrome, and multiple pterygium syndromes. These disorders, which may represent a phenotypic continuum of a single entity, are most often inherited in an autosomal recessive manner. Slow-channel CMS secondary to AChR gene mutations is mostly inherited as a dominant condition.

Description of This Particular Test: The following genes are tested in the order specified by the client. Testing is accomplished by amplifying the coding exons and ~50 bp of adjacent noncoding sequence, then determining the nucleotide sequence using standard dideoxy sequencing methods and a capillary electrophoresis instrument.

Reference Sequences:

Gene:	CMS Subtype:	Genomic: NC_	mRNA: NM_	Protein: NP_	CCDS:
<i>CHAT</i>	presynaptic CMS+episodic apnea	000010.10	020549.4	065574.3	7232.1
<i>COLQ</i>	synaptic AChE deficiency	000003.11	005677.3	005668.2	33709.1
<i>CHRNE</i>	postsynaptic AChR deficiency	000017.10	000080.2	000071.1	11058.1
<i>CHRNA1</i>	postsynaptic AChR deficiency	000002.11	001039523.2	001034612.1	33331.1
<i>CHRNBI</i>	postsynaptic AChR deficiency	000017.10	000747.2	000738.2	11106.1
<i>CHRND</i>	postsynaptic AChR deficiency	000002.11	000751.1	000742.1	2494.1
<i>MUSK</i>	postsynaptic AChR deficiency	000009.11	005592.2	005583.1	48005.1
<i>DOK7</i>	postsynaptic AChR deficiency	000004.10	173660.3	775931.3	3370.2
<i>RAPSN</i>	postsynaptic rapsyn deficiency	000011.8	005055.3	005046.2	7936.1

Indication for Testing: A comprehensive diagnostic algorithm can be found in (*GeneReviews, Abicht and Lochmüller, 2006*).

Sensitivity of Test: Sensitivity for CMS testing is at least 50% overall; 30% for *CHRNE*, 10% for *RAPSN*, and 7.5% for *COLQ* (*GeneReviews, Abicht and Lochmüller, 2006*).

Turnaround Time: Maximum of 80 days.

Specimen Requirements: See page 4 of the Requisition Form.

CPT codes and Price: Sequential Testing of: *CHAT, COLQ, CHRNE, CHRNA1, CHRNBI, CHRND, MUSK, DOK7, RAPSN*

CPT	<i>CHAT</i>	<i>COLQ</i>	<i>CHRNE</i>	<i>CHRNA1</i>	<i>CHRNBI</i>	<i>CHRND</i>	<i>MUSK</i>	<i>DOK7</i>	<i>RAPSN</i>	Panel
83890	\$ 30 x1	\$ 30 x1	\$ 30 x1	\$ 30 x1	\$ 30 x1	\$ 30 x1	\$ 30 x1	\$ 30 x1	\$ 30 x1	\$ 30 x1
83891	\$ 40 x1	\$ 40 x1	\$ 40 x1	\$ 40 x1	\$ 40 x1	\$ 40 x1	\$ 40 x1	\$ 40 x1	\$ 40 x1	\$ 40 x1
83898	\$300 x17	\$280 x16	\$210 x11	\$190 x10	\$190 x10	\$ 230 x12	\$280 x16	\$140 x8	\$160 x9	\$ 1960 x109
83904	\$440 x17	\$420 x16	\$320 x11	\$290 x10	\$290 x10	\$ 340 x12	\$420 x16	\$210 x8	\$230 x9	\$ 2950 x109
83894	\$ 60 x1	\$ 60 x1	\$ 50 x1	\$ 50 x1	\$ 50 x1	\$ 50 x1	\$ 60 x1	\$ 40 x1	\$ 50 x1	\$ 450 x1
83912	\$ 90 x1	\$ 90 x1	\$ 80 x1	\$ 80 x1	\$ 80 x1	\$ 80 x1	\$ 90 x1	\$ 80 x1	\$ 80 x1	\$ 340 x1
Totals:	\$ 960	\$ 920	\$ 730	\$ 680	\$ 680	\$ 770	\$ 920	\$ 540	\$ 590	\$ 5,770*

*When five or more of the genes on this panel are sequentially tested, a 15% discount will apply to the total cost.

Accreditation: CLIA ID #: 52D1027685 (expires 1/18/13) (CAP#: 7185561, AU ID: 1407125 expires 12/20/12)

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