Lambert-Eaton myasthenic syndrome (LEMS)

Get to know this rare neuromuscular disorder with a devastating impact

LEMS is a rare, immune-mediated disorder of the neuromuscular junction[1-3]

LEMS affects an estimated 3,000 individuals in the US, most of whom are adults[4,5]

Debilitating muscle weakness and fatigue characterize LEMS[6]

PREVALENCE

LEMS is the second-most common disorder of neuromuscular transmission.[2,3]

Affects 1/100,000 individuals in the United States[4,5]

As many as 50% of individuals suffering from LEMS are currently **undiagnosed or misdiagnosed**[5]

CLINICAL PRESENTATION

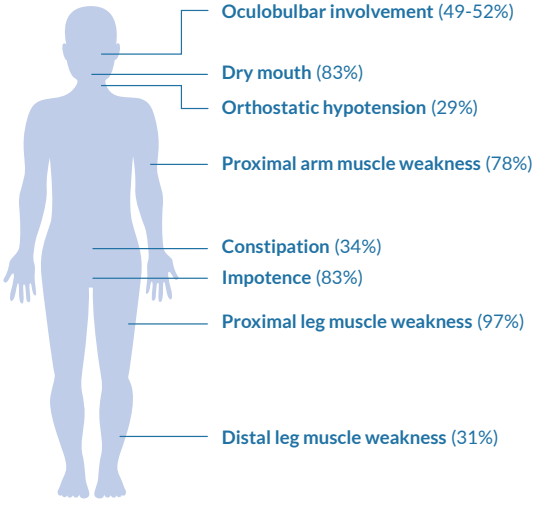
LEMS symptoms are insidious and progressive, characteristically beginning with[5,6]:

- Lower limb weakness and generalized fatigue
- Difficulty rising from a seated position and climbing stairs
- Dry mouth, impotence, or orthostatic hypotension

LEMS is often suspected and diagnosed based on a triad of symptoms[4,5,7-13]:

- Proximal muscle weakness with a caudal-to-cranial progression
- Autonomic nervous system dysfunction in most patients
- Hyporeflexia or areflexia in some patients

Neuromuscular and Autonomic Symptoms and Prevalence



Patients with LEMS report health-related quality of life (HRQoL) scores comparable to debilitating neurological disorders, such as multiple sclerosis.[6]

ETIOLOGY

LEMS is caused by pathogenic autoantibodies that target P/Q-type voltage-gated calcium channels (VGCCs) in the presynaptic membrane of the motor nerve terminal.[14,15]

Pathogenic Autoantibodies Inhibit Neuromuscular Transmission[14,15]

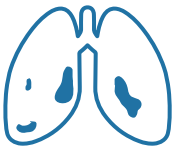
Impairs entry of calcium ions into the presynaptic nerve terminal of motor neurons

Decreased exocytosis of acetylcholine-containing vesicles into the neuromuscular junction

Leading to generalized fatigue and symmetric, proximal muscle weakness of striated skeletal muscles

SUBSETS OF LEMS

The underlying etiology that drives autoantibody production against VGCCs varies depending on the form of LEMS.



50% to 60%

Paraneoplastic LEMS[5]

- Small cell lung cancer (SCLC) is the most predominant malignancy associated with LEMS[11,16]
  - Screening for a suspected underlying tumor is imperative: ~96% of SCLC cases can be diagnosed within a year of LEMS diagnosis, given regular oncologic surveillance[16]
- Tumor LEMS often displays a more rapid, progressive course than non-tumor LEMS[8]

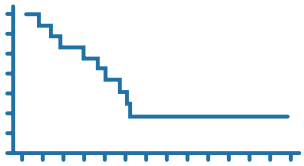
40% to 50%

Non-Tumor LEMS[5]

- Preexisting autoimmune conditions have frequently been observed in this patient population[17]
- Two-thirds of patients with LEMS display a characteristic HLA genotype (HLA-B8, HLA-DR3, and HLA-DQ2)[17]
- Non-tumor LEMS progresses more slowly than tumor LEMS, with fluctuating symptoms[5]

PROGRESSION/BURDEN

LEMS progresses over time and can result in severe debilitation.[6]
In the first 2 years after the onset of LEMS, the prevalence of specific symptoms related to muscle weakness and autonomic dysfunction increases regardless of the type of LEMS.[8]

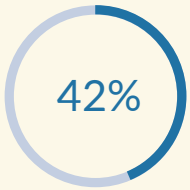


Even with long-term immunosuppressive therapy, **less than half of patients with non-tumor LEMS achieve sustained clinical remission**[18]

1 in every 4 patients with LEMS requires a wheelchair all the time or for mobilization when away from home[18]

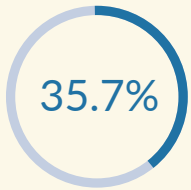
MISDIAGNOSIS

Misdiagnosis of LEMS is common, with up to 50% of patients being misdiagnosed or undiagnosed.[5]



received a **correct initial diagnosis** of LEMS

received **at least 1 misdiagnosis**



received a **diagnosis of myasthenia gravis**

LEMS is often confused with a number of other conditions, including[5]:

- Myasthenia gravis
- Generalized myopathies
- Peripheral nerve abnormalities
- Intracranial/spinal cord abnormalities
- Depression

A 2012 cross-sectional study found that the average time lapse between a patient's first consultation with a physician and a confirmed diagnosis of LEMS was 4.4 years.[6]

DIAGNOSTIC METHODS FOR CONFIRMING LEMS

Clearly identifying LEMS symptoms can result in a quicker confirmed diagnosis and effective treatment course.[5]

LEMS may be suspected based on clinical symptomatology and physical signs.[5] Diagnosis of LEMS may be further confirmed by use of one or both of the following methods:

Anti-Voltage-Gated Calcium Channel Antibody Testing

The presence of anti-VGCC antibodies can be detected in up to 90% of patients with LEMS. As these antibodies are highly specific to LEMS, a positive VGCC antibody test can help rule out other causes of muscular weakness.[5]

Electrodiagnostic Testing

Electrodiagnostic testing demonstrating an increment on high-frequency repetitive nerve stimulation or post-exercise potentiation is a hallmark of LEMS.[5]

Ask your regional account manager about a free diagnostic testing program provided by Catalyst Pharmaceuticals.

References: 1. Muppidi S, Wolfe GI, Barohn RJ. Diseases of the neuromuscular junction. In: Swaiman K, Ashwal S, Ferriero D, Schor N, eds. *Pediatric Neurology: Principles and Practice.* 5th ed. Philadelphia, PA: Elsevier; 2011:1549-1569. **2.** Deenen JC, Horlings CG, Verschuuren JJ, et al. The epidemiology of neuromuscular disorders: a comprehensive overview of the literature. *J Neuromuscul Dis.* 2015;2(1):73-85. **3.** Simon JI, Herbison GJ, Levy G. Case report: a case review of Lambert-Eaton myasthenic syndrome and low back pain. *Curr Rev Musculoskelet Med.* 2011;4(1):1-5. **4.** Sanders DB. Lambert-Eaton myasthenic syndrome: diagnosis and treatment. *Ann NY Acad Sci.* 2003;998:500-508. **5.** Titulaer MJ, Lang B, Verschuuren JJ. Lambert-Eaton myasthenic syndrome: from clinical characteristics to therapeutic strategies. *Lancet Neurol.* 2011;10(12):1098-1107. **6.** Harms L, Sieb JP, Williams AE, et al. Long-term disease history, clinical symptoms, health status, and healthcare utilization in patients suffering from Lambert Eaton myasthenic syndrome: results of a patient interview survey in Germany. *J Med Econ.* 2012;15(3):521-530. **7.** O'Neill JH, Murray NM, Newsom-Davis J. The Lambert-Eaton myasthenic syndrome. A review of 50 cases. *Brain.* 1988;111(Pt 3):577-596. **8.** Wirtz PW, Wintzen AR, Verschuuren JJ. Lambert-Eaton myasthenic syndrome has a more progressive course in patients with lung cancer. *Muscle Nerve.* 2005;32(2):226-229. **9.** Lorenzoni PJ, Scola RH, Kay CS, Parolin SF, Werneck LC. Non-paraneoplastic Lambert-Eaton myasthenic syndrome: a brief review of 10 cases. *Arq Neuropsiquiatr.* 2010;68(6):849-854. **10.** Titulaer MJ, Maddison P, Sont JK, et al. Clinical Dutch-English Lambert-Eaton myasthenic syndrome (LEMS) tumor association prediction score accurately predicts small-cell lung cancer in the LEMS. *J Clin Oncol.* 2011;29(7):902-908. **11.** Wirtz PW, Smallegange TM, Wintzen AR, Verschuuren JJ. Differences in clinical features between the Lambert-Eaton myasthenic syndrome with and without cancer: an analysis of 227 published cases. *Clin Neurol Neurosurg.* 2002;104(4):359-363. **12.** Young JD, Leavitt JA. Lambert-Eaton myasthenic syndrome: ocular signs and symptoms. *J Neuroophthalmol.* 2016;36(1):20-22. **13.** Merino-Ramírez MÁ, Bolton CF. Review of the diagnostic challenges of Lambert-Eaton syndrome revealed through three case reports. *Can J Neurol Sci.* 2016;43(5):635-647. **14.** Lennon VA, Kryzer TJ, Griesmann GE, et al. Calcium-channel antibodies in the Lambert-Eaton syndrome and other paraneoplastic syndromes. *N Engl J Med.* 1995;332(22):1467-1474. **15.** Motomura M, Lang B, Johnston I, Palace J, Vincent A, Newsom-Davis J. Incidence of serum anti-P/Q-type and anti-N-type calcium channel autoantibodies in the Lambert-Eaton myasthenic syndrome. *J Neurol Sci.* 1997;147(1):35-42. **16.** Titulaer MJ, Wirtz PW, Willems LN, et al. Screening for small-cell lung cancer: a follow-up study of patients with Lambert-Eaton myasthenic syndrome. *J Clin Oncol.* 2008;26(26):4276-4281. **17.** Gilhus NE. Lambert-Eaton myasthenic syndrome; pathogenesis, diagnosis, and therapy. *Autoimmune Dis.* 2011;2011:973808. **18.** Maddison P, Lang B, Mills K, Newsom-Davis J. Long term outcome in Lambert-Eaton myasthenic syndrome without lung cancer. *J Neurol Neurosurg Psychiatry.* 2001;70(2):212-217.

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