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.

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Printed in USA. 20LEM0221 July 2020

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

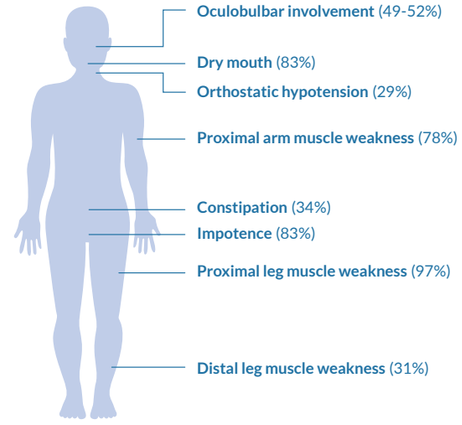
LEMS symptoms are insidious and progressive, characteristically beginning with[5,6]:

- 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]

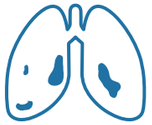
Impairs entry of calcium ions into the presynaptic nerve terminal of motor neurons

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]

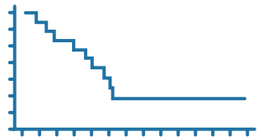
- Small cell lung cancer (SCLC) is the most predominant malignancy associated with LEMS[11,16]
  - Screening for a suspected underlying tumor is imperative: ~96% of SCLC cases can be diagnosed within a year of LEMS diagnosis, given regular oncologic surveillance[16]
- Tumor LEMS often displays a more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

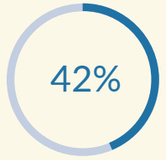


Even with long-term immunosuppressive therapy, **less than half of patients with non-tumor LEMS achieve sustained clinical remission**[18]

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]