

Voltage-Gated Calcium Channel Autoantibody Testing

FOR CONFIRMATION AND MONITORING OF AUTOANTIBODIES IN PATIENTS WITH LAMBERT-EATON MYASTHENIC SYNDROME (LEMS)

Clinical Background

- Lambert-Eaton myasthenic syndrome is an autoimmune presynaptic disorder characterized by proximal muscle weakness and mild autonomic symptoms (diminished salivary secretion, diminished sweating, and impotence).
- Symptoms result from impaired calcium-dependent release of acetylcholine, which causes insufficient minimum end-plate potential change required for muscle contraction.
- Autoantibodies against P/Q-type voltage-gated calcium channel (VGCC) have been identified in 85 to 90 percent of patients with idiopathic LEMS and in 95 to 100 percent of patients with paraneoplastic LEMS.
- A relatively high association has been reported for P/Q-type VGCC antibodies and cancer, particularly small-cell lung carcinoma. Antigenic mimicry of VGCC antigens by cancer cells has been proposed to account for this association; however, the etiology of idiopathic LEMS remains unclear.
- Autoantibodies that recognize the P/Q-type voltage-gated calcium channel on the presynaptic neuromuscular junction membrane have been identified in the majority of patients with Lambert-Eaton myasthenic syndrome.
- Antibodies to the P/Q-type VGCC have been detected in patients with other paraneoplastic neurologic disorders, in patients with cancer without neurologic symptoms, and 25 percent of patients with amyotrophic lateral sclerosis; thus, these antibodies cannot be considered diagnostic for LEMS.
- Antibodies to N-type voltage-gated calcium channels have also been identified in approximately 75 percent of patients with paraneoplastic LEMS.

Epidemiology

- Incidence and prevalence information for LEMS are limited; the annual incidence is estimated to be approximately 0.5 per million, with a prevalence of around four per thousand in the United States.

Indications for Ordering

- Confirmation of diagnosis and monitoring of patients with Lambert-Eaton myasthenic syndrome.
- Included in the differential diagnosis of other neuromuscular disorders (e.g., myasthenia gravis, neuromyotonia), paraneoplastic syndromes, neurological disorders, and autoimmune neuropathological syndromes.

Interpretation

- Negative: 0.0–24.5 pmol/L
- Indeterminate: 24.6–45.6 pmol/L
- Positive: 45.7 pmol/L or greater
- The presence of VGCC antibodies should be used in conjunction with clinical findings and should not be used as the sole criteria for diagnosis.

Limitations

- Antibodies detected are isotype-restricted to IgG immunoglobulin.
- Antibodies detected are restricted to the P/Q-type VGCC.

References

1. Lennon VA, et al. Calcium-channel antibodies in the Lambert-Eaton syndrome and other paraneoplastic syndromes. *N Engl J Med* 1995; 332:1467–74.
2. Takamori T. Lambert-Eaton myasthenic syndrome: Search for alternative autoimmune targets and possible compensatory mechanisms based on presynaptic calcium homeostasis. *J Neuroimmunol* 2008;201–2:145–52.
3. Harper CM, Lennon VA. Lambert-Eaton syndrome. In *Myasthenia gravis and related disorders*, 2nd ed. Kaminski HJ, ed. 2009; Totowa, NJ: Humana Press, 209–25.

Test Information

0092628

Voltage-Gated Calcium Channel (VGCC) Antibody

For specific collection, transport, and testing information, refer to the ARUP website at www.aruplab.com.

For information on test selection, ordering, and interpretation, refer to ARUP Consult[®] at www.arupconsult.com.