

Voltage-Gated Potassium Channel (VGKC) Autoantibody Testing

FOR THE DIAGNOSIS OF PERIPHERAL NERVE HYPEREXCITABILITY, LIMBIC ENCEPHALITIS, AUTONOMIC INVOLVEMENT, OR MORVAN SYNDROME

Test Highlights

- Autoantibodies against voltage-gated potassium channels (VGKC) may cause hyperexcitability of the peripheral and central nervous systems and are detected by radioimmunoassay (RIA).
- These antibodies may be associated with paraneoplastic or non-paraneoplastic (autoimmune) neurologic disorders.

Disease Overview

- Autoantibodies that recognize the voltage-gated potassium channels found at the neuromuscular junction (K_v 1.1, K_v 1.2, and K_v 1.4) have been identified in a spectrum of diseases. Peripheral nerve hyperexcitability resulting in muscle twitching, muscle cramps, and stiffness has been referred to by a variety of names, including neuromyotonia (NMT), Isaac syndrome, undulating myokymia, and Cramp-Fasciculation syndrome.
- A similar condition with additional symptoms of pain, excessive sweating, sleep disorders (i.e., insomnia, abnormal rapid eye movement), delirium, and cardiac arrhythmia was first described by the French physician Augustin Marie Morvan in 1890 and has been referred to as Morvan fibrillary chorea and Morvan syndrome.
- Autoantibodies that recognize voltage-gated potassium channels in the central nervous systems (K_v 1.1, K_v 1.2, and K_v1.6) have been detected in association with limbic encephalitis, frontotemporal dementia-like syndrome, and amnesia.
- Definitive differentiation among these diseases is problematic due to the presence of antibodies to proteins closely associated with the neuronal VGKC complex that may be precipitated in VGKC RIA assays. This may explain the variety of limbic encephalitis immunophenotypes, not all of which are associated with VGKC antibodies.
- NMT is a diverse family of disorders that may be confused with early stages of amyotrophic lateral sclerosis (ALS) characterized by muscle fasciculation and muscle weakness. It is critical to differentiate among these diseases since ALS demonstrates a fatal prognosis whereas NMT is rarely fatal.
- Palliative treatment of NMT usually consists of anticonvulsants, immunosuppressive therapy, or plasmapheresis.

Epidemiology

- Insufficient data is available regarding the incidence and prevalence of anti-VGKC antibodies.
- Generalized peripheral nerve hyperexcitability and NMT are divided into three categories: acquired, paraneoplastic, and hereditary, with the majority of cases classified as acquired.

- Both autonomic and central nervous system involvement are present in Morvan syndrome.
- Limbic encephalitis has been classified into three categories: VGKC antibody-associated, paraneoplastic, and idiopathic; it may be monophasic or relapsing/recurring in nature.

Indications for Ordering

- Confirmation of acquired neuromyotonia and Morvan syndrome
- Assessment and prognosis of limbic encephalitis.
- Differential diagnosis of other neuromuscular disorders (i.e., myasthenia gravis, Lambert-Eaton syndrome), paraneoplastic syndromes, neurological disorders, and autoimmune neuropathological syndromes.

Interpretation

- Negative: 0–31 pmol/L
- Indeterminant: 32–87 pmol/L
- Positive: >88 pmol/L
- The presence of VGKC antibodies should be used in conjunction with clinical manifestations and proposed diagnostic criteria for the neuromyotonia spectrum of disorders and VGKC antibody-associated limbic encephalitis; it should not be used as the sole criteria for diagnosis.

Limitations

- A sensitivity of 40–83 percent is reported for VGKC antibody detection by radioimmunoassay (RIA) assays using 125-iodine conjugated alpha-dendrotoxin labeled voltage-gated potassium channels.
- Antibodies detected are isotype-restricted to IgG immunoglobulin.
- VGKC receptor complex proteins may be co-precipitated by anti-VGKC antibodies, including leucine-rich, glioma inactivated 1 protein (LGI1), and contactin-associated protein 2 (Caspr-2).

References

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3. Kleopa KA, et al. Neuromyotonia and limbic encephalitis sera target mature Shaker-type K⁺ channels: subunit specificity correlates with clinical manifestations. *Brain* 2006;129:1570–84.
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5. Samarasekera SR, et al. Course and outcome of acute limbic encephalitis with negative voltage-gated potassium channel antibodies. *J Neurol Neurosurg Psychiatry* 2007;78:391–4.

Test Information

2004890 Voltage-Gated Potassium Channel (VGKC) 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.