Epilepsy, Autoimmune Evaluation, Spinal Fluid

**Useful For**
- Investigating new onset cryptogenic epilepsy with incomplete seizure control and duration of <2 years.
- Investigating new onset cryptogenic epilepsy plus 1 or more of the following accompaniments:
  - Psychiatric accompaniments (psychosis, hallucinations)
  - Movement disorder (myoclonus, tremor, dyskinesias)
  - Headache
  - Cognitive impairment/encephalopathy
  - Autoimmune stigmata (personal history or family history or signs of diabetes mellitus, thyroid disorder, vitiligo, premature graying of hair, myasthenia gravis, rheumatoid arthritis, systemic lupus erythematosus, idiopathic adrenocortical insufficiency) or "multiple sclerosis"
  - History of cancer
  - Smoking history (20+ pack years) or other cancer risk factors
  - Investigating seizures occurring within the context of a subacute multifocal neurological disorder without obvious cause, especially in a patient with past or family history of cancer

**Clinical Information**
Antiepileptic drugs (AEDs) are the mainstay of treatment for epilepsy, but seizures continue in one-third of patients despite appropriate AED therapeutic trials. The etiology of epilepsy often remains unclear. Seizures are a common symptom in autoimmune neurological disorders, including limbic encephalitis and multifocal paraneoplastic disorders. Seizures may be the exclusive manifestation of an autoimmune encephalopathy without evidence of limbic encephalitis.

Autoimmune epilepsy is increasingly recognized in the spectrum of neurological disorders characterized by detection of neural autoantibodies in serum or spinal fluid and responsiveness to immunotherapy. The advent of more sensitive and specific serological detection methods is increasingly revealing previously underappreciated autoimmune epilepsies. Neural autoantibodies specific for intracellular and plasma membrane antigens aid the diagnosis of autoimmune epilepsy, but no single antibody is specific for this diagnosis.

Autoantibody specificities currently most informative for autoimmune epilepsies include voltage-gated potassium channel-complex (VGKC-complex), glutamic acid decarboxylase-65 (GAD65), N methyl-D-aspartate receptor (NMDAR), alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptors (AMPA) and gamma aminobutyric acid type B receptor (GABABR) antibodies.

Autoantibodies recognizing onconeural proteins shared by neurons, glia, or muscle (eg, antineuronal nuclear antibody, type 1: ANNA 1; collapsin response-mediator protein-5 neuronal; CRMP-5-IgG; N-type calcium channel antibody, and acetylcholine receptor [muscle AChR] binding antibody) also serve as markers of paraneoplastic or idiopathic autoimmune epilepsies. A specific neoplasm is often predictable by the individual patient’s autoantibody profile.

Suspicion for autoimmune epilepsy on clinical grounds justifies comprehensive evaluation of cerebral spinal fluid and serum for neural autoantibodies. Selective autoantibody testing is not advised because no single neural antibody is definitively associated with seizures, and markers of occult cancer may be missed. Failure to detect a neural antibody does not exclude the diagnosis of autoimmune epilepsy when other clinical clues exist. A trial of immunotherapy is justifiable in those cases.

**Reflex Tests & Testing Algorithm**
Go to Mayo Medical Laboratories Test Catalog:
http://www.mayomedicallaboratories.com

Content and values subject to change. See the Mayo Medical Laboratories Test Catalog for current information.
Interpretation
Antibodies specific for neuronal, glial, or muscle proteins are valuable serological markers of autoimmune epilepsy and of a patient's immune response to cancer. These autoantibodies are not found in healthy subjects, and are usually accompanied by subacute neurological symptoms and signs. It is not uncommon for more than 1 of the following autoantibodies to be detected in patients with autoimmune epilepsy:
- Plasma membrane antibodies (N-methyl-D-aspartate [NMDA] receptor; 2-amino-3-[5-methyl-3-oxo-1,2-oxazol-4-yl] propanoic acid [AMPA] receptor; gamma-amino butyric acid [GABA-B] receptor). These autoantibodies are all potential effectors of dysfunction.
- Neuronal nuclear autoantibody, type 1 (ANNA-1) or type 3 (ANNA-3).
- Neuronal or muscle cytoplasmic antibodies (amphiphysin, Purkinje cell antibody-type 2 [PCA-2], collapsin response-mediator protein-5 neuronal [CRMP-5-IgG], or glutamic acid decarboxylase [GAD65] antibody).

A rising autoantibody titer in a previously seropositive patient suggests cancer recurrence.

Cautions
Negative results do not exclude autoimmune epilepsy or cancer.

The Epilepsy, Autoimmune Evaluation does not detect Ma2 antibody (alias: MaTa). Ma2 antibody has been described in patients with brainstem and limbic encephalitis in the context of testicular germ cell neoplasms. Scrotal ultrasound is advisable in men who present with unexplained subacute encephalitis.

Reference Values
To review all reference values go to http://www.mayomedicallaboratories.com

Analytic Time
3 days if negative / 5 days if positive

Clinical References

For additional interpretation information and clinical references, please visit the following website:
http://www.mayomedicallaboratories.com/test-catalog/Overview/61511