Lab Dept: Serology

Test Name: ENCEPHALOPATHY AUTOIMMUNE EVALUATION

General Information

Lab Order Codes: ENS1

Synonyms: Autoimmune Encephalopathy Evaluation

CPT Codes: 83519 x5 – Immunoassay for analyte other than infectious agent antibody or infectious agent antigen, quantitative by radioimmunassay
86255 x14 – Fluorescent noninfectious agent, antibody screen, each antibody
86341 – Islet cell antibody

Possible reflex testing (at an additional charge):

84182 x3 – Western blot, with interpretation and report, each
86255 x1 – Fluorescent noninfectious agent, antibody screen, each antibody
86256 x4 – Fluorescent noninfectious agent, titer, each antibody

Test Includes: If indirect immunofluorescence assay (IFA) suggests ANN1s, ANN2S, ANN3S, AMPHS, CRMS or AGN1S is indeterminate, then a paraneoplastic autoantibody Western blot is performed at an additional charge.

If IFA patterns suggests CRMP-5-IgG Western blot is performed at an additional charge.

If IFA pattern suggests amphiphysin antibody, then amphiphysin Western blot is performed at an additional charge.

If IFA pattern suggests NMO/AQP4-IgG, then NMO/QAP4-IgG FACS is performed at an additional charge.

If NMO/AQP4-IgG FACS screen assay requires further investigation, then NMO/AQP4-IgG FACS titration assay is performed at an additional charnge.

If IFA pattern suggests NMDA-R antibody and NMDA-R antibody CBA is positive, then aMPA-R titer is performed at an additional charge.

If IFA pattern suggests AMPA-R and AMPA-R antibody CBA is positive, then AMPA-R titer is performed at an additional charge.

If IFA pattern suggests GABA-B-R antibody and GABA-B_R andtibody CBA is positibe, then GABA-B-R titer is performed at an additional charge.

Western Blot: Native neuronal antigens, performed to confirm neuronal nuclear and cytoplasmic antibody specificities when IF screening is

uninterpretable.

Recombinanat human collapsin response-mediator protein 5: performed to confirm CRMP-5-IgG when IF screening is uninterpretable. Also performed for more sensitive detection on CRMP-5-IgG.

RIA: Confirmation of GAD65 antibodies when IF screening suggests GAD65 antibodies.

Logistics

Test Indications:

Evaluating new onset encephalopathy (noninfectious or metabolic) comprising confusional states, psychosis, delirium, memory loss, hallucinations, movement disorder, sensory or motor complaints, seizures, dyssonmnias, ataxias, nausea, vomiting, inappropriate antiduresis, coma, dysautonomias, or hypventialation in serum specimens.

The following accompaniments should increase suspicion for autoimmune encephalopathy:

- Headache
- Autoimmune stigmata (personal or family history or signs of diabetes mellitus, thyroid disorder, vitiligo, poliosis [premature graying], myasthenia gravis, rheumatoid arthritis, systemic lupus erythematosus)
- History of cancer
- Smoking history or other cancer risk factors
- Inflammatory cerebral spinal fluid (or isolated protein elevation)
- Neuroimaging signs suggesting inflammation
- Evaluating limbic encephalitis (noninfectious)
- Directing a focused search for cancer
- Investigating encephalopathy appearing in the course or wake of cancer therapy and not explainable by metastasis or drug effect

Autoimmune encephalopathies extend beyond the classically recognized clinical and radiological spectrum of “limbic encephalitis”. They encompass a diversity of neurological presentations with subacute or insidious onset, including confusional states, psychoses, delirium, memory loss, hallucinations, movement disorders, sensory or motor complaints, seizures, dyssomnias, ataxias, eye movement problems, nausea, vomiting, inappropriate antiduresis, coma, dysautonomias, or hypoventilation. A diagnosis of autoimmune encephalopathy should be suspected on the basis of clinical course, coexisting autoimmune disorder (eg, thyroiditis, diabetes), serological evidence of autoimmunity, spinal fluid evidence of intrathecal inflammation, neuroimaging or electroencephalographic abnormalities, and favorable response to trial of immunotherapy.

Detection of 1 or more neural autoantibodies aids the diagnosis of autoimmune encephalopathy and may guide a search for cancer. Pertinent autoantibody specificities include: 1) neurotransmitter receptors and ion channels such as neuronal voltage-gated potassium channels (and interacting synaptic and axonal proteins, LGI1 and CASPR2), ionotropic glutamate receptors (NMDA and AMPA), metabotrophic GAGA-B recptors; 2) enzymes, signaling molecules, and RNA-regulatory proteins in the cuytoplasm and nucleus of neurons (GAD65, CRMP-5, ANNA-1, and ANNA-2).

Importantly, autoimmune encephalopathies are reversible. Misdiagnosis as a progressive (currently irreversible) neurodegenerative conditions is not uncommon and has devastating consequences for the patient. Clinicians must consider the possibility of an autoimmune etiology in the differential diagnoses of encephalopathy. For example, a potentially reversible disorder justifies a trial of immunotherapy for the detection of neural autoantibodies in patients presenting with symptoms of personality change, executive dysfunction, and psychiatric manifestations.

A triad of clues helps to identifying patients with an autoimmune encephalopathy: 1) clinical presentation (subacute symptoms onset rapidlay progressive course and fluctuating symptoms) and radiological findings consistent with inflammation, 2) detection of neural autoantibodies in serum or cerebrospinal fluid (CSF), and 3) favorable respone to a trial of immunotherapy.

Detection of neural autoantibodies in serum or CSF informs the physician of a likely autoimmune etiology, and may heighten suspicion for a paraneoplastic basis and gude the search for cancer. Neurolgoical accompaniments of neural autoantibodies are generally not syndromic, but divers and multifocal. For example, neuronal voltage-gated potassium channel (VGKC)-complex antibodies were initially considered specific for autoimmune limbic encephalitis or disorders of peripheral nerve hyperexcitablilty. However, more diverse presentations are now recognized, including rapidly progressive cognitive decline mimicking frontotemporal dementia and Creutzfeldt-Jakob diseae.

Lab Testing Sections: Serology - Sendouts

Referred to: Mayo Clinic Laboratories (MML Test: ENS1)

Phone Numbers: MIN Lab: 612-813-6280

STP Lab: 651-220-6550

Test Availability: Daily, 24 hours

Turnaround Time: Results in 4-10 days

Special Instructions: N/A

Specimen

Specimen Type: Blood

Container: SST (Marble, gold or red)

Draw Volume: 12 mL (Minimum: 6 mL) blood

Processed Volume: 4 mL (Minimum: 2 mL) serum

Collection: Routine blood collection

Special Processing: Lab Staff: Centrifuge specimen, remove serum from cells, aliquot into a screw-capped round bottom vial. Store and ship at refrigerated temperatures.

Patient Preparation: None

Sample Rejection: Gross hemolysis; mislabeled or unlabeled specimens

Interpretive

Reference Range:

Antibody:	**Reference Range:**
Neuronal Nuclear Antibodies	
ANNA-1	<1:240
ANNA-2	<1:240
ANNA-3	<1:240
AGNA-1	<1:240
Neuronal and Muscle Cytoplamic Antibodies	
PCA-1	<1:240
PCA-2	<1:240
PCA-Tr	<1:240
Amphiphysin Ab	<1:240
CRMP-5-IgG	<1:240
Western Blot	
Paraneoplastic	Negative
CRMP-5-IgG	Negative
Amphiphysin	Negative
Islet Cell Antibodies	

GAD65 Ab	< or =0.02 nmol/L
Cation Channel Antibodies	
B-Type Calcium Channel Ab	< or =0.03 nmol/L
P/Q-Type Calcium Channel Ab	< or =0.02 nmol/L
AChR Gaglionic Neuronal Ab	< or =0.02 nmol/L
Neuronal VGKC Autoantibody	< or =0.02 nmol/L
ACHR Receptor Antibodies	
Ach Receptor (Muscle) Binding Ab	< or =0.02 nmol/L
Other Antibodies	
NMDA-R CBA IFA	Negative <1:120
AMPA-R CBA IFA	Negative <1:120
GABA-B-R CBA IFA	Negative <1:120
LGI1-IgG CBA	Negative
CASPR2-IgG CGA	Negative
NMO/AQP4 FACS	Negative

Critical Values: N/A

Limitations: N/A

Methodology:	ANN1S, ANN2S, ANN3S, AGN1S, PCAB2, PCATR, AMPHS,CRMS, PCABP, NMDIS, AMPIS, GABIS: Indirect Immunofluorescence Assay (IFA) VGKC, CCN, CCPQ, GANG, GD65S, ARBI: Radioimmunoassay (RIA) WBN, ABLOT: Western Blot AMPCS, GABCS, NMDCS, LG1CS, CS2CS: Cell Binding Assay (CBA)
References:	Mayo Clinical Laboratories January 2019