Autoimmune Epilepsy Panel, Serum and CSF

Content Review: May 2023 Last Update: February 2024

Autoimmune epilepsy is characterized by acute to subacute onset of epilepsy that is often refractory to standard treatment with antiseizure drugs but responds to immunotherapy.[1] Recognition of autoimmune causes of neurologic symptoms and detection of antineural antibodies may help to establish a diagnosis, support treatment decisions, serve as a prerequisite for enrollment in clinical trials, and guide the search for an associated malignancy.

Featured ARUP Testing

Autoimmune Epilepsy Panel, Serum 3006204

Method: Semi-Quantitative Cell-Based Indirect Fluorescent Antibody/Semi-Quantitative Indirect Fluorescent Antibody (IFA)/Qualitative Immunoblot/Semi-Quantitative Enzyme-Linked Immunosorbent Assay (ELISA)

Autoimmune Epilepsy Panel, CSF 3006205

Method: Semi-Quantitative Cell-Based Indirect Fluorescent Antibody/Semi-Quantitative Indirect Fluorescent Antibody (IFA)/Qualitative Immunoblot/Semi-Quantitative Enzyme-Linked Immunosorbent Assay (ELISA)

Disease Overview

Autoimmune epilepsy accounts for 15-20% of epilepsies previously considered to be cryptogenic.[2] In patients with new-onset seizure activity, the Antibody Prevalence in Epilepsy and Encephalopathy (APE^2) score can be used to predict the likelihood of the presence of an antineural antibody[3] and should therefore be considered before ordering antineural antibody testing. Factors associated with autoimmune epilepsy include autonomic dysfunction, brain magnetic resonance imaging (MRI) findings suggestive of encephalitis, elevated cerebrospinal fluid (CSF) protein or pleocytosis, faciobrachial dystonic seizures, history of autoimmunity, history of malignancy, neuropsychiatric changes, orofacial dyskinesias, seizures refractory to antiseizure drugs, and viral prodrome.[3] It is important to note that autoimmune epilepsy may exist in the absence of detectable, known antineural antibodies, and empiric immunotherapy trials may be considered in the appropriate clinical context.[4]

For more information about laboratory testing for autoimmune neurologic diseases, refer to the ARUP Consult Autoimmune Neurologic Disease - Antineural Antibody Testing topic.

Test Description

These serum and CSF antineural antibody panel tests can be used for the evaluation of patients with a neurologic phenotype consisting predominantly of new, acute to subacute onset of epilepsy that is refractory to more than two antiseizure medications. Testing for the presence of antineural antibodies in both serum and CSF is recommended to improve diagnostic yield.[5]

These phenotype-targeted panels test for the presence of antibodies associated with epilepsy. Clinical phenotypes for specific antineural antibody-associated syndromes often overlap, and phenotype-specific panels allow for rapid identification of associated antibodies, which may have implications for treatment, prognosis, and cancer screening.[6] Other panels may be more appropriate, depending on the patient's clinical phenotype:

ARUP Phenotype-Specific Panels to Consider for Autoimmune Neurologic Disease

ARUP Panel	Test Code	
	Serum	CSF
Autoimmune Movement Disorder Panel	3006206	3006207
Autoimmune Encephalopathy/Dementia Panel	3006201	3006202
Autoimmune Pediatric CNS Disorders Panel	3006210	3006211

Regardless of the panel chosen, order only one panel for serum and/or one panel for CSF; many antineural antibodies are redundant between these panels, and choosing based on the predominant phenotype will provide the most meaningful results. To compare these panels and the antibodies included, refer to ARUP Autoimmune Neurology Panel Components.

Testing for individual antibodies is also available separately.

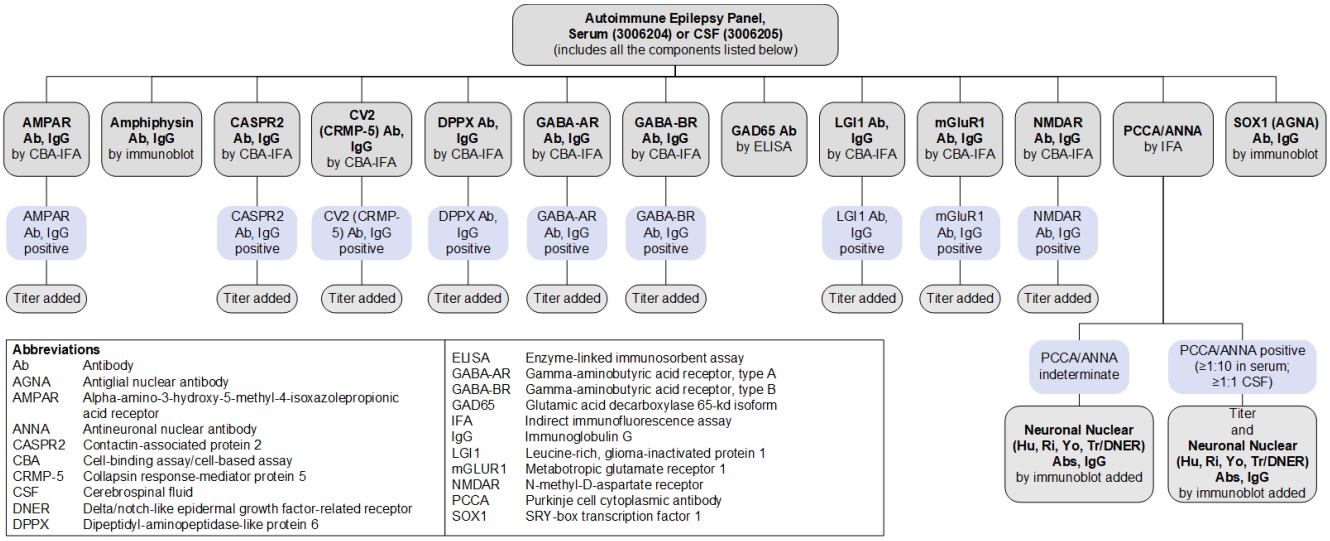
Antibodies Tested and Methodology

Autoimmune Epilepsy Panel, Serum (3006204) and Autoimmune Epilepsy Panel, CSF (3006205): Antibodies Tested and Methodology			
Autoantibody Markers	Methodology	Individual Autoantibody or Focused Panel Test Code	
		Serum	CSF
AMPAR Ab, IgG	CBA-IFA, reflex titer	3001260	3001257
Amphiphysin Ab, IgG	IB	2008893	3004510
ANNA-1 (Hu)	IFA, reflex IB, reflex titer	2007961	2010841
ANNA-2 (Ri)	IFA, reflex IB, reflex titer	2007961	2010841
CASPR2 Ab, IgG	CBA-IFA, reflex titer	2009452	3001986
CV2 (CRMP-5) Ab, IgG	CBA-IFA, reflex titer	3016999	3017001
DPPX Ab, IgG	CBA-IFA, reflex titer	3004359	3004512
GABA-AR Ab, IgG	CBA-IFA, reflex titer	3006008	3006003
GABA-BR Ab, IgG	CBA-IFA, reflex titer	3001270	3001267
GAD65 Ab	ELISA	2001771	3002788
LGI1 Ab, IgG	CBA-IFA, reflex titer	2009456	3001992
mGluR1 Ab, IgG	CBA-IFA, reflex titer	3006044	3006039
NMDAR Ab, IgG	CBA-IFA, reflex titer	2004221	2005164
PCCA-1 (Yo)	IFA, reflex IB, reflex titer	2007961	2010841
PCCA-Tr/DNER	IFA, reflex IB, reflex titer	2007961	2010841
SOX1 (AGNA) Ab, IgG	IB	3002885	3002886

Ab, antibody; AGNA, antiglial nuclear antibody; AMPAR, alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptor; ANNA-1, antineuronal nuclear antibody type 1; ANNA-2, antineuronal nuclear antibody type 2; CASPR2, contactin-associated protein 2; CBA, cell-binding assay/cell-based assay; CRMP-5, collapsin response-mediator protein 5; DNER, Delta/notch-like epidermal growth factor-related receptor; DPPX, dipeptidyl-aminopeptidase-like protein 6; ELISA, enzyme-linked immunosorbent assay; GABA-AR, gamma-aminobutyric acid receptor, type A; GABA-BR, gamma-aminobutyric acid receptor, type B; GAD65, glutamic acid decarboxylase 65-kd isoform; IB, immunoblot; IFA, indirect immunofluorescence assay; LGI1, leucine-rich, glioma-inactivated protein 1; mGluR1, metabotropic glutamate receptor 1; NMDAR, N-methyl-D-aspartate receptor; PCCA, Purkinje cell cytoplasmic antibody; SOX1, SRY-box transcription factor 1

Reflex Patterns

Autoimmune Epilepsy Panel, Serum (3006204) and Autoimmune Epilepsy Panel, CSF (3006205): Reflex Patterns



Limitations

This panel does not include every antibody that has been associated with autoimmune epilepsy:

- ANNA-3 and PCCA-2 are not included in this panel because they are extremely rare (present in approximately 0.0001% of specimens submitted for evaluation using a paraneoplastic antibody panel), and commercial assays to confirm the specificity of these antibodies are not currently available.[7]
- Glial fibrillary acidic protein (GFAP) and neurochondrin are not included because they have been only recently identified and their prevalence is currently not well established.
  - GFAP has been reported in 0.17% of samples screened, often co-occurring with other antineural antibodies.[8]
  - Neurochondrin has been reported in 0.002% of samples tested.[9]
- As testing for newly described antibodies becomes available and their clinical relevance is established, these panels will evolve to reflect these discoveries.

Test Interpretation

Results

Results must be interpreted in the clinical context of the individual patient; test results (positive or negative) should not supersede clinical judgment.

Autoimmune Epilepsy Panel, Serum (3006204) and Autoimmune Epilepsy Panel, CSF (3006205): Results Interpretation

Result	Interpretation
Positive for ≥1 autoantibodies	Autoantibody(ies) detected Supports a clinical diagnosis of autoimmune epilepsy Consider a focused search for malignancy based on antibody-tumor associations
Negative	No autoantibodies detected A diagnosis of autoimmune epilepsy is not excluded Immunotherapy trials may be considered in the appropriate clinical context

References

1. Jang Y, Kim DW, Yang KI, et al. Clinical approach to autoimmune epilepsy. *J Clin Neurol*. 2020;16(4):519-529.

2. Dubey D, Singh J, Britton JW, et al. Predictive models in the diagnosis and treatment of autoimmune epilepsy. *Epilepsia*. 2017;58(7):1181-1189.

3. Dubey D, Kothapalli N, McKeon A, et al. Predictors of neural-specific autoantibodies and immunotherapy response in patients with cognitive dysfunction. *J Neuroimmunol*. 2018;323:62-72.

4. Lee WJ, Lee ST, Byun JI, et al. Rituximab treatment for autoimmune limbic encephalitis in an institutional cohort. *Neurology*. 2016;86(18):1683-1691.

5. Flanagan EP, Drubach DA, Boeve BF. Autoimmune dementia and encephalopathy. *Handb Clin Neurology*. 2016;133:247-267.

6. Budhram A, Dubey D, Sechi E, et al. Neural antibody testing in patients with suspected atoimmune encephalitis. *Clin Chem*. 2020;66(12):1496-1509.

7. Horta ES, Lennon VA, Lachance DH, et al. Neural autoantibody clusters aid diagnosis of cancer. *Clin Cancer Res*. 2014;20(14):3862-3869.

8. Dubey D, Pittock SJ, Kelly CR, et al. Autoimmune encephalitis epidemiology and a comparison to infectious encephalitis. *Ann Neurol*. 2018;83(1):166-177.

9. Shelly S, Kryzer TJ, Komorowski L, et al. Neurochondrin neurological autoimmunity. *Neurol Neuroimmunol Neuroinflamm*. 2019;6(6):e612.

Related Information

ARUP Autoimmune Neurology Panel Components

Autoimmune Neurologic Diseases - Antineural Antibody Testing

ARUP Laboratories is a nonprofit enterprise of the University of Utah and its Department of Pathology. 500 Chipeta Way, Salt Lake City, UT 84108
(800) 522-2787 | (801) 583-2787 | aruplab.com | arupconsult.com