AUTOIMMUNE ENCEPHALITIS TESTING

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When testing for autoimmune or paraneoplastic causes of neurologic symptoms, it is best to send either the **autoimmune encephalopathy** or **paraneoplastic antibody panel**. Typically only one is needed as these panels mostly overlap. The autoimmune encephalopathy panel is generally sufficient, unless there are concerns for a paraneoplastic process in the peripheral nervous system (as the extra tests on the paraneoplastic antibody panel relate to the peripheral nervous system).

Send both serum and CSF panels (the antibodies can have different sensitivities in each; notably NMDA-R has greater sensitivity in CSF). Anti-Ma and anti-Ta are not tested by these panels and should be ordered separately if concerned (details below).

Tests are performed by immunofluorescence assay (IFE), enzyme immunoassay, radioimmunoassay (RIA), western blot (WB), cell-binding assay or flow cytometry. Most are IFE and then reflex tested to confirm by western blot or quantified with an assay listed above.

The table below is adapted from Linnoila and Pittock [1] and the Mayo Clinic Laboratories antibody matrix:

ANTIBODY	TYPE	ASSOCIATED CANCER(S)[A]	CLINICAL SYMPTOMS[B]
AChR binding	Surface	Thymoma	Myasthenia gravis
AChR ganglionic	Surface	Multiple carcinomas	Autonomic dysfunction
AGNA (SOX1)	Intracellular	Small cell lung cancer	Lambert Eaton myasthenic syndrome
AMPA-R	Surface	Thymoma, lung cancer, breast cancer	Limbic encephalitis[c]
Amphiphysin	Intracellular	Breast cancer, small cell lung cancer	Wide clinical spectrum including stiff person syndrome, cerebellar ataxia, encephalomyelitis
ANNA-1 (Hu)	Intracellular	Small cell lung cancer, neuroblastoma, thymoma	Wide clinical spectrum including sensory neuropathy, encephalomyelitis, limbic encephalitis, cerebellar ataxia
ANNA-2 (Ri)	Intracellular	Small cell lung cancer, breast cancer	Opsoclonus myoclonus, cerebellar ataxia, brainstem encephalitis
ANNA-3	Intracellular	Lung cancer	Sensory neuropathy, cerebellar ataxia, encephalomyelitis

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ANTIBODY	TYPE	ASSOCIATED CANCER(S)[A]	CLINICAL SYMPTOMS[B]
CASPR2	Surface	Thymoma	Morvan syndrome[d]
CRMP-5	Intracellular	Small cell lung cancer, thymoma	Wide clinical spectrum including cerebellar ataxia, encephalomyelitis, sensory neuropathy, optic neuritis, chorea
DPPX	Surface	B-cell cancers	Encephalitis with CNS hyperexcitability
GABA-B-R	Surface	Small cell lung cancer, neuroendocrine cancer	Limbic encephalitis
GAD65	Intracellular	Only occasional (lung cancer, thymoma)	Wide clinical spectrum including stiff person syndrome, cerebellar ataxia, encephalitis
Glycine receptor	Surface	Infrequent	Wide clinical spectrum including stiff person syndrome, PERM[e]
LGI-1	Surface	Thymoma, small cell lung cancer	Limbic encephalitis, faciobrachial dystonic seizures
Ma1/Ma2 (Ta)	Intracellular	Ma1 & Ma2: multiple carcinomas Ma2 (only): testicular cancer	Brainstem and cerebellar dysfunction
mGluR1	Surface	Hodgkin lymphoma	Cerebellar ataxia
NMDA-R	Surface	Ovarian teratoma	Progressive symptoms. Psychiatric symptoms → seizures and autonomic dysfunction → catatonia and coma
PCA-1 (Yo)	Intracellular	Gynecologic cancer (especially ovarian), breast cancer	Cerebellar ataxia
PCA-2	Intracellular	Small cell lung cancer	Encephalomyelitis, cerebellar ataxia
PCA-Tr	Surface	Hodgkin lymphoma	Cerebellar ataxia
Striational	Intracellular	Thymoma	Myasthenia gravis
VGCC (P/Q and N-type)	Surface	Lung, breast, gynecologic cancer	Lambert Eaton myasthenic syndrome, cerebellar ataxia
VGKC complex	Surface	Mostly due to associated LGI-1/CASPR2 antibodies (see those antibodies)	

[a] Many antibodies may be associated with future cancers (or no cancer); the cancers listed are considered the "classic" associations

[b] Many antibodies may have clinical symptoms beyond the key symptoms listed

[c] Symptoms of limbic encephalitis include short-term memory loss, focal seizures, irritability, depression, and cognitive issues

[d] Morvan syndrome involves neuromyotonia (muscle twitching) alongside autonomic and central nervous system dysfunction

[e] Progressive encephalomyelitis with rigidity and myoclonus

REFERENCE

1. Linnoila J, Pittock SJ. Autoantibody-associated central nervous system neurologic disorders. Semin Neurol. 2016;36(04):382–96. Thieme Medical Publishers.