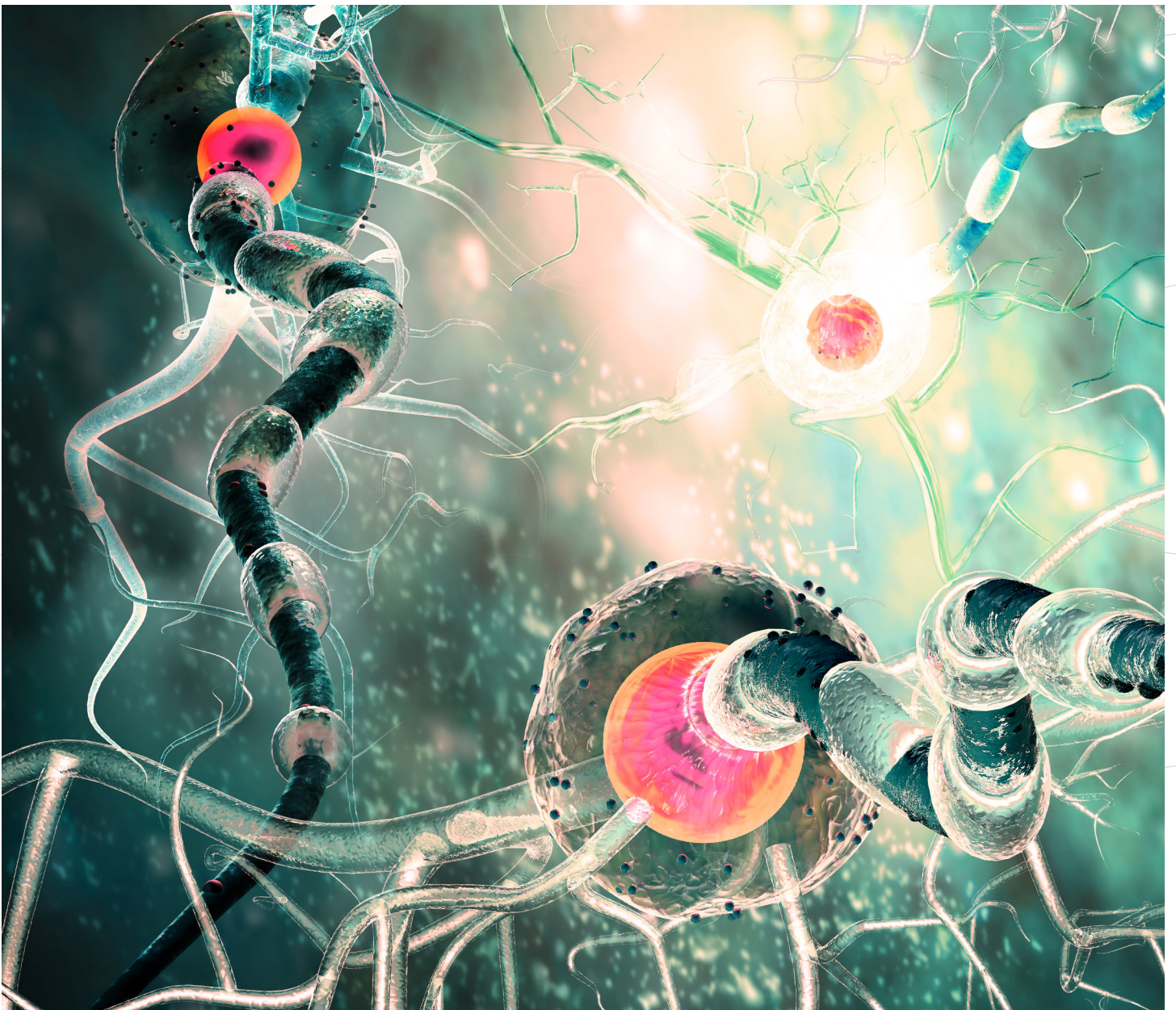




MAYO CLINIC
Mayo Medical Laboratories

AUTOIMMUNE DEMENTIA

AUTOANTIBODY EVALUATIONS TO EXPEDITE DIAGNOSIS AND TREATMENT



WHAT IS AUTOIMMUNE DEMENTIA?

Recent case series and clinical-serological observations have shown that autoimmune encephalopathies do not always present with delirium, but sometimes present as a rapidly progressive dementia. Additionally, some cases may be paraneoplastic.

CLUES HELPFUL IN IDENTIFYING PATIENTS WITH AN AUTOIMMUNE DEMENTIA:

- 1 Relatively rapid onset and progression of symptoms or radiological findings suggesting inflammation
- 2 Serum autoantibody or cerebrospinal fluid markers of inflammation (e.g., elevated protein or leukocytosis)
- 3 Objective evidence of improvement with immunotherapy trial

WHY CONSIDER AN AUTOIMMUNE ETIOLOGY IN NEW ONSET DEMENTIA?

TO AVOID MISDIAGNOSIS OF NEURODEGENERATIVE DISORDERS

- ▶ Misdiagnosing a potentially reversible condition as a progressive neurodegenerative disorder may delay a correct diagnosis beyond the window of reversibility (6-12 months), resulting in devastating consequences for the patient and family.
- ▶ Among Mayo Clinic patients diagnosed with and treated for an autoimmune dementia, 35% were initially misdiagnosed as having a neurodegenerative disorder.

BECAUSE EARLY DIAGNOSIS CAN MAKE A MEANINGFUL DIFFERENCE

- ▶ CNS disorders previously considered neurodegenerative and untreatable are increasingly recognized as having an autoimmune cause.
- ▶ Early-initiated immunotherapy gives patients the best possible outcome. Informative serological testing may also expedite the search for a limited stage cancer.

WHEN SHOULD I TEST FOR AN AUTOIMMUNE ETIOLOGY?*

CONSIDER AN AUTOIMMUNE ETIOLOGY WITH NEW ONSET DEMENTIA OR IN THE CASE OF COGNITIVE IMPAIRMENT INCLUDING ONE OR MORE OF THE FOLLOWING:

- ▶ Rapid onset and progression
- ▶ Fluctuating course
- ▶ Psychiatric accompaniments (psychosis, hallucinations)
- ▶ Movement disorder (myoclonus, tremor, dyskinesia)
- ▶ Headache
- ▶ Autoimmune stigmata (e.g., physical signs or personal or family history of diabetes, thyroid disorder, vitiligo, premature graying, myasthenia gravis, rheumatoid arthritis, systemic lupus erythematosus)
- ▶ Smoking history (20+ pack years) or other cancer risk factors
- ▶ History of cancer
- ▶ Inflammatory cerebrospinal fluid
- ▶ Neuroimaging atypical for degenerative etiology

* *We strongly advise obtaining serum and CSF before starting immunotherapy*

MAYO MEDICAL LABORATORIES: YOUR PARTNER IN COMMUNITY LABORATORY MEDICINE

With a strong emphasis on patient care and community-based medicine, we do more than deliver testing solutions. We connect you with our neurologists and laboratory experts who help you work with your results every step of the way.

FOR INFORMATION ABOUT DIAGNOSIS AND TREATMENT OF AUTOIMMUNE DEMENTIA, CONTACT US AT 855-516-8404

WHICH TESTS SHOULD I ORDER?

- > Dementia Autoimmune Evaluation, CSF
(Mayo ID: DEMEC)
TAT: 3 days negative / 5 days positive
- > Dementia Autoimmune Evaluation, Serum
(Mayo ID: DEMES)
TAT: 4 days negative / 7 days positive

WHY TEST BOTH CSF AND SERUM?

Some neural autoantibodies are detected more readily in serum (e.g., VGKC-complex IgG), while others can be detected more readily in CSF (e.g., NMDA receptor IgG). Testing both, simultaneously or sequentially, maximizes diagnostic yield.

NEURAL ANTIBODIES EVALUATED

NUCLEAR AND CYTOPLASMIC SPECIFICITIES

ANTIBODY	ONCOLOGICAL ASSOCIATION	APPROX. FREQUENCY OF CANCER
ANNA-1	Small-cell lung carcinoma, neuroblastoma, thymoma	90%
ANNA-2	Small-cell lung carcinoma, breast adenocarcinoma	90%
ANNA-3	Aerodigestive carcinoma	90%
AGNA-1 (SOX1)	Small-cell lung carcinoma	90%
PCA-2	Small-cell lung carcinoma	90%
PCA-Tr	Hodgkin lymphoma	90%
CRMP-5	Small-cell lung carcinoma, thymoma, thyroid, or renal carcinoma	90%
Amphiphysin	Small-cell lung carcinoma, breast adenocarcinoma	90%
GAD65	Occasionally (e.g., thymoma)	< 10%

PLASMA MEMBRANE SPECIFICITIES

ANTIBODY	ONCOLOGICAL ASSOCIATION	APPROX. FREQUENCY OF CANCER
VGKC-complex* (Kv1 potassium channel)	Small-cell lung carcinoma, thymoma, adenocarcinoma of breast, prostate	< 15%
NMDA receptor	Teratoma (ovarian or extra-ovarian)	50%
AMPA receptor	Thymoma, lung and breast carcinoma	70%
GABA-B receptor	Small-cell lung carcinoma, other neuroendocrine neoplasm	70%
P/Q and N-type calcium channel	Lung, breast or gynecologic carcinoma	15%
Muscle AChR	Thymoma, lung, breast, gynecologic, or prostate carcinoma	< 15%
Neuronal ganglionic AChR	Miscellaneous carcinomas, thymoma	< 15%

*VGKC radioimmunoassay sensitively detects antibodies to LGI1, CASPR2, and other VGKC-complex antigens.

Abbreviations: AGNA, anti-gliial/neuronal nuclear antibody; ANNA, antineuronal nuclear antibody; PCA, Purkinje cell cytoplasmic antibody; CRMP-5, collapsin response-mediator protein-5; GAD65, glutamic acid decarboxylase-65; VGKC, voltage-gated potassium channel; NMDA, N-methyl D-aspartate; AMPA, α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid; GABA, gamma-aminobutyric acid; AChR, acetylcholine receptor.

NEUROLOGISTS STAFFING THE CLINICAL LABORATORY ARE AVAILABLE FOR CONSULTATION AND ASSISTANCE IN THE INTERPRETATION OF AUTOANTIBODY EVALUATIONS



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CLINICAL REFERENCES FOR AUTOIMMUNE DEMENTIA

- Flanagan EP, McKeon A, Lennon VA, et al. Autoimmune dementia: clinical course and predictors of immunotherapy response. *Mayo Clin Proc.* Oct 2010;85(10):881-897
- McKeon A, Lennon, VA, Pittock, SJ. Immunotherapy Responsive Dementias and Encephalopathies. *Continuum Lifelong Learning* 2010;16(2):80-101

TAP INTO THE EXPERTISE OF MAYO CLINIC

The Mayo Clinic Neuroimmunology Laboratory was the first to introduce comprehensive serological evaluations to aid the diagnosis of neurological autoimmunity. The laboratory continues to discover and clinically validate novel autoantibody profiles that inform neurological decision-making and guide the search for cancer.

The clinical and research activities of the Mayo Clinic Neuroimmunology Laboratory focus on autoimmunity affecting the brain, optic nerve, retina, spinal cord, autonomic and somatic nerves and muscle. The neuroimmunology laboratory complements Mayo Clinic's Autoimmune Neurology Clinic.

FOR MORE INFORMATION ABOUT AUTOIMMUNE NEUROLOGY TESTING

MayoMedicalLaboratories.com/neurology