Test Definition: AN3TC

Antineuronal Nuclear Antibody Type 3 (ANNA-3) Titer, Spinal Fluid

Overview

Useful For

Evaluating patients who present with a subacute neurological disorder of undetermined etiology and have risk factors for primary lung carcinoma

Reporting an end titer result from cerebrospinal fluid specimens

Testing Algorithm

If the indirect immunofluorescence (IFA) pattern suggests antineuronal nuclear antibody type 3 (ANNA-3), then this test will be performed at an additional charge.

Method Name

Only orderable as a reflex. For more information see:
-DMC2 / Dementia, Autoimmune/Paraneoplastic Evaluation, Spinal Fluid
-ENC2 / Encephalopathy, Autoimmune/Paraneoplastic Evaluation, Spinal Fluid
-EPC2 / Epilepsy, Autoimmune/Paraneoplastic Evaluation, Spinal Fluid
-MDC2 / Movement Disorder, Autoimmune/Paraneoplastic Evaluation, Spinal Fluid
-MAC1 / Myelopathy, Autoimmune/Paraneoplastic Evaluation, Spinal Fluid

Indirect Immunofluorescence Assay (IFA)

NY State Available

Yes

Specimen

Specimen Type

CSF

Ordering Guidance

Serum is preferred. Spinal fluid testing is particularly useful if interfering antibodies are present in the serum.

Specimen Required

Only orderable as a reflex. For more information see:
-DMC2 / Dementia, Autoimmune/Paraneoplastic Evaluation, Spinal Fluid
-ENC2 / Encephalopathy, Autoimmune/Paraneoplastic Evaluation, Spinal Fluid
-EPC2 / Epilepsy, Autoimmune/Paraneoplastic Evaluation, Spinal Fluid
-MDC2 / Movement Disorder, Autoimmune/Paraneoplastic Evaluation, Spinal Fluid
-MAC1 / Myelopathy, Autoimmune/Paraneoplastic Evaluation, Spinal Fluid

Container/Tube: Sterile vial
Specimen Volume: 4 mL

Specimen Minimum Volume
2 mL

Reject Due To

Gross hemolysis	Reject
Gross lipemia	Reject
Gross icterus	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
CSF	Refrigerated (preferred)	28 days	
	Ambient	72 hours	
	Frozen	28 days	

Clinical & Interpretive

Clinical Information
Antineuronal nuclear autoantibodies (ANNA) are recognized clinically as markers of a patient's immune response to specific cancers (paraneoplastic autoantibodies).

In 1985, an antineuronal nuclear autoantibody (now known as ANNA-1 or anti-Hu)(1) was described as a serological accompaniment of subacute sensory neuropathy related to small-cell lung carcinoma (SCLC). ANNA-1 was subsequently recognized as an IgG marker for a spectrum of encephalomyeloradiculoneuropathy (including gastrointestinal dysmotilities) related to SCLC,(2) childhood neuroblastoma, and thymoma. The second antineuronal nuclear antibody to be recognized (known as ANNA-2 or anti-Ri) is an IgG marker of neurological autoimmunity related to SCLC and breast carcinoma.(3)

ANNA-3 is an IgG marker of an immune response to SCLC in patients presenting with a subacute, usually multifocal, paraneoplastic neurologic disorder.(4) Paraneoplastic sensorimotor neuropathy, cerebellar ataxia, and limbic encephalopathy are the most common presentations. However, an ANNA-3-positive patient may present with any element of an encephalomyeloradiculoneuropathy.

Other autoantibody markers of immune responses to SCLC include amphiphysin, collapsin response-mediated protein-5 (CRMP-5) IgG, Purkinje cell antibody type 2 (PCA-2), antiglial nuclear antibody, calcium channel antibodies (P/Q-type), and muscle acetylcholine receptor antibodies.

Reference Values

Only orderable as a reflex. For more information see:
-DMC2 / Dementia, Autoimmune/Paraneoplastic Evaluation, Spinal Fluid
-ENC2 / Encephalopathy, Autoimmune/Paraneoplastic Evaluation, Spinal Fluid
-EPC2 / Epilepsy, Autoimmune/Paraneoplastic Evaluation, Spinal Fluid
-MDC2 / Movement Disorder, Autoimmune/Paraneoplastic Evaluation, Spinal Fluid
-MAC1 / Myelopathy, Autoimmune/Paraneoplastic Evaluation, Spinal Fluid

<1:2
Neuron-restricted patterns of IgG staining that do not fulfill criteria for antineuronal nuclear antibody type 3 may be reported as "unclassified antineuronal IgG. "Complex patterns that include nonneuronal elements may be reported as "uninterpretable."

Interpretation

A positive result confirms that a patient's subacute neurological disorder has an autoimmune basis and predicts with 90% certainty that the patient has an aerodigestive carcinoma, usually a small-cell lung carcinoma (SCLC) that is new or recurrent and confined to the chest.

Fifteen percent of patients who are eventually proven to have small-cell carcinoma have an unrelated often more obvious cancer, either coexisting or in the past.

Antineuronal nuclear autoantibody type 3 (ANNA-3) has not yet been encountered in healthy subjects (n=100) or patients with lung carcinoma without a neurological accompaniment (n=100) or with other cancers (n=300).

Cautions

Antineuronal nuclear autoantibody type 3 (ANNA-3) is not detectable when it coexists with ANNA-1 or ANNA-2 unless its titer exceeds that of coexisting neuronal nuclear antibodies or is demonstrable by Western blot.

Clinical Reference

1. Graus F, Cordon-Cardo C, Posner JB: Neuronal antinuclear antibody in sensory neuropathy from lung cancer. Neurology. 1985 April;35(4):538-543
2. Lucchinetti CF, Kimmel DW, Lennon VA: Paraneoplastic and oncologic profile of patients seropositive for type 1 antineuronal nuclear autoantibodies. Neurology. 1998 Mar;50(3):652-657
3. Vernino S, Eggenberger ER, Rogers LR, Lennon VA: Paraneoplastic neurological autoimmunity associated with ANNA-1 autoantibody and thymoma. Neurology. 2002 Sep 24;59(6):929-932
4. Pittock SJ, Lucchinetti CF, Lennon VA: Anti-neuronal nuclear autoantibody-type 2: paraneoplastic accompaniments. Ann Neurol. 2003 May;53(5):580-587
5. Chan KH, Vernino S, Lennon VA: ANNA-3 anti-neuronal nuclear antibody: marker of lung cancer-related autoimmunity. Ann Neurol. 2001 Sep;50(3):301-311
6. Pittock SJ, Kryzer TJ, Lennon VA: Paraneoplastic antibodies coexist and predict cancer, not neurological syndrome. Ann Neurol. 2004 Nov;56(5):715-719
7. Horta ES, Lennon VA, Lachance DH, et al: Neural autoantibody clusters aid diagnosis of cancer. Clin Cancer Res. 2014 Jul 15;20(14):3862-3869

Performance

Method Description

The patient's specimen is tested by a standardized immunofluorescence assay that uses a composite frozen section of mouse cerebellum, kidney, and gut tissues. After incubation with the specimen and washing, fluorescein-conjugated goat-antihuman IgG is applied. Neuron-specific autoantibodies are identified by their characteristic fluorescence staining patterns. Specimens that are scored positive for any neuronal nuclear or cytoplasmic autoantibody are titrated. Interference by coexisting non-neuron-specific autoantibodies can usually be eliminated by serologic absorption.(Honorat JA, Komorowski L, Josephs KA, et al. IgLON5 antibody: Neurological accompaniments and outcomes in 20 patients. Neurol Neuroimmunol Neuroinflamm. 2017;4[5]:e385. Published 2017 Jul 18. doi:10.1212/NXI.0000000000000385)

Western blot is performed, as needed, to confirm seropositivity.

PDF Report

No

Day(s) Performed

Monday through Sunday

Report Available

6 to 8 days

Specimen Retention Time

5 weeks

Performing Laboratory Location

Mayo Clinic Laboratories - Rochester Main Campus

Fees & Codes

Fees

- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their account representative. For assistance, contact Customer Service.

Test Classification

This test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. It has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information

86256

Test Definition: AN3TC

Antineuronal Nuclear Antibody Type 3 (ANNA-3) Titer, Spinal Fluid

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
AN3TC	ANNA-3 Titer, CSF	94358-9

Result ID	Test Result Name	Result LOINC® Value
43442	ANNA-3 Titer, CSF	94358-9