Test Definition: AN3TC

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

Overview

Useful For

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

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

Directing a focused search for cancer

Investigating neurological symptoms that appear during, or after, cancer therapy, and are not explainable my metastasis

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

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Ordering Guidance

Both serum and spinal fluid testing are suggested. 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

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 autoantibody type 3 (ANNA-3) is an IgG marker of an immune response to a malignancy, most often of neuroendocrine origin, in patients presenting with subacute, usually multifocal, paraneoplastic neurologic disorders.(1) Ninety percent of the patients have evidence of a malignancy, most commonly neuroendocrine malignancy, particularly small-cell lung carcinoma (SCLC). Neurologic presentations include sensorimotor or sensory neuronopathy, cerebellar ataxia, encephalopathy or multifocal involvement. Half of the patients have serologic evidence of other neuroendocrine-tumor predicting antibodies, including neuronal intermediate filament (NIF) antibody, collapsin-response-mediator-protein-5 (CRMP5) antibody, voltage-gated calcium channel (P/Q type) antibody, ANNA-1, and Purkinje-cell-autoantibody-type-2/microtubule-associated-protein-1B (PCA-2/MAP1B).

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

Interpretation

Detection of antineuronal nuclear autoantibodies type 3 (ANNA-3) in serum or spinal fluid of patients with a compatible neurologic disorder:
-Identifies the neurologic problem as autoimmune and almost certainly paraneoplastic
-Prompts a search for underlying malignancy (small-cell lung cancer and other neuroendocrine lineage malignancies are the most common cancers encountered)

Antineuronal nuclear autoantibody type 3 is specific for the Dachshund homolog 1 (DACH1) protein.

Cautions

Antineuronal nuclear autoantibody type 3 (ANNA-3) may not be detectable when it coexists with ANNA-1 or ANNA-2 unless its titer exceeds that of coexisting neuronal nuclear antibodies. Presence of nonneural specific antibodies in a patient's specimen may hinder interpretation of ANNA-3 results by tissue indirect immunofluorescence.

Clinical Reference

1. Pittock SJ, Lucchinetti CF, Lennon VA: Anti-neuronal nuclear autoantibody-type 2: paraneoplastic accompaniments. Ann Neurol. 2003 May;53(5):580-587
2. Chan KH, Vernino S, Lennon VA. ANNA-3 anti-neuronal nuclear antibody: marker of lung cancer-related autoimmunity. Ann Neurol. 2001;50(3):301-311
3. Zekeridou A, Yang B, Lennon VA, et al. Anti-Neuronal Nuclear Antibody 3 Autoimmunity Targets Dachshund Homolog 1. Ann Neurol. 2022;91(5):670-675. doi:10.1002/ana.26320
4. Zekeridou A. Paraneoplastic Neurologic Disorders. Continuum (Minneap Minn). 2024;30(4):1021-1051. doi:10.1212/CON.0000000000001449

Performance

Method Description

The patient's specimen is tested by a standardized immunofluorescence assay that uses a composite frozen section of mouse cerebrum, 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.(Unpublished Mayo method)

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

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PDF Report
No

Day(s) Performed
Monday through Sunday

Report Available
6 to 8 days

Specimen Retention Time
2 days

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

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