Test Definition: AN2TC

Antineuronal Nuclear Antibody Type 2
(ANNA-2) 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

Serological evaluation of patients who present with a subacute neurological disorder and signs of midbrain/cerebellar/brain stem disorder and/or myelopathy, especially women with a previous history of breast cancer, and both sexes if there is a history of tobacco use or passive exposure

Directing a focused search for cancer

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

Reporting an end titer result from cerebrospinal fluid specimens

Testing Algorithm

If the indirect immunofluorescence pattern suggests antineuronal nuclear antibody type 2 (ANNA-2), then this test will be performed at an additional charge.

Method Name

Only orderable as a reflex. For more information see:
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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

Both serum and spinal fluid testing are suggested. Spinal fluid testing is particularly useful when interfering antibodies are present in the serum.

Specimen Required

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DMC2 / Dementia, Autoimmune/Paraneoplastic Evaluation, Spinal Fluid
ENC2 / Encephalopathy, Autoimmune/Paraneoplastic Evaluation, Spinal Fluid
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MDC2 / Movement Disorder, Autoimmune/Paraneoplastic Evaluation, Spinal Fluid
MAC1 / Myelopathy, Autoimmune/Paraneoplastic Evaluation, Spinal Fluid

Specimen Minimum Volume

1 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 2 (ANNA-2), also known as anti-Ri, is an IgG serologic marker of paraneoplastic neurologic autoimmunity and reflects an immune response to neuronal antigens expressed in certain breast, lung, or gynecologic cancers. These carcinomas are often occult, with the patients presenting with a paraneoplastic neurological syndrome. ANNA-2 is far less common than ANNA-1. It is one of the rarest paraneoplastic antibodies encountered in the Mayo Clinic Neuroimmunology Laboratory.

Patients who are seropositive for ANNA-2 usually present to a neurologist with signs of midbrain, brain stem, cerebellar, or spinal cord dysfunction. Opsoclonus-myoclonus, laryngospasm, or jaw-opening dystonia may be prominent. Peripheral neuropathic signs and symptoms may occur. These often reflect coexisting autoimmunity to other onconeural

proteins (eg, ANNA-1, collapsin response-mediator protein-5 [CRMP-5]); coexisting paraneoplastic autoantibodies are found in 73% of cases.

Antineuronal nuclear autoantibody type 2 positive patients are female in 64% of cases. Most have primary carcinoma of breast or lung; gynecologic cancer is less frequent.

Antineuronal nuclear autoantibody type 2 is not detected in serum or spinal fluid of healthy individuals. It is found in fewer than 2% of patients who have small-cell lung carcinoma without evidence of neurologic dysfunction.

Antineuronal nuclear autoantibody type 2 is identified by an indirect immunofluorescence assay. It characteristically stains neurons in the central nervous system and spares neurons in the peripheral nervous system. ANNA-2 is confirmed by a line blot assay.

Reference Values

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DMC2 / Dementia, Autoimmune/Paraneoplastic Evaluation, Spinal Fluid
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MAC1 / Myelopathy, Autoimmune/Paraneoplastic Evaluation, Spinal Fluid

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Interpretation

Detection of antineuronal nuclear autoantibodies type 2 (ANNA-2) 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 (breast, lung, or gynecologic)

Antineuronal nuclear autoantibody type 2 is specific for the nova1/nova2 proteins.

Cautions

Presence of non-neural specific antibodies in a patient’s specimen may hinder interpretation of antineuronal nuclear autoantibody type 2 (ANNA-2) 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;53(5):580-587
2. Horta ES, Lennon VA, Lachance DH, et al: Neural autoantibody clusters aid diagnosis of cancer. Clin Cancer Res. 2014;20(14):3862-3869
3. Zekeridou A. Paraneoplastic neurologic disorders. Continuum (Minneap Minn). 2024;30(4):1021-1051. doi:10.1212/CON.0000000000001449

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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)

If antineuronal nuclear autoantibody type 1 (ANNA-1), antinuclear antibody, or antimitochondrial antibody titers equal or exceed ANNA-2, Western blot analysis may be required to establish ANNA-2 specificity with certainty.

PDF Report

No

Day(s) Performed

Monday through Sunday

Report Available

5 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

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LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
AN2TC	ANNA-2 Titer, CSF	94357-1

Result ID	Test Result Name	Result LOINC® Value
43441	ANNA-2 Titer, CSF	94357-1