MAYO CLINIC LABORATORIES

Test Definition: NSE

Neuron-Specific Enolase, Serum

Overview

Useful For

A follow-up marker in patients with neuron-specific enolase-secreting tumors of any type

An auxiliary test in the diagnosis of small cell lung carcinoma

An auxiliary test in the diagnosis of carcinoids, islet cell tumors, and neuroblastomas

An auxiliary tool in the assessment of comatose patients

Method Name

Homogeneous Time-Resolved Fluorescence

NY State Available

Yes

Specimen

Specimen Type

Serum

Specimen Required

Supplies: Sarstedt Aliquot Tube, 5 mL (T914)
Collection Container/Tube:
Preferred: Red top
Acceptable: Serum gel
Submission Container/Tube: Plastic vial
Specimen Volume: 0.5 mL
Collection Instructions:
1. **Specimens should not be transported by tube system prior to centrifugation**.
2. Centrifuge and aliquot serum into a plastic vial.

Forms

If not ordering electronically, complete, print, and send an Oncology Test Request (T729) with the specimen.

Specimen Minimum Volume

0.3 mL

Reject Due To

Gross	Reject

hemolysis	
Gross lipemia	OK
Gross icterus	Reject
Hemolysis at any level	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Serum	Refrigerated (preferred)	7 days	
	Ambient	5 days	

Clinical & Interpretive

Clinical Information

Enolase is a glycolytic enzyme that catalyzes the conversion of 2-phosphoglycerate to phosphoenolpyruvate. Enolase exists in the form of several tissue-specific isoenzymes, consisting of homo or heterodimers of 3 different monomer-isoforms (alpha, beta, and gamma). Neuron-specific enolase (NSE) is a 78 kDa gamma-homodimer and represents the dominant enolase-isoenzyme found in neuronal and neuroendocrine tissues. Its levels in other tissues, except erythrocytes, are negligible. The biological half-life of NSE in body fluids is approximately 24 hours.

Due to this organ-specificity, concentrations of NSE in serum or, more commonly, cerebrospinal fluid (CSF) are often elevated in diseases that result in relative rapid (hours/days to weeks rather than months to years) neuronal destruction. Measurement of NSE in serum or CSF can therefore assist in the differential diagnosis of a variety of neuron-destructive and neurodegenerative disorders. The most common application is in the differential diagnosis of dementias, where elevated CSF concentrations support the diagnosis of rapidly progressive dementias, such as Creutzfeldt-Jacob Disease. NSE may also have utility as a prognostic marker in neuronal injury. For example, there is increasing evidence that elevated serum NSE levels correlate with a poor outcome in coma, particularly when caused by hypoxic insult.

Neuron-specific enolase is frequently overexpressed by neural crest-derived tumors. Up to 70% of patients with small cell lung carcinoma (SCLC) have elevated serum NSE concentrations at diagnosis. Approximately 90% of patients with advanced SCLC will have serum levels above the healthy reference range. Other neuroendocrine tumors with frequent expression of NSE include carcinoids (up to 66% of cases), islet cell tumors (typically <40% of cases), and neuroblastoma (exact frequency of NSE expression unknown). NSE levels in NSE-secreting neoplasms correlate with tumor mass and tumor metabolic activity. High levels have, therefore, some negative prognostic value. Falling or rising levels are often correlated with tumor shrinkage or recurrence, respectively.

Reference Values

< or =15 ng/mL

Serum markers are not specific for malignancy, and values may vary by method.

Interpretation

Serum neuron-specific enolase (NSE) measurement has its greatest utility in the follow-up of patients with tumors of any

type that have been shown to secrete NSE. With successful treatment, serum concentrations should fall with a half-life of approximately 24 hours. Persistent NSE elevations in the absence of other possible causes (see Cautions) suggest persistent tumor. Rising levels indicate tumor spread or recurrence in patients who had previously become NSE negative.

In the context of a patient with a lung mass, disseminated malignancy of unknown origin, or symptoms suggestive of paraneoplastic disease without identifiable tumor, elevated NSE levels suggest an underlying small cell lung carcinoma (SCLC).

In patients with suspected carcinoid, islet cell tumor, or neuroblastoma, who have no clear elevations in the primary tumor markers used to diagnose these conditions, an elevated serum NSE level supports the clinical suspicion.
-Carcinoid: chromogranin A, urinary 5-hydroxyindoleacetic acid, serum/blood 5-hydroxytryptamine (serotonin)
-Islet cell tumors: variety of peptide and amine-derived hormones, chromogranin A
-Neuroblastoma: vanillylmandelic acid and homovanillic acid

When considered alongside established outcome predictors of coma, such as Glasgow coma scale and other clinical predictors (papillary light responses, corneal reflexes, motor responses to pain, myoclonus, status epilepticus), electroencephalogram, sensory evoked potentials, measurement of serum NSE concentrations provides additional information. Elevated levels are indicative of a poor outcome. Currently, no established algorithms exist to combine serum NSE concentrations and the various other predictors into a composite score that gives clear predictive outcome information. The NSE measurement, therefore, needs to be considered in a qualitative or semi-quantitative fashion and carefully weighed against other predictors by a physician experienced in examining and managing coma patients.

Cautions

All neuron-specific enolase (NSE) test results must be considered in the clinical context, and interferences or artifactual elevations should be suspected if the clinical NSE test results are at odds with the clinical picture or other tests.

Hemolysis can lead to significant artifactual NSE elevations since erythrocytes contain NSE.

Hemoglobin concentrations as low as 20 mg/dL were found to have an adverse effect on NSE testing.

Proton pump inhibitor treatment, hemolytic anemia, hepatic failure, and kidney failure can also result in artifactual NSE elevations.

Other false-positive results depend on the treating context. When performing NSE testing for tumor diagnosis or follow-up, epileptic seizure, brain injury, encephalitis, stroke, and rapidly progressive dementia might result in false-positive results. On the other hand, when NSE testing is performed to assist in neurological diagnosis, NSE-secreting tumors can represent a source of false-positive results.

Neuron-specific enolase values can vary significantly between methods/assays. Serial follow-up should be performed with the same assay. If assays are changed, patients should have their baseline level reestablished.

This assay is an immunometric assay and can, in rare situations, be affected by false-low results in the presence of extremely high NSE concentrations ("hooking") or autoantibodies to NSE.

In rare cases, some individuals can develop antibodies to mouse or other animal antibodies (often referred to as human anti-mouse antibodies [HAMA] or heterophile antibodies), which may cause interference in some immunoassays. Caution should be used in interpretation of results, and the laboratory should be alerted if the result does not correlate with the clinical presentation.

Clinical Reference

1. Burghuber OC, Worofka B, Schernthaner G, et al. Serum neuron-specific enolase is a useful tumor marker for small cell lung cancer. Cancer. 1990;65(6):1386-1390
2. Lamberts SW, Hofland LJ, Nobels FR. Neuroendocrine tumor markers. Front Neuroendocrinol. 2001;22(4):309-339
3. Aksamit AJ Jr, Preissner CM, Homburger HA. Quantitation of 14-3-3 and neuron-specific enolase proteins in CSF in Creutzfeldt-Jacob disease. Neurology. 2001;57(4):728-730
4. Riley RD, Heney D, Jones DR, et al. A systematic review of molecular and biological tumor markers in neuroblastoma. Clin Cancer Res. 2004;10(1 Pt 1);4-12
5. Portela-Gomes GM, Hacker GW, Weitgasser R. Neuroendocrine cell markers for pancreatic islets and tumors. Appl Immunohistochem Mol Morphol. 2004;12(3):183-192
6. Wijdicks EFM, Hijdra A, Young GB, Bassetti CL, Wiebe S. Quality Standards Subcommittee of the American Academy of Neurology: Practice parameter: prediction of outcome in comatose survivors after cardiopulmonary resuscitation (an evidence-based review). Neurology. 2006;67(2):203-210
7. Huang L, Zhou JG, Yao WX, et al. Systematic review and meta-analysis of the efficacy of serum neuron-specific enolase for early small cell lung cancer screening. Oncotarget. 2017;8(38):64358–64372
8. Cheng F, Yuan Q, Yang J, Wang W, Liu H. The prognostic value of serum neuron-specific enolase in traumatic brain injury: systematic review and meta-analysis. PLoS One. 2014;9(9):e106680
9. Isgro MA, Bottoni P, Scatena R. Neuron-specific enolase as a biomarker: Biochemical and clinical aspects. Adv Exp Med Biol. 2015;867:125-143. doi:10.1007/978-94-017-7215-0_9

Performance

Method Description

Neuron-specific enolase is measured in this homogeneous automated immunofluorescent assay on the BRAHMS Kryptor. The Kryptor uses TRACE (time resolved amplified cryptate emission) technology based on a nonradioactive transfer of energy. This transfer occurs between 2 fluorescent tracers: the donor (europium cryptate) and the acceptor (XL665). In the NSE assay, 2 monoclonal antibodies are labeled, 1 with europium cryptate and 1 with XL665. NSE is sandwiched between the 2 antibodies, bringing them into close proximity. When the antigen-antibody complex is excited with a nitrogen laser at 337 nm, some fluorescent energy is emitted at 620 nm, and the rest is transferred to XL665. This energy is then emitted as fluorescence at 665 nm. A ratio of the energy emitted at 665 nm to that emitted at 620 nm (internal reference) is calculated for each sample. Signal intensity is proportional to the number of antigen-antibody complexes formed and, therefore, to antigen concentration.(Unpublished Mayo method)

PDF Report

No

Day(s) Performed

Monday through Saturday

Test Definition: NSE

Neuron-Specific Enolase, Serum

Report Available
1 to 3 days

Specimen Retention Time
2 weeks

Performing Laboratory Location
Mayo Clinic Laboratories - Rochester Superior Drive

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
83520

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
NSE	Neuron Specific Enolase, S	15060-7

Result ID	Test Result Name	Result LOINC® Value
NSE	Neuron Specific Enolase, S	15060-7