

Overview

Useful For

Assessing neuronal damage related to various neurodegenerative diseases

Method Name

Chemiluminescent Enzyme Immunoassay

NY State Available

Yes

Specimen

Specimen Type

EDTA Plasma

Specimen Required

Supplies: Sarstedt Aliquot Tube, 5 mL (T914)

Collection Container/Tube:

Preferred: Lavender top (EDTA)

Acceptable: None

Submission Container/Tube: Plastic screw-top vial

Specimen Volume: 0.6 mL

Collection Information: Centrifuge and aliquot plasma into a plastic vial. **Do not submit specimen in original tube.**

Forms

[If not ordering electronically, complete, print, and send a Neurology Specialty Testing Client Test Request \(T732\)](#) with the specimen.

Specimen Minimum Volume

0.50 mL

Reject Due To

Gross hemolysis	Reject
Gross lipemia	Reject
Gross icterus	OK

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
EDTA Plasma	Refrigerated (preferred)	14 days	
	Ambient	7 days	
	Frozen	90 days	

Clinical & Interpretive

Clinical Information

Neurofilaments (NF) are exclusively located in the neuronal cytoskeleton and are released to the interstitial fluid upon axonal injury or neurodegeneration. NF concentrations in cerebrospinal fluid (CSF) and blood have been shown to correlate with the extent of axonal damage or neurodegeneration in various neurodegenerative diseases. Of the family of NF proteins, neurofilament light chain (NfL) has gained the most interest as a candidate marker of neurodegeneration. During axonal damage, NfL is released into the CSF, and eventually into the blood where concentrations are 40-fold lower than in the CSF. Concentrations of NfL in plasma have been shown to be approximately 5% to 10% lower than those measured in serum.

Circulating NfL concentrations increase with age with at a rate approximately 2% to 3% per year of age in both male and female individuals. While the specific cause of this increase has not been elucidated, it is believed to be related to the aging process as well as to the development of subclinical ischemic events. NfL concentrations in blood (plasma or serum) reflect the extent of axonal damage, making them a generic marker of disease activity. Increases in NfL concentrations have been reported in individuals with traumatic brain injury, amyotrophic lateral sclerosis, multiple sclerosis, frontotemporal dementia, Alzheimer disease (AD), and other neurodegenerative diseases.

Plasma neurofilament light chain (NfL) is a non-specific marker of neuro-axonal injury showing promising associations with outcomes in several neurological conditions. In neurodegenerative diseases, NfL may also serve as a prognostic marker of disease progression and drug efficacy biomarker of experimental therapies. In a meta-analysis of AD, frontotemporal dementia, and amyotrophic lateral sclerosis, plasma NfL concentrations were elevated in patients compared to controls with utility in differentiating neurodegenerative conditions from non-neurodegenerative mimics. However, due to a lack of specificity to a particular neurodegenerative disease, its role as a diagnostic marker may be limited.

Reference Values

<2.5 years: < or =12.8 pg/mL

2.5 to 4 years: < or =11.8 pg/mL

5 to 9 years: < or =10.4 pg/mL

10 to 14 years: < or =8.8 pg/mL

15 to 19 years: < or =9.2 pg/mL

20 to 24 years: < or =10.4 pg/mL

25 to 29 years: < or =11.9 pg/mL

30 to 34 years: < or =13.5 pg/mL

35 to 39 years: < or =15.3 pg/mL

40 to 44 years: < or =17.3 pg/mL

45 to 49 years: < or =19.7 pg/mL

50 to 54 years: < or =22.4 pg/mL

55 to 59 years: < or =25.4 pg/mL

60 to 64 years: < or =28.8 pg/mL

65 to 69 years: < or =32.7 pg/mL

70 to 74 years: < or =37.1 pg/mL

75 to 79 years: < or =42.1 pg/mL

80 to 84 years: < or =47.8 pg/mL

> or =85 years: < or =54.3 pg/mL

Interpretation

Interpretation of plasma neurofilament light chain (NfL) concentrations depends on the clinical context.

Normal plasma NfL concentrations are generally consistent with the absence of neurodegeneration. In patients receiving therapy for multiple sclerosis (MS), normal or decreased NfL concentrations would suggest treatment response and a more favorable prognosis.

Increased plasma NfL concentrations are consistent with the presence of neurodegeneration. In patients with a known neurologic condition, elevated NfL or increased concentrations from an established, patient-specific baseline may indicate poorer prognosis and/or disease progression.

In multiple sclerosis, NfL is most valuable as a prognostic indicator for severity of disease, disease progression, and as an indicator of response to therapy. Baseline plasma NfL concentrations are a valuable contribution to the initial workup in patients with diagnosed or suspected MS and should be interpreted in the context of other clinical information. The Consortium of Multiple Sclerosis Centers recommends measurement of blood NfL at baseline and regular follow-up (3-6 months) for obtaining prognostic information and evaluating treatment response.(1) Elevated baseline or increasing NfL concentrations can predict multiple sclerosis relapses and other disease activity. The use of blood NfL in serial disease monitoring and treatment response has been evaluated in various prospective clinical trials. Reductions in NfL concentrations after different treatments tend to follow the hierarchy of treatment efficacy, with greatest reductions observed with the most intensive treatments. A study that included over 1000 patients with MS receiving various treatments, reported the largest reductions in plasma NfL concentrations following alemtuzumab treatment (54% reduction), and the smallest reduction with teriflunomide treatment (7%).(2)

Pediatric-onset MS prevalence and incidence rates are increasing globally. Between 3% and 10% of patients with MS present under 16 years of age. Guidelines for pediatric MS recommend that treatment can be started early in the disease course. Plasma NfL is helpful to predict disease severity and to guide treatment decisions in patients with pediatric MS. Elevated blood NfL concentrations were significantly associated with higher numbers of cerebral and spinal MRI lesions at baseline. High concentrations of circulating NfL may be predictive of MS disease events within four months.(3,4)

The nonspecific increase of NfL in a number of neurodegenerative disorders reduces the utility of NfL for differentiation of Alzheimer Disease (AD) from other cause of dementia. Measuring NfL in the context of AD likely has limited clinical utility.

In amyotrophic lateral sclerosis (ALS), NfL concentrations have been suggested to be able to discriminate ALS from ALS-mimics. NfL concentrations at symptom onset may be prognostic of disease progression rate and may be used to stratify patients into groups with a similar prognosis in clinical trials. Blood NfL concentrations remain relatively stable

throughout the disease. A longitudinal decline in NfL concentrations has been described with some ALS treatments. For example, the US Food and Drug Administration has approved Qalsody (tofersen) to treat patients with ALS associated with a genetic variant in the superoxide dismutase 1 (*SOD1*) gene. The approval was based on a reduction in plasma NfL concentrations at the end treatment compared to the placebo arm. For other ALS therapies such as riluzole, NfL concentrations have been reported not to be useful for monitoring treatment effects.

Parkinson disease (PD) patients with elevated NfL concentrations have been reported to have worse cognitive decline, brain cortical atrophy, and motor scores. Blood NfL concentrations in atypical forms of Parkinson disease are higher than in PD and may be used to help differentiate PD from atypical parkinsonian disorders such as progressive supranuclear palsy, corticobasal degeneration, and multiple system atrophy.

In frontotemporal dementia (FTD), NfL concentrations differ according to the underlying mutation - they are highest in people with the *GRN* mutation and lowest in people with the *MAPT* mutation. These levels rise in the presymptomatic stages of FTD, and the timing of preclinical increases differs with the underlying mutation.

In traumatic brain injury (TBI), blood NfL concentrations have been evaluated both in the context of mild TBI (mTBI) diagnosis (acute setting) and prognosis (outcome prediction). In the acute setting, the utility of NfL in identifying mTBI within 24 hours of an injury has been controversial, likely due to the different timepoints used in studies for evaluating NfL concentrations after the injury (ranging from 1-, 4-, 6-, 12-, and 24-hours post-injury). A recent 2022 review describes the findings of six different publications looking at the role of NfL in acute mTBI concluding that, although the clinical usefulness of blood NfL for acute diagnosis of mild TBI is uncertain, the biomarker shows promise for the prognosis of complications of mild TBI, neuroimaging findings and recovery when measured during the first days to weeks after injury.(5)

In hypoxic-ischemic brain injury, NfL is a promising prognostic marker after cardiac arrest. NfL concentrations increase within the first 24 hours after cardiac arrest and the increased concentrations persist for days to months. A recent meta-analysis showed that elevated NfL concentrations 48 hours after cardiac arrest predict poor neurological outcomes.(6) Several studies have shown that the prognostic value of blood NfL in this context is higher than that of other blood biomarkers routinely used for cardiac arrest prognosis including neuron-specific enolase, S100 and total-Tau.

Cautions

Increases in neurofilament light chain (NfL) are not disease specific. Results should only be used in conjunction with other clinical information when evaluating patients with neurodegeneration.

Higher concentrations of NfL may be found in persons with history of stroke, atrial fibrillation, myocardial infarction, chronic kidney disease, pregnancy, and diabetes.

Lower concentrations of NfL may be found in individuals with a body mass index of 30 or more.

Neurofilament light chain concentrations obtained with different methods may be different and cannot be used interchangeably.

All immunometric assays can, on rare occasions, be subject to a hooking effect at extremely high analyte concentrations (false-low results), heterophilic antibody interference (false-high results), or autoantibody interference (unpredictable

effects). If the laboratory result does not fit the clinical picture, these possibilities should be considered.

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

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6. Wang SL, Li N, Feng SY, Li Y. Serum neurofilament light chain as a predictive marker of neurologic outcome after cardiac arrest: a meta-analysis. *BMC Cardiovasc. Disord.* 2023;23(1):193
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12. Ashrafzadeh-Kian S, Figdore D, Larson B, et al. Head-to-head comparison of four plasma neurofilament light chain (NfL) immunoassays. *Clin Chim Acta*. 2024;561:119817. doi: 10.1016/j.cca.2024.119817
13. Figdore DJ, Ashrafzadeh-Kian S, Pazdernik VK, Algeciras-Schimrich A, Bornhorst JA. Determination of pediatric and adult reference intervals for neurofilament light chain (NfL) in blood and a comparison to other recent studies. *J Lab Precis Med*. 2024;9:29. doi:10.21037/jlpm-24-33

Performance

Method Description

Plasma calibrator or specimen are added to particle solution. Neurofilament Light (NfL) in specimens or calibrators specifically binds to anti-NfL monoclonal antibody (mouse) on the particles and antigen-antibody immunocomplexes are

formed. The particles are washed and rinsed to remove unbound materials. Alkaline phosphatase (ALP)-labeled anti-NfL monoclonal antibodies (mouse) are added and specifically bind to the prior formed immunocomplexes on the particles, and additional immunocomplexes are formed. The particles are washed and rinsed to remove unbound materials. Substrate solution is added and mixed with the particles and 3-(2'-spiroadamantane)-4-methoxy-4-(3"-phosphoryloxy) phenyl-1,2-dioxetane disodium salt (AMPPD) contained in the substrate solution is dephosphorylated by the catalysis of ALP indirectly conjugated to particles. Luminescence (at a maximum wavelength of 477 nm) is generated by the cleavage reaction of dephosphorylated AMPPD. The luminescent signal reflects the amount of NfL in the sample.(Unpublished Mayo method)

PDF Report

No

Day(s) Performed

Monday through Friday

Report Available

1 to 3 days

Specimen Retention Time

3 months

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

83884

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
NFLP	Neurofilament Light Chain, P	101281-4

Result ID	Test Result Name	Result LOINC® Value
NFLP	Neurofilament Light Chain, P	101281-4