MAYO CLINIC LABORATORIES

Test Definition: A1ALC

Alpha-1-Antitrypsin Proteotype S/Z, LC-MS/MS, Serum

Overview

Useful For

Identification of homozygous and heterozygous S and Z proteotypes of alpha-1-antitrypsin deficiency

Profile Information

Test Id	Reporting Name	Available Separately	Always Performed
A1ASZ	A1AT Proteotype S/Z, LC-MS/MS	No	Yes
AATP	Alpha-1-Antitrypsin, S	Yes, (order AAT)	Yes

Reflex Tests

Test Id	Reporting Name	Available Separately	Always Performed
A1APR	Alpha-1-Antitrypsin Phenotype, S	Yes, (order A1APP)	No

Testing Algorithm

If the mass spectrometry proteotype and quantitative serum level are discordant, then phenotyping will be added and performed at an additional charge.

For more information see Alpha-1-Antitrypsin-A Comprehensive Testing Algorithm

Special Instructions

- Alpha 1 Antitrypsin-A Comprehensive Testing Algorithm
- Alpha-1-Antitrypsin Testing Result Table

Method Name

A1ASZ: Liquid Chromatography Tandem Mass Spectrometry (LC-MS/MS)
AATP: Nephelometry
A1APR: Isoelectric Focusing

NY State Available

Yes

Specimen

Specimen Type

Test Definition: A1ALC

Alpha-1-Antitrypsin Proteotype S/Z, LC-MS/MS, Serum

Serum

Specimen Required

Collection Container/Tube:
Preferred: Red top
Acceptable: Serum gel
Submission Container/Tube: Plastic vial
Specimen Volume: 1.25 mL
Collection Instructions: Centrifuge and aliquot serum into a plastic vial.

Forms

If not ordering electronically, complete, print, and send a Gastroenterology and Hepatology Test Request (T728) with the specimen.

Specimen Minimum Volume

0.5 mL

Reject Due To

Gross hemolysis	OK
Gross lipemia	Reject
Gross icterus	OK

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Serum	Refrigerated (preferred)	28 days	
	Ambient	28 days	
	Frozen	28 days	

Clinical & Interpretive

Clinical Information

Alpha-1-antitrypsin (A1A) is a protein that inhibits the enzyme neutrophil elastase. It is predominantly synthesized in the liver and secreted into the bloodstream. The inhibition function is especially important in the lungs because it protects against excess tissue degradation. Tissue degradation due to A1A deficiency is associated with an increased risk for early onset panlobular emphysema, which initially affects the lung bases (as opposed to smoking-related emphysema, which presents with upper-lung field emphysema). Patients may become symptomatic in their 30s and 40s. The most frequent symptoms reported in a National Institute of Health study of 1129 patients with severe deficiency (mean age 46 years) included cough (42%), wheezing (65%), and dyspnea with exertion (84%). Many patients were misdiagnosed as having asthma. It is estimated that approximately one-sixth of all lung transplants are for A1A deficiency. Liver disease can also occur, particularly in children; it occurs much less commonly than emphysema in adults.

A1A deficiency is a relatively common disorder in those of Northern European ancestry. The diagnosis of A1A deficiency is initially made by quantitation of protein levels in serum followed by determination of specific allelic variants by isoelectric focusing (IEF). While there are many different alleles in this gene, only 3 are common. The 3 major alleles include: M (full functioning, normal allele), S (associated with reduced levels of protein), and Z (disease-causing variant associated with liver disease and premature emphysema). The S and Z alleles account for the majority of the abnormal alleles detected in affected patients. As a codominant disorder, both alleles are expressed. An individual of SZ or S-null genotype may have a small increased risk for emphysema (but not liver disease) due to slightly reduced protein levels. On the other hand, an individual with the ZZ genotype is at greater risk for early onset liver disease and premature emphysema. Smoking appears to hasten development of emphysema by 10 to 15 years. These individuals should be monitored closely for lung and liver function.

Historically, IEF has been the primary method for characterizing variants, although in some cases, the interpretation is difficult and prone to error. Serum quantitation is helpful in establishing a diagnosis but can be influenced by other factors. A proteomic method using trypsin-digested sera can detect the mutated peptides of the S and Z alleles but can miss disease alleles other than the S and Z alleles. This test combines all of these methods to provide a comprehensive result.

Reference Values

ALPHA-1-ANTITRYPSIN:
100-190 mg/dL

ALPHA-1-ANTITRYPSIN PROTEOTYPE:
Negative for S and Z phenotype (Non S Non Z)

Interpretation

For each of the possible alpha-1-antitrypsin (A1A) genotypes there is an expected range for the total serum level of A1A. However, a number of factors can influence either the A1A serum level or the A1A proteotype results, including acute illness (A1A is an acute-phase reactant), protein replacement therapy, the presence of other rare variants, or the presence of rare DNA alterations (ie, polymorphisms). When the serum level differs from what is expected for that proteotype (ie, discordant), additional studies are performed to ensure the most appropriate interpretation of test results. Additional follow-up may include A1A phenotyping by isoelectric focusing, obtaining additional clinical information, and DNA sequencing. See Alpha-1-Antitrypsin Testing Result Table.

Cautions

This assay will not detect 5% of the known genetic variants that cause alpha-1-antitrypsin deficiency. Therefore, the absence of a detectable genetic variant does not rule out the possibility that an individual is a carrier of, or affected with, this disease.

Test results should be interpreted in the context of clinical findings, family history, and other laboratory data. Errors in the interpretation of results may occur if information given is inaccurate or incomplete.

Rare variants exist that could lead to false-negative or false-positive results. If results obtained do not match the clinical findings, additional testing should be considered.

Errors in interpretation may occur if patients have had a recent blood transfusion or are on A1A replacement therapy.

Clinical Reference

1. Stoller JK, Aboussouan LS. Alpha-1-antitrypsin deficiency. Lancet. 2005;365(9478):2225-2236
2. McElvaney NG, Stoller JK, Buist AS, et al. Baseline characteristics of enrollees in the National Heart, Lung and Blood Institute Registry of alpha 1-antitrypsin deficiency. Alpha 1-Antitrypsin Deficiency Registry Study Group. Chest. 1997;111(2):394-403
3. Murray JD, Willrich MA, Krowka et al. Liquid chromatography-tandem mass spectrometry based alpha1-antitypsin (AAT) testing, Am J Clin Clin Pathol. 2021;155(4):547-552

Performance

Method Description

Alpha-1-Antitrypsin Proteotype S/Z:
Proteins from patient sera are denatured, reduced, and digested with trypsin to form peptides. Labeled internal standards are added to the peptide mixture and subjected to selective reaction monitoring (SRM) liquid chromatograph-tandem mass spectrometry analysis. The presence or absence of the S and Z mutated peptides are determined by SRM peptide-specific m/z values for both the mutated and nonmutated peptides.(Chen Y, Snyder MR, Zhu Yi, et al: Simultaneous phenotyping and quantification of alpha-1-antitrypsin by liquid chromatography-tandem mass spectrometry. Clin Chem. 2011;57[8]:1161-1168)

Alpha-1-Antitrypsin:
In this Siemens Nephelometer II method, the light scattered onto the antigen-antibody complexes is measured. The intensity of the measured scattered light is proportional to the amount of antigen-antibody complexes in the sample under certain conditions. If the antibody volume is kept constant, the signal behaves proportionally to the antigen volume.

A reference curve is generated by a standard with a known antigen content on which the scattered light signals of the samples can be evaluated and calculated as an antigen concentration. Antigen-antibody complexes are formed when a sample containing antigen and the corresponding antiserum are put into a cuvette. A light beam is generated with a light emitting diode (LED), which is transmitted through the cuvette. The light is scattered onto the immuno-complexes that are present. Antigen and antibody are mixed in the initial measurement, but no complex is formed yet. An antigen-antibody complex is formed in the final measurement.

The result is calculated by subtracting value of the final measurement from the initial measurement. The distribution of intensity of the scattered light depends on the ratio of the particle size of the antigen-antibody complexes to the radiated wavelength.(Instruction manual: Siemens Nephelometer II. Siemens, Inc; Version 2.3, 2008; Addendum to the Instruction Manual 2.3, 08/2017)

PDF Report

No

Day(s) Performed

Monday, Thursday

Report Available
7 to 14 days

Specimen Retention Time
14 days

Performing Laboratory Location
Rochester

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
82103
82542
82104 (if appropriate)

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
A1ALC	A1AT Proteotype S/Z, LC-MS/MS, S	102082-5

Result ID	Test Result Name	Result LOINC® Value
AATP	Alpha-1-Antitrypsin, S	6771-0
34855	A1AT Proteotype S/Z, LC-MS/MS	49244-7