Overview

Useful For
Determining the specific proteotype for prognosis and genetic counseling for patients with alpha-1-antitrypsin deficiency

Profile Information

<table>
<thead>
<tr>
<th>Test ID</th>
<th>Reporting Name</th>
<th>Available Separately</th>
<th>Always Performed</th>
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</thead>
<tbody>
<tr>
<td>A1ASZ</td>
<td>A1AT Proteotype S/Z, LC-MS/MS</td>
<td>No</td>
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<tr>
<td>AATP</td>
<td>Alpha-1-Antitrypsin, S</td>
<td>Yes, (order AAT)</td>
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Reflex Tests

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<th>Reporting Name</th>
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<tr>
<td>A1APR</td>
<td>Alpha-1-Antitrypsin Phenotype, S</td>
<td>Yes, (order A1APP)</td>
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</tbody>
</table>

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

See Alpha-1-Antitrypsin-A Comprehensive Testing Algorithm in Special Instructions.

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
Serum
Test Definition: A1ALC
A1AT Proteotype S/Z, LC-MS/MS, S

Specimen Required
Container/Tube:

Preferred: Red top
Acceptable: Serum gel

Specimen Volume: 1.25 mL

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

Specimen Minimum Volume
0.5 mL

Reject Due To

<table>
<thead>
<tr>
<th>Gross hemolysis</th>
<th>OK</th>
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<tbody>
<tr>
<td>Gross lipemia</td>
<td>Reject</td>
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<tr>
<td>Gross icterus</td>
<td>OK</td>
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Specimen Stability Information

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<tr>
<th>Specimen Type</th>
<th>Temperature</th>
<th>Time</th>
<th>Special Container</th>
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<tbody>
<tr>
<td>Serum</td>
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<tr>
<td></td>
<td>Ambient</td>
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</tr>
<tr>
<td></td>
<td>Frozen</td>
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Clinical and 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 1,129 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 Northern European Caucasians. 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
Test Definition: A1ALC
A1AT Proteotype S/Z, LC-MS/MS, S

include: M (full functioning, normal allele), S (associated with reduced levels of protein), and Z (disease-causing mutation 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, though 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 DNA 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 in Special Instructions.

**Cautions**

This assay will not detect 5% of the known mutations that cause alpha-1-antitrypsin (A1A) deficiency. Therefore, the absence of a detectable mutation 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 our interpretation of results may occur if information given is inaccurate or incomplete.

Rare mutations 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**


Performance

Method Description
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 (LC-MS/MS) 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)


PDF Report
No

Day(s) and Time(s) Test Performed
Monday, Thursday; 10 a.m.

Analytic Time
7 days

Maximum Laboratory Time
14 days

Specimen Retention Time
14 days

Performing Laboratory Location
Rochester

Fees and 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 Regional Manager. 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. This test has not been cleared or approved by the U.S. Food and Drug Administration.

CPT Code Information
82103-Alpha-1-antitrypsin

82542-A1AT proteotype S/Z, LC-MS/MS

82104-Alpha-1-antitrypsin phenotype (if appropriate)

LOINC® Information
### Test Definition: A1ALC
A1AT Proteotype S/Z, LC-MS/MS, S

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<th>Test Order Name</th>
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