**Overview**

**Useful For**
Determining the biochemical phenotype for galactosemia when enzymatic and molecular results are incongruent

**Highlights**
Galactose-1-phosphate uridyltransferase (GALT) deficiency is the most common cause of galactosemia and requires lifelong restriction of dietary galactose.

When enzymatic and molecular results are incongruent for galactosemia, biochemical phenotype in conjunction with GALT enzyme analysis distinguishes between classic galactosemia and other phenotypes.

**Additional Tests**

<table>
<thead>
<tr>
<th>Test ID</th>
<th>Reporting Name</th>
<th>Available Separately</th>
<th>Always Performed</th>
</tr>
</thead>
<tbody>
<tr>
<td>GALT</td>
<td>Gal-1-P Uridyltransferase, RBC</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

**Testing Algorithm**
A quantitative galactose-1-phosphate uridylyltransferase (GALT) level is used in addition to the isoelectric focusing for accurate interpretation. If recent GALT test results are not provided, GALT will be automatically performed at an additional charge. However, if previous GALT results are provided, GALT testing will be cancelled and not charged.

See Galactosemia Testing Algorithm in Special Instructions.

**Special Instructions**
- Informed Consent for Genetic Testing
- Galactosemia Testing Algorithm
- Biochemical Genetics Patient Information
- Informed Consent for Genetic Testing (Spanish)

**Method Name**
GALTP: Isoelectric Focusing
GALT: Enzyme Reaction Followed by Liquid Chromatography-Tandem Mass Spectrometry (LC-MS/MS)

**NY State Available**
Yes

**Specimen**

**Specimen Type**
Whole Blood EDTA

**Advisory Information**
GCT / Galactosemia Reflex, Blood is the preferred test to evaluate for possible diagnosis of galactosemia, routine carrier screening, and follow-up of abnormal newborn screening results.
For monitoring of dietary compliance, see GAL1P / Galactose-1-Phosphate (Gal-1-P), Erythrocytes.

**Necessary Information**

Patient's age is required.

**Specimen Required**

**Container/Tube:** Lavender top (EDTA)

**Specimen Volume:** 3 mL

**Forms**

1. **New York Clients-Informed consent is required.** Document on the request form or electronic order that a copy is on file. The following documents are available in Special Instructions:
   - [Informed Consent for Genetic Testing](T576)
   - [Informed Consent for Genetic Testing-Spanish](T826)

2. [Biochemical Genetics Patient Information](T602) in Special Instructions.

3. If not ordering electronically, complete, print, and send an [Inborn Errors of Metabolism Test Request](T798) with the specimen.

**Specimen Minimum Volume**

2 mL

**Reject Due To**

| Gross hemolysis | Reject |

**Specimen Stability Information**

<table>
<thead>
<tr>
<th>Specimen Type</th>
<th>Temperature</th>
<th>Time</th>
<th>Special Container</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whole Blood EDTA</td>
<td>Refrigerated (preferred)</td>
<td>28 days</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ambient</td>
<td>14 days</td>
<td></td>
</tr>
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</table>

**Clinical and Interpretive**

**Clinical Information**

Galactosemia is an autosomal recessive disorder that results from a deficiency of any 1 of the 3 enzymes catalyzing the conversion of galactose to glucose: galactose-1-phosphate uridylyltransferase (GALT), galactokinase (GALK), and uridine diphosphate galactose-4-epimerase (GALE). GALT deficiency is the most common cause of galactosemia and is often referred to as classic galactosemia. The complete or near-complete deficiency of GALT enzyme is life-threatening if left untreated. Complications in the neonatal period include failure to thrive, liver failure, sepsis, and death; even with survival, long-term intellectual disability can result.

Galactosemia is treated by a galactose-restricted diet, which allows for rapid recovery from the acute symptoms and a generally good prognosis. Despite adequate treatment from an early age, individuals with galactosemia remain at
increased risk for developmental delays, speech problems, and abnormalities of motor function. Females with galactosemia are at increased risk for premature ovarian failure. Based upon reports by newborn screening programs, the frequency of classic galactosemia in the United States is approximately 1 in 30,000, although literature reports range from 1 in 10,000 to 1 in 60,000 live births.

Duarte-variant galactosemia (compound heterozygosity for the Duarte mutation, N314D, and a classic mutation) is generally associated with higher levels of enzyme activity (5%-20%) than classic galactosemia (<5%); however, this may be indistinguishable by newborn screening assays. Typically, individuals with Duarte-variant galactosemia have a milder phenotype, but are also often treated with a low galactose diet during infancy. The LA variant, which consists of N314D and a second mutation, L218L, is associated with higher levels of GALT enzyme activity than the Duarte-variant allele.

In general, molecular genetic analysis with a panel of common mutations is typically performed to determine the specific genotype. If the enzymatic and molecular results are incongruent, biochemical phenotyping and/or molecular sequence analysis may be beneficial to help clarify results to determine a treatment strategy and recurrence risks.

See Galactosemia Testing Algorithm in Special Instructions for additional information.

Reference Values

Descriptive report

Interpretation

An interpretive report will be provided.

A quantitative galactose-1-phosphate uridylytransferase level (GALT / Galactose-1-Phosphate Uridyltransferase [GALT], Blood) is required for accurate interpretation.

See Galactosemia Testing Algorithm in Special Instructions for additional information.

Cautions

A more comprehensive interpretation can be provided when parental specimens are also submitted for testing.

Since transfusion results in replacement of significant number of red cells, the assay should be deferred for 90 days posttransfusion.

Clinical Reference


Performance

Method Description

Isoelectric focusing is used to resolve the isoenzymes of galactose-1-phosphate uridylytransferase (GALT). The band patterns, when used in conjunction with a quantitative GALT result, can be used to predict the GALT phenotype of an individual.
In isoelectric focusing, a pH gradient is established across an agarose gel by adding a select mixture of amphoteric molecules to the gel and applying an electric field to the gel. Each protein (isoenzyme) has its own unique isoelectric point, a pH at which the net charge of the protein is equal to zero. Therefore, if a protein is applied to the gel, it will migrate through the pH gradient in the gel until it reaches its isoelectric point. There the protein will stop and "focus" into distinct bands.

In this procedure, an RBC hemolysate is focused on a 5% agarose gel containing ampholytes of a 5 to 7 pH range. The isoenzyme bands are then visualized by applying a substrate mixture that results in a series of reactions (shown below). The final product, nicotinamide adenine dinucleotide phosphate (NADPH; reduced form), is stained a blue-violet color when it reacts with phenazine methosulfate (PMS) and 3-(4-5 dimethylthiazol-2-yl)l-2,5-diphenyltetrazolium bromide (MTT). (Shin YS, Niedermeier HP, Endres W, et al: Agarose gel isoelectrofocusing of UDP-galactose pyrophosphorylase and galactose-1-phosphate uridylytransferase: developmental aspect of UDP-galactose pyrophosphorylase. Clin Chim Acta 1987;166:27-35, modified to acrylamide as described by Leclerc P, Forest JC: Electrophoretic determination of isoamylases in serum with commercially available reagents. Clin Chem 1982;28:37-40)

<table>
<thead>
<tr>
<th>GALT</th>
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<tbody>
<tr>
<td>Gal-1-P + UDP-Glu</td>
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</tr>
<tr>
<td>Phosphoglucomutase</td>
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<tr>
<td>Glu-1-P + Glu-1-6 diP</td>
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<tr>
<td>Glu-6-P-Dehydrogenase</td>
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<tr>
<td>Glu-6-P + NADP</td>
<td>---------------&gt;</td>
</tr>
<tr>
<td>NADPH + MTT + PMS</td>
<td>---------------&gt;</td>
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</tbody>
</table>

PDF Report
No

Day(s) and Time(s) Test Performed
Thursday; 9 a.m.

Analytic Time
8 days

Maximum Laboratory Time
15 days

Specimen Retention Time
Processed RBC stored 2 months

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.
Test Definition: GALTP
Gal-1-Phos Urdyltrns Phenotype,RBC

- 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
82664
82775

LOINC® Information

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<tr>
<td>GALTP</td>
<td>Gal-1-Phos Urdyltrns Phenotype,RBC</td>
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<table>
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<th>Result LOINC Value</th>
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<td>Gal-1-Phos Urdyltrns Phenotype,RBC</td>
<td>33780-8</td>
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<td>Reviewed By</td>
<td>18771-6</td>
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