Overview

Useful For
Distinguishing between primary and secondary hyperoxaluria
Distinguishing between primary hyperoxaluria types 1, 2, and 3

Genetics Test Information
Primary hyperoxalurias (PH), classified into types 1, 2, and 3, are genetic disorders of oxalate metabolism characterized by increased urinary excretion of oxalic acid and kidney stone formation.

Secondary hyperoxaluria is an acquired condition resulting from either increased intake of dietary oxalate or altered intestinal oxalate absorption.

Highlights
A diagnostic workup in an individual with hyperoxaluria demonstrates increased concentration of oxalate in urinary metabolite screening. If glycolate, glycerate, or 4-hydroxy-2-oxoglutarate is present, a primary hyperoxaluria is indicated.

Each type is distinguished from the others based on the urine profile.

Testing Algorithm
See Hyperoxaluria Diagnostic Algorithm in Special Instructions.

Special Instructions
- Hyperoxaluria Diagnostic Algorithm

Method Name
GasChromatography-MassSpectrometry(GC-MS)

NY State Available
Yes

Specimen
Specimen Type
Urine

Specimen Required
Supplies: Urine Tubes, 10 mL (T068)

Container/Tube: Plastic, 10-mL urine tube

Specimen Volume: 10 mL

Collection Instructions:
1. Have patient void the first-morning specimen, then collect specimen within 2 hours of first-morning void. 2. No preservative.
3. Immediately freeze specimen.

**Forms**

If not ordering electronically, complete, print, and send 1 of the following forms with the specimen:

- [Inborn Errors of Metabolism Test Request](#) (T798)
- [Renal Diagnostics Test Request](#) (T830)

**Specimen Minimum Volume**

1.1 mL

**Reject Due To**

All specimens will be evaluated at Mayo Clinic Laboratories for test suitability.

**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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<tr>
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</tr>
<tr>
<td></td>
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**Clinical and Interpretive**

**Clinical Information**

Increased urinary oxalate frequently leads to renal stone formation and renal insufficiency. Identifying the cause of hyperoxaluria has important implications in therapy, management and prognosis.

Hyperoxalurias are classified as primary and secondary. Primary hyperoxaluria is an inherited disorder of oxalate metabolism while secondary hyperoxaluria is an acquired condition resulting from either increased intake of dietary oxalate or altered intestinal oxalate absorption. Primary hyperoxalurias are classified into types 1, 2, and 3.

Hyperoxaluria type 1 (PH1) is an autosomal recessive disorder resulting in a deficiency of peroxisomal alanine:glyoxylate aminotransferase due to variants in the *AGXT* gene. It is characterized by increased urinary oxalic, glyoxylic, and glycolic acids. PH1 is the most common type with manifestations that include deposition of calcium oxalate in the kidneys (nephrolithiasis, nephrocalcinosis), and end-stage renal disease. Calcium oxalate deposits can be further deposited in other tissues such as the heart and eyes, and lead to a variety of additional symptoms. Age of onset is variable with a small percentage of patients presenting in the first year of life with failure to thrive, nephrocalcinosis, and metabolic acidosis. Approximately half of affected individuals show manifestations of PH1 in late childhood or early adolescence, and the remainder present in adulthood with recurrent renal stones. Some individuals with PH1 respond to supplemental pyridoxine therapy.

Hyperoxaluria type 2 (PH 2) is due to a defect in *GRHPR* gene resulting in a deficiency of the enzyme hydroxypyruvate reductase. PH2 is inherited in an autosomal recessive manner and is identified by an increase in urinary oxalic and glyceric acids. Like PH1, PH2 is characterized by deposition of calcium oxalate in the kidneys (nephrolithiasis, nephrocalcinosis), and end-stage renal disease. Most individuals have symptoms of PH2 during childhood, and it is thought that PH2 is less common than PH1.
Hyperoxaluria type 3 (PH3), due to recessive variants in *HOGA1* (formerly *DHDPSL*), occurs in a small percentage of individuals with primary hyperoxaluria. *HOGA1* encodes a mitochondrial 4-hydroxy-2-oxoglutarate aldolase that catalyzes the 4th step in the hydroxyproline pathway. PH3 is characterized biochemically by increased urinary excretion of oxalate and 4-hydroxy-2-oxoglutarate (HOG). As with PH types 1 and 2, PH type 3 is characterized by calcium-oxalate deposition in the kidneys or kidney stone formation. Most individuals with PH3 have early onset disease with recurrent kidney stones and urinary tract infections as common symptoms. End-stage renal disease is not a characteristic of PH3. Of note, individuals with heterozygous variants in *HOGA1* can have variable and intermittent elevations of urine oxalate.

Secondary hyperoxalurias are due to hyperabsorption of oxalate (enteric hyperoxaluria); total parenteral nutrition in premature infants; ingestion of oxalate, ascorbic acid, or ethylene glycol; or pyridoxine deficiency, and may respond to appropriate therapy.

A diagnostic workup in an individual with hyperoxaluria demonstrates increased concentration of oxalate in urinary metabolite screening. If glycolate, glycerate, or HOG is present, a primary hyperoxaluria is indicated. Additional analyses can include molecular testing for PH1 (AGXTZ / *AGXT* Gene, Full Gene Analysis), PH2 (GRHPZ / *GRHPR* Gene, Full Gene Analysis, Varies), or PH3 (*HOGA1* sequencing).

**Reference Values**

**REPORTING/INTERPRETING RESULTS**

**Reference Intervals (Normal Ranges):**

**GLYCOLATE**

\[< \text{or} = 17 \text{ years}: < \text{or} = 75 \text{ mg/g creatinine} \]
\[
> \text{or} = 18 \text{ years}: < \text{or} = 50 \text{ mg/g creatinine}
\]

**GLYCERATE**

\[< \text{or} = 31 \text{ days}: < \text{or} = 75 \text{ mg/g creatinine} \]

\[
32 \text{ days} - 4 \text{ years}: < \text{or} = 125 \text{ mg/g creatinine}
\]

\[
5 - 10 \text{ years}: < \text{or} = 55 \text{ mg/g creatinine}
\]

\[
> \text{or} = 11 \text{ years}: < \text{or} = 25 \text{ mg/g creatinine}
\]

**OXALATE**

\[< \text{or} = 6 \text{ months}: < \text{or} = 400 \text{ mg/g creatinine} \]

\[
7 \text{ months} - 1 \text{ year}: < \text{or} = 300 \text{ mg/g creatinine}
\]

\[
2 - 6 \text{ years}: < \text{or} = 150 \text{ mg/g creatinine}
\]

\[
7 - 10 \text{ years}: < \text{or} = 100 \text{ mg/g creatinine}
\]

\[
> \text{or} = 11 \text{ years}: < \text{or} = 75 \text{ mg/g creatinine}
\]
Test Definition: HYOX
Hyperoxaluria Panel, U

4-HYDROXY-2-OXOGLUTARATE (HOG)

< or =10 mg/g creatinine

**Interpretation**

Increased concentrations of oxalate and glycolate indicate type 1 hyperoxaluria.

Increased concentrations of oxalate and glycerate indicate type 2 hyperoxaluria.

Increased concentrations of oxalate and 4-hydroxy-2-oxoglutarate indicate type 3 hyperoxaluria.

Increased concentrations of oxalate with normal concentrations of glycolate, glycerate, and 4-hydroxy-2-oxoglutarate indicate secondary hyperoxaluria.

**Cautions**

Ascorbic acid (vitamin C) will falsely elevate oxalic acid results.

**Clinical Reference**


**Performance**

**Method Description**

Urine samples corresponding to 0.25 mg of creatinine (not to exceed 1 mL of urine) are oximated by reaction with methoxyamine hydrochloride to stabilize one of the target analytes, 4-hydroxy-2-oxoglutaric (HOG). The urine is then acidified and extracted with ethyl acetate:isopropanol. After evaporation, the dry residue is silylated with BSTFA/1%TMCS:pyridine and analyzed by capillary gas chromatography/mass spectrometry (GC/MS). (Unpublished Mayo method)

**PDF Report**

No

**Day(s) and Time(s) Test Performed**

Thursday; 8 a.m.

**Analytic Time**

14 days
Specimen Retention Time
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.
- 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
82542

LOINC® Information

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