Overview

Useful For
Distinguishing type 1 from type 2 diabetes mellitus

Identifying individuals at risk of type 1 diabetes (including high-risk relatives of patients with diabetes)

Predicting future insulin requirement treatment in patients with adult-onset diabetes

Highlights
This evaluation consisting of tests for 4 antibodies targeting islet cell antigens (GAD65, IA-2, ZnT8, and insulin) gives optimum sensitivity and specificity for the diagnosis of type 1 diabetes mellitus.

Profile Information

<table>
<thead>
<tr>
<th>Test ID</th>
<th>Reporting Name</th>
<th>Available Separately</th>
<th>Always Performed</th>
</tr>
</thead>
<tbody>
<tr>
<td>DMEI</td>
<td>Diabetes Interpretation, S</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>GD65S</td>
<td>GAD65 Ab Assay, S</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>INAB</td>
<td>Insulin Abs, S</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>IA2</td>
<td>IA-2 Ab, S</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>EZNT8</td>
<td>ZnT8 Ab, S</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Method Name
GD65S, INAB, IA2: Radioimmunoassay (RIA)

EZNT8: Enzyme-Linked Immunosorbent Assay (ELISA)

DMEI: Interpretive Comments

NY State Available
Yes

Specimen

Specimen Type
Serum

Specimen Required

Container/Tube:

Preferred: Red top

Acceptable: Serum gel

Specimen Volume: 4 mL
Specimen Minimum Volume
2 mL

Reject Due To

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Gross hemolysis</td>
<td>Reject</td>
</tr>
<tr>
<td>Gross lipemia</td>
<td>Reject</td>
</tr>
<tr>
<td>Gross icterus</td>
<td>Reject</td>
</tr>
</tbody>
</table>

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>Serum</td>
<td>Refrigerated (preferred)</td>
<td>28 days</td>
<td></td>
</tr>
<tr>
<td>Frozen</td>
<td>28 days</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ambient</td>
<td>72 hours</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Clinical and Interpretive

Clinical Information

Islet cell autoantibodies have been known to be associated with type 1 diabetes mellitus since the 1970s. Since 1988, several autoantigens against which islet antibodies are directed have been identified. These include the insulinoma-associated protein 2 (IA-2), glutamic acid decarboxylase 65 (GAD65), insulin and, most recently, the zinc transporter ZnT8.(1) Only 4% to 7% of patients with type 1 diabetes are autoantibody negative, fewer than 10% have only 1 marker, and around 70% have 3 or 4 markers. These findings have been confirmed in multiple specialty laboratories internationally.

One or more of these autoantibodies are detected in 93% to 96% of patients with type 1 diabetes, both adults and children. These antibodies are also detectable in relatives of type 1 diabetic patients at risk for developing diabetes, before clinical onset.(2) Some patients with type 1 diabetes are initially diagnosed as having type 2 diabetes because of symptom-onset in adulthood, societal obesity, and initial insulin-independence. These patients with either "latent autoimmune diabetes in adulthood" or type 1 diabetes mellitus may be distinguished from those patients with type 2 diabetes by detection of 1 or more islet autoantibodies (including ZnT8 antibody). Patients with gestational diabetes can also be stratified for future diabetes risk by detection of 1 or more islet autoantibodies.

Reference Values

GLUTAMIC ACID DECARBOXYLASE (GAD65) ANTIBODY

< or =0.02 nmol/L

Reference values apply to all ages.

INSULIN ANTIBODIES

< or =0.02 nmol/L

Reference values apply to all ages.
ISLET ANTIGEN 2 (IA-2) ANTIBODY
< or =0.02 nmol/L
Reference values apply to all ages.

ZINC Transporter 8 (ZnT8) ANTIBODY
< 15.0 U/mL
Reference values apply to all ages.

Interpretation
Seropositivity for 1 or more islet cell autoantibodies is supportive of:

- A diagnosis of type 1 diabetes. Only 2% to 4% of patients with type 1 diabetes are antibody negative; 90% have more than 1 antibody marker, and 70% have 3 or 4 markers.(1) Patients with gestational diabetes who are antibody seropositive are at high risk for diabetes postpartum. Rarely, diabetic children test seronegative, which may indicate a diagnosis of maturity-onset diabetes of the young in clinically suspicious cases.

- A high risk for future development of diabetes. Among 44 first-degree relatives of patients with type 1 diabetes, those with 3 antibodies had a 70% risk of developing type 1 diabetes within 5 years.(2)

- A current or future need for insulin therapy in patients with diabetes. In the UK Prospective Diabetes Study, 84% of those classified clinically as having type 2 diabetes and seropositive for glutamic acid decarboxylase 65 required insulin within 6 years, compared to 14% that were antibody negative.(3)

Cautions
Negative results do not exclude the diagnosis of or future risk for type 1 diabetes mellitus. The risk of developing type 1 diabetes may be stratified further by testing for HLA genetic markers. Careful monitoring of hyperglycemia is the mainstay for determining the requirement for insulin therapy.

Clinical Reference


Performance
Method Description

Immunoprecipitation assays:

(125)I-labeled recombinant human antigen (glutamic acid decarboxylase 65, islet antigen 2, insulin) is added to the test serum. If antibody is present, it forms a soluble complex with the (125)I-labeled antigen. Subsequent addition of goat-antihuman IgG and IgM precipitates the complex. The amount of radioactivity in the precipitate is proportional to

ELISA

ZnT8 antibodies are principally directed against the C terminal domain of ZnT8. The ZnT8 autoantibody ELISA is based on the bridging principle that employs the ability of divalent ZnT8 autoantibodies to bind to ZnT8 coated on to the plate well with one arm, and to liquid ZnT8-biotin with the other arm. Calibrators or undiluted serum samples in duplicate are added to ZnT8 coated plate wells and incubated overnight. ZnT8-biotin is added to each well and plates. After further incubation, aspiration and wash, streptavidin-peroxidase is added to each well. After further incubation, aspiration and wash, peroxidase substrate is added. After further incubation, 0.5 mol/L H2S04 stop solution is added to each well. Absorbance is measured at 450nm, blanked against wells containing peroxidase substrate and H2S04 only. (Petruzelkova L, Ananieva-Jordanova R, Vcelakova J, et al: The dynamic changes of zinc transporter 8 autoantibodies in Czech children from the onset of Type 1 diabetes mellitus. Diabet Med 2014;31:165-171).

PDF Report

No

Day(s) and Time(s) Test Performed

Monday through Thursday, Sunday; 10 p.m.

GAD65 antibody: Monday through Friday; 4 a.m.; 4 p.m.

Insulin antibodies: Monday, Wednesday, Friday; 4 a.m.

IA-2 antibody: Tuesday, Thursday; 4 a.m.

Zinc Transporter 8 Antibody: Tuesday and Thursday, 10 a.m.

Analytic Time

7 days

Maximum Laboratory Time

10 days

Specimen Retention Time

28 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

See Individual Components
**CPT Code Information**

- 86337-Insulin antibodies
- 86341 x3-Islet cell antibody

**LOINC® Information**

<table>
<thead>
<tr>
<th>Test ID</th>
<th>Test Order Name</th>
<th>Order LOINC Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>DBS1</td>
<td>Diabetes Mellitus Type 1 Evaluation</td>
<td>In Process</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Result ID</th>
<th>Test Result Name</th>
<th>Result LOINC Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>81596</td>
<td>GAD65 Ab Assay, S</td>
<td>30347-9</td>
</tr>
<tr>
<td>89588</td>
<td>IA-2 Ab, S</td>
<td>81155-4</td>
</tr>
<tr>
<td>8666</td>
<td>Insulin Abs, S</td>
<td>60463-7</td>
</tr>
<tr>
<td>34268</td>
<td>Diabetes Interpretation, S</td>
<td>69048-7</td>
</tr>
<tr>
<td>64926</td>
<td>ZnT8 Ab, S</td>
<td>76651-9</td>
</tr>
</tbody>
</table>