

## 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

### Profile Information

Test Id	Reporting Name	Available Separately	Always Performed
DMEI	Diabetes Interpretation, S	No	Yes
GD65S	GAD65 Ab Assay, S	Yes	Yes
INAB	Insulin Abs, S	Yes	Yes
IA2	IA-2 Ab, S	Yes	Yes
EZNT8	ZnT8 Ab, S	Yes	Yes

### 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.

### 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

**Collection Container/Tube:**

**Preferred:** Red top

**Acceptable:** Serum gel

**Submission Container/Tube:** Plastic vial

**Specimen Volume:** 4 mL

**Collection Instructions:** Centrifuge and aliquot serum into a plastic vial.

### Specimen Minimum Volume

2 mL

### Reject Due To

Gross hemolysis	Reject
Gross lipemia	Reject
Gross icterus	Reject

### Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Serum	Ambient	72 hours	
	Refrigerated (preferred)	28 days	
	Frozen	28 days	

## Clinical & 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

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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 (GAD65) 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 human leukocyte antigen genetic markers. Careful monitoring of hyperglycemia is the mainstay for determining the requirement for insulin therapy.

**Clinical Reference**

1. Bingley PJ. Clinical applications of diabetes antibody testing. *J Clin Endocrinol Metab.* 2010;95(1):25-33
2. Bingley PJ, Gale EA. Progression to type 1 diabetes in islet cell antibody-positive relatives in the European Nicotinamide Diabetes Intervention Trial: the role of additional immune, genetic and metabolic markers of risk. *Diabetologia.* 2006;49(5):881-890
3. Turner R, Stratton I, Horton V, et al. UKPDS 25: autoantibodies to islet-cell cytoplasm and glutamic acid decarboxylase for prediction of insulin requirement in type 2 diabetes. UK Prospective Diabetes Study Group. *Lancet.* 1997;350(9087):1288-1293
4. Thomas NJ, Jones AG. The challenges of identifying and studying type 1 diabetes in adults [published online ahead of print, 2023 Sep 20]. *Diabetologia.* 2023;10.1007/s00125-023-06004-4. doi:10.1007/s00125-023-06004-4

**Performance****Method Description**

Radioimmunoassay:

(125)I-labeled recombinant human antigen is incubated with patient sample. Anti-human IgG is then added to form an immunoprecipitate. After washing the immunoprecipitate, the amount of (125)I-labeled antigen in the

immunoprecipitate is measured using a gamma-counter. The amount of gamma emission in the precipitate is proportional to the amount of antigen-specific IgG in the sample. Results are reported as units of precipitated antigen (nMol) per L of patient sample. (Masuda M, Powell M, Chen S, et al. Autoantibodies to IA-2 in insulin-dependent diabetes mellitus. Measurements with a new immunoprecipitation assay. Clin Chim Acta. 2000;291(1):53-66; Walikonis JE, Lennon VA. Radioimmunoassay for glutamic acid decarboxylase [GAD65] autoantibodies as a diagnostic aid for stiff-man syndrome and a correlate of susceptibility to type 1 diabetes mellitus. Mayo Clin Proc. 1998;73[12]:1161-1166; Horta ES, Lennon VA, Lachance DH, et al. Neural autoantibody clusters aid diagnosis of cancer. Clin Cancer Res. 2014;20[14]:3862-9386)

#### Enzyme-Linked Immunosorbent Assay

Zinc transporter 8 (ZnT8) antibodies are principally directed against the C terminal domain of ZnT8. The ZnT8 autoantibody enzyme-linked immunosorbent assay 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 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 sulfuric acid stop solution is added to each well. Absorbance is measured at 450nm, blanked against wells containing peroxidase substrate and sulfuric acid 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(2):165-171)

#### PDF Report

No

#### Day(s) Performed

GAD65 antibody: Monday through Friday

Insulin antibodies: Monday, Wednesday, Friday

IA-2 antibody, Zinc Transporter 8 Antibody: Tuesday, Thursday

#### Report Available

7 to 10 days

#### Specimen Retention Time

28 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**

See Individual Test IDs

**CPT Code Information**

86337

86341 x3

**LOINC® Information**

Test ID	Test Order Name	Order LOINC® Value
DBS1	Diabetes Mellitus Type 1 Evaluation	104673-9

Result ID	Test Result Name	Result LOINC® Value
81596	GAD65 Ab Assay, S	30347-9
89588	IA-2 Ab, S	81155-4
8666	Insulin Abs, S	60463-7
34268	Diabetes Interpretation, S	69048-7
64926	ZnT8 Ab, S	76651-9