Test Definition: DBS1

Diabetes Mellitus Type 1 Evaluation

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

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

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

Gross hemolysis	Reject
Gross lipemia	Reject
Gross icterus	Reject

Specimen Stability Information

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

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

1. Bingley PJ: Clinical applications of diabetes antibody testing. J Clin Endocrinol Metab 2010;95:25-33

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;49:881-890

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;350:1288-1293

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

the level of antibody in the serum.(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;291:53-66)

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) 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 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

Test Definition: DBS1

Diabetes Mellitus Type 1 Evaluation

Test ID	Test Order Name	Order LOINC Value
DBS1	Diabetes Mellitus Type 1 Evaluation	In Process

Result ID	Test Result Name	Result LOINC Value
81596	GAD65 Ab Assay, S	94345-6
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