MAYO CLINIC LABORATORIES

Test Definition: INAB

Insulin Antibodies, Serum

Overview

Useful For

Predicting the future development of type 1 diabetes in asymptomatic children, adolescents, and young adults, when used in conjunction with family history, human leukocyte antigen-typing, and other autoantibodies, including glutamic acid decarboxylase (GAD65) and islet cell antigen 2 (IA-2) antibodies

Differential diagnosis of type 1 versus type 2 diabetes

Evaluating diabetics with insulin resistance in patients with established diabetes (type 1 or type 2)

Investigation of hypoglycemia in nondiabetic subjects

Method Name

Radioimmunoassay (RIA)

NY State Available

Yes

Specimen

Specimen Type

Serum

Specimen Required

Supplies: Sarstedt Aliquot Tube, 5 mL (T914)
Collection Container/Tube:
Preferred: Red top
Acceptable: Serum gel
Submission Container/Tube: Plastic vial
Specimen Volume: 1.5 mL
Collection Instructions: Centrifuge and aliquot serum into a plastic vial.

Specimen Minimum Volume

1 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 & Interpretive

Clinical Information

The onset of autoimmune diabetes mellitus (type 1 diabetes mellitus) is preceded (and accompanied) by the appearance of autoantibodies to a variety of pancreatic islet cell antigens in serum, including insulin. The level of these autoantibodies is generally low and may even fall during follow-up. In genetically predisposed, but disease-free, individuals (first degree relatives of patients with type 1 diabetes or individuals with permissive human leukocyte antigen [HLA] alleles), detection of multiple islet cell autoantibodies is a strong predictor for subsequent development of type I diabetes.

Once type 1 diabetes has fully manifested, insulin autoantibody levels usually fall to low or undetectable levels. However, after insulin therapy is initiated, autoantibody production may recur as a memory response. Insulin autoantibody production is more common when therapeutic insulin of animal origin is used (rarely used in contemporary practice). Larger therapeutic doses may be required because of antibody-induced insulin resistance.

Insulin antibodies may be found in nondiabetic individuals complaining of hypoglycemic attacks. In this setting their presence can be an indicator of "factitious hypoglycemia" due to the surreptitious injection of insulin, rather than to a clinical problem (eg, insulinoma). However, insulin autoantibodies in nondiabetic subjects can occasionally develop without exposure to exogenous insulin and may rarely become a cause of episodic hypoglycemia. Anti-idiotypic autoantibodies against insulin autoantibodies have been demonstrated in some cases. Interaction of these antibodies with insulin autoantibodies could displace bound insulin from the insulin autoantibodies, resulting in hypoglycemia.

In addition to IgG and IgM insulin autoantibodies, IgE antibodies (identified by the fluorescence enzyme immunoassay) may occur. IgE insulin autoantibodies result in immediate hypersensitivity reactions, such as urticaria, but do not lead to insulin resistance or hypoglycemia as can be seen with the IgG antibodies. This test only determines the presence of IgG and IgM antibodies, not IgE antibodies.

In conjunction with family history, HLA-typing and measurement of other islet cell autoantibodies (glutamic acid decarboxylase [GAD65] antibody and islet cell antigen 2 antibody [IA-2]), insulin autoantibody testing helps predict the future development of type I diabetes in asymptomatic children, adolescents, and young adults. Inclusion of a recently described fourth autoantibody (zinc transporter 8: ZnT8) further enhances the prediction of type 1 diabetes occurrence and its distinction from type 2 diabetes.

Reference Values

< or =0.02 nmol/L

Reference values apply to all ages.

Interpretation

Seropositivity (> or =0.03 nmol/L) in a patient never treated with insulin is consistent with predisposition to type 1 diabetes. Seropositivity is not as informative of type 2 diabetes status as other islet cell antibodies in patients who are receiving (or have received) insulin therapy because this antibody can arise secondary to therapy. It is thought that high levels of insulin autoantibodies might contribute to insulin resistance.

A family history of type 1 diabetes, other organ-specific autoimmunity and a diabetes-permissive human leukocyte antigen phenotype strengthens the prediction of type 1 diabetes development. The detection of multiple islet cell antibodies is indicative of the likely development of future type 1 diabetes.

In patients presenting with hypoglycemia, the presence of insulin autoantibodies may indicate surreptitious insulin administration or, rarely, insulin autoantibody-related hypoglycemia. The differential diagnosis cannot be made on the basis of insulin autoantibody detection alone. C-peptide and insulin measurements are always required in addition to insulin autoantibody measurements in the diagnosis of hypoglycemia.

Cautions

This test should not be requested in patients who have recently received radioisotopes, therapeutically or diagnostically, because of potential assay interference. The specific waiting period before specimen collection will depend on the isotope administered, the dose given and the clearance rate in the individual patient. Specimens will be screened for radioactivity prior to analysis. Radioactive specimens received in the laboratory will be held 1 week and assayed if sufficiently decayed, or canceled if radioactivity remains.

Clinical Reference

1. Schernthaner G. Immunogenicity and allergenic potential of animal and human insulins. Diabetes Care. 1993;16 Suppl3:155-165
2. Lernmark A. Type 1 diabetes. Clin Chem. 1999;45(8 Pt 2):1331-1338
3. Eisenbarth GS, Jeffery J. The natural history of type 1A diabetes. Arq Bras Endocrinol Metabol. 2008;52(2):146-155
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

(125)I-labeled recombinant human insulin 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 Insulin-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)

PDF Report
No

Day(s) Performed
Sunday, Wednesday

Report Available
3 to 9 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
This test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. It has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information
86337

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
INAB	Insulin Abs, S	60463-7

Result ID	Test Result Name	Result LOINC® Value
8666	Insulin Abs, S	60463-7