

## Overview

### Useful For

Assessing susceptibility to autoimmune (type 1, insulin-dependent) diabetes mellitus and related endocrine disorders (eg, thyroiditis and pernicious anemia)

Distinguishing between patients with type 1 and type 2 diabetes

Confirming a diagnosis of stiff-man syndrome, autoimmune encephalitis, autoimmune ataxia, brain stem encephalitis, autoimmune epilepsy, autoimmune myelopathy; titers generally greater than or equal to 20.0 nmol/L

### Method Name

Radioimmunoassay (RIA)

### NY State Available

Yes

## Specimen

### Specimen Type

Serum

### Ordering Guidance

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.

### Specimen Required

#### Container/Tube:

**Preferred:** Red top

**Acceptable:** Serum gel

**Specimen Volume:** 1.5 mL

### Forms

[If not ordering electronically, complete, print, and send 1 of the following forms with the specimen:](#)

[-General Request \(T239\)](#)

[-Neurology Specialty Testing Client Test Request \(T732\)](#)

### Reject Due To

Gross hemolysis    Reject

Gross lipemia      Reject

Gross icterus      Reject

### Specimen Minimum Volume

1 mL

**Specimen Stability Information**

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

**Clinical & Interpretive****Clinical Information**

Glutamic acid decarboxylase (GAD) is a neuronal enzyme involved in the synthesis of the neurotransmitter gamma-aminobutyric acid (GABA). Antibodies directed against the 65-kD isoform of GAD (GAD65) are encountered at high titers ( $>$  or  $\approx$ 20 nmol/L) in a variety of autoimmune neurologic disorders including stiff-person (Moersch-Woltman) syndrome, autoimmune cerebellitis, brain stem encephalitis, seizure disorders, and other myelopathies.

GAD65 antibody is also the major pancreatic islet antibody and an important serological marker of predisposition to type 1 diabetes. GAD65 autoantibody also serves as a marker of predisposition to other autoimmune disease that occur with type 1 diabetes, including thyroid disease (eg, thyrotoxicosis, Grave disease, Hashimoto thyroiditis, hypothyroidism), pernicious anemia, premature ovarian failure, Addison disease, (idiopathic adrenocortical failure) and vitiligo. GAD65 antibodies are found in the serum of approximately 8% of healthy subjects older than age 50, usually in low titer but often accompanied by related "thyrogastic" autoantibodies.

**Reference Values**

$<$  or  $\approx$ 0.02 nmol/L

Reference values apply to all ages.

**Interpretation**

High titers ( $>$  or  $\approx$ 20.0 nmol/L) are found in classic stiff-person syndrome (93% positive) and in related autoimmune neurologic disorders (eg, acquired cerebellar ataxia, some acquired non-paraneoplastic encephalomyelopathies). Diabetic patients with polyendocrine disorders also generally have glutamic acid decarboxylase (GAD65) antibody values 0.02 nmol/L or above.

Values in patients who have type 1 diabetes without a polyendocrine or autoimmune neurologic syndrome are usually 0.02 nmol/L or below. Low titers (0.03-19.9 nmol/L) are detectable in the serum of approximately 80% of type 1 diabetic patients. Conversely, low titers are detectable in the serum of less than 5% of patients with type 2 diabetes. Testing for autoimmune type 1 diabetes is complimented by testing for insulin, IA-2 and ZnT8 antibodies.

Eight percent of healthy Olmsted County residents over age 50 have low-positive values, and may be at risk for future autoimmune disease.

Values 0.03 nmol/L or above are consistent with susceptibility to autoimmune (type 1) diabetes and related endocrine disorders (thyroiditis and pernicious anemia).

**Cautions**

Antibodies specific for glutamic acid decarboxylase (GAD65) account for most, but not all, antibodies detected in the islet cell antibody test (IA-2). IA-2 (a protein tyrosine kinase-like protein) insulin and zinc transporter-8 antibodies are complementary islet cell antibodies.

---

**Clinical Reference**

1. McKeon A, Tracy JA: GAD65 neurological autoimmunity. *Muscle Nerve*. 2017 Jul;56(1):15-27. doi: 10.1002/mus.25565.
2. Pittock SJ, Yoshikawa H, Ahlskog JE, et al: Glutamic acid decarboxylase autoimmunity with brainstem, extrapyramidal and spinal cord dysfunction. *Mayo Clin Proc*. 2006;81:1207-1214
3. McKeon A, Robinson MT, McEvoy KM, et al: Stiff-man syndrome and variants: clinical course, treatments, and outcomes. *Arch Neurol*. 2012 Feb;69(2):230-238
4. Steriade C, Britton J, Dale RC, et al: Acute symptomatic seizures secondary to autoimmune encephalitis and autoimmune-associated epilepsy: Conceptual definitions. *Epilepsia*. 2020 Jul;61(7):1341-1351
5. Bingley PJ. Clinical applications of diabetes antibody testing. *J Clin Endocrinol Metab*. 2010 Jan;95(1):25-33

**Performance****Method Description**

(125)I-labeled recombinant human glutamic acid decarboxylase (GAD65) is incubated with the patient's diluted serum. Antihuman IgG are then added to form an immunoprecipitate. After washing the precipitated immune complexes, specific antibodies are detected by counting gamma-emission from the pellet's bound (125)I-GAD65. (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 December;73[12]:1161-1166; Horta ES, Lennon VA, Lachance DH, et al: Neural autoantibody clusters aid diagnosis of cancer. *Clin Cancer Res*. 2014;20:3862-9386)

**PDF Report**

No

**Specimen Retention Time**

28 days

**Performing Laboratory Location**

Rochester

**Fees & Codes****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 US Food and Drug Administration.

**CPT Code Information**

86341