
Overview

Useful For

Second-order testing for evaluation of patients with clinical signs and symptoms of humoral immunodeficiency or combined immunodeficiency (cellular and humoral)

Testing Algorithm

Testing includes total immunoglobulin G (IgG) as well as the 4 subclasses of IgG.

See [Celiac Disease Diagnostic Testing Algorithm](#) in Special Instructions

Special Instructions

- [Celiac Disease Diagnostic Testing Algorithm](#)

Method Name

Nephelometry

NY State Available

Yes

Specimen

Specimen Type

Serum

Ordering Guidance

If testing for immunoglobulin (Ig) G4-related diseases, the more appropriate test to order is IGGS4 / Immunoglobulin Subclass IgG4, Serum.

Specimen Required

Patient Preparation: Fasting preferred but not required

Container/Tube:

Preferred: Serum gel

Acceptable: Red top

Specimen Volume: 1 mL

Forms

If not ordering electronically, complete, print, and send a [General Request](#) (T239) with the specimen.

Reject Due To

Gross hemolysis OK
 Gross lipemia Reject
 Gross icterus OK

Specimen Minimum Volume

0.5 mL

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Serum	Refrigerated (preferred)	14 days	
	Ambient	14 days	
	Frozen	14 days	

Clinical & Interpretive
Clinical Information

The most abundant immunoglobulin in human serum is immunoglobulin G (IgG) (approximately 80% of the total). IgG protein is comprised of molecules of 4 subclasses designated IgG1 through IgG4. Each subclass contains molecules with a structurally unique gamma heavy chain. Of total IgG, approximately 65% is IgG1, 25% is IgG2, 6% is IgG3, and 4% is IgG4. Molecules of different IgG subclasses have somewhat different biologic properties (eg, complement fixing ability and binding to phagocytic cells), which are determined by structural differences in gamma heavy chains. Clinical interest in IgG subclasses concerns potential immunodeficiencies (eg, subclass deficiencies) and IgG4-related diseases (eg, IgG4 elevations). This assay is best for deficiency testing, and the IgG4 assay (IGGS4 / Immunoglobulin Subclass IgG4, Serum) is best for IgG4-related disease testing.

Diminished concentrations of IgG subclass proteins may occur in the context of hypogammaglobulinemia (eg, in common variable immunodeficiency where all immunoglobulin classes are generally affected) or deficiencies may be selective, usually involving IgG2. Deficiency of IgG1 usually occurs in patients with severe immunoglobulin deficiency involving other IgG subclasses. Deficiency of IgG2 is more heterogeneous and can occur as an isolated deficiency or in combination with deficiency of immunoglobulin A (IgA), or of IgA and other IgG subclasses. Most patients with IgG2 deficiency present with recurrent infections, usually sinusitis, otitis, or pulmonary infections. Children with deficiency of IgG2 often have deficient antibody responses to polysaccharide antigens including bacterial antigens associated with *Haemophilus influenzae* type B and *Streptococcus pneumoniae*. Isolated deficiencies of IgG3 or IgG4 occur rarely, and the clinical significance of these findings is not clear.

IgG subclass 4-related disease is a recently recognized syndrome of unknown etiology most often occurring in middle-aged and older men. Several organ systems can be involved and encompasses many previous and newly described diseases such as type 1 autoimmune pancreatitis; Mikulicz disease and sclerosing sialadenitis; inflammatory orbital pseudotumor; chronic sclerosing aortitis; Riedel thyroiditis, a subset of Hashimoto thyroiditis; IgG4-related interstitial pneumonitis; and IgG4-related tubulointerstitial nephritis. Each of these entities is characterized by tumor-like swelling of the involved organs with infiltrative, predominately IgG4-positive, plasma cells with accompanying "storiform" fibrosis. In addition, elevated serum concentrations of IgG4 are found in 60% to 70% of patients diagnosed with IgG4-related disease.

The diagnosis of IgG4-related disease requires a tissue biopsy of the affected organ demonstrating the aforementioned histological features. It is recommended that patients suspected of having an IgG4-related disease have their serum IgG4 level measured.

Testing for IgG subclass levels may be indicated in patients with clinical evidence of a possible immunodeficiency with hypogammaglobulinemic patients or normal concentrations of total serum IgG.

Reference Values

TOTAL IgG

0-<5 months: 100-334 mg/dL

5-<9 months: 164-588 mg/dL

9-<15 months: 246-904 mg/dL

15-<24 months: 313-1,170 mg/dL

2-<4 years: 295-1,156 mg/dL

4-<7 years: 386-1,470 mg/dL

7-<10 years: 462-1,682 mg/dL

10-<13 years: 503-1,719 mg/dL

13-<16 years: 509-1,580 mg/dL

16-<18 years: 487-1,327 mg/dL

> or =18 years: 767-1,590 mg/dL

IgG1

0-<5 months: 56-215 mg/dL

5-<9 months: 102-369 mg/dL

9-<15 months: 160-562 mg/dL

15-<24 months: 209-724 mg/dL

2-<4 years: 158-721 mg/dL

4-<7 years: 209-902 mg/dL

7-<10 years: 253-1,019 mg/dL

10-<13 years: 280-1,030 mg/dL

13-<16 years: 289-934 mg/dL

16-<18 years: 283-772 mg/dL

> or =18 years: 341-894 mg/dL

IgG2

0-<5 months: < or =82 mg/dL

5-<9 months: < or =89 mg/dL

9-<15 months: 24-98 mg/dL

15-<24 months: 35-105 mg/dL

2-<4 years: 39-176 mg/dL

4-<7 years: 44-316 mg/dL

7-<10 years: 54-435 mg/dL

10-<13 years: 66-502 mg/dL

13-<16 years: 82-516 mg/dL

16-<18 years: 98-486 mg/dL

> or =18 years: 171-632 mg/dL

IgG3

0-<5 months: 7.6-82.3 mg/dL

5-<9 months: 11.9-74.0 mg/dL

9-<15 months: 17.3-63.7 mg/dL

15-<24 months: 21.9-55.0 mg/dL

2-<4 years: 17.0-84.7 mg/dL

4-<7 years: 10.8-94.9 mg/dL

7-<10 years: 8.5-102.6 mg/dL

10-<13 years: 11.5-105.3 mg/dL

13-<16 years: 20.0-103.2 mg/dL

16-<18 years: 31.3-97.6 mg/dL

> or =18 years: 18.4-106.0 mg/dL

IgG4

0-<5 months: < or =19.8 mg/dL

5-<9 months: < or =20.8 mg/dL

9-<15 months: < or =22.0 mg/dL

15-<24 months: < or =23.0 mg/dL

2-<4 years: 0.4-49.1 mg/dL

4-<7 years: 0.8-81.9 mg/dL

7-<10 years: 1.0-108.7 mg/dL

10-<13 years: 1.0-121.9 mg/dL

13-<16 years: 0.7-121.7 mg/dL

16-<18 years: 0.3-111.0 mg/dL

> or =18 years: 2.4-121.0 mg/dL

Interpretation

Diminished concentrations of all immunoglobulin G (IgG) subclasses are found in common variable immunodeficiency, combined immunodeficiency, ataxia telangiectasia, and other primary and acquired immunodeficiency diseases.

A diminished concentration of IgG2 protein may be clinically significant in the context of recurrent sinopulmonary infection and may occur with or without concomitant immunoglobulin A deficiency.

Elevated levels of IgG4 are consistent with, but not diagnostic of, IgG4-related disease.

Slightly diminished concentrations of 1 or more IgG subclass proteins are not uncommon, and usually have little clinical significance.

Conversely, some individuals with deficient specific antibody responses to polysaccharide antigens may have normal serum levels of IgG subclasses.

Cautions

Measurement of immunoglobulin G (IgG) subclass proteins is not a first-order test in patients suspected of having an immunodeficiency disease. Quantitation of IgG, immunoglobulin A, and immunoglobulin M levels, along with other first-order tests for immunodeficiency, should be performed first.

Elevations in serum IgG4 concentrations are not specific to IgG4-related disease; they are also found in disorders such as multicentric Castleman disease, allergic disorders, Churg-Strauss syndrome, sarcoidosis, and a large number of other conditions.

Clinical Reference

Umetsu DT, Ambrosino DM, Quinti I, et al: Recurrent sinopulmonary infection and impaired antibody response to bacterial capsular polysaccharide antigen in children with selective IgG-subclass deficiency. *N Engl J Med*

1985;313:1247-1251

Performance

Method Description

In this Siemens Nephelometer II method, the light scattered onto the antigen-antibody complexes is measured. The intensity of the measured scattered light is proportional to the amount of antigen-antibody complexes in the sample under certain conditions. If the antibody volume is kept constant, the signal behaves proportionally to the antigen volume.

A reference curve is generated by a standard with a known antigen content on which the scattered light signals of the samples can be evaluated and calculated as an antigen concentration. Antigen-antibody complexes are formed when a sample containing antigen and the corresponding antiserum are put into a cuvette. A light beam is generated with a light emitting diode (LED), which is transmitted through the cuvette. The light is scattered onto the immuno-complexes that are present. Antigen and antibody are mixed in the initial measurement, but no complex is formed yet. An antigen-antibody complex is formed in the final measurement.

The result is calculated by subtracting value of the final measurement from the initial measurement. The distribution of intensity of the scattered light depends on the ratio of the particle size of the antigen-antibody complexes to the radiated wavelength. (Instruction manual: Siemens Nephelometer II, Siemens, Inc, Newark, DE, Version 3, 2008; Schauer U, Stemberg F, Rieger CH, et al: IgG subclass concentration in certified reference material 470 and reference values for children and adults determined with The Binding Site Reagents. Clin Chem 2003;49[11]:1924-1929)

PDF Report

No

Specimen Retention Time

14 days

Performing Laboratory Location

Rochester

Fees & Codes

Test Classification

This test has been cleared, approved, or is exempt by the US Food and Drug Administration and is used per manufacturer's instructions. Performance characteristics were verified by Mayo Clinic in a manner consistent with CLIA requirements.

CPT Code Information

82784

82787 x 4

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
IGGS	IgG Subclasses, S	47289-4

Result ID	Reporting Name	LOINC®
T_IGG	Total IgG	2465-3
IGG1	IgG 1	2466-1
IGG2	IgG 2	2467-9
IGG3	IgG 3	2468-7
IGG4	IgG 4	2469-5