MAYO CLINIC LABORATORIES

Test Definition: IGGS

IgG Subclasses, Serum

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 IgG as well as the 4 subclasses of IgG.

For more information see Celiac Disease Diagnostic Testing Algorithm

Special Instructions

- Celiac Disease Diagnostic Testing Algorithm

Method Name

Turbidimetry

NY State Available

No

Specimen

Specimen Type

Serum

Ordering Guidance

If testing for immunoglobulin subclass IgG4-related disease, the most appropriate test to order is IGGS4 / IgG4, Immunoglobulin Subclasses, Serum.

Specimen Required

Patient Preparation: Fasting preferred but not required
Collection Container/Tube:
Preferred: Serum gel
Acceptable: Red top
Submission Container/Tube: Plastic vial
Specimen Volume: 1 mL
Collection Instructions: Centrifuge and aliquot serum into a plastic vial.

Forms

If not ordering electronically, complete, print, and send General Request (T239)

Specimen Minimum Volume

See Specimen Required

Reject Due To

Gross hemolysis	Reject
Gross lipemia	Reject
Gross icterus	OK

Specimen Stability Information

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

Clinical & Interpretive

Clinical Information

The most abundant immunoglobulin isotype in human serum is IgG. IgG immunoglobulins are comprised of 4 subclasses designated IgG1 through IgG4. Of total IgG, approximately 65% is IgG1, 25% is IgG2, 6% is IgG3, and 4% is IgG4. Each IgG subclass contains structurally unique portions of the constant region of the gamma heavy chain.

The half-life of IgG1, IgG2, and IgG4 is around 22 days, while IgG3 has a half-life of approximately 7 days. The complement classical pathway is activated most strongly by IgG1 and IgG3 followed by weak strength in activation by IgG2. IgG4 does not activate complement. Clustering of multiple IgG molecules is required to activate complement. Both IgG1 and IgG3 bind Fc receptors on phagocytic cells, activate killer monocytes, and cross the placenta via receptor-mediated active transport. IgG1 is the principal IgG to cross the placenta, and neonatal concentrations are similar to maternal concentrations. Neonates have low production of IgG as the result of immaturity of their immune systems, and IgG concentrations fall through infancy, as the maternally-acquired antibody repertoire is cleared.

Measurement of the concentrations of IgG subclass proteins in serum is useful in evaluating patients with clinical signs and symptoms of humoral immunodeficiency or combined immunodeficiency (cellular and humoral). Diminished concentrations of one or more IgG subclass protein may occur in the context of hypogammaglobulinemia, eg, common variable immunodeficiency or deficiencies may be selective, usually involving IgG subclass 2. Deficiency of IgG subclass 1 usually occurs in patients with severe immunoglobulin deficiency involving other IgG subclasses. Deficiency of IgG subclass 2 is more heterogeneous and can occur as an isolated deficiency or in combination with deficiency of IgA or IgA and other IgG subclasses. Most patients with IgG2 deficiency present with recurrent infections, usually sinusitis, otitis, or pulmonary infections. Children with deficiency of IgG subclass 2 often have deficient antibody responses to polysaccharide antigens, including bacterial antigens associated with *Haemophilus influenzae* type B and *Streptococcus pneumoniae*. Isolated deficiencies of IgG subclass 3 or 4 occur rarely, and the clinical significance of these findings is not clear.

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: < or =49.1 mg/dL
4-<7 years: < or =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: < or =121.7 mg/dL
16-<18 years: < or=111.0 mg/dL
> or =18 years: 2.4-121.0 mg/dL

Interpretation

Diminished concentrations of all 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 IgA deficiency.

Elevated concentration of IgG4 is 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 concentrations of IgG subclasses.

Cautions

Measurement of IgG subclass proteins is not a first-order test in patients suspected of having an immunodeficiency disease. Quantitation of IgG, IgA, and IgM, 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 other conditions.

Clinical Reference

1. Schauer U, Stemberg F, Rieger CHL, 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
2. Dietzen DJ. Amino acids, peptides, and proteins. In: Rifai N, Horvath AR, Wittwer C, eds. Tietz Textbook of Clinical Chemistry and Molecular Diagnostics. 6th ed. Elsevier; 2018:393-394
3. Vidarsson G, Dekkers G, Rispens T. IgG subclasses and allotypes: From structure to effector functions. Front Immunol. 2014;5:520
4. Napodano C, Marino M, Stefanile A, et al. Immunological role of IgG subclasses. Immunol Invest. 2021;50(4):427-444
5. Barton JC, Barton JC, Bertoli LF, Acton RT. Factors associated with IgG levels in adults with IgG subclass deficiency. BMC Immunol. 2021;22(1):53

Performance

Method Description

The determination of the soluble antigen concentration by turbidimetric methods involves the reaction with specific antiserum to form insoluble complexes. When light is passed through the suspension formed a portion of the light is transmitted and focused onto a photodiode by an optical lens system. The amount of transmitted light is indirectly proportional to the specific protein concentration in the test sample.

Concentrations are automatically calculated by reference to a calibrations curve stored within the instrument.(Package inserts: Optilite IgG Kit. The Binding Site Group, Ltd: ver.11, 08/2015; Optilite IgG1. The Binding Site Group, Ltd: ver.23, 07/2019; Optilite IgG2. The Binding Site Group, Ltd: ver.23, 07/2019; Optilite IgG3. The Binding Site Group, Ltd: ver.8, 12/2014; Optilite IgG4. The Binding Site Group, Ltd: ver.23, 07/2019)

PDF Report

No

Day(s) Performed

Monday through Friday, Sunday

Report Available

Same day/1 to 3 days

Specimen Retention Time

14 days

Performing Laboratory Location

Jacksonville

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 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	Test Result Name	Result LOINC® Value
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