MAYO CLINIC LABORATORIES

Test Definition: IGFPN

Insulin-Like Growth Factor 1 and Insulin-Like Growth Factor Binding Protein 3 Growth Panel, Serum

Overview

Useful For

Evaluation of growth disorders

Evaluation of growth hormone deficiency or excess in children and adults

Monitoring of recombinant human growth hormone treatment

Follow-up of individuals with acromegaly and gigantism

Profile Information

Test Id	Reporting Name	Available Separately	Always Performed
IGF1S	Insulin-Like Growth Factor 1, S	Yes	Yes
IGFB3	IGFBP-3, S	Yes	Yes

Method Name

IGF1S: Chemiluminescence
IGFB3: Enzyme-Labeled Chemiluminescent Immunometric Assay

NY State Available

Yes

Specimen

Specimen Type

Serum

Necessary Information

Necessary Information

Indicate patient's age and sex.

Specimen Required

Patient Preparation: For 12 hours before specimen collection, patient **should not** take multivitamins or dietary supplements (eg, hair, skin, and nail supplements) containing biotin (vitamin B7).
Collection Container/Tube:

Preferred: Red top
Acceptable: Serum gel
Submission Container/Tube: 2 Plastic vials
Specimen Volume: 1.6 mL Serum
Collection Instructions: Centrifuge and aliquot serum into 2 plastic vials, each containing 0.8 mL of serum.

Specimen Minimum Volume

Serum: 0.5 mL

Reject Due To

Gross hemolysis	Reject
Gross lipemia	OK
Gross icterus	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Serum	Frozen (preferred)	14 days	
	Ambient	72 hours	
	Refrigerated	72 hours	

Clinical & Interpretive

Clinical Information

Insulin-like growth factor 1 (IGF-1) is a 70-amino acid polypeptide (molecular weight [MW] 7.6 kDa).IGF-1 is the major mediator of the anabolic and growth-promoting effects of growth hormone (GH). IGF-1 is mostly bound to protein, in particular insulin-like growth factor binding protein 3 (IGFBP-3), which also controls its bioavailability and half-life. Noncomplexed IGF-1 and IGFBP-3 have short half-lives (t1/2) of 10 and 30 to 90 minutes, respectively, while the IGFBP-3/IGF-1 complex is cleared with a much slower t1/2 of 12 hours.

Insulin-like growth factor binding protein 3 is a 264-amino acid peptide (MW 29 kDa) produced by the liver. It is the most abundant of a group of IGFBPs that transport and control bioavailability and half-lives of IGFs, in particular IGF-1, the major mediator of the anabolic- and growth-promoting effects of GH. In addition to its IGF binding function, IGFBP-3 also exhibits intrinsic growth-regulating effects that are not yet fully understood but have evoked interest with regards to a possible role of IGFBP-3 as a prognostic tumor marker.

Insulin-like growth factor 1 is produced by many tissues, but the liver is the main source of circulating IGF-1. IGF-1 synthesis in the liver is under the control of GH. The secretion patterns of IGF-1 and IGFBP-3 mimic each other. Unlike GH secretion, which is pulsatile and demonstrates significant diurnal variation, IGF-1 and IGFBP-3 levels show only minor fluctuations. IGF-1 and IGFBP-3 serum levels therefore represent a stable and integrated measurement of GH production

and tissue effect.

Low IGF-1 and IGFBP-3 levels are observed in GH deficiency or GH resistance. If acquired in childhood, these conditions result in short stature. Childhood GH deficiency can be an isolated abnormality or associated with deficiencies of other pituitary hormones. Some of the latter cases may be due to either pituitary or hypothalamic tumors or result from cranial radiation or intrathecal chemotherapy for childhood malignancies. Most GH resistance in childhood is mild-to-moderate, with causes ranging from poor nutrition to severe systemic illness (eg, kidney failure). These individuals may have IGF-1 and IGFBP-3 levels within the reference range. Severe childhood GH resistance is rare and usually due to GH-receptor defects. Both GH deficiency and mild-to-moderate GH resistance can be treated with recombinant human GH (rhGH) injections. The prevalence and causes of adult GH resistance are uncertain, but adult GH deficiency is seen mainly in pituitary tumor patients. It is associated with decreased muscle bulk and increased cardiovascular morbidity and mortality, but replacement therapy remains controversial.

Elevated serum IGF-1 and IGFBP-3 levels indicate a sustained overproduction of GH or excessive rhGH therapy. Endogenous GH excess is caused mostly by GH-secreting pituitary adenomas, resulting in gigantism if acquired before epiphyseal closure and in acromegaly thereafter. Both conditions are associated with generalized organomegaly, hypertension, diabetes, cardiomyopathy, osteoarthritis, compression neuropathies, a mild increase in cancer risk (breast, colon, prostate, lung), and diminished longevity. It is plausible, but unproven, that long-term rhGH overtreatment may result in similar adverse outcomes.

Malnutrition results in low IGF-1 levels, which recover with restoration of adequate nutrition.

Reference Values

INSULIN-LIKE GROWTH FACTOR 1
Male:
<1 year: 27.0-157.0 ng/mL
1 year: 29.7-166.8 ng/mL
2 years: 33.9-183.9 ng/mL
3 years: 39.0-204.5 ng/mL
4 years: 44.3-225.0 ng/mL
5 years: 50.0-245.5 ng/mL
6 years: 56.2-267.1 ng/mL
7 years: 63.4-291.9 ng/mL
8 years: 72.4-323.1 ng/mL
9 years: 83.6-361.6 ng/mL
10 years: 96.9-406.6 ng/mL
11 years: 111.6-454.4 ng/mL
12 years: 126.1-498.7 ng/mL
13 years: 138.6-532.5 ng/mL
14 years: 147.5-551.2 ng/mL
15 years: 152.2-553.5 ng/mL
16 years: 152.9-541.8 ng/mL
17 years: 150.6-520.6 ng/mL

18 years: 146.2-493.6 ng/mL
19 years: 140.2-462.7 ng/mL
20 years: 133.1-430.0 ng/mL
21-25 years: 115.2-354.8 ng/mL
26-30 years: 97.9-281.6 ng/mL
31-35 years: 88.3- 246.0 ng/mL
36-40 years: 83.4-232.7 ng/mL
41-45 years: 74.9-216.4 ng/mL
46-50 years: 66.9-205.1 ng/mL
51-55 years: 60.6-200.3 ng/mL
56-60 years: 54.3-194.2 ng/mL
61-65 years: 48.8-187.7 ng/mL
66-70 years: 46.5-191.9 ng/mL
71-75 years: 40.9-179.2 ng/mL
76-80 years: 37.1-172.0 ng/mL
81-85 years: 33.8-165.4 ng/mL
86-90 years: 32.2-166.1 ng/mL

Females:
<1 year: 17.9-125.6 ng/mL
1 year: 19.5-132.3 ng/mL
2 years: 22.2-145.4 ng/mL
3 years: 25.9-164.2 ng/mL
4 years: 30.7-187.8 ng/mL
5 years: 36.2-214.4 ng/mL
6 years: 42.0-240.4 ng/mL
7 years: 48.6-269.6 ng/mL
8 years: 56.9-305.3 ng/mL
9 years: 67.2-349.4 ng/mL
10 years: 79.5-400.3 ng/mL
11 years: 92.6-452.6 ng/mL
12 years: 105.3- 499.1 ng/mL
13 years: 115.9-533.4 ng/mL
14 years: 123.4-552.0 ng/mL
15 years: 127.4-554.2 ng/mL
16 years: 127.9-541.5 ng/mL
17 years: 125.3-517.3 ng/mL
18 years: 120.5-485.8 ng/mL
19 years: 114.4-450.8 ng/mL
20 years: 107.8-416.0 ng/mL
21-25 years: 92.9-342.0 ng/mL
26-30 years: 78.4-270.0 ng/mL
31-35 years: 73.1-243.0 ng/mL

36-40 years: 69.0-227.0 ng/mL
41-45 years: 61.5-204.4 ng/mL
46-50 years: 56.8-194.5 ng/mL
51-55 years: 53.0-189.6 ng/mL
56-60 years: 45.6-172.4 ng/mL
61-65 years: 42.2-169.0 ng/mL
66-70 years: 38.3-162.5 ng/mL
71-75 years: 36.6-164.7 ng/mL
76-80 years: 34.7-164.8 ng/mL
81-85 years: 34.4-172.4 ng/mL
86-90 years: 33.6-177.8 ng/mL

Tanner stage reference intervals:
Males:
I : 81.3-255.3 ng/mL
II: 106.2-432.3 ng/mL
III: 244.9-511.4 ng/mL
IV: 222.6-577.7 ng/mL
V: 227.4-517.8 ng/mL
Females:
I: 85.9-323.0 ng/mL
II: 117.5-451.3 ng/mL
III: 258.3-528.5 ng/mL
IV: 224.2-585.8 ng/mL
V: 188.2-511.6 ng/mL
Tanner Stage reference source: Bindlingmaier M, Friedrich N, Emeny RT,et al. Reference intervals for insulin-like growth factor-1 (IGF-1) from birth to senescence: results from a multicenter study using a new automated chemiluminescence IGF-I immunoassay conforming to recent international recommendations. J Clin Endocrinol Metab. 2014;99(5):1712-1721

Note: Puberty onset (transition from Tanner stage I to Tanner stage II) occurs for boys at a median age of 11.5 (+/-2) years and for girls at a median age of 10.5 (+/-2) years. There is evidence that it may occur up to 1 year earlier in obese girls and in African American girls. For boys, there is no definite proven relationship between puberty onset and body weight or ethnic origin. Progression through Tanner stages is variable. Tanner stage V (young adult) should be reached by age 18.

INSULIN-LIKE GROWTH FACTOR BINDING PROTEIN 3
1-7 days: < or =0.7 mcg/mL
8-14 days: 0.5-1.4 mcg/mL
15 days-11 months: Unavailable
1 year: 0.7-3.6 mcg/mL
2 years: 0.8-3.9 mcg/mL
3 years: 0.9-4.3 mcg/mL

4 years: 1.0-4.7 mcg/mL
5 years: 1.1-5.2 mcg/mL
6 years: 1.3-5.6 mcg/mL
7 years: 1.4-6.1 mcg/mL
8 years: 1.6-6.5 mcg/mL
9 years: 1.8-7.1 mcg/mL
10 years: 2.1-7.7 mcg/mL
11 years: 2.4-8.4 mcg/mL
12 years: 2.7-8.9 mcg/mL
13 years: 3.1-9.5 mcg/mL
14 years: 3.3-10 mcg/mL
15 years: 3.5-10 mcg/mL
16 years: 3.4-9.5 mcg/mL
17 years: 3.2-8.7 mcg/mL
18 years: 3.1-7.9 mcg/mL
19 years: 2.9-7.3 mcg/mL
20 years: 2.9-7.2 mcg/mL
21-25 years: 3.4-7.8 mcg/mL
26-30 years: 3.5-7.6 mcg/mL
31-35 years: 3.5-7.0 mcg/mL
36-40 years: 3.4-6.7 mcg/mL
41-45 years: 3.3-6.6 mcg/mL
46-50 years: 3.3-6.7 mcg/mL
51-55 years: 3.4-6.8 mcg/mL
56-60 years: 3.4-6.9 mcg/mL
61-65 years: 3.2-6.6 mcg/mL
66-70 years: 3.0-6.2 mcg/mL
71-75 years: 2.8-5.7 mcg/mL
76-80 years: 2.5-5.1 mcg/mL
81-85 years: 2.2-4.5 mcg/mL

Tanner Stages:
Males
Stage I: 1.4-5.2 mcg/mL
Stage II: 2.3-6.3 mcg/mL
Stage III: 3.1-8.9 mcg/mL
Stage IV: 3.7-8.7 mcg/mL
Stage V: 2.6-8.6 mcg/mL

Females
Stage I: 1.2-6.4 mcg/mL
Stage II: 2.8-6.9 mcg/mL
Stage III: 3.9-9.4 mcg/mL

Stage IV: 3.3-8.1 mcg/mL
Stage V: 2.7-9.1 mcg/mL

Note: Puberty onset (transition from Tanner stage I to Tanner stage II) occurs for boys at a median age of 11.5 (+/-2) years and for girls at a median age of 10.5 (+/-2) years. There is evidence that it may occur up to 1 year earlier in obese girls and in African American girls. By contrast, for boys there is no definite proven relationship between puberty onset and body weight or ethnic origin. Progression through Tanner stages is variable. Tanner stage V (young adult) should be reached by age 18.

Interpretation

Both insulin-like growth factor 1 (IGF-1) and insulin-like growth factor binding protein 3 (IGFBP-3) measurements can be used to assess growth hormone (GH) excess or deficiency. However, for all applications, IGF-1 measurement has generally been shown to have superior diagnostic sensitivity and specificity and should be used as the primary test. In particular, in the diagnosis and follow-up of acromegaly and gigantism, IGFBP-3 measurement adds little, if anything, to IGF-1 testing. The combination of IGF-1 and IGFBP-3 measurements appears superior to determining either analyte alone in the diagnosis of GH deficiency and resistance and in the monitoring of recombinant human GH (rhGH) therapy.

Insulin-like growth factor 1 and IGFBP-3 levels below the 2.5th percentile for age are consistent with GH deficiency or severe GH resistance, but patients with incomplete GH deficiency or mild-to-moderate GH resistance may have levels within the reference range. In GH deficiency, GH levels may also be low and can show suboptimal responses in stimulation tests (eg, exercise, clonidine, arginine, ghrelin, growth hormone-releasing hormone, insulin-induced hypoglycemia), while in severe GH resistance, GH levels are substantially elevated. However, dynamic GH testing is not always necessary for diagnosis. If it is undertaken, it should be performed and interpreted in endocrine testing centers under the supervision of a pediatric or adult endocrinologist.

The aim of both pediatric and adult GH replacement therapy is to achieve IGF-1 and IGFBP-3 levels within the reference range, ideally within the middle-to-upper third. Higher levels are rarely associated with any further therapeutic gains but could potentially lead to long-term problems of GH excess.

Elevated IGF-1 and IGFBP-3 levels support the diagnosis of acromegaly or gigantism in individuals with appropriate symptoms or signs. In successfully treated patients, both levels should be within the normal range. In both diagnosis and follow-up, IGF-1 levels correlate better with clinical disease activity than IGFBP-3 levels.

After transsphenoidal removal of pituitary tumors in patients with acromegaly, IGF-1 concentration starts to decrease and returns to normal levels in most patients postoperatively by the fourth day.(1)

Individuals with anorexia or malnutrition have low values of IGF-1. IGF-1 is a more sensitive indicator than prealbumin, retinol-binding protein, or transferrin for monitoring nutritional repletion.

Cautions

Insulin-like growth factor 1 (IGF-1) and insulin-like growth factor binding protein 3 (IGFBP-3) reference ranges are highly age dependent, and results must always be interpreted within the context of the patient's age.

Increased concentrations of IGF-1 are normal during pregnancy, however reference intervals on this population have not been formally established.

Discrepant IGF-1 and IGFBP-3 results can sometimes occur due to liver and kidney disease; however, this is uncommon and such results should alert laboratories and other healthcare professionals to the possible occurrence of a preanalytical or analytical error.

The use of biotin-containing supplements may lead to inaccurately reduced IGF-1 measurements.

Currently, IGF-1 or IGFBP-3 cannot be reliably used as risk indicators or prognostic markers in breast, colon, prostate, or lung cancer.

Insulin-like growth factor 1 and IGFBP-3 assays exhibit variability among platforms and manufacturers. Results obtained with different assay methods or kits should not be used interchangeably.

All immunometric assays can, on rare occasions, be subject to a hooking effect at extremely high analyte concentrations (falsely low results) or heterophilic antibody interference (most often falsely high results). If the laboratory result does not fit the clinical picture, these possibilities should be considered.

Clinical Reference

1. Bidlingmaier M, Friedrich N, Emeny RT, et al. Reference intervals for insulin-like growth factor-1 (IGF-1) from birth to senescence: results from a multicenter study using a new automated chemiluminescence IGF-1 immunoassay conforming to recent international recommendations. J Clin Endocrinol Metab. 2014; 99(5): 1712-1721
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3. Grimberg A, DiVall SA, Polychronakos C, et al. Guidelines for growth hormone and insulin-like growth factor-I treatment in children and adolescents: growth hormone deficiency, idiopathic short stature, and primary insulin-like growth factor-I deficiency. Horm Res Paediatr. 2016;86(6):361-397
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6. Katznelson L, Laws ER, Melmed S, et al. Acromegaly: An endocrine society clinical practice guideline. J Clin Endocrinol Metab. 2014;99(11):3933-3951
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8.Tzanela M. Dynamic tests and basal values for defining active acromegaly. Neuroendocrinology. 2006;83(3-4):200-204
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12. Parama C, Fluiters E, de la Fuente J, Andrade A, Garcia-Mayor RV. Monitoring of treatment success in patients with acromegaly: the value of serum insulin-like growth factor binding protein-3 and serum leptin measurements in comparison to plasma insulin-like growth factor 1 determination. Metabolism. 2001;50(9):1117-1121
13. Monzavi R, Cohen P. IGFs and IGFBPs: Role in health and disease. Best Pract Res Clin Endocrinol Metab. 2002;16(3):433-447
14. Boquete HR, Sobrado PGV, Fideleff HL, et al: Evaluation of diagnostic accuracy of insulin-like growth factor (IGF)-1 and IGF-binding protein-3 in growth hormone-deficient children and adults using ROC plot analysis. J Endocrinol Metab. 2003;88(10):4702-4708
15. Shen Y, Zhang J, Zhao Y, Yan Y, Liu Y, Cai J. Diagnostic value of serum IGF-1 and IGFBP-3 in growth hormone deficiency: a systematic review with meta-analysis. Eur J Pediatr. 2015;174(4):419-427
16. Inoue-Lima TH, Vasques GA, Nakaguma M, et al. A Bayesian approach to diagnose growth hormone deficiency in children: Insulin-like growth factor type 1 is valuable for screening and IGF-binding protein type 3 for confirmation. Horm Res Paediatr. 2020;93(3):197-205

Performance

Method Description

Insulin-Like Growth Factor 1:
Insulin-like growth factor 1 (IGF-1) testing is performed using the IDS iSYS instrument. The assay is based on chemiluminescence technology. Ten microliters of patient sample are incubated with an acidic solution to dissociate IGF-I from the binding proteins. A portion of this, along with neutralization buffer is incubated with a biotinylated anti-IGF-I monoclonal antibody and an acridinium labelled anti-IGF-I monoclonal antibody. Streptavidin-labelled magnetic particles are then added. The magnetic particles are captured using a magnet, and a wash step performed to remove any unbound analyte. Trigger reagents are added; the resulting light emitted by the acridinium label is directly proportional to the concentration of IGF-I in the original sample.(Package insert: IDS-iSYS Insulin-like Growth Factor-I (IGF-I). Immunodiagnostic Systems Inc. IS-3900PLv13. 3/15/2025)

Insulin-Like Growth Factor-Binding Protein 3:
The Immulite 2000 insulin-like growth factor-binding protein 3 (IGFBP-3) assay is a solid-phase, enzyme-linked chemiluminescent immunoassay based on murine monoclonal antibodies. The patient sample and alkaline phosphatase-conjugated anti- IGFBP-3 antibodies are simultaneously incubated with an antibody-coated bead. During this time, IGFBP-3 in the sample forms an antibody sandwich complex that binds to the streptavidin on the bead. Unbound enzyme conjugate is then removed by washing, after which substrate is added. The chemiluminescent substrate, a phosphate ester of adamantyl dioxetane, undergoes hydrolysis in the presence of alkaline phosphatase to yield an unstable intermediate. The continuous production of this intermediate results in the sustained emission of light. The photon output is directly proportional to the concentration of IGFBP-3 in the sample.(Package insert: Immulite 2000 IGFBP-3 PIL2KGB-15. Siemens Healthcare Diagnostics; 03/2018)

PDF Report

No

Day(s) Performed
Monday through Friday

Report Available
1 to 3 days

Specimen Retention Time
2 weeks

Performing Laboratory Location
Mayo Clinic Laboratories - Rochester Superior Drive

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
83520
84305

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
IGFPN	IGF-1, IGFBP-3 Growth Panel	In Process

Result ID	Test Result Name	Result LOINC® Value
IGFB3	IGFBP-3, S	2483-6
IGF1Z	Z-score	73561-3
IGFZ1	Z-score	73561-3
IGF1C	Insulin-Like Growth Factor 1, S	2484-4