Test Definition: IGFB3

Insulin-Like Growth Factor-Binding Protein 3, Serum

Overview

Useful For

Diagnosing growth disorders

Diagnosing adult growth hormone deficiency

Monitoring of recombinant human growth hormone treatment

As a possible adjunct to insulin-like growth factor 1 and growth hormone in the diagnosis and follow-up of acromegaly and gigantism

Method Name

Enzyme-Labeled Chemiluminescent Immunometric Assay

NY State Available

Yes

Specimen

Specimen Type

Serum

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).
Supplies: Sarstedt Aliquot Tube, 5 mL (T914)
Collection Container/Tube:
Preferred: Red top
Acceptable: Serum gel
Submission Container/Tube: Plastic vial
Specimen Volume: 0.8 mL
Collection Instructions: Centrifuge promptly and aliquot serum into a plastic vial.

Specimen Minimum Volume

0.3 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 binding protein 3 (IGFBP-3) is a 264-amino acid peptide (molecular weight 29 kDa) produced by the liver. It is the most abundant of a group of IGFBPs that transport and control bioavailability and half-life of the IGFs, in particular IGF-1, the major mediator of the anabolic- and growth-promoting effects of growth hormone (GH). Noncomplexed IGFBP-3 and IGF-1 have short half-lives (t1/2) of 30 to 90 minutes and 10 minutes, respectively, while the IGFBP-3/IGF-1 complex is cleared with a much slower t1/2 of 12 hours. 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 as a prognostic tumor marker.

The secretion patterns of IGFBP-3 and IGF-1 mimic each other; their respective syntheses are primarily controlled by GH. Unlike GH secretion, which is pulsatile and demonstrates significant diurnal variation, IGFBP-3 and IGF-1 levels show only minor fluctuations. IGFBP-3 and IGF-1 serum levels therefore represent a stable and integrated measurement of GH production and tissue effect.

Low IGFBP-3 and IGF-1 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 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 IGFBP-3 and IGF-1 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, and diminished longevity. It is plausible, but unproven, that long-term rhGH-overtreatment may result in similar adverse outcomes.

Reference Values

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, ie, the transition from Tanner stage I (prepubertal) to Tanner stage II (early pubertal), occurs for girls at a median age of 10.5 (+/-2) years and for boys at a median age of 11.5 (+/-2) years. There is evidence that it may occur up to 1 year earlier in girls who are obese 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 years.

Interpretation

For all applications, insulin-like growth factor 1 (IGF-1) measurement has generally been shown to have superior diagnostic sensitivity and specificity compared with IGF-binding protein 3 (IGFBP-3). IGFBP-3 testing should, therefore, usually be combined with IGF-1 testing. The combination of IGF-1 and IGFBP-3 measurements appears superior to determining either analyte alone in the diagnosis of growth hormone (GH) deficiency and resistance and in the monitoring of recombinant human GH therapy. By contrast, in the diagnosis and follow-up of acromegaly and gigantism, IGFBP-3 measurement adds little if anything to IGF-1 testing.

Insulin-like growth factor 1 and IGFBP-3 levels below the 2.5th percentile for age are consistent with GH deficiency or severe 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 are also low and 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 an 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, ideally within the

lower third. In both diagnosis and follow-up, IGF-1 levels correlate better with clinical disease activity than IGFBP-3 levels.

Cautions

Insulin-like growth factor 1 (IGF-1) and IGF-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.

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

At this time, IGFBP-3 cannot be reliably used as a prognostic marker in breast, colon, prostate, or lung cancer.

Insulin-like growth factor-binding protein 3 assays exhibit significant variability among platforms and manufacturers. Direct comparison of results obtained by different assays is problematic. Reestablishing a patient's baseline concentration is preferred if assays are changed.

In rare cases, some individuals can develop antibodies to mouse or other animal antibodies (often referred to as human anti-mouse antibodies [HAMA] or heterophile antibodies), which may cause interference in some immunoassays. Caution should be used in interpretation of results, and the laboratory should be alerted if the result does not correlate with the clinical presentation.

Clinical Reference

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3. Granada ML, Murillo J, Lucas A, et al. Diagnostic efficiency of serum IGF-1, IGF-binding protein-3 (IGFBP-3), IGF/IGFBP-3 molar ratio and urinary GH measurements in the diagnosis of adult GH deficiency: importance of an appropriate reference population. Eur J Endocrinol. 2000;142(3):243-253
4. 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
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7. 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
8. 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

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 Saturday

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

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value

IGFB3	IGFBP-3, S	2483-6

Result ID	Test Result Name	Result LOINC® Value
IGFB3	IGFBP-3, S	2483-6