MAYO CLINIC LABORATORIES

Test Definition: APGH

Alpha-Subunit Pituitary Tumor Marker, Serum

Overview

Useful For

Adjunct in the diagnosis of pituitary tumors

As part of the follow-up of treated pituitary tumor patients

Differential diagnosis of thyrotropin-secreting pituitary tumor versus thyroid hormone resistance

Differential diagnosis of constitutional delay of puberty versus hypogonadotrophic hypogonadism

Method Name

Immunochemiluminescent Assay

NY State Available

Yes

Specimen

Specimen Type

Serum

Ordering Guidance

This test should not be ordered on pregnant patients.

Specimen Required

Supplies: Sarstedt Aliquot Tube, 5 mL (T914)
Collection Container/Tube:
Preferred: Serum gel
Acceptable: Red top
Submission Container/Tube: Plastic vial
Specimen Volume: 1 mL serum
Collection Instructions: Centrifuge and aliquot serum into a plastic vial

Forms

If not ordering electronically, complete, print, and send an Oncology Test Request (T729) with the specimen.

Specimen Minimum Volume

Serum: 0.35 mL

Reject Due To

Gross hemolysis	Reject
Gross lipemia	OK
Gross icterus	OK

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Serum	Frozen (preferred)	90 days	
	Refrigerated	7 days	

Clinical & Interpretive

Clinical Information

Three human pituitary glycoprotein hormones (luteinizing hormone (LH), follicle-stimulating hormone (FSH), and thyrotropin) and the placenta-derived chorionic gonadotropin are closely related tropic hormones. They signal through G-protein-coupled receptors, regulating hormonal activity of their respective endocrine target tissues. Each is composed of an alpha- and a beta-subunit, coupled by strong noncovalent bonds. The alpha-subunits of all 4 hormones are essentially identical (92 amino acids; molecular weight [MW] of the "naked" protein:10,205 Da), being transcribed from the same gene and showing only variability in glycosylation (MW of the glycosylated proteins: 13,000-18,000 Da). Alpha-subunits are essential for receptor transactivation. By contrast, all the different beta-subunits are transcribed from separate genes, show less homology, and convey the receptor specificity of the dimeric hormones.

Under physiological conditions, alpha- and beta-chain synthesis and secretions are tightly coupled, and only small amounts of monomeric subunits are secreted. However, under certain conditions, coordinated production of intact glycoprotein hormones may be disturbed and disproportionate quantities of free alpha-subunits secreted. In particular, some pituitary adenomas may overproduce alpha subunits. Although most commonly associated with gonadotroph- or thyrotroph-derived tumors, alpha-subunit secretion has also been observed in corticotroph, lactotroph, and somatotroph pituitary adenomas. Overall, depending on cell type and tumor size, 5% to 30% of pituitary adenomas will produce sufficient free alpha-subunits to result in elevated serum levels, which usually fall with successful treatment. Stimulation testing with hypothalamic releasing factors (eg, gonadotropin-releasing hormone [GnRH] or thyrotropin-releasing hormone [TRH]) may result in further elevations disproportionate to those seen in individuals without tumors.

Measurement of free alpha-subunit after GnRH-stimulation testing can also be useful in the differential diagnosis of constitutional delay of puberty (CDP) versus hypogonadotrophic hypogonadism (HH). CDP is a benign, often familial, condition in which puberty onset is significantly delayed but eventually occurs and then proceeds normally. By contrast, HH represents a disease state characterized by lack of gonadotropin production. Its causes are varied, including hypothalamic and pituitary inflammatory or neoplastic disorders, a range of specific genetic abnormalities, as well as unknown causes. In children, HH results in complete failure to enter puberty without medical intervention. In children with CDP, in normal pubertal children, in normal adults and, to a lesser degree, in normal prepubertal children, GnRH administration results in increased serum LH, FSH, and alpha-subunit levels. This response is greatly attenuated in patients with HH, particularly regarding the post-GnRH rise in alpha-subunit concentrations.

Reference Values

PEDIATRIC
< or =5 days: < or =50 ng/mL
6 days-12 weeks: < or =10 ng/mL
3 months-17 years: < or =1.2 ng/mL
Tanner II-IV*: < or =1.2 ng/mL

ADULTS
Males: < or =0.5 ng/mL
Premenopausal females: < or =1.2 ng/mL
Postmenopausal females: < or =1.8 ng/mL

Pediatric and adult reference values based on Mayo studies.

*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 proven relationship between puberty onset and body weight or ethnic origin. Progression through Tanner stages is variable. Tanner stage V (adult) should be reached by age 18.

Interpretation

In the case of pituitary adenomas that do not produce significant amounts of intact tropic hormones, diagnostic differentiation between sellar- and suprasellar tumors of non-pituitary origin (eg, meningiomas or craniopharyngiomas) can be difficult. In addition, if such nonsecreting adenomas are very small, they can be difficult to distinguish from physiological pituitary enlargements.

In a proportion of these cases, free alpha-subunit may be elevated, aiding in diagnosis. Overall, 5% to 30% of pituitary adenomas produce measurable elevation in serum free alpha-subunit concentrations. There is also evidence that an exuberant free alpha-subunit response to thyrotropin-releasing hormone (TRH) administration may occur in some patients with pituitary adenoma that do not have elevated baseline free alpha-subunit levels. A more than 2-fold increase in free alpha-subunit serum concentrations at 30 to 60 minutes following intravenous administration of 500 mcg of TRH is generally considered abnormal, but some investigators consider any increase of serum free alpha-subunit that exceeds the reference range as abnormal. TRH testing is not performed in the laboratory but in specialized clinical testing units under the supervision of a physician.

In pituitary tumor patients with pre-treatment elevations of serum free alpha-subunit, successful treatment is associated with a reduction of serum free alpha-subunit levels. Failure to lower levels into the normal reference range may indicate incomplete cure, and secondary rises in serum free alpha-subunit levels can indicate tumor recurrence.

Small thyrotropin (TSH)-secreting pituitary tumors are difficult to distinguish from thyroid hormone resistance. Both types of patients may appear clinically euthyroid or mildly hyperthyroid and may have mild-to-modest elevations in peripheral thyroid hormone levels along with inappropriately (for the thyroid hormone level) detectable TSH, or mildly-to-modestly elevated TSH. Elevated serum free alpha-subunit levels in such patients suggest a TSH secreting tumor, but genetic variant screening of the thyroid hormone receptor gene may be necessary for a definitive diagnosis.

Constitutional delay of puberty (CDP) is a benign, often familial condition in which puberty onset is significantly delayed but eventually occurs and then proceeds normally. By contrast, hypogonadotrophic hypogonadism (HH) represents a

disease state characterized by lack of gonadotropin production. Its causes are varied, ranging from idiopathic over specific genetic abnormalities to hypothalamic and pituitary inflammatory or neoplastic disorders. In children, it results in complete failure to enter puberty without medical intervention. CDP and HH can be extremely difficult to distinguish from each other. Intravenous administration of 100 mcg gonadotropin-releasing hormone (GnRH) results in much more substantial rise in free alpha-subunit levels in CDP patients, compared with HH patients. A greater than 6-fold rise at 30- or 60-minutes post-injection is seen in more than 75% of patients with CDP, while a less than 2-fold rise appears diagnostic of HH. Increments between 2- and 6-fold are nondiagnostic.

Cautions

False-positive elevations in serum free alpha-subunit levels may be seen in some women if blood specimens are drawn within 24 hours of ovulation.

Patients with kidney failure may have serum free alpha-subunit concentrations of up to 6-times the upper limit of reference range.

Elevated alpha-subunit results on patients with elevated thyrotropin (TSH) should be interpreted with caution due to TSH cross-reactivity with the assay.

Assisted reproduction involving ovarian hyperstimulation or in vitro fertilization may be associated with the elevation in serum free alpha-subunit levels.

Pregnancy is associated with very substantial, physiological elevations in serum free alpha-subunit levels, paralleling chorionic gonadotropin (hCG) secretion. This test should not be ordered on pregnant patients.

Thyrotropin-releasing hormone and gonadotropin releasing hormone testing are not performed in the laboratory, but in specialized clinical testing units under the supervision of a physician.

Clinical Reference

1. Preissner CM, Klee GG, Scheithauer BW, Abboud CF. Free alpha subunit of the pituitary glycoprotein hormones. Measurement in serum and tissue of patients with pituitary tumors. Am J Clin Pathol. 1990;94(4):417-421
2. Samejima N, Yamada S, Takada K, et al. Serum alpha-subunit levels in patients with pituitary adenomas. Clin Endocrinol. 2001:54(4):479-484
3. Mainieri AS, Elnecave RH. Usefulness of the free alpha-subunit to diagnose hypogonadotropic hypogonadism. Clin Endocrinol. 2003;59(3):307-313
4. Socin HV, Chanson P, Delemer B, et al. The changing spectrum of TSH-secreting pituitary adenomas: diagnosis and management in 43 patients. Eur J Endocrinol. 2003;148(4):433-442
5. Solarski M, Rotondo F, Syro LV, Cusimano MD, Kovacs K. Alpha subunit in clinically non-functioning pituitary adenomas: An immunohistochemical study. Pathol Res Pract. 2017;213(9):1130-1133

Performance

Method Description

Alpha-subunit pituitary glycoprotein hormone is measured using an immunochemiluminescent assay sandwich procedure. Standards, controls, and specimens are first incubated with monoclonal antibody-coated beads for 2 hours.

After washing, a different monoclonal antibody labeled with acridinium ester is added and incubated for 1 hour. After washing, the beads (with attached labeled antibody) are counted in a luminometer. The resulting chemiluminescent light units are directly proportional to the amount of alpha-subunit pituitary glycoprotein hormone present in the sample.(Unpublished Mayo method)

PDF Report
No

Day(s) Performed
Friday

Report Available
2 to 8 days

Specimen Retention Time
14 days

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 was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. It has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information
82397

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
APGH	AlphaSubunit Pituitary Tumor Marker	14170-5

Result ID	Test Result Name	Result LOINC® Value
9003	AlphaSubunit Pituitary Tumor Marker	14170-5