MAYO CLINIC LABORATORIES

Test Definition: BHCG

Beta-Human Chorionic Gonadotropin, Quantitative, Serum

Overview

Useful For

Monitoring patients for retained products of conception

Aiding in the diagnosis of gestational trophoblastic disease (GTD), testicular tumors, ovarian germ cell tumors, teratomas, and, rarely, other human chorionic gonadotropin (hCG)-secreting tumors

Serial measurement of hCG following treatment for:
-Monitoring therapeutic response in GTD or in hCG-secreting tumors
-Detecting persistent or recurrent GTD or hCG-secreting tumors

This test is **not intended to** detect or monitor pregnancy.

Method Name

Electrochemiluminescence Immunoassay (ECLIA)

NY State Available

No

Specimen

Specimen Type

Serum

Ordering Guidance

If human chorionic gonadotropin (hCG) during pregnancy is indicated, order THCG / Human Chorionic Gonadotropin (hCG), Quantitative, Pregnancy, Serum.

If hCG testing requested on cerebrospinal fluid specimens to aid in the diagnosis of brain metastases of testicular cancer or extragonadal intracerebral germ cell tumors, order BHSF / Beta-Human Chorionic Gonadotropin, Quantitative, Spinal Fluid.

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: Serum gel
Acceptable: Red top

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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 an Oncology Test Request (T729) with the specimen.

Specimen Minimum Volume

0.75 mL

Reject Due To

Gross hemolysis	Reject
Gross lipemia	OK

Specimen Stability Information

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

Clinical & Interpretive

Clinical Information

Human chorionic gonadotropin (hCG) is a glycoprotein hormone (molecular weight: MW approximately 36,000 Da) consisting of 2 noncovalently bound subunits. The alpha subunit (92-amino acids; "naked" protein MW 10,205 Da) is essentially identical to that of luteinizing hormone (LH), follicle-stimulating hormone, and thyrotropin (previously known as thyroid-stimulating hormone: TSH). The alpha subunit is essential for receptor transactivation. The different beta subunits of the above hormones are transcribed from separate genes, show less homology, and convey the receptor-specificity of the dimeric hormones. The chorionic gonadotropin, beta gene (coding for a 145-amino acid, "naked" protein MW 15,531 Da, glycosylated subunit MW approximately 22,500 Da) is highly homologous to the beta subunit of LH and acts through the same receptor. However, while LH is a classical tropic pituitary hormone, hCG does not usually circulate in significant concentrations. In pregnant primates (including humans) it is synthesized in the placenta and maintains the corpus luteum and, hence, progesterone production, during the first trimester. Thereafter, the placenta produces steroid hormones, diminishing the role of hCG. hCG concentrations fall, leveling off around week 20, significantly above prepregnancy levels. After delivery, miscarriage, or pregnancy termination, hCG falls with a half-life of 24 to 36 hours, until prepregnancy levels are reached.

Outside of pregnancy, hCG may be secreted by abnormal germ cell, placental, or embryonal tissues, in particular seminomatous and nonseminomatous testicular tumors; ovarian germ cell tumors; gestational trophoblastic disease (hydatidiform mole and choriocarcinoma); and benign or malignant nontesticular teratomas. Rarely, other tumors

including hepatic, neuroendocrine, breast, ovarian, pancreatic, cervical, and gastric cancers may secrete hCG, usually in relatively modest quantities.

During pathological hCG production, the highly coordinated secretion of alpha and beta subunits of hCG may be disturbed. In addition to secreting intact hCG, tumors may produce disproportionate quantities of free alpha-subunits or, more commonly, free beta-subunits. Assays that detect both intact hCG and free beta-hCG, including this assay, tend to be more sensitive in detecting hCG-producing tumors.

With successful treatment of hCG-producing tumors, hCG levels should fall with a half-life of 24 to 36 hours, and eventually return to the reference range.

Reference Values

Children(1,2)
Males
Birth-3 months: < or =50 IU/L*
>3 months-<18 years: <1.4 IU/L
Females
Birth-3 months: < or =50 IU/L*
>3 months-<18 years: <1.0 IU/L

*Human chorionic gonadotropin (hCG), produced in the placenta, partially passes the placental barrier. Newborn serum beta-hCG concentrations are approximately 1/400th of the corresponding maternal serum concentrations, resulting in neonate beta-hCG levels of 10-50 IU/L at birth. Clearance half-life is approximately 2 to 3 days. Therefore, by 3 months of age, levels comparable to adults should be reached.

Adults (97.5th percentile)
Males: <1.4 IU/L
Females
Premenopausal, nonpregnant: <1.0 IU/L
Postmenopausal: <7.0 IU/L

Pediatric reference values based on:
1. Chen RJ, Huang SC, Chow SN, Hsieh CY. Human chorionic gonadotropin pattern in maternal circulation. Amniotic fluid and fetal circulation in late pregnancy. J Reprod Med. 1993;38(2):151-154
2. Schneider DT, Calaminus G, Göbel U. Diagnostic value of alpha 1-fetoprotein and beta-human chorionic gonadotropin in infancy and childhood. Pediatr Hematol Oncol. 2001;18(1):11-26

Interpretation

After delivery, miscarriage, or pregnancy termination, human chorionic gonadotropin (hCG) falls with a half-life of 24 to 36 hours, until prepregnancy levels are reached. An absent or significantly slower decline is seen in patients with retained products of conception.

Gestational trophoblastic disease (GTD) is associated with very considerable elevations of hCG, usually above 2 multiples of the medians for gestational age persisting or even rising beyond the first trimester.

Serum hCG levels are elevated in approximately 40% to 50% of patients with nonseminomatous testicular cancer and 20% to 40% of patients with seminoma. Markedly elevated levels of hCG (>5000 IU/L) are uncommon in patients with pure seminoma and indicate the presence of a mixed testicular cancer.

Ovarian germ cell tumors (approximately 10% of ovarian tumors) display elevated hCG levels in 20% to 50% of cases. Teratomas in children may overproduce hCG, even when benign, resulting in precocious pseudopuberty. Levels may be elevated to similar levels as seen in testicular cancer.

Among nonreproductive tumors, hepatobiliary tumors (hepatoblastomas, hepatocellular carcinomas, and cholangiocarcinomas) and neuroendocrine tumors (eg, islet cell tumors and carcinoids) are those most commonly associated with hCG production.

Many hCG-producing tumors also produce other embryonic proteins or antigens, in particular alpha fetoprotein (AFP). AFP should, therefore, also be measured in the diagnostic workup of such neoplasms.

Complete therapeutic response in hCG-secreting tumors is characterized by a decline in hCG levels with an apparent half-life of 24 to 36 hours and eventual return to concentrations within the reference range. GTD and some tumors may produce hyperglycosylated hCG with a longer half-life, but an apparent half-life of more than 3 days suggests the presence of residual hCG-producing tumor tissue.

A rise in hCG levels above the reference range in patients with hCG-producing tumors that had previously been treated successfully, suggests possible local or distant metastatic recurrence.

Cautions

Despite strenuous efforts at standardization, different human chorionic gonadotropin (hCG) assays show only modest agreements with each other. Therefore, whenever serial monitoring of hCG concentration is required, the same assay should be used for all measurements.

Transient elevations of serum hCG can occur following chemotherapy in patients with susceptible tumors, due to massive tumor cell lysis; these transient elevations should not be confused with tumor progression.

Normal serum levels of hCG do not always exclude tumor persistence since tumors may undergo transition to differentiated teratomas, which may not produce hCG.

In individuals with incomplete or complete primary hypogonadism (eg, menopausal women, XXY males, surgically or medically castrated individuals who are receiving inadequate sex steroid-replacement therapy), increased luteinizing hormone (LH)-gene transcription results in minor "leaky" transcription of hCG, and hCG levels of 3 to 5 IU/L and, in some cases, levels as high as 25 IU/L, may be seen. In postmenopausal women, hCG levels ranging from 3.5 to 32 IU/L have been reported. In these cases, measurements of serum concentrations of sex hormones (LH and follicle-stimulating hormone) might be indicated.

End-stage renal failure is associated with up to 10-fold elevations in serum hCG levels.

Among immunometric assays, hCG assays have been found uniquely susceptible to heterophile antibody interference, resulting in occasional false-positive results. Our current assay has been proven robust in this respect, but rare interferences still occur. Typically, the observed false-positive elevations are modest, ranging from just above the reference range to levels of 50 to 60 IU/L. If such results are seen and are discordant with the clinical picture or other biochemical or imaging tests, then the laboratory should be alerted. Rerunning the specimen in question after additional blocking treatment may resolve the issue. For patients with apparent serum hCG concentrations above 15 to 20 IU/L, hCG should also be detectable in urine, if it is truly elevated. Failure to detect urinary hCG in such patients, supports a false-positive serum hCG test.

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. The presence of antibodies to streptavidin or ruthenium can rarely occur and may also interfere in this assay. 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

1. Cole LA, Khanlian SA, Muller CY. Detection of perimenopause or postmenopause human chorionic gonadotropin: an unnecessary source of alarm. Am J Obstet Gynecol. 2008;198:275.e1-275.e7
2. Schneider DT, Calaminus G, Gobel U. Diagnostic value of alpha 1-fetoprotein and beta-human chorionic gonadotropin in infancy and childhood. Pediatr Hematol Oncol. 2001;18(1):11-26
3. Cole LA, Butler S. Detection of hCG in trophoblastic disease. The USA hCG reference service experience. J Reprod Med. 2002;40(6):433-444
4. von Eyben FE. Laboratory markers and germ cell tumors. Crit Rev Clin Lab Sci. 2003;40(4):377-427
5. Sturgeon CM, Duffy MJ, Stenman UH, et al. National Academy of Clinical Biochemistry laboratory medicine practice guidelines for use of tumor markers in testicular, prostate, colorectal, breast, and ovarian cancers. Clin Chem. 2008;54(12):e11-e79
6. Franks CE, Li J, Martinez M, et al. Utility of commercially available quantitative hCG immunoassays as tumor markers in trophoblastic and non-trophoblastic disease. Clin Chem. Published online May 19, 2023. doi:10.1093/clinchem/hvad045

Performance

Method Description

Testing is performed on the Roche cobas e801. The Roche Elecsys HCG+beta (human chorionic gonadotropin) assay is a 2-site immunometric sandwich assay using electrochemiluminescence detection. Patient specimen, biotinylated monoclonal HCG-specific antibody, and monoclonal HCG-specific antibody labeled with a ruthenium react to form a complex. Streptavidin-coated microparticles act as the solid phase to which the complex becomes bound. Voltage is applied to the electrode inducing a chemiluminescent emission from the ruthenium, which is then measured against a calibration curve to determine the amount of HCG in the patient specimen.(Package insert: Elecsys HCG+beta. Roche Diagnostics; V 1.0, 05/2024)

PDF Report

No

Day(s) Performed
Monday through Saturday

Report Available
1 to 3 days

Specimen Retention Time
7 days

Performing Laboratory Location
Mayo Clinic Jacksonville Clinical Lab

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 modified from the manufacturer's instructions. Its performance characteristics were determined by Mayo Clinic in a manner consistent with CLIA requirements. This test has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information
84702

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
BHCG	Beta-HCG, Quantitative, S	21198-7

Result ID	Test Result Name	Result LOINC® Value
BHCG	Beta-HCG, Quantitative, S	21198-7