MAYO CLINIC LABORATORIES

Test Definition: CPR

C-Peptide, Serum

Overview

Useful For

Diagnostic workup of hypoglycemia:
-Diagnosis of factitious hypoglycemia due to surreptitious administration of insulin
-Evaluation of possible insulinoma
-Surrogate measure for the absence or presence of physiological suppressibility of endogenous insulin secretion during diagnostic insulin-induced hypoglycemia (C-peptide suppression test)

Assessing insulin secretory reserve in selected diabetic patients (as listed below) who either have insulin autoantibodies or who are receiving insulin therapy:
-Assessing residual endogenous insulin secretory reserve
-Monitoring pancreatic and islet cell transplant function
-Monitoring immunomodulatory therapy aimed at slowing progression of preclinical, or very early-stage type 1 diabetes mellitus

Method Name

Electrochemiluminescence Immunoassay (ECLIA)

NY State Available

Yes

Specimen

Specimen Type

Serum

Specimen Required

Patient Preparation:
1. Fasting: 8 hours, required
2. 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
Submission Container/Tube: Plastic vial
Specimen Volume: 1 mL
Collection Instructions: Centrifuge and aliquot serum into a plastic vial within 2 hours of collection.

Forms

If not ordering electronically, complete, print, and send 1 of the following forms with the specimen:
-General Request (T239)
-Kidney Transplant Test Request

Specimen Minimum Volume
0.75 mL

Reject Due To

Gross hemolysis	Reject
Gross lipemia	OK
Gross icterus	OK
Autopsy specimen	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Serum	Frozen (preferred)	30 days	
	Refrigerated	7 days	

Clinical & Interpretive

Clinical Information
C-peptide (connecting peptide), a 31-amino-acid polypeptide, represents the midportion of the proinsulin molecule. Proinsulin resembles a hairpin structure, with an N-terminal and C-terminal, which correspond to the A and B chains of the mature insulin molecule, oriented parallel to each other and linked by disulfide bonds. The looped portion of the hairpin between the A and B chains is called C-peptide. During insulin secretion, C-peptide is enzymatically cleaved off and cosecreted in equimolar proportion with mature insulin molecules.

Following secretion, insulin and C-peptide enter the portal circulation and are routed through the liver where at least 50% of the insulin binds to receptors, initiates specific hepatic actions (stimulation of hepatic glucose uptake and suppression of glycogenolysis, gluconeogenesis, and ketogenesis), and is subsequently degraded. Most of the insulin molecules that pass through the liver into the main circulation bind to peripheral insulin receptors, promoting glucose uptake, while the remaining molecules undergo renal elimination. Unlike insulin, C-peptide is subject to neither hepatic nor significant peripheral degradation but is mainly removed by the kidneys. As a result, C-peptide has a longer half-life than insulin (30-35 minutes versus 5-10 minutes), and the molar ratio of circulating insulin to circulating C-peptide is generally below 1, despite equimolar secretion. Until recently, C-peptide was thought to have no physiological function, but it now appears that there may be specific C-peptide cell-surface receptors (most likely belonging to the super-family of G-protein coupled receptors), which influence endothelial responsiveness and skeletal and renal blood flow.

In most disease conditions associated with abnormal serum insulin levels, the changes in serum C-peptide levels parallel insulin-related alterations (insulin to C-peptide molar ratio < or =1). Both serum C-peptide and serum insulin levels are

elevated in kidney failure and in disease states that lead to augmented primary endogenous insulin secretion (eg, insulinoma, sulfonylurea intoxication). Both also may be raised in any disease states that cause secondary increases in endogenous insulin secretion mediated through insulin resistance, primarily obesity, glucose intolerance, and early type 2 diabetes mellitus (DM), as well as endocrine disorders associated with hypersecretion of insulin-antagonistic hormones (eg, Cushing syndrome, acromegaly). Failing insulin secretion in type 1 DM and longstanding type 2 DM is associated with corresponding reductions in serum C-peptide levels.

Discordant serum insulin and serum C-peptide abnormalities are mainly observed in 2 situations: exogenous insulin administration and the presence of anti-insulin autoantibodies. Factitious hypoglycemia due to surreptitious insulin administration results in appropriate suppression of endogenous insulin and C-peptide secretion. At the same time, the peripherally administered insulin bypasses the hepatic first-pass metabolism. In these situations, insulin levels are elevated and C-peptide levels are decreased. In patients with insulin antibodies, insulin levels are increased because of the prolonged half-life of autoantibody-bound insulin. Some patients with anti-idiotypic anti-insulin autoantibodies experience episodic hypoglycemia caused by displacement of autoantibody-bound insulin.

Reference Values

1.1-4.4 ng/mL
Reference interval applies to fasting patients.
Reference intervals have not been formally verified in-house for pediatric patients. The published literature indicates that reference intervals for adult and pediatric patients are comparable.

Interpretation

To compare insulin and C-peptide concentrations (ie, insulin to C-peptide ratio):
-Convert insulin to pmol/L: insulin concentration in mcIU/mL x 6.945 = insulin concentration in pmol/L
-Convert C-peptide to pmol/L: C-peptide concentration in ng/mL x 331 = C-peptide concentration in pmol/L

Factitious hypoglycemia due to surreptitious insulin administration results in elevated serum insulin levels and low or undetectable C-peptide levels, with a clear reversal of the physiological molar insulin to C-peptide ratio (< or =1) to an insulin to C-peptide ratio of greater than 1. By contrast, insulin and C-peptide levels are both elevated in insulinoma and the insulin to C-peptide molar ratio is 1 or less. Sulfonylurea ingestion also is associated with preservation of the insulin to C-peptide molar ratio of 1 or less.

In patients with insulin autoantibodies, the insulin to C-peptide ratio may be reversed to greater than 1, because of the prolonged half-life of autoantibody-bound insulin.

Dynamic testing may be necessary in the workup of hypoglycemia; the C-peptide suppression test is most frequently employed. C-peptide levels are measured following induction of hypoglycemia through exogenous insulin administration. The test relies on the demonstration of the lack of suppression of serum C-peptide levels within 2 hours following insulin-induced hypoglycemia in patients with insulinoma.

Reference intervals have not been formally verified in-house for pediatric patients. The published literature indicates that reference intervals for adult and pediatric patients are comparable.

Cautions

Significant hemolysis will result in artifactually lower C-peptide levels, and such specimens are usually rejected. However, even mild hemolysis can lead to modest decrements in C-peptide values.

There is significant (>20%) cross-reactivity between C-peptide and proinsulin. There is no significant cross-reactivity with other pancreatic islet cell peptides or neuroendocrine peptides.

Very high C-peptide levels (>180 ng/mL) may result in artifactually low measurements (hook effect). Such levels are very unlikely to occur in patients, but if individuals are suspected of having serum levels above 180 ng/mL, the laboratory should be alerted to allow dilution of the specimen prior to testing.

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 also 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.

In the assessment of hypoglycemia, neither C-peptide nor insulin measurements are useful, or indicated, if serum blood glucose levels exceed 60 mg/dL.

In the diagnosis and management of diabetes mellitus, measurement of serum insulin levels usually provides superior information to that of serum C-peptide.

Patients with a body mass index above 25 may have elevated fasting C-peptide levels.

In rare cases, interference due to extremely high titers of antibodies to ruthenium or streptavidin can occur.

Clinical Reference

1. Service FJ, O'Brien PC, Kao PC, Young WF Jr. C-peptide suppression test: effects of gender, age, and body mass index; implications for the diagnosis of insulinoma. J Clin Endocrinol Metab. 1992;74:204-210
2. Lebowitz MR, Blumenthal SA. The molar ratio of insulin to C-peptide. An aid to the diagnosis of hypoglycemia due to surreptitious (or inadvertent) insulin administration. Arch Int Med. 1993;153(5):650-655
3. Leighton E, Sainsbury CA, Jones GC. A practical review of C-peptide testing in diabetes. Diabetes Ther. 2017;8(3):475-487
4. Jones AG, Hattersley AT. The clinical utility of C-peptide measurement in the care of patients with diabetes. Diabet.Med. 2013;30(7):803-817. doi:10.1111/dme.12159
5. Ahn CH, Kim LK, Lee JE, et al. Clinical implications of various criteria for the biochemical diagnosis of insulinoma. Endocrinol Metab (Seoul). 2014;29(4):498-504. doi:10.3803/EnM.2014.29.4.498
6. Young DS, Huth EJ. SI Units for Clinical Measurement. American College of Physicians; 1998

Performance

Method Description

The Roche Elecsys C-peptide assay is a 2-site immunometric (sandwich) assay using electrochemiluminescence detection. Patient specimen, biotinylated monoclonal C-peptide specific antibody, and monoclonal C-peptide-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 C-peptide in the patient specimen.(Package insert: Elecsys C-peptide. Roche Diagnostics; V 2.0 English, 10/2022)

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
84681

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
CPR	C-Peptide, S	13037-7

Result ID	Test Result Name	Result LOINC® Value
CRPN	C-Peptide, S	13037-7