

Overview

Useful For

Diagnosis and differential diagnosis of hypercalcemia

Diagnosis of primary, secondary, and tertiary hyperparathyroidism

Diagnosis of hypoparathyroidism

Monitoring end-stage kidney failure patients for possible renal osteodystrophy

Method Name

Electrochemiluminescence

NY State Available

Yes

Specimen

Specimen Type

Serum

Specimen Required

Patient Preparation:

1. For 12 hours before specimen collection do not take multivitamins or dietary supplements containing biotin (vitamin B7), which is commonly found in hair, skin, and nail supplements and multivitamins.
2. Patient should be fasting for 12 hours

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.

Forms

If not ordering electronically, complete, print, and send a [Renal Diagnostics Test Request](#) (T830) 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	Frozen (preferred)	180 days	
	Refrigerated	72 hours	
	Ambient	8 hours	

Clinical & Interpretive

Clinical Information

Parathyroid hormone (PTH) is produced and secreted by the parathyroid glands, which are located along the posterior aspect of the thyroid gland. The hormone is synthesized as a 115-amino acid precursor (pre-pro-PTH), cleaved to pro-PTH, and then to the 84-amino acid molecule, PTH (numbering, by universal convention, starting at the amino terminus). The precursor forms generally remain within the parathyroid cells.

Secreted PTH undergoes cleavage and metabolism to form carboxyl-terminal fragments (PTH-C), amino-terminal fragments (PTH-N), and mid-molecule fragments (PTH-M). Only those portions of the molecule that carry the amino terminus (ie, the whole molecule and PTH-N) are biologically active. The active forms have half-lives of approximately 5 minutes. The inactive PTH-C fragments, with half-lives of 24 to 36 hours, make up more than 90% of the total circulating PTH and are primarily cleared by the kidneys. In patients with kidney failure, PTH-C fragments can accumulate to very high levels. PTH 1-84 is also elevated in these patients, with mild elevations being considered a beneficial compensatory response to end organ PTH resistance, which is observed in kidney failure.

The serum calcium level regulates PTH secretion via negative feedback through the parathyroid calcium sensing receptor (CASR). Decreased calcium levels stimulate PTH release. Secreted PTH interacts with its specific type II G-protein receptor, causing rapid increases in renal tubular reabsorption of calcium and decreased phosphorus reabsorption. It also participates in long-term calciostatic functions by enhancing mobilization of calcium from bone and increasing kidney synthesis of 1,25-dihydroxy vitamin D, which, in turn, increases intestinal calcium absorption. In rare inherited syndromes of parathyroid hormone resistance or unresponsiveness, and in kidney failure, PTH release may not increase serum calcium levels.

Hyperparathyroidism causes hypercalcemia, hypophosphatemia, hypercalcuria, and hyperphosphaturia. Long-term consequences are dehydration, kidney stones, hypertension, gastrointestinal disturbances, osteoporosis, and sometimes neuropsychiatric and neuromuscular problems. Hyperparathyroidism is most commonly primary and caused by parathyroid adenomas. It can also be secondary in response to hypocalcemia or hyperphosphatemia. This is most commonly observed in kidney failure. Long-standing secondary hyperparathyroidism can result in tertiary hyperparathyroidism, which represents the secondary development of autonomous parathyroid hypersecretion. Rare cases of mild, benign hyperparathyroidism can be caused by inactivating *CASR* genetic variants.

Hypoparathyroidism is most commonly secondary to thyroid surgery but can also occur on an autoimmune basis or due

to activating *CASR* genetic variants. The symptoms of hypoparathyroidism are primarily those of hypocalcemia with weakness, tetany, and possible optic nerve atrophy.

Reference Values

<1 month: 7.0-59 pg/mL

4 weeks-11 months: 8.0-61 pg/mL

12 months-10 years: 11-59 pg/mL

11 years-17 years: 15-68 pg/mL

18 years and older: 15-65 pg/mL

Interpretation

Approximately 90% of the patients with primary hyperparathyroidism have elevated parathyroid hormone (PTH) levels. The remaining patients have normal (inappropriate for the elevated calcium level) PTH levels. Approximately 40% of the patients with primary hyperparathyroidism have serum phosphorus levels below 2.5 mg/dL, and about 80% have serum phosphorus levels below 3.0 mg/dL.

A (appropriately) low PTH level and high phosphorus level in a hypercalcemic patient suggests that the hypercalcemia is not caused by PTH or PTH-like substances.

A (appropriately) low PTH level with a low phosphorus level in a patient with hypercalcemia suggests the diagnosis of paraneoplastic hypercalcemia caused by parathyroid-related peptide (PTHrP). PTHrP shares N-terminal homology with PTH and can transactivate the PTH receptor. It can be produced by many different tumor types.

A low or normal PTH in a patient with hypocalcemia suggests hypoparathyroidism, provided the serum magnesium level is normal. Low magnesium levels inhibit PTH release and action and can mimic hypoparathyroidism.

Low serum calcium and high PTH levels in a patient with normal kidney function suggest resistance to PTH action (pseudohypoparathyroidism type 1a, 1b, 1c, or 2) or, very rarely, bio-ineffective PTH.

A limited number of the PTH-C fragments, which accumulate in kidney failure, chiefly PTH 7-84, cross-react in this and other intact PTH assays. PTH 1-84 is also elevated in kidney failure, with mild elevations being considered beneficial. Consequently, when measured with an intact PTH assay, concentrations of 1.5 to 3 times the upper limit of the healthy reference range appear to represent the optimal range for end-stage kidney failure patients. Lower concentrations may be associated with adynamic renal bone disease, while higher levels suggest possible secondary or tertiary hyperparathyroidism, which can result in high-turnover renal osteodystrophy.

Some patients with moderate hypercalcemia and equivocal phosphate levels, who have either mild elevations in PTH or (inappropriately) normal PTH levels, may be suffering from familial hypocalciuric hypercalcemia, which is due to inactivating *CASR* genetic variants. The molar kidney calcium to creatinine clearance is typically less than 0.01 in these individuals. The condition can be confirmed by *CASR* gene sequencing; see *CASRZ / CASR Gene, Full Gene Analysis, Varies*.

Cautions

Parathyroid hormone (PTH) values should be interpreted in conjunction with serum calcium and phosphorus levels, and the overall clinical presentation and history of the patient.

Do not interpret an elevated PTH value with a normal serum calcium result as necessarily indicative of primary hyperparathyroidism. It is possible that the elevation in PTH is due to secondary causes, the most likely being vitamin D deficiency.

Normal reference ranges may vary based on geographical locations of the populations studied.

The carboxyl-terminal (PTH-C) fragment 7-84, which accumulates in kidney failure, shows substantial cross-reactivity in this assay. Healthy population reference ranges, therefore, do not apply in kidney failure.

As with all tests containing monoclonal mouse antibodies, erroneous findings may be obtained from specimens taken from patients previously treated with monoclonal mouse antibodies or have received them for diagnostic purposes.

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

Clinical Reference

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3. Brossard JH, Cloutier M, Roy L, Lepage R, Gascon-Barre M, D'Amour P: Accumulation of a non-(1-84) molecular form of parathyroid hormone (PTH) detected by intact PTH assay in renal failure: importance in the interpretation of PTH values. *J Clin Endocrinol Metab.* 1996 Nov;81(11):3923-3929
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Performance

Method Description

The Roche cobas assay for determining intact parathyroid hormone employs a sandwich test principle in which a biotinylated monoclonal antibody reacts with the N-terminal fragment (1-37) and a monoclonal antibody labeled with a ruthenium complex reacts with the C-terminal fragment (38-84). Application of a voltage to the electrode then induces

chemiluminescent emission, which is measured by a photomultiplier. The antibodies used in this assay are reactive with epitopes in the amino acid regions 26-32 and 37-42. (Package insert: Elecsys PTH reagent. Roche Diagnostics; V 2.0 English, 02/2020)

PDF Report

No

Day(s) Performed

Monday through Saturday

Report Available

Same day/1 to 2 days

Specimen Retention Time

3 months

Performing Laboratory Location

Rochester

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

83970

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
PTH2	Parathyroid Hormone (PTH), S	2731-8

Result ID	Test Result Name	Result LOINC® Value
PTH2	Parathyroid Hormone (PTH), S	2731-8