# Test Definition: PTH2

Parathyroid Hormone, Serum

## Overview

### Useful For

Diagnosis and differential diagnosis of hypercalcemia

Diagnosis of primary, secondary, and tertiary hyperparathyroidism

Diagnosis of hypoparathyroidism

Monitoring kidney failure patients for possible renal osteodystrophy

### Method Name

Electrochemiluminescence

### NY State Available

Yes

## Specimen

### Specimen Type

Serum

### Specimen Required

**Patient Preparation:**

1. Fasting: 12 hours, preferred but not 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.

### Forms

If not ordering electronically, complete, print, and send 1 of the following forms with the specimen:
-Kidney Transplant Test Request
-Renal Diagnostics Test Request (T830)

### 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 | |
| | Ambient | 8 hours | |
| | Refrigerated | 72 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 184 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 patient with hypercalcemic 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 patients with kidney failure. 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 renal calcium to creatinine clearance is typically less than 0.01 in these individuals. The condition can be confirmed by *CASR* gene sequencing; see CASRG / *CASR* Full Gene Sequencing with Deletion/Duplication, Varies.

## Cautions

Serum biotin concentrations up to 1200 ng/mL do not interfere with this assay. Concentrations up to 1200 ng/mL may be present in specimens collected from patients taking extremely high doses of biotin up to 300 mg per day.(1) In a study among 54 healthy volunteers, supplementation with 20 mg/day biotin resulted in a maximum serum biotin concentration of 355 ng/mL 1-hour post-dose.(2)

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.

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 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. Saint Paul LP, Debruyne D, Bernard D, Mock DM, Defer GL. Pharmacokinetics and pharmacodynamics of MD1003 (high-dose biotin) in the treatment of progressive multiple sclerosis. Expert Opin Drug Metab Toxicol. 2016;12(3):327-344. doi:10.1517/17425255.2016.1136288
2. Grimsey P, Frey N, Bendig G, et al. Population pharmacokinetics of exogenous biotin and the relationship between biotin serum levels and in vitro immunoassay interference. J Pharmacokinet Pharmacodyn. 2017;2(4),247-256
3. Boudou P, Ibrahim F, Cormier C, Chabas A, Sarfati E, Souberbielle JC. Third- or second-generation parathyroid hormone assays: a remaining debate in the diagnosis of primary hyperparathyroidism. J Clin Endocrinol Metab. 2005;90(12):6370-6372
4. Silverberg SJ, Bilezikian JP. The diagnosis and management of asymptomatic primary hyperparathyroidism. Nat Clin Pract Endocrinol Metab. 2006;2(9):494-503
5. 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;81(11):3923-3929
6. Garfield N, Karaplis AC. Genetics and animal models of hypoparathyroidism. Trends Endocrinol Metab. 2001;12(7):288-294
7. Sakhaee K. Is there an optimal parathyroid hormone level in end-stage renal failure: the lower the better? Curr Opin Nephrol Hypertens. 2001;10(3):421-427
8. Vetter T, Lohse MJ. Magnesium and the parathyroid. Curr Opin Nephrol Hypertens. 2002;11(4):403-410
9. Bilezikian JP, Potts JT Jr, Fuleihan GEH, et al. Summary statement from a workshop on asymptomatic primary hyperparathyroidism: a perspective for the 21st century. J Clin Endocrinol Metab. 2002;87(12):5353-5361
10. Minisola S, Pepe J, Piemonte S, Cipriani C. The diagnosis and management of hypercalcaemia. BMJ. 2015;350:h2723

11. Cooper MS. Disorders of calcium metabolism and parathyroid disease. Best Pract Res Clin Endocrinol Metab. 2011;25(6):975-983. doi:10.1016/j.beem.2011.07.001
12. De Sanctis V, Soliman A, Fiscina B. Hypoparathyroidism: from diagnosis to treatment. Curr Opin Endocrinol Diabetes Obes. 2012;19(6):435-442. doi:10.1097/MED.0b013e3283591502

## 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. Roche Diagnostics; V 4.0 English, 05/2023)

### PDF Report
No

### Day(s) Performed
Monday through Saturday

### Report Available
Same day/1 to 2 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 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.

# Test Definition: PTH2

Parathyroid Hormone, Serum

## 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 |