# Test Definition: PTHRP

Parathyroid Hormone-Related Peptide, Plasma

## Overview

### Useful For

Aiding in the evaluation of individuals with hypercalcemia of unknown origin

Aiding in the evaluation of individuals with suspected humoral hypercalcemia of malignancy

The test **should not be used** to exclude cancer or screen individuals with tumors for humoral hypercalcemia of malignancy.

### Method Name

Immunochemiluminometric Assay (ICMA)

### NY State Available

Yes

## Specimen

### Specimen Type

Plasma EDTA

### Specimen Required

**Supplies:** Sarstedt Aliquot Tube, 5 mL (T914)
**Collection Container/Tube:** Ice-cooled, lavender top (EDTA)
**Submission Container/Tube:** Plastic vial
**Specimen Volume:** 0.7 mL Plasma
**Collection Instructions:**
1. Centrifuge specimen in a refrigerated centrifuge or in chilled centrifuge cups.
2. Aliquot plasma into plastic vial and freeze.

### Forms

If not ordering electronically, complete, print, and send a General Request (T239) with the specimen.

### Specimen Minimum Volume

Plasma: 0.25 mL

### Reject Due To

| | |
|---|---|
| Gross hemolysis | Reject |
| Gross lipemia | OK |
| Gross icterus | OK |

### Specimen Stability Information

| Specimen Type | Temperature | Time | Special Container |
|---|---|---|---|
| Plasma EDTA | Frozen | 30 days | |

## Clinical & Interpretive

### Clinical Information

Parathyroid hormone-related peptide (PTHrP) exists in several isoforms, ranging in size from 60 to 173 amino acids, which are created by differential splicing and posttranslational processing by prohormone convertases. PTHrP is produced in low concentrations by virtually all tissues. The N-terminus and the secondary structure of multiple isoforms of PTHrP resemble parathyroid hormone (PTH), allowing PTHrP to bind to the same receptor as PTH.

The physiological role of PTHrP can be divided into 5 categories:
1) Transepithelial calcium transport, particularly in the kidney and mammary gland
2) Smooth muscle relaxation in the uterus, bladder, gastrointestinal tract, and arterial wall
3) Regulation of cellular proliferation
4) Cellular differentiation and apoptosis of multiple tissues
5) As an indispensable component of successful pregnancy and fetal development (embryonic gene deletion is lethal in mammals)

Humoral hypercalcemia of malignancy (HHM) is a common complication of cancer. Elevations of PTHrP are the most common cause of malignancy-associated hypercalcemia. PTHrP leads to hypercalcemia by stimulating calcium resorption from bone and reabsorption in the kidneys. It also plays a significant function in osteolysis in bony metastases, particularly in breast cancer, and has been postulated to play a role in malignancy-associated cachexia through induction of orexigenic peptides.

Various malignancies secrete PTHrP resulting in HHM. PTHrP production is most commonly seen in carcinomas of breast, lung (squamous), head and neck (squamous), kidney, bladder, cervix, uterus, and ovary. Neuroendocrine tumors may also occasionally produce PTHrP. Most other carcinomas, sarcomas, and hematolymphoid malignancies only sporadically produce PTHrP, with the exception of T-cell lymphomas and myeloma. In HHM, the typical laboratory presentation includes elevated calcium and PTHrP, decreased PTH, and suppressed serum 1,25 dihydroxyvitamin D3 levels. Patients with HHM may have increased PTHrP values before treatment. PTHrP level decreases and PTH level increases, accompanied by decreased serum calcium values, are observed with successful treatment.

### Reference Values

< or =4.2 pmol/L

Reference values have not been established for patients younger than 1 year.

### Interpretation

Depending on the patient population, up to 80% of individuals with malignant tumors and hypercalcemia will be suffering from humoral hypercalcemia of malignancy (HHM). Of these, 50% to 70% might have an elevated parathyroid

hormone-related peptide (PTHrP) level. These patients will also usually show typical biochemical changes of excess parathyroid hormone (PTH)-receptor activation, namely, besides the hypercalcemia, they might have hypophosphatemia, hypercalcuria, hyperphosphaturia, and elevated serum alkaline phosphatase. Their PTH levels will typically be less than 30 pg/mL or undetectable.

In patients with biochemical findings that suggest, but do not prove, primary hyperparathyroidism (eg, hypercalcemia, but normal or near-normal serum phosphate, and a PTH level that is within the population reference range but above 30 pg/mL), HHM should be considered as a diagnostic possibility, particularly if the patient is an older adult, has a history of malignancy, or has risk factors for malignancy. An elevated PTHrP level in such a patient is highly suggestive of HHM as the cause for the hypercalcemia.

### Cautions

Parathyroid hormone-related peptide (PTHrP) can be elevated in pregnant and lactating women and in newborn infants.

Nonmalignant conditions that have been described in association with elevated plasma PTHrP levels include systemic lupus erythematosus, HIV-associated lymphadenopathy, lymphedema of chest or pleural cavities, and with benign tumors of the ovary, kidney, and the neuroendocrine system.

Because of the complexity of PTHrP isoforms, the differences between various PTHrP assays and the lack of a common calibration standard, PTHrP measurements performed with different assays cannot be compared easily.

The complex isoform mixture of PTHrP can occasionally lead to pronounced nonlinearity on dilution of patient specimens. In these situations an accurate measurement of PTHrP concentrations might be impossible.

Like all immunometric assays, PTHrP assays are susceptible to false-low results at extremely high analyte concentrations ("hooking") and to rare false-positive results due to heterophile antibody interference. Therefore, if test results are incongruent with the clinical picture, the laboratory should be contacted.

### Clinical Reference

1. Donovan PJ, Achong N, Griffin K, Galligan J, Pretorius CJ, McLeod DS. PTHrP-mediated hypercalcemia: causes and survival in 138 patients. J Clin Endocrinol Metab. 2015;100(5):2024-2029
2. Goltzman D. Nonparathyroid hypercalcemia. Front Horm Res. 2019;51:77-90
3. Jacobs TP, Bilezikian JP. Clinical Review: Rare causes of hypercalcemia. J Clin Endocrinol Metab. 2005;90(11):6316-6322
4. Mundy GR, Edwards JR. PTH-related peptide (PTHrP) in hypercalcemia. J Am Soc Nephrol. 2008;19(4):672-675

## Performance

### Method Description

The parathyroid hormone-related peptide (PTHrP) assay is a plate-based chemiluminescent assay utilizing an anti-PTHrP rabbit-polyclonal antibody for capture and an acridinium ester anti-PTHrP goat-polyclonal antibody for detection. The assay targets 1 to 86 PTHrP.(Ashrafzadeh-Kian S, Bornhorst J, Algeciras-Schimnich A. Development of a PTHrP chemiluminescent immunoassay to assess humoral hypercalcemia of malignancy. Clin Biochem. 2022;105-106:75-80. doi:10.1016/j.clinbiochem.2022.04.005)

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### PDF Report
No

### Day(s) Performed
Monday through Thursday

### Report Available
2 to 5 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 |
|---|---|---|
| PTHRP | PTH-Related Peptide | 15087-0 |

| Result ID | Test Result Name | Result LOINC® Value |
|---|---|---|
| 81774 | PTH-Related Peptide | 15087-0 |