

## Technical Bulletin

*Detailed information concerning methodology, specimen requirements, and reference ranges on new and specialized tests.*

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• Test Name:	<b>Intact PTH (Parathyroid Hormone, Intact)</b>
• Test Order Number:	762 (includes total calcium)
• CPT code:	83970 (PTH), 82310 (Calcium)
• Department:	Clinical Chemistry (400)
• Testing Schedule:	Monday, Wednesday, Friday evenings
• Specimen Requirement:	2 mL EDTA Plasma, lavender top tube, spin and separate freeze immediately. 2 mL serum is required for calcium, refrigerate.
• Reference Range:	12-72 pg/mL
• Methodology:	Chemiluminescence
• Turn Around Time:	48 hours

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### Clinical Significance

Intact parathyroid hormone (parathyrin, PTH-I), a single-chain polypeptide containing 84 amino acids, exerts significant influence in the maintenance of optimal calcium ion concentrations. PTH raises serum ionized calcium levels through direct action on bone and the kidneys: it increases the rate of calcium ion flow from bone to the extracellular fluid, and increases both the renal tubular reabsorption of ionized calcium and the renal excretion of phosphate. Long-term regulation of total body calcium by PTH occurs through its stimulation of vitamin D metabolism, which results in enhanced intestinal absorption of ionized calcium.<sup>1</sup>

In healthy individuals, PTH is secreted in response to circulating calcium ion levels. Any reduction below an individual's normal level triggers a pronounced increase in PTH secretion. Calcium levels returning to normal exert a negative feedback effect, thus inhibiting PTH secretion by the parathyroid glands.

PTH undergoes proteolysis to a lesser extent in the parathyroid glands but mostly peripherally, especially in the liver but also in the kidneys and bone, to yield N-terminal fragments and longer lived C-terminal and midregion fragments. The N-terminal fragments contain the region that confers bioactivity. C-terminal (biologically inert) and N-terminal fragments are initially generated in equivalent amounts, but the N-terminal fragments disappear rapidly. The C-terminal assays (as well as midregion assays) are likely to be unreliable in chronic renal failure, where increased PTH is typically a reflection of impaired renal clearance of C-terminal fragments.<sup>1,2</sup>

For the intact hormone, the in vivo half-life is 2 to 5 minutes.<sup>3</sup> In patients with normal renal function intact PTH is the majority of PTH-like bioactivity.<sup>4</sup> Hypercalcemia is most commonly due to hyperparathyroidism or hypercalcemia of malignancy. Patients with hyperparathyroidism generally have elevated values of PTH-I and calcium.

Patients with hypercalcemia of malignancy generally have elevated calcium values with low PTH-I values. However, malignant tumors generally produce PTH-related peptide, (PTH-rP) and depending on the assay some older PTH assays will produce elevated PTH results. PTH levels are also characteristically high in secondary hyperparathyroidism, usually associated with renal failure, as a result of stimulation of the parathyroid gland by low calcium levels. Hypocalcemia accompanied by a low PTH level, on the other hand, is to be expected in hypoparathyroidism, either postsurgical or idiopathic.

## Method

Intact PTH is a solid-phase, two-site chemiluminescent enzyme-labeled immunometric assay.<sup>5</sup> Previously, immunoassays specific for various PTH fragments were developed. Most relied on antisera specific for a discrete region: the C-terminal, N-terminal, or midmolecule. The antisera employed in such assays recognize not only the specific region, but similar fragments as well. Recent assays for intact PTH have the necessary sensitivity for detecting circulating intact PTH in the normal population and for discriminating between the normal population and those with primary hyperparathyroidism. These assays also appear to discriminate better between primary hyperparathyroidism and hypercalcemia of malignancy compared with previous assays, and do so virtually without any significant overlap between these groups.

## Patient Preparation

Sampling after 10:00 AM has been suggested for optimum discrimination between the normal population and those with mild primary hyperparathyroidism because of a pronounced nocturnal rise in intact PTH levels observed in a small experimental male population.

## Intra-operative PTH

Serial PTH measurements made during surgery can be used as a "biochemical biopsy" to help determine if all of the overactive parathyroid tissue has been removed. The short biological half-life (2-5 minutes) of intact PTH and the suppression of the normal parathyroid gland combined with rapid laboratory assays allow a period for monitoring during an operative procedure. Several samples taken at 5-10 minute intervals (0 min, 5 min, 10 min) are used to monitor the rapid fall in plasma values. **For technical reasons, intra-operative PTH specimens must be scheduled ahead of time with the laboratory so instruments can be adjusted specifically for this PTH assay.**

## References

1. Armitage, EK, Parathyrin (parathyroid hormone): metabolism and methods of assay. Clin Chem 32: 418-424, 1986.
2. Blind E et al, Two-site assay of intact parathyroid hormone in the investigation of primary hyperthyroidism and other disorders of calcium metabolism compared with a mid-region assay. J Clin Endocrinol Metab 67:353-360, 1988.
3. Kao, PC, et al, Clinical performance of parathyroid hormone immunometric assays, Mayo Clin Proc, 67: 637-645, 1992.
4. Measuring the PTH level, Lancet, (Jan 16) 94-95, 1988.
5. Immulite 2000 Intact PTH, package insert, June 28, 2001.

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