Parathyrin (Parathyroid Hormone): Metabolism and Methods for Assay

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Parathyrin (parathyroid hormone) radioimmunoenzyme assay is a commonly ordered endocrine assay. I discuss here the metabolism of the hormone and the effect information on this metabolism has had on the development of radioimmunoassays for parathyrin. Although radioimmunoassay is the most widely accepted technique for the routine assay for parathyrin, "high-performance" liquid chromatography, cytochemical bioassay, and homologous bioassay have also been developed for this analyte. Accordingly, I briefly review the clinical utility of these assays in terms of their ability to assess the functional activity of the parathyroid gland.

Additional Keyphrases: endocrine hormones · radioimmunoassay · chromatography, reversed-phase · cytochemical and homologous bioassays · hyperparathyroidism · Ca²⁺ transport

Calcium ions play a major role in many biological processes, such as metabolic actions, neurotransmitter release, hormone secretion, and muscle contraction (1, 2). Critical shifts of calcium ions into or out of cells or subcellular organelles are apparently involved in various regulated reactions or functions. The molecular level of action of Ca²⁺ involves a homologous class of intracellular Ca²⁺-binding proteins that serve as receptors for Ca²⁺ (1). The concentration of intracellular cytosolic Ca²⁺ ranges from 10⁻⁸ to 10⁻⁷ mol/L, compared with a concentration in extracellular fluid of 10⁻³ mol/L (3, 4). A transient increase of intracellular Ca²⁺ to 10⁻⁶ mol/L suffices to cause the Ca²⁺-binding proteins to form an active complex by binding Ca²⁺; this complex can regulate numerous enzymatic and cytoplasmic functions (1). The precise concentration of intracellular cytosolic Ca²⁺ is maintained by plasma membrane Ca²⁺ transporters (3). In humans, regulation of the concentration of calcium in the extracellular fluid involves a system of endocrine effects and organ-specific actions.

Calcium homeostasis in humans is maintained by the actions of parathyrin (parathyroid hormone, PTH), vitamin D, and calcitonin. Vitamin D and PTH are the major factors in controlling the concentration of calcium in extracellular fluid within narrow limits (5). PTH is secreted from the parathyroid gland at a rate that is inversely proportional to the Ca²⁺ concentration in serum. PTH acts to increase Ca²⁺ in serum via actions on the bone, kidney, and, through vitamin D, on the gut. Vitamin D increases absorption from the gut and bone re-absorption of calcium. The production of the most active vitamin D metabolite, 1,25-dihydroxycholecalciferol, is directly enhanced by hypophosphatemia and indirectly by hypocalcemia via PTH secretion. Calcitonin is secreted at a rate directly proportional to the Ca²⁺ concentration in serum. Calcitonin acts to inhibit resorption of bone; therefore, it antagonizes the effects of vitamin D and PTH.

The physiological function of PTH is the maintenance of the extracellular calcium concentration and the prevention of hypocalcemia. Its secretion is closely regulated by the concentration of serum Ca²⁺; any decrease in serum Ca²⁺ below the normal concentration for an individual causes a sharp increase in PTH secretion (6). As the concentration of Ca²⁺ in serum returns to normal, by negative feedback it inhibits the parathyroid gland to decrease the secretion of PTH.

PTH increases the concentrations of serum Ca²⁺ by direct actions on the bone and kidney and indirect actions on the intestine. By increasing the rate of bone reabsorption, it thereby increases the flow of Ca²⁺ from the bone to the extracellular fluid (5). It increases the renal tubular reabsorption of Ca²⁺, increases the renal excretion of phosphate, and increases the renal metabolism of 25-hydroxycholecalciferol to 1,25-dihydroxycholecalciferol. PTH enhances the intestinal absorption of Ca²⁺ indirectly through its action on the renal metabolism of vitamin D. The hormone's effect on bone and, to a lesser degree, on kidney results in rapid changes in the concentration of Ca²⁺ in serum, whereas the maintenance of total body calcium depends on chronic effects of PTH on the intestine via the stimulation of vitamin D metabolism to enhance the efficiency of intestinal Ca²⁺ absorption.

The mode of action of PTH at the target cells is the stimulation of adenylate cyclase (EC 4.6.1.1) activity, which increases the concentration of 3',5'-cyclic adenosine monophosphate (cAMP) in tissues (5). This, in turn, activates cytosolic protein kinases and other enzymatic reactions, which lead to the physiological effects of PTH.

Metabolism

Berson and Yalow (7) first reported that the PTH assayed in serum was immunochemically different from the PTH extracted from the parathyroid gland. This heterogeneity of circulating endogenous hormone is now known to be the result of proteolytic metabolism of PTH after its biosynthesis. This occurs both within the parathyroid gland and outside of it (5, 6). The biological significance of this proteolytic metabolism is of major interest. Is its function to
destroy the hormone or does this proteolysis result in the generation of needed biologically active fragments?

Initially, some concluded that only intact PTH was secreted by the parathyroid glands, and that all the fragments of the hormone in serum were due to peripheral metabolism (8, 9). Another group (10) reported that hormone extracted directly from the gland showed multiple immunoactive peaks on gel filtration, which were similar to the peaks detected in plasma. They also concluded that all of the biologically inactive (carboxyl-terminal, C-terminal) fragments in the plasma of uremic patients could be accounted for by glandular secretion and that this was the result of the prolonged t½ of the fragments, which was more than 100-fold longer than the t½ for intact PTH in uremic patients. From this evidence, they suggested (10) that glandular secretion instead of peripheral metabolism could account for all of the immunoactive forms of the hormone in serum. Subsequent studies have shown that the parathyroid gland secretes substantial amounts of C-terminal and possibly some also amino-terminal (N-terminal) fragments together with intact PTH (11, 12).

That there is, or can be, peripheral proteolysis of PTH has been shown by injecting intact PTH into dogs and calves and monitoring both the disappearance of the administered hormone from the plasma and the appearance of fragments (13–16)—fragments that immunochemically and physicochemically are identical to endogenously produced hormone fragments (5). From current evidence, one can conclude that intact PTH undergoes both intraglandular and peripheral proteolysis; we still do not know, however, which is the predominant site of metabolism.

Numerous studies (15, 17–20) have shown that the liver and kidney are involved in the metabolism of PTH. The liver takes up intact PTH with high efficiency and generates C-terminal fragments similar to those present in the circulation (17, 18). Moreover, one or more N-terminal fragment(s) that are biologically active are generated by the hepatic metabolism of PTH (17). Metabolism in the liver has been further confirmed by studies of Segre et al. (19); using heparctomized and sham-treated rats, they showed that no C-terminal fragments with N-terminal residues at positions 34 and 37 were detected after hepatectomy, whereas the typical C-terminal fragments having positions 34 and 37 of the intact hormone sequence as their N-terminal residues were found in the sham-treated rats. This study clearly established the liver as the principal peripheral organ involved in the generation of C-terminal fragments. Segre et al. also showed (20) that Kupffer cells, the intrasinusoidal macrophages, possess the specific enzyme(s) involved in PTH metabolism. The PTH fragments resulting from metabolism in Kupffer cells are immunoactively and chemically indistinguishable from those found in plasma when intact hormone is injected. The initial proteolytic attack on intact PTH is via an endopeptidase, generating both N- and C-terminal fragments. Initially the quantities of N-terminal fragments formed are equivalent to the C-terminal fragments, but the former then disappear rapidly from the medium (20). These results are similar to the findings obtained from the study of plasma: high concentrations of C-terminal fragments and low concentrations of N-terminal fragments. The rate of disappearance of intact PTH in Kupffer cell suspensions is similar to the rate in vivo, the t½ being 12 (SEM 4) min (20).

Intraglandular metabolism of PTH was studied by using porcine parathyroid cells incubated in vitro; two C-terminal fragments, in addition to intact PTH, were isolated from the incubation medium (21). PTH(37-84) and PTH(34-84) were identical to the fragments isolated from in vivo hepatic metabolism of PTH (19, 21). Purified cathepsin B from porcine parathyroid glands cleaved PTH and pro-PTH between residues 36 and 37, yielding a major C-terminal and lesser N-terminal fragments (22). The N-terminal fragments were further degraded by the removal of small peptides from their carboxyl end; the enzyme acted no further on the PTH(37-84) fragment. Cleavage of the hormonal substrates by purified liver cathepsin B was identical to that of the parathyroid gland enzyme (22). Cathepsin B (EC 3.4.22.1) accounts for the glandular metabolism that yields the PTH(37-84) fragment, but whether it can also generate the PTH(34-84) fragment remains to be established.

The kidney appears to be responsible for clearance of the C-terminal fragments, once they are formed (19, 23). Renal uptake of C-terminal PTH fragments apparently depends on glomerular filtration; reabsorption and degradation involves the tubular cells (24). Intact hormone is removed by both peritubular uptake and glomerular filtration with subsequent reabsorption. Besides removing PTH and its fragments from circulation, the kidney may also act as a source of PTH fragments; in vitro degradation of PTH with the production of PTH fragments by kidney tissue has been demonstrated (23, 25). The C-terminal and N-terminal fragments observed on gel filtration are similar to those taken from the circulation of intact experimental animals and from humans. The kidney appears to have less of a quantitative effect in the metabolism of intact PTH and release of PTH fragments than the liver does (19).

The major interest in metabolism is whether a particular process generates the biologically active fragments necessary for the organism's functioning. Martin et al. reported (23, 26) that only a bovine N-terminal [PTH(1-34)] fragment stimulates the production of cAMP in isolated, perfused bone. The rate of uptake of the N-terminal fragment by the bone from circulation was high, whereas uptake of intact bovine PTH was only minimal. Moreover, there were only minimal increases in the concentrations of cAMP in the presence of high concentrations of intact bovine PTH(1-84). These authors (23) concluded that PTH uptake in bone differs from that in kidney and liver. These studies suggest that peripheral metabolism of intact PTH may play a major role in regulating the effect of PTH on bone tissue (26). Conversely, intact PTH is capable of activating adenylyl cyclase in skeletal tissue in vitro without prior cleavage (27). In addition, bone cells and skeletal tissue may metabolize bovine PTH(1-84) and contribute to the immunoheterogeneity of circulating PTH in rats (28). Further studies are required to resolve this issue of whether metabolism of the hormone is or is not required for biological activity in bone tissue.

Proteolytic metabolism of PTH in the parathyroid gland and in peripheral organs (liver, kidney, and bone) results in a short-lived N-terminal fragment, and a C-terminal fragment, which is longer lived, in the circulation. Roe et al. (29) have suggested that a higher order of complexity for PTH metabolism exists, given the detection of a small midregion PTH fragment. Midregion PTH fragments, whether from glandular secretion or produced in the circulation, reportedly have similar size and immunochromatic characteristics (29, 30). As I will discuss next, this diversity of PTH fragments in serum has also resulted in a diversity of assays and antisera for PTH.
Assays of PTH Concentrations

Radioimmunoassays

Since the introduction of a radioimmunoassay for PTH in 1963, the PTH assay has become a commonly ordered endocrine test (31). However, the development of antisera for PTH has been complicated by the heterogeneity of circulating immunoreactive PTH. In general, PTH radioimmunoassays fall into one of four groups: (a) those with antisera directed towards the N-terminal region of PTH, which recognize intact hormone as well as N-terminal PTH fragments; (b) those with antisera directed towards the C-terminal region of PTH, which recognize intact hormone and C-terminal fragments of PTH; (c) those with antisera directed towards the middle region of PTH (mid-molecule assay), which recognize intact PTH and the fragments of the hormone containing the midregion sequence of PTH; and (d) intact PTH assays, with either an antiserum against the region where PTH is metabolized, or two antisera, one each directed towards the N-terminal and C-terminal regions. In addition to radioimmunoassays of PTH, assays developed to measure PTH include "high-performance" liquid chromatography, cytochemical bioassay, and a homologous bioassay.

N-terminal assays. Several authors (10, 32-35) have described radioimmunoassays of PTH in which antisera with specificity predominantly directed to the N-terminal region of the PTH molecule [PTH(1-34)] are used. Because the structural requirements for biological activity of the hormone are met in the first 34 amino acids of the molecule (17), one would expect N-terminal assays to show good correlation with the clinical status of patients; to date, however, this has not been the case for the diagnosis of primary hyperparathyroidism. The reason for the poor discrimination provided by N-terminal assays is not known, but could involve some of following factors. Because the concentrations of intact PTH and (or) of PTH(1-34) in serum are low, the N-terminal-specific antisera must have a high affinity constant (in the 10^-11 L/mol range) to be effective (35). In addition, the plasma half-lives of intact hormone and of the N-terminal fragments are extremely short, and some evidence indicates that the secretion of PTH is somewhat episodic (36); therefore, hyperparathyroidism may not necessarily result in increased concentrations of N-terminal PTH. Finally, the poor discrimination of the early N-terminal assays could be due to nonspecific immunoreactivity of the antisera involved; newer N-terminal assays appear to better distinguish patients with primary hyperparathyroidism from patients with normal parathyroid function (35, 37, 38).

C-terminal assays. C-terminal assays for PTH are based on antisera that have been shown to react with fragments enzymatically derived from the C-terminal region of PTH, such as the 53-84 sequence, and that react with the different C-terminal fragments found in the circulation (10, 29, 39-42). The C-terminal fragment of PTH is biologically inactive and has a longer half-life than does either intact PTH or PTH(1-34). In general, C-terminal assay results will be higher than N-terminal assay results because of the longer half-life of the C-terminal fragment (40). In patients with chronic renal failure, results of C-terminal assay are generally much higher than those of N-terminal assays because the normal renal clearance of C-terminal PTH is severely compromised by the disease (43). Clinical experience shows that the C-terminal assays more clearly discriminate between states of normal and abnormal parathyroid function in most cases than the N-terminal assays do, because of the longer half-life and fragment accumulation of C-terminal PTH in serum.

Mid-molecule assays. The availability of several synthetic fragments of PTH has allowed for the development of antisera directed towards the middle region of the PTH molecule. Mallette et al. (44) described an antisera against the synthetic peptide human PTH(43-68); this midmolecule assay detects both intact hormone and fragments which contain the middle region. Similar assays that detect PTH(44-68) have also been developed (28, 30, 32, 45, 46). Mid-molecule assays also detect in serum an additional PTH fragment; it contains the midregion but not the C-terminal region of PTH (29, 30). This additional circulating PTH fragment is similar in size and immunochemical characteristics to the midregion fragment found in parathyroid gland extracts (30). Roos et al. suggested (29) that the midregion immunoreactivity somehow specifically reflects increased parathyroid secretory activity, because it is absent from normal and basal sera but is present in sera from persons with increased PTH secretion. Little N-terminal immunoreactivity is associated with the midregion fragment of PTH; therefore, it is unlikely that the midregion fragment possesses any biological activity. Mid-molecule assays are reportedly useful for distinguishing primary hyperparathyroidism, secondary hyperparathyroidism, primary hypoparathyroidism, and secondary hypoparathyroidism (45, 46).

Assays of intact PTH. The final approach to radioimmunoassay of PTH has been to detect only intact hormone by using either (a) antisera against PTH(24-48), i.e., the proteolytic region of intact PTH, or (b) sequential immunoeXtraction of N-terminal fragments, followed by midregion radioimmunoassay (47, 48). Mallette (47) reported developing six high-titer anti-human PTH(28-48) antisera; the resulting assay detected the intact hormone or the PTH(28-48) peptide but not hormone fragments resembling those thought to be formed in vivo. Because the most sensitive of the antisera could detect only 20 fmol or more of intact PTH per assay tube (normal concentration in serum is less than 2 fmol/mL), assay sensitivity will have to be improved before the system will detect normal concentrations of intact PTH in serum (47). Lindall et al. (48) reported a two-step immunochromatographic method for estimating the concentration of intact PTH in serum. The first step involved extraction and concentration of serum PTH moieties by using solid-phase-bound anti-N-terminal antibody. The PTH immunorextract was then assayed with a radioimmunoassay of mid-molecule PTH. Using this assay, the authors estimated normal values for intact PTH as 4.8 ± 0.3 pmol/L (mean ± SEM for 52 normal sera) (48). In these same sera, total anti-midmolecule immunoreactivity was 67.0 (SEM 1.7) pmol/L; therefore, in normal patients, intact PTH represented 7.0% of the total mid-molecule PTH measured, whereas in 18 patients with primary hyperparathyroidism the intact PTH (101 ± 7.6 pmol/L) represented 68.1% of the total midmolecule PTH (167 ± 19 pmol/L) (49). Using this assay, the authors were able to distinguish all of the normal patients from the primary hyperparathyroid patients (48).

Liquid Chromatographic Assay

"High-performance" liquid chromatography (HPLC) with reversed-phase techniques have been used to either purify or analyze PTH (49-51). In general, the HPLC assay
involves extracting plasma or supernates of tissue homogenates on octadecylsilyle-silica, then assaying the extracts by reversed-phase HPLC with a solvent system composed of a linear gradient of aqueous acetonitrile. Although monitoring eluates by ultraviolet absorbance and (or) endogenous tryptophan fluorescence has been used for quantification, in most of the HPLC assays radioimmunoassay is used to detect PTH in the collected fractions of column effluent (51). Immunoreactivity profiles of parathyroid tissue contain three main elution peaks (51): the first appears to be equivalent to the C-terminal fragment of PTH; the pooled products of the second showed weak bioactivity and immunoreactivity with N-terminal, mid-molecule, and C-terminal radioimmunoassays; the third consisted of immunoreactive components associated with intact PTH—intact human PTH being composed of three or four closely associated components. These results suggest that the biological degradation of human PTH is more complex than first believed and that reversed-phase HPLC offers a new dimension in PTH analysis (51). However, HPLC assay of PTH is still dependent on micro-scale chemical analysis and biological assessment; it has not been used to assay multiple patients’ samples.

Bioassays of PTH

The cytochemical bioassay for PTH, used to characterize the biological activity of circulating forms of the hormone (52), depends on the stimulation of glucose-6-phosphate dehydrogenase activity in the distal convoluted tubules of segments of guinea-pig kidney maintained in vitro; the activity of the enzyme is measured by microdensitometry (53). The responses to synthetic bovine PTH(1-34) and human PTH(1-34) were parallel and equinominal to that for intact bovine PTH (52). The concentration of biologically active PTH in human circulation appears to be between 1 and 30 ng/L (52, 54). Results of the bioassay suggest that the concentration of biologically active PTH in the circulation is less than 10% of the circulating PTH measured by radioimmunoassay (54, 55). The bioassay reportedly is capable of distinguishing hormonal activity in plasma from normal, hypoparathyroid, and hyperparathyroid humans (52, 54, 55). This technique, which is cumbersome to perform, is not a practical alternative to radioimmunoassay, but may provide a comparison procedure for assessing radioimmunoassay methods (55).

An assay for endogenous biologically active human PTH, based on the use of guanylyl nucleotide-amplified renal adenylate cyclase, has been reported for both canine and human renal cortical plasma membranes (56, 57). The principle of the procedure is biological activation by human PTH of adenylate cyclase in membrane-enriched homogenized renal cortex tissue; the adenylate is quantitated by radioimmunoassay of the generated cAMP (57). Both intact PTH and biologically active fragments are measured. In normal patients the concentrations of biologically active PTH were near the detection limit of the assay, but most of the patients with surgically proven hyperparathyroidism had increased concentrations of circulating active PTH. In patients with hyperparathyroidism secondary to chronic renal disease, at least 90% of the circulating C-terminal immunoreactive PTH was biologically inert; nonetheless, the majority of these patients did have increases in biologically active PTH (56, 57). This bioassay is not as sensitive as the cytochemical bioassay, but may be more practical; reportedly 10 to 20 test samples may be assayed daily, with final results obtained in one to two days (56).

Clinical Utility of PTH Assays

Assessment of the functional activity of the parathyroid glands is required in clinical evaluations of hypercalcemic and hypocalcemic states. Of the numerous disorders that present with hypercalcemia, primary hyperparathyroidism and cancer are among the most common. In primary hyperparathyroidism, most of the patients have increased PTH in serum because of adenoma, hyperplasia, or carcinoma of the parathyroid gland, with subsequent increases in calcium concentrations in serum. Malignancies can produce hypercalcemia via osteolytic bone metastases, which increase the efflux of calcium from the skeleton into the serum, or via the secretion of factors that increase bone reabsorption (58). In most malignancies, the patients may have severe hypercalcemia, but the concentrations of PTH, as measured by radioimmunoassay, may be low or undetectable. However, in hypercalcemic patients with carcinoma of the lung and kidney, the concentrations of immunoreactive PTH may be increased enough to overlap with those for patients with primary hyperparathyroidism. In most other clinical conditions characterized by hypercalcemia, the high concentrations of calcium suppress the release of PTH, resulting in low or undetectable PTH measured by radioimmunoassay.

The most common cause of hypocalcemia is renal insufficiency; the hypocalcemia triggers the release of PTH, and the patients develop secondary hyperparathyroidism. Gastrointestinal disorders with calcium malabsorption and vitamin D deficiency can also cause hypocalcemia with secondary hyperparathyroidism. Hyperparathyroidism, either congenital or secondary to surgery, is characterized by low or undetectable concentrations of PTH, plus hypocalcemia.

Interpretation of PTH radioimmunoassay results is complicated by the presence of several immunoreactive PTH species in human serum. The major problem has been the ability to distinguish between normal subjects and those with hyperparathyroidism (35). Although the primary clinical use of the PTH assay is the diagnosis of hyperparathyroidism, the various PTH assays differ in their ability to distinguish hyperparathyroidism from normal.

Because the N-terminal fragment contains the biologically active portion of PTH, one would expect that the N-terminal assays would be the most useful for clinical purposes; however, the experience of several authors has shown extremely variable discrimination between normal and hyperparathyroid patients (Table 1). Evaluating the N-terminal PTH assay results in conjunction with the concentrations of calcium in serum somewhat improves the clinical utility of the assay (36). Only the newer assays can distinguish patients with primary hyperparathyroidism from normal subjects more than 90% of the time (35, 37, 38). Other than the more-recent, more-sensitive N-terminal assays, this essay has not met the demand of being able to confirm or deny a diagnosis of primary hyperparathyroidism. However, N-terminal PTH assays are useful for evaluating parathyroid status of patients with chronic or acute renal failure (58, 59) and for evaluating the contents of venous catheterization samples in diagnosing patients with hypercalcemia and malignancy (36).

Paradoxically, the C-terminal and midmolecule PTH assays have provided a clearer clinical discrimination between normal and abnormal parathyroid function (Table 1), even though they measure the biologically inactive fragments as well as intact PTH (36). Because the biologically inactive PTH fragments are removed from plasma by glomerular filtration, they tend to accumulate in patients with chronic
Table 1. Clinical Sensitivities of Radioimmunoassays for PTH

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<tr>
<th>Source</th>
<th>Antiserum</th>
<th>1st HPT patients with absolute increase in PTH</th>
<th>Normals with PTH &lt;ULN</th>
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<td>89</td>
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<td>G36</td>
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1st HPT, surgically proven primary hyperparathyroidism; ULN, upper limit of normal range in study cited; nr, not reported.

renal failure (58). Nevertheless, results of C-terminal and mid-molecule PTH assays still correlate with the evidence of PTH activity on bone (36, 58). Arnaud et al. (32) have suggested that the results of C-terminal PTH assays correlate better with parathyroid gland activity because the longer half-lives of the C-terminal fragments in plasma permit a better assessment of the integrated activity of the parathyroid glands. The finding that a small midregion PTH fragment may reflect parathyroid secretory activity (29) may make the mid-molecule assay more clinically useful in the future, but the chemistry and the biological significance of this small midregion fragment require further study. To date, the C-terminal assays have performed slightly better than the mid-molecule assays for the evaluation of hyperparathyroidism. The best approach may be to use an antiserum with mixed C-terminal and mid-molecule reactivity, such as CH 9 antiserum (see Table 1).

As discussed earlier, the procedure for intact PTH—immunoextraction of PTH by anti-N-terminal antibody followed by mid-molecule radioimmunoassay—differenciated normal subjects and patients with hyperparathyroidism well. All 18 primary hyperparathyroid patients were clearly separated from 52 normal persons, intact PTH in the primary hyperparathyroid group averaging 20-fold that in the normal group (48). This procedure needs further clinical studies with more patients. However, it may not be readily adaptable to the clinical laboratory for use with large numbers of patients' samples because of the immunoextraction step.

The cytochemical bioassay shows good clinical correlation for both hypoparathyroidism and hyperparathyroidism in small clinical studies—in general, less than 10 patients per group (see Table 2). However, this assay is not suitable for routinely measuring PTH in the large number of patients' samples tested in the clinical laboratory. As already mentioned, it may provide a comparison method for evaluating other procedures for measuring concentrations of PTH (35).

Perhaps some of the newer approaches to measuring PTH activity will lead to increased clinical utility in the future. The new, more-sensitive N-terminal radioimmunoassays, intact PTH radioimmunoassay, reversed-phase HPLC, or a homologous bioassay may become the method of choice in the future. But so far, even though imperfect, the C-terminal assays have shown the greatest clinical utility for discriminating between normal persons and primary hyperparathyroid patients.

References


