42 Laboratory Testing, PTH Measurement of Needle Aspirates, and Intra Operative PTH Technologies

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Introduction

Parathyroid hormone (PTH) is synthesized by the parathyroid glands and secreted directly into circulation in order to regulate calcium and phosphate homeostasis. The full-length hormone, which is comprised of 84 amino acids, has a plasma half-life of less than 5 min. PTH is measured to aid in the differential diagnoses of calcium-related disorders and to monitor bone metabolism in patients with chronic kidney disease. Rapid PTH assays are currently the best intraoperative adjunct for monitoring for an adequate response to resection of one or more hyperfunctional parathyroid tumor(s). Significant variability exists among commercially available PTH assays. This chapter describes these assays and their relative characteristics.

Pre-analytical Variability

Circulating Heterogeneity

$PTH_{1–84}$ is synthesized and secreted by the parathyroid glands largely in response to changes in serum calcium [1, 2]. Circulating PTH fragments, containing carboxyl (C)-terminal or amino (N)-terminal peptides, arise from the intraglandular (chief cell) and peripheral (primarily hepatic) degradation of $PTH_{1–84}$ [3, 4]. While the

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half-life of $PTH_{1–84}$ is between 2 and 4 min, the half-life of C-terminal fragments ranges between 10 and 50 min [5, 6].

In the setting of normocalcemia, the composition of PTH in circulation is approximately [6–8]:

$PTH_{1–84}$	20 %	(Range 5–30 %)
N-terminal fragments	2 %	(Range 0–5 %)
C-terminal fragments	80 %	(Range 75–95 %)

PTH with an N-terminal structure (or the first 34 amino acids) is biologically active and equipotent compared to the full-length hormone. For example, recombinant $PTH_{1–34}$ or teriparatide (Forteo®, Eli Lilly and Company) is a widely available drug for men and women with severe osteoporosis [9]. Despite the biological significance of $PTH_{1–84}$ and $PTH_{1–34}$, these molecular forms account for only a fifth of total PTH in circulation.

C-terminal fragments, in contrast, account for most (~80 %) of the PTH in circulation. While historically regarded as biologically inert, increasing evidence suggests that some C-terminal fragments can interact with non-classical PTH receptors and induce biological actions that are independent and opposite to those of $PTH_{1–84}$ or $PTH_{1–34}$ [6, 10]. Small C-terminal fragments, which altogether lack a N-terminal structure (e.g., $PTH_{37–84}$, $PTH_{38–84}$), are the most prevalent molecular form in circulation (~70–75 %). Large C-terminal fragments (e.g., $PTH_{7–84}$), which are often referred to as non-$PTH_{1–84}$ in the literature and have truncated N-terminal structures, are relatively less common but can accumulate in the setting of renal failure [7, 11–13].

Pathophysiological Variability and Expected Results

There is inherent biological variability in PTH patterns over time; in general, PTH levels rise with age and body mass index [14]. In healthy persons, PTH secretion is circadian, with the highest levels being released in the nighttime hours [15–18]. Physical exercise and seasonal behaviors can also influence PTH levels [19].

PTH levels also vary according to changes in serum calcium and renal function. In the setting of hypercalcemia or elevated $1,25(OH)_2D$, PTH secretion is reduced but favors a relatively higher C-terminal fragment to $PTH_{1–84}$ ratio [3, 6, 20]. Concurrent high calcium and high PTH concentrations may indicate an etiology of primary hyperparathyroidism while the absence of PTH elevation may indicate hypercalcemia of malignancy.

In the setting of acute or chronic hypocalcemia, the parathyroid glands secrete primarily $PTH_{1–84}$ and few C-terminal fragments. Concurrent low PTH and calcium levels are indicative of hypoparathyroidism (e.g., postsurgical or idiopathic etiology). Elevated PTH concentration in the absence of hypercalcemia is consistent with secondary hyperparathyroidism, which is often caused by hypovitaminosis D or reduced renal function. Continual overproduction of PTH results in renal osteodystrophy [21–23].

Analytical Determination

Competitive (First-Generation) Assays

In 1963, Berson and Yalow developed the first radioimmunoassay for PTH [24] (Fig. 42.1). Their early first-generation (competitive) assay employed polyclonal sera from guinea pigs and rabbits raised against bovine PTH [24]. Because of the assay's low sensitivity, circulating PTH levels had to be significantly elevated (e.g., patients with hyperparathyroidism) to be detected. A decade later, Arnaud and colleagues (Mayo Clinic) enhanced the assay's sensitivity for human PTH by using antibodies raised against porcine (rather than bovine) PTH, which allowed for measurement of PTH levels within the normal human range [25].

Fig. 42.1 The first PTH assay. Solomon Berson and Rosalyn Yalow first measured PTH via a radioimmunoassay in the early 1960s. In 1977, Dr. Yalow won the Nobel Prize for radioimmunoassay measurement of peptide hormones (including PTH); Dr. Berson died from a heart attack in 1972

Intact (Second-Generation) Assays

However, because of high cross-reactivity with small C-terminal fragments and insufficient sensitivity for measuring intact hormone, first-generation assays were replaced by two-site (noncompetitive) immunometric or "sandwich assays" [26]. Second-generation or "intact" PTH assays employ a C-terminal capture antibody (e.g., epitopes 39–44) bound to a solid phase and a second enzyme-labeled N-terminal reporter or signal antibody (e.g., epitopes 13–34) [27] (Fig. 42.2).

While initially thought to measure only intact hormone, later characterization of the assay demonstrated that the detection antibodies cross-react with large C-terminal fragments, which have truncated N-terminal structures (e.g., $PTH_{7–84}$) [12]. Depending on the assay, large C-terminal fragments can account for up to 10–30 % of immunoreactive PTH in patients with normal renal function, and up to half in patients with renal failure [6, 13]. Despite these limitations, intact assays are still widely used in many clinical laboratories, and reliable reference ranges have now been established in many patient populations.

Bioactive (Third-Generation) Assays

To eliminate cross-reactivity with all C-terminal fragments, third-generation or "bioactive" ("whole" or "bio-intact") PTH assays were developed. Bioactive PTH assays employ a similar capture antibody compared to intact assays but use detection antibodies directed against epitopes located at the extreme N-terminal region (e.g., epitopes 1–4) [28–31] (Fig. 42.2).

The detection antibodies were later demonstrated to cross-react with yet another PTH molecular form, which had not previously been appreciated [32]. This newly discovered molecular form, referred to as N-PTH, is not a PTH fragment but rather a posttranslational modification (possibly a phosphorylated serine at position 17) of $PTH_{1–84}$ [28, 30, 31, 33]. Because the modification exists within epitopes 15–20, intact assays do not detect N-PTH. While the physiological relevance of the modified PTH remains unknown, N-PTH appears to be over-secreted in the setting of severe hyperparathyroidism and in parathyroid cancer [34, 35].

Because bioactive assays do not cross-react with large C-PTH fragments, the third-generation-to-second-generation PTH ratio is

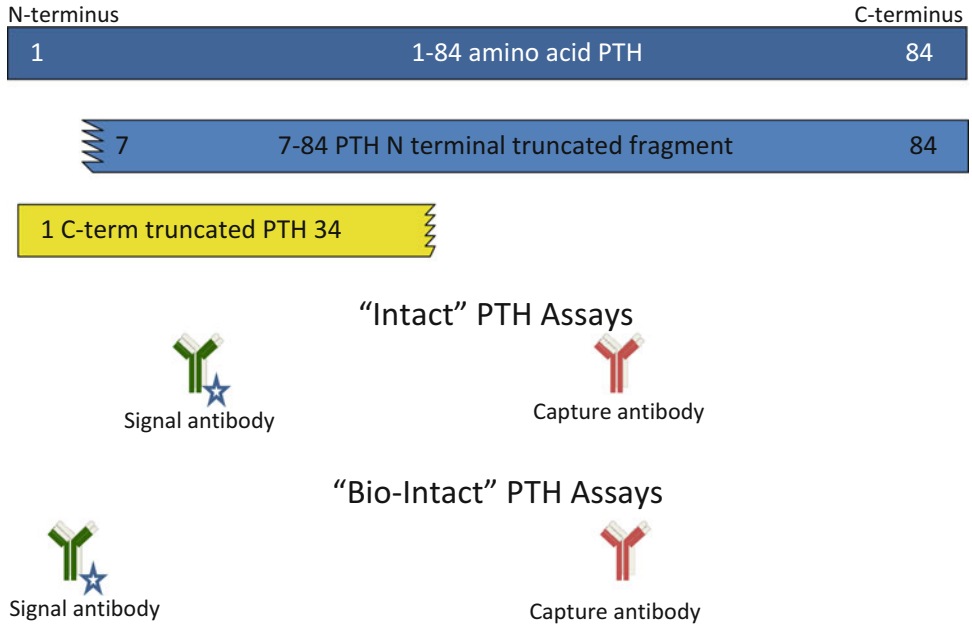

Fig. 42.2 Immunometric PTH assays. Intact PTH assays employ a C-terminal (e.g., epitopes 39–44) capture antibody bound to a solid phase and a second enzyme-labeled N-terminal (e.g., epitopes 13–34) reporter or signal antibody. Third-generation or bioactive ("whole" or "bio-intact") assays employ a similar capture antibody compared to intact assays but use detection antibodies directed against epitopes located at the extreme N-terminal region

generally less than one. However, in the setting of parathyroid cancer, this does not appear to be the case. Interestingly, a third-generation-to-second-generation PTH ratio >1 has a sensitivity of 83.3 %, and a specificity of 100 % for diagnosing parathyroid carcinoma in patients presenting with primary hyperparathyroidism [34, 35]. While more studies are needed, this ratio may be a useful adjunct for diagnosing parathyroid carcinoma earlier in the disease course, and identifying those patients who are at higher risk for recurrent disease [34, 35].

Next-Generation Assays

Liquid chromatography coupled to tandem mass spectrometry (LC-MS/MS) detection has traditionally been limited to the quantitative analysis of small molecules (e.g., testosterone, vitamin D metabolites). However, MS techniques are rapidly being developed and refined for their ability to quantify larger and more complex molecules, such as $PTH_{1–84}$ [36]. To date, the primary challenge preventing widespread implementation of MS for PTH measurement is the significant amount of interference caused by several different modified PTH molecular forms (e.g., oxidized and phosphorylated PTH variants), which can rapidly accumulate in some patient samples. For example, in patients requiring dialysis, a large proportion of PTH becomes oxidized and biologically less active. Thus, results obtained using conventional assays (which include non-oxidized and oxidized PTH) likely over-estimate the true level of biologically active hormone in this patient population.

With this in mind, a variant of the intact PTH assay was recently developed to help improve the specificity of PTH measurements in dialysis patients. First, a monoclonal antibody is used to immobilize and subsequently eliminate all oxidized PTH (identified via methionine residues located at position 8 and/or 18); all remaining PTH is then measured with a conventional intact assay, which employs antibodies against epitopes

26–32 and epitopes 55–64 for capture and detection, respectively [37]. In the original study, a large (but highly variable) proportion (~90 %) of the starting PTH concentration in the dialysis patient samples were determined to be oxidized (biologically less active) [37]. While promising, the clinical implications of differentiating oxidized versus non-oxidized PTH in circulation remain speculative.

Collection, Storage, and Potential Contaminants

Approximately 3–4 mL (minimum 1 mL) of whole blood is collected via venipuncture in a pre-chilled EDTA plasma tube (lavender top). After collection, EDTA whole blood is centrifuged immediately. To avoid hemolysis (which decreases PTH values), the collection tube should not be filled completely, and the sample should remain relatively stable and upright throughout collection, transport, and processing. The specimen is then gently inverted (but NOT shaken) several times to allow mixing. EDTA whole blood is stable for a maximum of 2 h at ambient temperature and 4 h on wet ice.

> [*Note: Serum (red top) tubes, while a less stable reservoir for PTH compared to EDTA plasma, are also acceptable. However, when using serum tubes, the whole blood sample must be allowed to clot, which can take approximately 30 min (potentially longer in patients receiving anticoagulation therapy) after sample collection. Centrifuging serum samples before clotting occurs can result in fibrin formation. While the time required for whole blood to clot may not be critical for routine clinical or laboratory testing, it can be a source of significant delay in the intraoperative setting (see below).*

The plasma (anticoagulated blood) or serum (after a clot has formed) is then separated from the supernatant using a refrigerated centrifuge (10 min at $2095 \times g$). After centrifugation, EDTA plasma is stable for approximately 4 h at ambient temperature, 24 h at 4 °C, 2–4 months at −20 °C, and 2–24 months at −80 °C [38]. Of note, bioactive (third-generation) assays are associated with greater PTH stability compared to their intact (second-generation) counterparts [39].

Heterophile antibodies in human serum, which may be present in up to 11 % of the population, can potentially bridge the assay immunoglobulins (i.e., the capture and signal antibodies) and falsely elevate in vitro diagnostic results [19, 39, 40]. Heterophile antibodies are becoming increasingly prevalent in the USA because of enhanced exposure to monoclonal antibodies for the treatment of chronic inflammatory disorders, cancer, and transplantation [40]. When heterophile antibodies are suspected, re-analysis of the patient's serum may be performed using blocking agents that are specific to the immunoassay [40]. Unusual fragments or genetic variations in PTH have been implicated in falsely low measured PTH concentrations for some assays [41].

PTH Standards and Reference Intervals

The International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) established a PTH working group with the intentions of (1) "[defining the] inclusion/exclusion requirements for an appropriate panel of sera and plasma with which to establish reference intervals and establishment of such a panel with support from the clinical community and diagnostic manufacturers," and (2) "development of a reference measurement procedure for $PTH_{1–84}$ to a standard that would enable its adoption by the IFCC reference laboratory network [42]."

Thus, at present, there remains no PTH standard or reference by which to compare PTH assays, and there is little to suggest that any such announcement is coming any time soon. Regardless of whether a PTH standard is available or not, best practice in regard to measuring PTH in human circulation always involves knowing what the assay *actually* measures and interpreting assay results in the context of other laboratory parameters, in addition to the patient's clinical history and exam findings.

Modern or commercially available PTH assays (i.e., intact and bioactive assays) generally yield reference intervals somewhere between 10 and 100 pg/mL. Intact and bioactive assays pos-

sess sufficient sensitivity and reproducibility to measure PTH concentrations at the low end of the reference range in the normal population (~10 pg/mL) [43]. When reference subjects with vitamin D levels less than 20 nmol/L (which raises serum PTH levels) are excluded, the upper limit of the normal population PTH reference interval is approximately 50 pg/mL.

Significant variability in results obtained by immunometric assays has repeatedly been demonstrated in the literature [44]. Despite all of the discrepancy, there are no known clinically significant differences in the diagnostic sensitivities between intact (second-generation) and bioactive (third-generation) assays for the diagnosis of primary hyperparathyroidism in patients with normal renal function [45–48]. Moreover, bioactive PTH assays have not yet proved any significant advantage over intact assays in the diagnoses of bone disease or other clinical manifestations of secondary hyperparathyroidism in uremic patients [45].

Assays belonging to the same generation can vary by as much as 4.2-fold in magnitude between the lowest and highest reading methods [44, 49, 50]. The difference in the PTH levels between any two assays, however, is generally proportional throughout the range of measurements. There is some evidence that applying dynamic reference intervals (based on a range of serum PTH values obtained by acute modification of serum calcium concentrations in healthy subjects) instead of Gaussian intervals (based on PTH values observed in individuals with normocalcemic concentrations) may significantly improve the clinical sensitivity of PTH assays ([51]; Lepage 1988). In one study, dynamic reference intervals increased the average clinical sensitivity for detecting primary hyper- and hypoparathyroidism from 68 to 100 % [51].

Intraoperative PTH Assays

Rapid PTH Model

In 1988, Samuel Nussbaum (Massachusetts General Hospital) and colleagues presented a small case series ($N = 13$) at the American Association of Endocrine Surgeons (AACE) meeting in Boston suggesting that their PTH immunoradiometric assay (turnaround time 15 min) could be used as an intraoperative adjunct for guiding the extent of neck exploration during parathyroidectomy [27]. In 1993, after Nichols Institute Diagnostics had made available the equipment and labeled antibody for use in an immunochemiluminometric (no longer requiring radioactive isotopes) assay, Dr. George Irvin (University of Miami, Jackson Memorial Hospital) popularized the assay as an adjunct to image-guided, focused parathyroidectomy [52].

Because the plasma half-life of PTH is less than 5 min, intraoperative PTH monitoring enables the surgeon to detect a decline in PTH after the primary source(s) of the excess hormone is excised. The Miami criterion, established by Irvin and continuing to be used today, requires obtaining at least four intraoperative PTH samples (pre-skin incision, pre-gland excision, 5 min post-gland excision, 10 min post-gland excision). A 50 % reduction in PTH levels at 5 or 10 min post-excision is indicative of surgical success. The criteria can be modified or adapted depending on the desired sensitivity and/or specificity [5, 53–55]. For example, many surgeons often also obtain a 20-min sample after gland removal if there is a delayed drop in PTH, which does not meet or is close to the 50 % requirement, before continuing further exploration.

Rapid PTH assays have a turnaround time ranging between 8 and 20 min. Some manufacturers offer a relatively "slower" laboratory mode for routine clinical analysis and a "faster" (e.g., "rapid" or "turbo") mode for intraoperative analysis. For example, the Access® Immunoassay System (Beckman Coulter, Pasadena, CA) offers "routine" (~30 min) and "intraoperative" (~15 min) modes. According to the manufacturer, when PTH levels are >12 pg/ml, the routine and intraoperative modes' imprecision levels are ≤8 % and ≤12 %, respectively. In our experience, the Beckman intraoperative mode yields about 5 % lower PTH levels compared to the routine mode and the differences in precision were within the manufacturer's reported ranges (7 % vs. 6 %).

Table 42.1 Commonly used commercially available (past and/or present) intraoperative PTH assays

Platform (manufacturer)	Setting	Form	Fragments	Reference (pg/ml)	Time (min)
STAT-IO-I-PTH (Future Diagnostics)	Point of care	Intact	$PTH_{1–84}$ Non-$PTH_{1–84}$	10–65	8
Advantage[a] (Nichols Diagnostics)	Point of care	Bioactive	$PTH_{1–84}$ N-PTH	6–40	12
Access Intraoperative Mode (Beckman Coulter)	Central Lab	Intact	$PTH_{1–84}$ Non-$PTH_{1–84}$	12–88	15
Turbo Intact PTH (Diagnostic Products)	Central Lab	Intact	$PTH_{1–84}$ Non-$PTH_{1–84}$	12–72	16
Elecsys 2010/1010/E170 Stat Assay (Roche Diagnostics)	Central Lab	Intact	$PTH_{1–84}$ Non-$PTH_{1–84}$	15–65	9

[a]The Nichols Advantage kit was introduced in 1996 and was the first widely available rapid intraoperative PTH assay. The US Food and Drug Administration removed the assay from the market in 2005 [57]. Future Diagnostics (Wijchen, Netherlands) released a new version of the point-of-care (POC) intraoperative PTH assay called the STAT-IO-I-PTH

See Table 42.1 for other commonly used and commercially available (past and present) intraoperative PTH platforms.

While statistically significant variations among various intraoperative assays have been reported (predominantly in the setting of renal insufficiency), the clinical significance of the variation among commercially available assays is not well established. Technical and patient factors that can cause an insufficient decline in PTH levels include decreased renal clearance in patients with chronic renal disease, significant baseline sample hemolysis or hemodilution (both decrease baseline PTH value), a missed peak, and laboratory errors. Technical factors such as post-excision sample dilution or hemolysis (both decrease PTH value) can lead to a falsely adequate drop in PTH, which in turn can lead to missed parathyroid disease.

Cost-Effectiveness of Intraoperative PTH Monitoring

The cost-effectiveness of intraoperative PTH monitoring is difficult to measure because one must balance the ability of the technique to prevent missed multiglandular disease with the total assay-related costs over time [56]. Additionally, a number of institution-specific factors influence the relative value of intraoperative PTH monitoring. Total assay costs include the platform/instrumentation, reagents, quality controls, calibration material, labor, inspection/service, repairs, and operating room time.

In a literature review involving 4280 patients identified in 17 different studies, Morris et al. concluded that intraoperative PTH monitoring increases the cure rate of minimally invasive parathyroidectomy only marginally (98.8 % vs. 96.3 %) while incurring approximately 4 % additional cost. However, intraoperative PTH monitoring can potentially compensate for itself by reducing operating room times and eliminating the need for frozen sections. Intraoperative PTH reduced overall treatment costs only when total assay-related costs were less than $110 per case (Fig. 42.3). The intraoperative PTH assay was cost saving when the rate of unrecognized multiglandular disease exceeded 6 % or if the cost of the reoperation exceeded $12,000 (compared with initial minimally invasive parathyroidectomy, $3733).

An emerging debate among those who use intraoperative PTH monitoring routinely is whether it costs more or less to perform the PTH assay at the point of care (POC) or via a central laboratory. If POC testing decreases operating room time (estimated at $88–$94 per min), then high-volume thyroid and parathyroid surgical centers may experience considerable cost savings

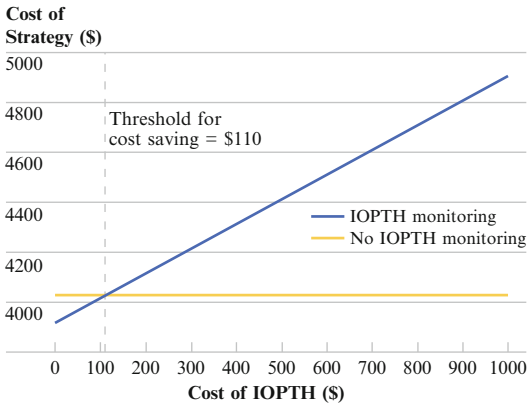

Fig. 42.3 Cost threshold for intraoperative monitoring. Intraoperative PTH monitoring is cost saving when the test-related costs fall below $110. This value considers both the cost of the test and the cost of the operating room time spent waiting for results. Permissions: Morris LF, Zanocco K, Ituarte PHG, et al. The value of intraoperative parathyroid hormone monitoring in localized primary hyperparathyroidism: a cost analysis. Ann Surg Oncol. 2010; 17:679–85

(e.g., $1400 per patient, assuming that POC testing reduces OR time by 17 min) [57, 58]. However, POC assay savings are offset, at least in part, by capital costs of equipment (~$30,000), higher reagents/quality control costs (central lab $3.61 vs. POC $37), and labor (~$28 per hour) [59].

Needle Aspirates

Intraoperative PTH, which is obtained by fine-needle aspiration (FNA), can be used to differentiate parathyroid from non-parathyroid tissue (e.g., thyroid, lymph node, thymus, muscle, fat) with a specificity of 100 % [60, 61]. Generally, FNA is performed with a 3- or 5-mL syringe and a 23- or 25-G needle. The desired tissue is drawn into the syringe and then diluted in about 3 mL of normal saline. The sample is then agitated and centrifuged. The supernatant is analyzed using conventional intraoperative PTH measurements [62, 63]. While the risks of this procedure may be low, they are not negligible and can be severe (e.g., infection, hemorrhage) [64, 65].

Evidence on the efficacy of FNA PTH concentration determination methods as a surrogate "biochemical frozen section" has continued to accumulate [66]. In a large study of 255 parathyroid aspirates and 104 non-parathyroid aspirates, a median (with ± S.D.) of 8120 ± 2711 was found in parathyroid gland tissue aspirates versus 0.8 ± 9.29 for non-parathyroid aspirates. In this large study, the use of PTH measurements of FNA tissue aspirates was 100 % sensitive and 100 % specific, which has also been observed in other studies [62, 67]. Much less distinction in PTH concentrations and a lack of complete sensitivity and specificity have been seen in comparing pathological and non-pathological parathyroid glands [67]. Using POC PTH measurements resulted in a reduction in assay time of 12 min versus 19 min for frozen section results in one institution, although a large number of factors can influence relative times of the two investigations [62].

Alternatively, a "Na-wash" or saline washout method can be utilized in conjunction with cytology. In this method, following collection of cytology samples, FNA saline washes are obtained by washing the empty FNA syringes with 0.5–1.0 mL of saline. Washes from multiple needles can then be pooled and the subsequent saline solution analyzed by PTH determination. Utilizing the Na-wash technique, a comparison of parathyroid FNA determination with a PTH washout procedure exhibited a sensitivity of 84 % and specificity of 100 %, resulting in a positive predictive value of 100 % for parathyroid tissue. In this study, an arbitrary cutoff of 1,000 pg/mL was used for detection of parathyroid tissue. The authors indicated that this cutoff could be lowered. Importantly, this study seemingly indicated that in patients with difficulty in localization of a parathyroid adenoma, FNA with PTH determinations performed better than parathyroid scanning or ultrasonography alone [65]. In addition, the ability of the washout technique to reliably distinguish parathyroid tissue from other tissue has been shown to have application in thyroidectomy to prevent inadvertent damage to the parathyroid [68].

There are analytical considerations or potential interferences for the measurement of PTH in

saline solutions as described previously for plasma PTH. Again, PTH measurements vary widely between different PTH assays. As these sample types are much less well characterized, appropriate cutoffs are not well established and are often arbitrary and technique dependent. Published cutoffs for detection of parathyroid tissue, while not always rigorously evaluated, are relatively similar (100 and 138 pg/mL, for example) [64, 66]. Caution should be used in consideration of appropriate cutoff levels, as they will affect observed sensitivity and specificity. Ideally, some form of validation of the appropriateness of cutoff levels should be attempted in individual institutions. Furthermore, while the PTH assays used to determine PTH in plasma have been FDA approved, they are not approved for alternate sample types such as saline washes from tissue aspirates.

Thus, these assays used in conjunction with saline sample are considered laboratory-determined testing and require additional stability and accuracy validations, as there may be matrix affects or differences in stability as compared to plasma PTH determinations. Furthermore, if proposed FDA guidelines on laboratory-determined tests are finalized, extensive laboratory validation may be required, potentially limiting testing availability for non-validated specimen types [69].

Summary

Measuring PTH in circulation is an important element of the diagnostic assessment for hypocalcemia, hypercalcemia, metabolic bone disease, and parathyroid gland tumors. Assay techniques have evolved over the past 50 years in parallel with our understanding of the PTH molecule. Major advances include the use of nonradioactive isotopes, increased sensitivity and specificity for "intact" or "bioactive" hormone, and reduced incubation times. Intact or bioactive PTH hormone is highly labile and subject to fragmentation. Instability of the molecule is largely dependent upon time and temperature. The ability to rapidly and adequately test for intraoperative PTH has spurred a number of applications and surgical improvement.

Society Guidelines

- CKD-MBD: Monitor serum levels of calcium, phosphorus, PTH, and alkaline phosphatase activity beginning in CKD stage 3 (adults) and in stage 2 (children).

Best Practices

- Assay-specific normative ranges should be established for each assay before making therapeutic decisions for individual patients. This includes establishing normative ranges for particular populations (e.g., patients with chronic kidney disease).
- Intact (second-generation) and bioactive (third-generation) PTH assays are currently used in routine clinical and surgical practice. Fragment-specific assays may increasingly provide insight into the relative contribution of PTH and its fragments to mineral homeostasis in normal and pathophysiological conditions.
- Results obtained by intact and bioactive PTH assays are highly correlated, and both assays can be used for the diagnosis and monitoring of hyperparathyroidism and renal bone disease. The combination of results obtained from intact and bioactive PTH assays may aid in diagnosing parathyroid carcinoma.
- Clinicians and surgeons must always be aware of the particular assay being used and the normal values that are associated with their use.

Expert Opinion

The evolving utilization of intraoperative PTH testing has served as an invaluable and cost-effective tool in parathyroidectomy. A thorough understanding of the clinical chemistry involved with intraoperative PTH analysis, as well as an understanding of pre-analytical and practical testing considerations, contributes to optimization of clinical practice.

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