Interpretation of Plasma PTH Concentrations According to 25OHD Status, Gender, Age, Weight Status, and Calcium Intake: Importance of the Reference Values

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Context: Reference values for plasma PTH assessment were generally established on small samples of apparently healthy subjects, without considering their 25-hydroxyvitamin D (25OHD) status or other potential modifiers of PTH concentration.

Objective: Our objective was to assess ranges of plasma PTH concentration in a large sample of adults, stratifying by 25OHD status, age, gender, weight status, and calcium intake.

Design, Setting, and Participants: This cross-sectional survey is based on 1824 middle-aged Caucasian adults from the Supplémentation en Vitamines et Minéraux Antioxydants study (1994).

Main Outcome Measures: Plasma PTH and 25OHD concentrations were measured by an electrochemoluminescent immunoassay. Extreme percentiles of plasma PTH concentrations were assessed specifically in subjects who had plasmatic values of 25OHD of 20 ng/mL or greater and 30 ng/mL or greater.

Results: Among subjects with 25OHD status of 20 ng/mL or greater, the 97.5th percentile of plasma PTH concentration was 45.5 ng/L. By using this value as a reference, 5% of the subjects with plasma 25OHD less than 20 nmol/L had a high plasma PTH level, reflecting secondary hyperparathyroidism. Among vitamin D-replete subjects (25OHD status of 20 ng/mL or greater), the 97.5th percentile of plasma PTH was higher in overweight/obese subjects (51.9 vs 43.5 ng/L among normal weight subjects).

Conclusions: The reference value for plasma PTH defined in this vitamin D-replete population was far below the value currently provided by the manufacturer (65 ng/L) and varied according to overweight status. These results may contribute to improve the diagnosis of primary and secondary hyperparathyroidism and subsequent therapeutic indication. (J Clin Endocrinol Metab 99: 1196–1203, 2014)
Excessive PTH secretion may be due to problems in the parathyroid glands themselves [primary hyperparathyroidism (PHPT), which leads to hypercalcemia] or may also occur in response to a decrease in serum ionized calcium concentration, as encountered in various situations such as vitamin D deficiency [secondary hyperparathyroidism (SHPT)] (1). In most cases, high PTH secretion maintains a normal calcemia but increases the bone turnover and fragility and, at least in the elderly, enhances the risk of osteoporotic fracture, mainly at cortical sites (2). Furthermore, in prospective population-based studies, PTH concentrations in the upper normal range have been associated with an increased incidence of cardiovascular events (3).

Whereas measurement of blood PTH concentration is frequently done in clinical practice, reference values for blood PTH concentration provided by kit manufacturers were generally established on small samples of apparently healthy but poorly described subjects. In addition, although low levels of 25-hydroxyvitamin D (25OHD) are common in normal people (4), vitamin D status had not generally been taken into account in the previously published reference values for the current PTH assays as reviewed elsewhere (5). Nevertheless, it is now well established that PTH and 25OHD concentrations are inversely correlated (6), that PTH increases when 25OHD concentrations are below a certain value (7), and that PTH decreases when vitamin D-insufficient subjects are given vitamin D supplementation. Therefore, PTH reference values should be revised to take into consideration this phenomenon.

We previously proposed to include only vitamin D-sufficient subjects to establish a reference range for serum PTH (8–10). By doing this with different PTH assays, we systematically found that the upper limit of the PTH concentrations measured in vitamin D-replete subjects was lower than the upper normal limit proposed by the manufacturers’ kits. The difference between our normal values and those of the manufacturers varied greatly from one kit to another (8).

However, these studies were conducted on relatively small samples. In addition, PTH concentrations have been reported to be influenced by a number of other factors. For example, the aldosterone and the whole renin angiotensin aldosterone system may impact on PTH levels (11). An increase in PTH has also been described in older individuals (12), in blacks compared with whites (13), in obese individuals (14), and in those with low calcium intake (6). However, the establishment of PTH reference ranges did not usually take into account these other factors.

For these reasons, it was concluded in the Third International Workshop on Asymptomatic Primary Hyperparathyroidism (15) that further studies were required to establish reference intervals using large population cohorts of vitamin D-replete subjects with an additional stratification by other potential PTH modifiers. Thus, our objective was to assess ranges of plasma PTH concentration (2.5th and 97.5th percentiles) in a large sample of Caucasian adults by stratifying not only by 25OHD status but also by age, gender, overweight status, and calcium intake.

Materials and Methods

Study population

The Supplémentation en Vitamines et Minéraux Antioxydants (SU.VI.MAX) study is a population-based, double-blind, placebo-controlled, randomized trial (clinical trial number NCT00272428) initially designed to assess the effect of a 7.5-year daily antioxidant supplementation on the incidence of cardiovascular disease and cancer (16). Subjects were advised not to take any spontaneous supplementation during the study period. A total of 13,017 subjects were enrolled in 1994–1995. Subjects provided written informed consent, and the study was approved by the Ethical Committee for Studies with Human Subjects at the Paris-Cochin Hospital (Comité Consultatif de Protection des Personnes se Prêtant à des Recherches Biomédicales number 706) and the Commission Nationale de l’Informatique et des Libertés (number 334641). Potential conflicts of interest have been disclosed to the study participants.

A nested case-control study was set up to investigate the association between 25OHD, PTH, and cancer risk and thus included all first primary incident cancer cases diagnosed between 1994 and 2007 (n = 928) and one or two matched controls per case (n = 1850). Controls were randomly selected among the participants of identical sex, age, intervention group, and season of blood draw and without cancer diagnosis by the end of follow-up. The present study focuses on the controls of this nested case-control study.

Baseline data collection

At enrollment, all participants had a clinical examination and anthropometric measurements by study nurses and physicians. They completed self-administered questionnaires on sociodemographic data, smoking, physical activity, medication use, and health status. Dietary intake data were collected by repeated 24 hour-records (one every 2 months). Mean daily calcium intake was estimated using a published French food composition table (17).

A 35-mL venous blood sample was collected at baseline in vacutainer tubes from participants who had been fasting for 12 hours at the time of the visit. All blood draws occurred between October and April. Blood samples were centrifuged immediately after the blood draw, and plasma aliquots were stored in dry ice less than 1 hour after blood draw for shipment toward the central biobank (maximum 24 h), at which they were stored frozen in liquid nitrogen (−196°C).
Laboratory analyses

Baseline (1994) plasma samples were analyzed in 2012–2013 to determine the concentration of PTH and 25OHD. Plasma PTH concentrations were assessed with the Roche Cobas electrochemoluminescent immunometric assay (Roche Diagnostics), a second-generation PTH assay that uses two anti-PTH antibodies, one directed toward the 26–32 portion of the PTH molecule and another directed toward the 53–84 portion (18). The reference values provided by the manufacturer for this PTH assay are 15–65 ng/L, but no data are provided about the characteristics of the reference population from which these values are derived. We found that the interassay coefficient of variation (CV) was less than 2.9% (three samples of various PTH concentrations tested in 42 separate runs), whereas the intraassay CV was less than 1.4% (the same three samples tested 21 times in the same run).

Plasma 25OHD was measured with the Roche Cobas electrochemoluminescent total 25OHD assay, based on the principle of competitive binding (19). We found that the interassay CV was less than 10% (eight samples of various 25OHD concentrations tested in 42 separate runs), whereas the intraassay CV was less than 6.6% (the same eight samples tested 21 times in the same run).

The Jean Verdier Hospital is member of a program developed by the manufacturer Roche (TIQCon-) and an external quality control of Bio-Rad Laboratories (EQAS). The performance characteristics of the vitamin D assays were as follows: target mean, 34.20 ng/mL; mean, 36.02 ng/mL; confidence interval (CI), 34.27–37.78 ng/mL; SD, 0.59; CV, 1.63%; bias, 5.33%; Z score, 3.45. The performance characteristics of the PTH assays were as follows: target mean, 197.0 pg/mL; mean, 191.5 pg/mL; CI, 167.9–215.1 pg/mL; SD, 7.9; CV, 4.10%; bias, −2.79%; Z score, 0.32.

Statistical analyses

First, the distribution of PTH was computed overall, and in subjects with 25OHD of 20 ng/mL or greater and 30 ng/mL or greater, respectively. Second, the Pearson correlation coefficient between PTH and 25OHD plasma concentrations was calculated. Then the nonlinear association between plasma PTH concentration and 25OHD status was modeled by using the SAS NLIN Procedure. Next, the mean and SD of PTH concentrations were computed by plasma 25OHD status. Lastly, the extreme percentiles (2.5 and 97.5) of plasma PTH concentrations were computed overall and stratified by 25OHD status (≥20 ng/mL and ≥ 30 ng/mL), gender, age, overweight status, and calcium intake. Because the distribution of PTH was not considered as being strictly normal according to the Shapiro-Wilk and Kolmogorov-Smirnov tests, the nonparametric method was applied. All analyses were performed with SAS software (version 9.3).

Table 1: Characteristics of the Study Population (n = 1824)

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Table 2 provides values of PTH concentrations according to the level of plasma 25OHD. The linear Pearson correlation coefficient between PTH and 25OHD plasma concentrations was −0.20 (P < .0001). However, the relationship between PTH and 25OHD concentration was nonlinear and modeled by the following equation: PTH = 23.7 + 13.7 exp(−0.1×25OHD) (Figure 2). This equation suggested a plasma PTH plateau level at 24 ng/L and a 25OHD level in which this plateau was reached corresponding to about 30 ng/mL. When plasma 25OHD values were lower than 30 ng/mL, the plasma PTH values began to increase.

Results

Among the 1850 participants to the SU.VI.MAX cohort eligible for the present study, several were excluded for the following reasons: taking a medication containing vitamin D (n = 12), phosphorus (n = 1), or loop diuretic (n = 1), antecedent of epilepsy (n = 3), chronic renal failure (n = 3), or celiac disease (n = 2) or less than two dietary records provided within the first 2 years of the study (n = 4). Thus, 1824 subjects remained for analyses. Characteristics of this study population are described in Table 1. Participants were Caucasian middle-aged men and women. Mean (±SD) plasma PTH concentration was 26.2 ± 9.3 ng/L. As shown in Figure 1, the distribution of PTH was slightly skewed to the right for the whole population but was not in vitamin D-replete subjects. Nine subjects had a PTH value above 65 ng/L (upper normal limit of the kit manufacturer). The proportions of subjects with 25OHD concentrations of 20 ng/mL or less and 30 ng/mL or less were 57.8% and 83.9%, respectively.
Table 3 provides extreme percentiles (2.5 and 97.5) of plasma PTH concentrations overall and stratified by 25OHD status, gender, age, overweight status, and calcium intake. Among subjects with 25OHD status of 20 ng/mL or greater, the 97.5th percentile of plasma PTH concentration was 45.5 ng/L. The corresponding value was similar (45.3 ng/L) among subjects with 25OHD status of 30 ng/mL or greater. This value was 30% lower than the upper normal value proposed by the kit manufacturer (65 ng/L) and slightly lower than the 50.8 ng/L value of the 97.5th percentile of PTH calculated without stratification by 25OHD status.

By using the value of 45.5 ng/L as the upper limit of the PTH reference range, 4.8% of the subjects with a plasma 25OHD concentration of 20 ng/mL or less had a high plasma PTH level, reflecting SHPT. This might be missed if the reference PTH values are those obtained in the entire group, as is usually done.

Among subjects with a 25OHD concentration of 20 ng/mL or greater, the value of the 97.5th percentile of plasma PTH concentration differed by weight status and by calcium intake (Table 3). However, this difference in the value of the 97.5th percentile of PTH according to calcium intake level was no longer observed in subjects with higher vitamin D status (≥30 ng/mL), whereas the difference persisted according to overweight status.

**Discussion**

In this study conducted on a large population-based sample of French Caucasian adults, we investigated plasma PTH values by stratifying not only by 25OHD status but also by age, gender, weight status, and calcium intake as recommended for the establishment of PTH reference val-

![Figure 1](https://example.com/fig1.png)

**Figure 1.** Distribution of plasma PTH concentration in the whole population and in subjects with 25OHD of 20 ng/mL or greater and 30 ng/mL or greater. A, Plasma PTH concentration in whole population (n = 1824). B, Plasma PTH concentration in subjects with 25OHD of 30 ng/mL or greater (n = 293). C, Plasma PTH concentration in subjects with 25OHD of 20 ng/mL or greater (n = 770).

![Figure 2](https://example.com/fig2.png)

**Figure 2.** Plasma PTH concentration according to 25OHD status (n = 1824). The relationship between plasma PTH concentration and 25OHD status was modeled by the following equation: PTH = 23.7 + 13.7exp(-0.1x25OHD).
ues by the expert panel who published the last recommendations for the diagnosis of asymptomatic PHPT (15).

The first step in establishing reference values for a given biological marker is to recruit a healthy reference population. Concerning PTH, exclusion criteria can be defined as any situation possibly inducing an increase or a decrease in PTH concentration. Some of these conditions such as the use of a treatment and/or the existence of a symptomatic disease are easily identified at inclusion, but others are mostly asymptomatic and are ignored if not searched. Among these conditions, vitamin D deficiency/insufficiency is very common in the general French adult population, as confirmed by our results. However, although an increased secretion of PTH in subjects with vitamin D insufficiency is well documented (12), the 25OHD concentration below which PTH levels begin to rise varies widely across studies. It ranged from 10 to 49 ng/mL in a systematic review of literature reporting a PTH-25OHD threshold (20). In the present study, we found that plasma PTH concentration increased when plasma 25OHD values fell below the threshold of 30 ng/mL, a finding consistent with what was previously observed in 1569 samples (different from those of the present study) of the same SU.VI.MAX cohort study in which PTH reached a plateau for a 25OHD concentration of about 31 ng/mL, similarly in all age and gender groups (7). Although part of the discrepancies between PTH-25OHD thresholds across studies may be related to a lack of standardization and operator variability in 25OHD assays (21), it must be noted that the PTH and 25OHD assays used in the present study and in another published report (7) were different.

We found that the 97.5th percentile of the distribution of the Plasma Cobas PTH values in our whole population was 50.8 ng/L, which is 22% lower than the upper normal value of 65 ng/L provided by the manufacturer of this kit. It decreased to 45.5 ng/L (30% lower than 65) in vitamin D-replete subjects. This is consistent with the results of several studies on smaller samples that we previously conducted (8, 9). For example, when excluding subjects with low 25OHD concentrations from a group of 280 healthy Caucasians aged 60–79 years, the upper limit of the PTH reference interval decreased by 29% and 23% with the Nichols Allegro assay and the Scantibodies CAP assay, respectively (9). More recently, we found that the 97.5th percentile of serum PTH concentrations measured with the same assay as in the present study in 240 healthy adults with a 25OHD greater than 30 ng/mL and an estimated glomerular filtration rate greater than 60 mL/min per 1.73 m² was 50 ng/L (8). Although close to the value of 45.3 ng/L found in the present study, it is slightly higher, which may be explained by the use of serum in that reported elsewhere (8) and plasma in the present study. Indeed, we previously showed that, with this PTH kit, plasma values are slightly lower than serum values (22).

Other authors have recently published PTH reference values in vitamin D-replete populations with the same PTH kit with contrasting results (23, 24). La’ulu and Roberts (23) found that the upper reference limit of serum PTH

| Table 3. Extreme Percentiles of Plasma PTH Concentrations According to 25OHD Status, Gender, Age, Weight Status, and Calcium Intake |
|----------------|----------------|----------------|
|                | All            | Plasma 25OHD ≥20 ng/mL | Plasma 25OHD ≥30 ng/mL |
|                | n              | Mean of Plasma PTH SD  | 2.5  | 97.5 | n              | Mean of Plasma PTH SD  | 2.5  | 97.5 | n              | Mean of Plasma PTH SD  | 2.5  | 97.5 |
| All            | 1824           | 26.2             | 9.3   | 14.3 | 50.8           | 247              | 7.9   | 13.5 | 45.5           | 293              | 7.4   | 13.3 | 45.3 |
| Subgroups      |                |                  |       |       |                |                  |       |       |                |                  |       |       |       |
| Men            | 833            | 27.1             | 9.6   | 14.6 | 53.0           | 412              | 8.0   | 13.5 | 49.1           | 167              | 7.3   | 13.3 | 45.3 |
| Women          | 991            | 25.5             | 9.0   | 14.1 | 48.5           | 359              | 7.9   | 12.6 | 44.3           | 126              | 7.5   | 11.7 | 46.7 |
| Age 35–44 y    | 287            | 25.0             | 8.9   | 14.3 | 50.1           | 111              | 8.6   | 13.1 | 50.1           | 43               | 8.3   | 14.7 | 49.1 |
| Age 45–49 y    | 481            | 26.0             | 9.9   | 13.7 | 50.6           | 190              | 8.3   | 11.6 | 45.3           | 63               | 8.2   | 9.4  | 45.4 |
| Age 50–54 y    | 463            | 26.2             | 9.0   | 14.4 | 49.1           | 193              | 6.8   | 13.1 | 44.3           | 66               | 5.7   | 9.7  | 38.1 |
| Age 55–65 y    | 593            | 27.1             | 9.2   | 14.6 | 53.9           | 277              | 8.1   | 14.0 | 50.8           | 121              | 7.4   | 13.8 | 45.5 |
| Non-overweighta | 1137           | 25.6             | 9.1   | 13.9 | 48.5           | 510              | 7.2   | 13.3 | 43.5           | 199              | 7.1   | 13.3 | 43.5 |
| Overweightab   | 678            | 27.9             | 9.6   | 15.2 | 53.9           | 261              | 9.0   | 13.5 | 51.9           | 94               | 8.1   | 11.3 | 50.8 |
| Calcium intake | 1467           | 26.4             | 9.4   | 14.5 | 51.0           | 619              | 8.1   | 14.4 | 49.1           | 235              | 7.6   | 13.5 | 45.5 |

a Overweight was defined as body mass index [weight in kilograms/(height in meters)²] ≥ 25 kg/m².
b Four subjects were excluded because they were taking a medication that contained calcium.
values was 73.5 ng/L in 252 apparently healthy subjects and 60.3 ng/L in the 133 subjects with 25OHD greater than 30 ng/mL. Rejnmark et al (24) found that the upper plasma PTH limit was 81 ng/L in 2316 apparently healthy women aged 17–84 years and slightly decreased to 72.6 ng/L and 67 ng/L in women with 25OHD greater than 32 ng/mL (n = 525) and 25OHD greater than 40 ng/mL (n = 182), respectively. No obvious explanation can be proposed for the differences between these results and especially those of the well-conducted study by Rejnmark et al and our results. Indeed, the fact that they explored only women should not explain their higher PTH limit as in the present study as well as in another report (8), and we did not find different PTH levels in men and in women. Similarly, we do not believe that the larger age range of the population in the study by Rejnmark et al may explain much of the difference because age was not a significant determinant of plasma PTH in our study. However, this deserves further investigation because age was significantly, albeit weakly, correlated with PTH in their study.

The probability that interlaboratory differences in PTH levels would explain discrepancies between the study by Rejnmark et al and ours is also low because the kit used in both studies presents a relatively low interlaboratory coefficient of variation (9.7% for PTH concentrations of 53 ng/L and 7.3% for PTH concentrations of 20 ng/L).

The most important reason for these different results probably pertains to the way blood samples were obtained [i.e., in the early morning after an overnight fast in our study and between 8:00 AM and 1:00 PM in a nonfasting state in the study by Rejnmark et al (24)]. Indeed, circadian variation of PTH concentration is well documented, with a higher concentration during the late morning-early afternoon period than during early morning hours (25–27). Contrary to our study in which the distribution of PTH in vitamin D-replete subjects was not skewed, it was skewed to the right in the study by Rejnmark et al. It is thus plausible that a subset of their population who had a blood sample at the latest hours influenced the distribution of the PTH values and was responsible for the higher upper limit. Interestingly, the 25OHD concentration below which PTH started to increase in the study by Rejnmark et al was 33 ng/mL, consistent with ours. In the study by La’ulu and Roberts (23), the upper PTH limit in subjects with a 25OHD level greater than 30 ng/mL was between our results and those of Rejnmark et al. They used serum samples (slightly higher values than with plasma with the Cobas kit) and provided no data on the timing and fasting/nonfasting state of blood samples. Moreover, the CI of their upper normal value was high, making their result statistically compatible with both studies.

In addition to considering the vitamin D status, we further stratified our analyses by other potential PTH modifiers. As discussed above, gender and age had no influence on PTH values. However, because only middle-aged subjects were included, age range may have been too narrow to obtain a sufficient PTH contrast between age groups. Our results suggest that the PTH reference value definition should integrate weight status and possibly calcium intake. In overweight vitamin D-replete subjects, the upper PTH value was higher than in their nonoverweight counterparts. In subjects with a 25OHD concentration of 20 ng/mL or greater, the 97.5th percentile for PTH was higher in those with lower calcium intake. This difference disappeared in those with a 25OHD status of 30 ng/mL or greater.

The clinical importance of decreasing the upper normal value of PTH concentrations may be questioned. The obvious consequence is that, in clinical practice, much more patients will be detected as having an increased PTH. It will be thus important to evaluate whether there are plausible reasons for an increased PTH secretion in these patients, a question that, in many cases, will need additional explorations. In 2003 (28), we validated in 708 well-documented consecutive osteopenic patients the upper PTH limit of 46 ng/L (compared with the 65 ng/L value of the manufacturer) that we found with the Nichols Allegro assay in vitamin D-replete subjects (9). We showed that our proposed reference values increased the detection of high PTH levels in normocalcemic patients having a potential reason for an abnormal PTH secretion (better sensitivity) with no more than 3% of patients with a PTH above 46 ng/L and no reason for an increased PTH secretion (no loss of specificity). The gain in sensitivity was important as among 348 patients with a potential cause of increased PTH, 46 (13.2%) had a concentration above 65 ng/L, whereas 126 (36.2%) had a concentration above 46 ng/L. Similarly, in a recent study on the effects of parathyroidectomy on bone mineral density, we found that more than half of our 39 patients with a surgically proven normocalcemic PHPT and 40% of those with a hypercalcemic but asymptomatic form of the disease had a PTH concentration measured with the same assay as in the present study below the manufacturer upper normal value of 63 ng/L (29). All data from our previous studies (8–10, 28, 29) were derived from samples obtained after an overnight fast.

Strengths of our study pertained to the large number of subjects, the population-based recruitment, the ability to stratify the PTH concentrations by 25OHD status, gender, age, weight status, and calcium intake. Some limitations should also be acknowledged. First, this study focused on middle-aged Caucasians; thus, additional studies...
are needed to investigate the same aspects in other ethnic groups and younger as well as older adults. In addition, caution is needed when extrapolating these results to the whole French middle-aged Caucasian people because our subjects were volunteers participating in a nutritional intervention study, who generally had a higher education level and occupational status. Second, information on plasma creatinine concentration was available for only 274 subjects. We verified that none of them had an estimated glomerular filtration rate (Modification of Diet in Renal Disease formula) below 60 mL/min per 1.73 m². In addition, three subjects who self-declared a chronic renal failure diagnosed by a physician were excluded from this study. Our results should be confirmed in future studies that precisely control for plasma creatinine concentration in all subjects. Third, measurement of calcium status would have been useful to investigate potential PHPT, but such information was not available in this study. However, this pathology is more prevalent (2%-3%) in women aged 50 years and older (30), which represent only 43% of this study population. Thus, the number of subjects with PHPT, if any, is probably very low. Fourth, the stability over time of PTH preserved in liquid nitrogen has not been documented. However, liquid nitrogen is considered as particularly appropriate for the cryopreservation of biofluids or tissues because its very low temperature strongly inhibits the activity of enzymes. In addition, as previously discussed, our results were very consistent with those of Chapuy et al (7) (on other subjects of the SU.VI.MAX cohort, for whom PTH levels were assessed between 1995 and 1997) in terms of mean PTH concentrations and value of the PTH plateau according to 25OHD levels. This suggests a high stability of the PTH analyte over time, which should be confirmed in ad hoc validation studies. Next, we used only one PTH assay to measure PTH in plasma samples obtained after an overnight fast. Because a huge intermethod variability in PTH results is well documented (8, 22, 31), this study should be extended to other PTH kits. Furthermore, because plasma and serum PTH levels are often different, some kits producing higher plasma concentrations and others producing higher serum concentrations (22, 32), and because the timing of sampling and the fasting/nonfasting status of the subjects/patients influence PTH concentration, a clear consensus statement on the preanalytical requirements for PTH testing (plasma or serum, fasting or not) should be released by an expert panel. Lastly, our results should be reexamined in the future, when the assessment method used for the determination of 25OHD status in this study is definitely calibrated against the recent reference method, based on isotope dilution and mass spectrometry (33).

In conclusion, because even small increases in PTH levels may have potentially harmful bone and possibly nonbone effects, correct detection of abnormal PTH values is of major clinical importance. The present work provided new insights for setting PTH reference values in a large sample of vitamin D-replete middle-aged French Caucasian adults, taking into account other potential modifiers, in line with recent recommendations (15). Our results suggest that the upper limit for plasma PTH measured by the Roche Cobas immunoassay in fasting subjects should be approximately 45 ng/L rather than the 65 ng/L value currently provided by the manufacturer. They also suggest that reference values for PTH could differ according to weight status and calcium intake. These results should contribute to improve the diagnosis of PHPT and SHPT and subsequent therapeutic indication. Further studies are required to evaluate the proposed upper limit for PTH in patient populations, eg, patients with PHPT.

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