mens, we confirmed a sample throughput of 75 specimens per hour; this is reduced by samples with glucose levels triggering ORDAC, or elevated creatinine levels. The results for a "stat" sample for all analytes appeared on the monitor in 135 s, with a printed report being available in 165 s; a single stat result was printed within 2 min.

**Discussion**

The Beckman Synchron CX3 is an eight-test biochemistry analyzer that can process a routine workload at 75 specimens (up to 600 tests) per hour. The instrument reports urinary calcium results, even though the manufacturer recommends that this assay not be performed.

The instrument is generally well designed and requires minimal daily maintenance. To achieve optimum analytical performance of the arsenazo calcium method, we found it necessary to clean the reaction cup and stirrer daily to remove blue deposit, as opposed to fortnightly as recommended. Also, accessibility to the creatinine module at the rear of the instrument is difficult. Operation during the one-month evaluation period was relatively trouble-free, although occasional "rebooting" of the instrument software was required after the appearance of undecipherable information on the video monitor. The software is "user-friendly," with duplicate analysis, easy data recall, special calculations (e.g., anion gap), user-defined comments, bar graph illustrating volumes of remaining reagents, and an automatic resample for over-range glucose results.

Features of software for on-line quality control, bidirectional interfacing, and reduced sample requirements were not available on the instrument tested. A large dead volume was required in relation to the actual volumes used for assay, rendering the instrument unsuitable for neonatal and pediatric specimens. Planned modifications to sample cup geometry and appropriate software should satisfactorily reduce dead-volume requirements. Apart from the problems noted, this well-conceived instrument performed satisfactorily during the evaluation period. We conclude that the performance characteristics make it an ideal routine or stat analyzer for commonly requested tests in the clinical chemistry laboratory.

We thank Mr. J. Glover for assistance with data processing, and Mrs. L. Milosevski and Ms. J.R. Burton for typing the manuscript.

**References**


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**Intact Parathyrin in Postmenopausal Women**

Lori J. Sokoll,1 Frank D. Morrow,2 Diane M. Quirbach,2 and Beas Dawson-Hughes1,3

To establish a reference range, we measured intact parathyrin (parathyroid hormone, PTH) in 245 healthy postmenopausal women, ages 42-75 years, with use of the Allegro Intact PTH Kit from Nichols Institute Diagnostics. We also assayed serum from a subset of 120 of the women with kits specific for mid-molecule PTH. The mean intact PTH concentration for the 245 women was 32 ng/L (95% confidence interval 14-60 ng/L). Intact PTH values in these subjects were not normally distributed, although calcium concentrations in the same samples were. There was positive, but not significant ($r = 0.12, P = 0.06$), correlation between intact PTH and age, and a significant negative correlation between serum calcium and intact PTH that was not observed between calcium and mid-molecule PTH. The improved sensitivity of the intact PTH assay makes it useful in studies of calcium homeostasis in the normal population.

**Additional Keyphrases:** reference interval • calcium • age-related effects • immunoradiometry

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Parathyrin (parathyroid hormone, PTH), an important regulator of calcium homeostasis, exerts a direct influence on bone. Small—15% to 20%—changes, both decreases (1-3) and increases (3), in the concentration of immunoreactive PTH have been demonstrated in serum from osteoporotic women. Investigation of PTH involvement in calcium homeostasis in a normal population requires a sensitive and specific assay capable of detecting even smaller differences. Circulating PTH consists primarily of peptide fragments, the results of intracellular degradation and peripheral metabolism of the intact 84-amino-acid molecule (4, 5). Most commercial kits contain antibodies specific for the carboxyl or the middle portions of the PTH molecule; these assays measure inert fragments as well as the biologically active intact hormone, the latter representing only 5% to 25% of total immunoreactive PTH (6, 7). The intact and amino-terminal fragments have a biological half-life of about 12 min, whereas the carboxyl-terminal fragments have a half-life of 30 to 40 min (8, 9). Measurement of the intact hormone has been shown to be especially sensitive to small changes in calcium concentrations in serum (10). A recently introduced commercially available kit, the Allegro Intact PTH kit (Nichols Institute Diagnostics, San Juan Capistrano, CA), has a detection limit of 1 pg/mL and has been shown to discriminate among patients with disturbances in calcium metabolism (11). In this two-site immunoradiome-
tric assay (IRMA), two different polyclonal antibodies are used. One, bound to polystyrene beads, is specific for mid-region and C-terminal PTH (39–84); the other, labeled with 125I, is specific for N-terminal PTH (1–34). The two antibodies form a sandwich complex with the intact PTH in the specimen.

Here we present an evaluation of the Allegro Intact PTH kit for use in measuring PTH in healthy postmenopausal women. We compare this assay with two different kits designed to measure mid-molecule PTH.

Materials and Methods

Participating in this study were 245 healthy postmenopausal women who were being enrolled in a field trial at the USDA Human Nutrition Research Center on Aging at Tufts University. Their ages ranged from 42 to 75 years, and their last menses had occurred at least one year before. None had a history of fracture of the hip, spine, or wrist, or evidence of vertebral fracture on roentgenograms of the thoracic and lumbar spine. Women with a history of parathyroid disease or other disorder known to affect calcitropic hormones were excluded.

All of the women had normal concentrations of creatinine and 25-hydroxyvitamin D in their sera. Sera and plasma were collected after an overnight fast. Calcium analyses were performed on fresh specimens; aliquots for PTH measurements were frozen in Cryotubes (Nunc, Inc., Newbury Park, CA) at −20 °C for up to eight months before analysis. PTH assays were performed on specimens less than 30 min after thawing.

We measured ionized calcium in anaerobic serum specimens, using the Nova 7 Total Calcium/Ionized Calcium Analyzer (Nova Biochemical, Waltham, MA). Total calcium was determined with the Roche calcium reagent and the Cobas Fara centrifugal analyzer (Roche Instruments, Belleville, NJ). We measured PTH in serum with the "C/MM PTH" radioimmunoassay kit and the Allegro Intact PTH kit from Nichols Institute Diagnostics and in plasma with the PTH Omega radioimmunoassay kit from Cambridge Medical Diagnostics, Inc., Billerica, MA. The PTH Omega kit is specific for the mid-molecule portion. The antiserum is specific for the 53–68 region and the tracer is 125I-labeled PTH (44–68). Synthetic human PTH (1–84) standards range from 500 to 15,000 pg/mL. Bound and free label are separated by using a second antibody after an overnight incubation.

The Nichols C/MM kit is specific for the 44–68 region; it contains antisera specific for this region and 125I-labeled PTH (44–68) tracer. Human standards are also specific for amino acids 44–68 and are supplied at concentrations of 60 to 2500 pg/mL. After a 5-h incubation of antibody with standard or patient's specimen, the tracer is added to the tube; a second antibody/polyethylene glycol reagent is introduced after an overnight incubation.

The Allegro Intact PTH kit utilizes intact (1–84) human standards; concentrations vary from lot to lot but generally range from 12 to 1350 pg/mL. Bound and free hormone are separated by washing the bead after a 22-h incubation. Our intra-assay CV was 5.6%, the inter-assay CV 6.6%.

Results

The distribution of intact PTH values for the 245 normal women is shown in Figure 1. The distribution of intact PTH values was not gaussian (by the Kolmogorov/Smirnov test) although that of serum calcium was. In a subset of 120

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decades were 30.0 and 30.3 pg/mL, respectively, increasing to 33.5 pg/mL for the seventh decade and 36.4 pg/mL for the eighth decade. The positive correlation between intact PTH and age was not statistically significant, however ($r = 0.12, P = 0.06$).

Table 2 summarizes the relationships between serum PTH concentration (assayed with three different PTH kits) and serum calcium (total, ionized, and ionized normalized to pH 7.4) in the subset of 120 women. Intact PTH in serum was significantly but negatively correlated with each of the measurements of serum calcium. However, there was no correlation between the mid-molecule PTH values obtained with either assay kit and serum calcium in this cohort.

Discussion

In this study, we determined reference values for intact PTH in serum of healthy menopausal women. Thirteen subjects (5.3%) who were within our normal range of 14 through 50 pg/mL had values exceeding the normal reference interval stated for the kit (10–55 pg/mL). Elsewhere, Nussbaum et al. (11) defined a normal reference interval of 12 to 65 pg/mL for 72 healthy subjects of unspecified ages. These results reinforce the need for each laboratory to determine its own reference intervals and also to extend the upper limit of the range for the elderly population.

The reason for the non-Gaussian distribution of values for intact PTH is unclear. However, it does not appear to be related to PTH degradation during sample processing or storage, to the age distribution of the subjects, or to the distribution of serum calcium values.

Mean values for intact PTH in serum increased slightly with age. When assays with antibodies directed towards the carboxyl portion of the PTH molecule are used (1, 13–15), the correlation with age is stronger ($r < 0.06$), presumably because more circulating, biologically inactive PTH fragments are being measured. Gallagher et al. (1) found that concentrations of PTH in serum increased by 80% between ages 20 and 90 years when the assay involved an antibody that recognized the mid-molecule portion of PTH (1). With use of an antibody directed towards the intact molecule, however, the increase in PTH was only 30% between ages 20 and 90 (1).

The healthy population displays a tightly-regulated inverse relationship between concentrations of calcium and PTH in serum. The increased sensitivity of the new assay of intact PTH now demonstrates this relationship in the serum of overnight-fasted healthy subjects.

The Nichols Allegro Intact PTH kit has previously been found to be effective in distinguishing surgically proven hyperparathyroidism from hypercalcemia associated with malignancy (11). Here we conclude that the Intact PTH assay is sufficiently sensitive to detect differences in PTH concentrations in a healthy population, which should be of value in the clinical investigation of calcium metabolism.

References


**Circulating Concentrations of Immunoreactive Peptide 7B2 in Certain Pathophysiological Conditions, and Response to Oral Glucose Load**


A peptide, 7B2, originally isolated from pituitary, is present in endocrine tumors, with high concentrations in pancreatic islet tumors. Plasma from most of these patients showed very high immunoreactivity to 7B2 (IR-7B2). To assess whether or not there is any alteration in circulating 7B2 concentrations due to age, sex, etc., we measured concentrations in plasma in 96 fasting healthy subjects, ages three months to 91 years; in patients with various other conditions, including pregnancy; and in cord blood. The response of circulating IR-7B2 to oral glucose was also evaluated. We found particularly high IR-7B2 concentrations in cord blood. Postnatally the concentrations were lower and decreased gradually with age to values for adults [15.6 (SE 2.9) pmol/L], increasing again significantly (P < 0.01) in persons older than 70 years [37.1 (SE 32) pmol/L]. There was no significant sex-related difference in values for plasma. For the pathological conditions studied, we observed significantly supranormal values in patients with chronic renal failure [175.1 (SE 35.9) pmol/L]. Some of the pregnant patients in their third trimester also showed high values. A small but significant increase in plasma IR-7B2 was observed after a glucose load, both in control subjects and diabetics. Perhaps the kidney plays a major role in 7B2 degradation.

**Additional Keyphrases:** pituitary peptides · pancreatic islet tumors · age-related changes · pregnancy · cord blood · possible tumor marker evaluated · renal failure

A pituitary protein, designated 7B2, has been isolated from porcine and human pituitary glands (1, 2). A subsequently developed radioimmunoassay (3–5) revealed its existence outside the pituitary gland. It was present in especially high concentrations in the endocrine pancreas (6) and adrenal medulla (4). Furthermore, this immunoreactive 7B2 (IR-7B2) was shown to be released from the PC12 pheochromocytoma cell line (7). Concentrations of IR-7B2 in plasma were also high in patients with pancreatic islet tumors (8), and such endocrine tumors themselves had a high 7B2 content. Little is known about IR-7B2 concentrations in plasma of persons of different age groups or with pathological conditions other than neoplastic diseases.

In this study we looked for changes in plasma IR-7B2 with age, gestational weeks, sex, or certain pathological conditions.

**Materials and Methods**

Subjects

We collected plasma from 96 fasting subjects, three months to 91 years old (mean age 37, SD 30 years; males 37, females 59), and from 23 umbilical cords. We also examined plasma samples from the following additional groups:

- Group 1, 101 diabetic patients, with or without diabetic complications.
- Group 2, 28 patients with hyperthyroidism.
- Group 3, seven patients with primary hypothyroidism.
- Group 4, 13 patients with hepatic cirrhosis.
- Group 5, 43 patients with chronic renal failure, regularly undergoing hemodialysis.
- Group 6, 35 patients with cerebral vascular accident (cerebral hemorrhage or infarction).
- Group 7, 36 pregnant patients (eight to 40 weeks of gestation).

All patients were definitively diagnosed in each case by a combination of clinical and laboratory features. All patients with thyroid disorders had also been assessed by radioimmunoassay of thyroid hormones or thyrotropin and serological examinations. Table 1 lists details of these patients.

To assess the effect of food intake, we gave a 75-g oral glucose load to seven normal subjects (mean age 56.6, SD 13.8 years; five men, two women), eight hyperthyroid patients (mean age 39.9, SD 15 years; two men, six women), and 33 diabetics (mean age 51.5, SD 18.3 years; 15 men, 18 women). Blood was sampled from 0 to 180 min after glucose ingestion from the antecubital vein. All blood samples were