Dear Sir,

Several in vitro studies have demonstrated that a higher extracellular calcium concentration is necessary to decrease PTH secretion from parathyroid glands taken from patients with secondary hyperparathyroidism [1, 2]. In these earlier reports, however, PTH secretion was analyzed in terms of percentage of maximum release, and the results were not discussed in relation to the intensity of hyperparathyroidism in uremic patients. Thus, it is still unknown how the secondary hyperparathyroidism progresses, and the optimal treatment remains to be established.

To evaluate the variation of PTH secretion in uremia, 8 patients with serum levels of intact PTH from 82 to 1117 pg/ml and serum total calcium less than 10 mg/100 ml were studied. They were receiving hemodialysis for 4–5 h, 3 times a week, and their predialysis phosphate levels were controlled below 6 mg/l00 ml with calcium carbonate alone. Four patients out of 8 had not been given any vitamin D analogues, and the others had been taking a minimum dose (0.25 µg/day) of lα-hydroxy-cholecalciferol [lα(OH)D3].

In these patients, lα(OH)D3 was started or gradually increased in dosage to elevate serum calcium concentration, and predialysis levels of serum ionized calcium and intact PTH (Allegro intact PTH assay) were determined weekly for more than 15 weeks. When the serum total calcium value exceeded 11.0 mg/100 ml, the doses of lα(OH)D3 were decreased. Increased doses of lα(OH)D3 were used to elevate the serum calcium, since PTH secretion is not suppressed directly by oral treatment with vitamin D analogues [3]. Throughout the study, predialysis phosphate levels were kept below 6 mg/l00 ml in every patient, but the doses of calcium carbonate were not changed. Calcium concentrations in the dialysate were

intact PTH
1000
Ionized Ca mmol/l
Fig. 1. Correlation curves between serum ionized calcium and intact PTH in patients with chronic renal failure.

Increased doses of 1α(OH)D3 brought about a gradual elevation in serum total and ionized calcium concentrations and a decrease in intact PTH levels. Correlation curves between ionized calcium and intact PTH observed in each patient are shown in figure 1. Comparing the correlation curves of the patients numbered 1, 2, and 3, whose initial intact PTH had exceeded 500 pg/ml, with the curves of other patients, the curves of the former patients were shifted to the right upper side with steeper slopes. In these 3 patients, moreover, small changes in ionized calcium around 1.5 mmol/l were accompanied by sharp changes in PTH toward the opposite direction.

Although we did not follow the time-course changes in the correlation curve in a given patient, the findings described above are considered to demonstrate the way of progression in secondary hyperparathyroidism. As secondary hyperparathyroidism progresses, higher levels of serum calcium are needed in order to suppress PTH release, and the basal secretion of PTH is also elevated as shown in figure 2. Furthermore, at the lower concentrations of serum calcium, small changes of it cause a sharp elevation or suppression of PTH in patients with advanced secondary hyperparathyroidism.

Recent studies [4, 5] have shown that intravenous 1,25(OH)2D3 shifts the correlation curve between serum ionized calcium and PTH secretion to the left. However, it is still uncertain whether this direct suppression of PTH is strong enough to replace surgical parathyroidectomy.

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