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TOPIC: CORRELATION BETWEEN PTH AND BONE ACTIVITY

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PTH measurements and other biochemical markers are often used as a means to assess the type and severity of renal osteodystrophy. Thus, one assumption would be that the bone response to PTH is uniform. But factors including among others phosphate, vitamin D status and treatment, and race (bone of black patients respond less to PTH) would be confounding variables that affect the bone response to PTH. These factors thus have the potential to alter the anticipated correlation between PTH and bone activity. Another confounding variable is that the relationship between PTH and serum calcium is bifunctional. In other words, hypo- and hypercalcemia respectively stimulate and suppress PTH values, but PTH also increases the serum calcium concentration. As shown in the figure below (JASN 6:1371, 1995), the predialysis (basal) PTH value can be similar over a range of serum calcium values (<8.5, 8.5 to 9.5, and >9.5 mg/dl) even though the secretory capacity of the parathyroid gland (maximal PTH) can vary by as much as

three-fold with maximal PTH being greater in the patients with higher serum calcium values. Thus, the higher serum calcium concentration acts to modify the predialysis (basal) PTH value. A reasonable question would seem to be whether the bone activity is only a function of the predialysis (basal) PTH value or does the magnitude of hyperparathyroidism also affect the bone activity.

In another study, the effect of hypo- and hypercalcemia on the ratio of whole PTH (1-84 PTH only) to intact PTH (1-84 and non 1-84 PTH) was evaluated (KI 64:1867, 2003). The induction of hypocalcemia increased the ratio of whole to intact PTH and the induction of hypercalcemia decreased the ratio of whole to intact PTH. While 1-84 PTH activity should increase bone activity, non 1-84 PTH has been shown to decrease the calcemic action of 1-84 PTH and thus

non 1-84 PTH may also decrease the bone activity of 1-84 PTH. Because a wide range of serum calcium values are seen in the dialysis patient, the ambient serum calcium concentration through its action on non 1-84 PTH production might modify the effect of 1-84 PTH on bone activity. Thus, differences in the serum calcium concentration in the dialysis patient might have the capacity to modify the expected relationship between PTH and bone activity in renal osteodystrophy.

The bone response to PTH is modified by phosphate with a high phosphate decreasing the calcemic action of PTH (Bone 25:279, 1999). Whether the high phosphate modifies the effect of PTH on bone activity and other biochemical markers of bone activity is not known, but would not be surprising. Finally, it has been shown in the dialysis patient that calcitriol treatment decreases bone activity even in the absence of a decrease in PTH. Calcitriol treatment also probably reduces the capacity of PTH to remove calcium from bone during hypocalcemia and for bone to buffer calcium during hypercalcemia (Nephron 71:218, 1995).

In summary, there is considerable evidence to suggest that the relationship between PTH and bone activity is not a simple linear relationship, but rather several confounding factors would be expected to alter the relationship.