

Direct Measurement of the Hormone 7-84 PTH

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In 1998, D'Amour et al. discovered that the iPTH assay measures 1-84 PTH and 7-84 PTH. In 2000, Slatopolsky et al. discovered that 7-84 PTH was hypocalcemic and was secreted by the parathyroid gland. In 2001, Malluche et al. demonstrated that the 1-84 PTH/7-84 PTH ratio was 94% accurate in predicting bone turnover (far exceeding iPTH or the newer 1-84 PTH assay.) In 2002, Divietti et al. demonstrated that the 7-84 PTH inhibited osteoclast formation and bone resorption (as opposed to 1-84 PTH) and mediated its actions through a PTH C-terminal receptor (as opposed to the 1-84 PTH N-terminal receptor.) In 2003, Malluche et al. demonstrated that the 7-84 PTH inhibited osteoblast formation, bound PTH target cells and lowered bone turnover. In 2003, Yamashita et al. discovered that 7-84 PTH has nearly twice the half life of 1-84 PTH. In 2003, Friedman et al. found that 7-84 PTH specifically down regulated the 1-84 PTH receptor on distal tubule cells, but not proximal tubule cells. In 2003, Waller et al. found that the 1-84 PTH/7-84 PTH measurement of total PTH (1-84 PTH + 7-84 PTH) and $7-84 \text{ PTH} = \text{tPTH} - (1-84 \text{ PTH})$. This indirect method of assessing 7-84 PTH can result in an amplified variance from variances in the CAP and tPTH assays. We describe a method for the direct assay of 7-84 PTH involving 2 steps. At first 250 microliters of patient plasma are incubated at room temperature for 5-8 hours in a tube coated with an amino terminal antibody that binds 1-84 PTH, but not the 7-84 PTH which remains soluble. Then, 200 microliters of the 7-84 PTH plasma is removed and placed into another tube to which is added a 3/16 inch bead coated with 39-84 PTH antibody along with 0.1 ml of 125-I labeled 7-34 PTH antibody. The assay of the 7-84 PTH proceeds at room temperature with rotation for 10-18 hours, after which time the bead is washed and assessed for gamma radiation which corresponds to the concentration of 7-84 PTH. The direct 7-84 PTH assay has been validated to specifically measure 7-84 PTH and not measure 1-84 PTH. This method improves the precision of the 1-84 PTH/7-84 PTH ratio.

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