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## ARTICLES

# Calcium modulation of adrenocorticotropin levels in women--a clinical research center study

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In vitro calcium modulation of anterior pituitary hormone secretion has been well described. In addition, several investigations performed in human subjects have documented modulation of the circulating levels of pituitary hormones by supraphysiological calcium concentrations. Recent data from our laboratory document the existence of an extracellular calcium-sensing receptor that is thought to mediate the effects of variations in extracellular calcium on the secretion of PTH and calcitonin. We have also demonstrated the presence of this receptor in pituitary-derived, ACTH-secreting AtT-20 cells as well as in the anterior pituitary of rats and mice. In the present study we investigated the effect on anterior pituitary hormone levels of variations in serum calcium within the physiological range. We serially measured serum levels of ionized calcium (Cai), ACTH, cortisol, TSH, and PRL during 90-min iv infusions (on separate days) of calcium, citrate, and dextrose in 10 healthy women with a mean age of 55 +/- 5 yr. During the calcium infusion, the serum Cai level increased significantly from 4.32 +/- 0.10 mg/dL at baseline to 4.86 +/- 0.08 mg/dL at completion ( $P = 0.002$ ), and this change was accompanied by a significant increment in the serum ACTH level from 9.87 +/- 1.32 to 16.31 +/- 2.84 pg/mL ( $P = 0.0008$ ). There was no change in the serum ACTH level during the citrate infusion despite significant decrements in serum Cai, nor were there changes in either Cai or ACTH during the dextrose infusion. Finally, changes in Cai did not alter TSH or PRL levels. In summary, our dynamic studies are the first to demonstrate an increase in baseline serum ACTH levels in response to physiological increments in Cai (i.e. increments within the normal range). This effect was specific for increments and not decrements in serum Cai and was selective for ACTH, as TSH and PRL levels did not change with any of the infusions.