58. LOW CONCENTRATIONS OF PLASMA CORTICOSTEROIDS IN RABBITS IMMUNIZED WITH CORTICOTROPHIN RELEASING FACTOR (CRF-41)

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Recently described corticotrophin releasing factor isolated from ovine hypothalamus and synthesized based on the recently described sequence containing 41 amino acids (CRF-41) was used for immunizations of White New Zealand rabbits. The synthetic peptide, CRF (Bachem), was coupled to bovine serum albumin and injected into three rabbits. All the rabbits developed antibodies as demonstrated by the binding of ^{125}I-CRF (iodinated tyrosine derivative). The titers were: 1:8000, 1:12000 and 1:16000. Sera from the control rabbits failed to bind the tracer. The immunized rabbits were found to have significantly lower corticosterone plasma concentrations (0.049 ± 0.003 µg/100 ml; n of samples=12;) than the controls (0.38 ± 0.28 µg/100 ml; n=27), $p < 0.01$. Plasma cortisol values were also significantly lower (0.22 ± 0.01 µg/100 ml vs 0.50 ± 0.07 µg/100 ml; $p < 0.01$). These results suggest a physiological role of CRF-41 in the regulation of the pituitary-adrenal system. (M.L. is currently on sabbatical leave from the Clinical Research Institute of Montreal; M.P.P. is currently on sabbatical leave as a Josiah Macy Fdn. Scholar.)

59. CRF REVERSES DEXAMETHASONE SUPPRESSION OF CORTICOSTERONE SECRETION IN RATS

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The ability of the newly sequenced peptide, CRF, to stimulate the pituitary-adrenal axis in rats was tested using a paradigm involving dexamethasone suppression, nembutal light anesthesia (tranquilization) and either saline or CRF intravenous administration. Adult male rats (Sprague-Dawley) were given either dexamethasone (400 µg) or saline i.p., 4 hours prior to nembutal tranquilization. CRF (or saline) was given 15 to 30 minutes after the nembutal in doses of 3.0, 10.0 or 24 µg/rat (average weight 270 gms). Dexamethasone suppressed bothcorticosterone (B) and aldosterone secretion. CRF elevated significantly plasma B in a weak dose-response fashion; near maximal stimulation was found with the lowest doses of CRF employed. The response profile was similar to that reported previously (Rivier et al., Endocrinology 110:272, 1982). However, contrary to their findings CRF reversed dexamethasone suppression by approximately 50%. The addition of morphine to the paradigm had not effect on the CRF reversal. It is concluded that while CRF is an endogenous regulator of plasma corticosterone, its sites of action and interaction with other regulatory factors remain to be elucidated completely. (MPP is currently on sabbatical as a Josiah Macy Jr. Foundation Scholar.)

60. INFLUENCE OF CORTISOL ON IN VITRO METABOLISM OF HUMAN TRABECULAR BONE

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The development of a procedure for incubating trabecular bone from the femoral heads of human hip replacement recipients has allowed us to investigate the metabolism of Ca^{++}, Mg^{++}, and phosphate (PO_4^{3-}) by bone under standard in vitro conditions. Upon incubating trabecular bone for 6 hours we observed a time-dependent uptake of Ca^{++} and Mg^{++} from and release of PO_4^{3-} into the incubation medium, accompanied by a concomitant rise in alkaline phosphatase (AP) concentration. Trabecular bone inactivated by boiling for 3o min showed a net uptake of all 3 electrolytes from the medium, while AP activity remained undetectable. Addition of cortisol to the medium led to a dose-dependent increase in the net uptake of Ca^{++} and Mg^{++} and a decrease in the release of PO_4^{3-} as well as a decrease in the activity of the AP.

Our incubation model responded to cortisol in a time- and dose-dependent manner, and may thus allow further evaluation of the direct effects of hormones on the mineral metabolism of human bone.