The effect of reserpine on pituitary-adrenocortical function in the rat

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Although the effect of reserpine on hypothalamo-pituitary-adrenocortical (HPA) function has been extensively studied there is still a great deal of confusion in the literature about this aspect of its action. Pituitary adrenocortical activity was assessed in male Sprague-Dawley rats and changes in adrenal ascorbic acid (Roe & Kuether, 1943) and plasma corticosterone (Zenker & Bernstein, 1958) concentrations were used as indices of corticotrophin (ACTH) release. One hour after a single intraperitoneal injection of either 1.25 or 2.5 mg/kg of reserpine adrenal ascorbic acid was depleted and the plasma corticosterone concentration was elevated. The effect persisted for 24 h suggesting that the drug causes prolonged hypersecretion of ACTH. Increased pituitary adrenocorticotrophic activity was evident in rats treated with the same volume of vehicle (1.0% glacial acetic acid in deionized water, pH 4) 1 h but not 24 h later. After 5-7 repeated, single, daily injections of the same doses of reserpine it was found that adrenal ascorbic acid and plasma corticosterone concentrations were normal 1 h after the final injection, indicating that the alkaloid no longer acted as a stressful stimulus, i.e. some form of 'adaptation' occurred. No similar 'adaptation' was observed in response to injection of vehicle alone. Rats 'adapted' to reserpine were exposed to cold (4° C for 1 h) either immediately or 24 h after the final injection. In animals 'adapted' to the higher dose of reserpine ACTH release no longer occurred and no change was seen in the concentrations of adrenal ascorbic acid and plasma corticosterone when the stress was applied immediately after the final injection. However, there was also an apparent inhibition of ACTH release in the corresponding vehicle treated rats. Twenty-four hours after the final injection the application of cold stress caused a rise in the plasma corticosterone concentration *without* a concomitant depletion of adrenal ascorbic acid in reserpine treated rats. The stress response in the corresponding vehicle treated controls was normal. It appears that, in certain conditions, reserpine can effectively inhibit the functional activity of the HPA system but in practice the use of different parameters of ACTH secretion and the neglect of proper controls can lead to widely different interpretations of the experimental data.

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References

ROE, J.H. & KUETHER, C.A. (1943). The determination of ascorbic acid in whole blood and urine through the 2.4-dinitrophenylhydrazine derivative of dehydroascorbic acid. *J. Biol. Chem.*, **147**, 399-407.

ZENKER, N. & BERNSTEIN, D.E. (1958). The estimation of small amounts of corticosterone in rat plasma. *J. Biol. Chem.*, **231**, 695-701.

Oestrogen dependence of enzyme activity and intracellular structure in the hamster submaxillary gland

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Recently we analysed the androgen dependence of individual estero-proteases and cell structures in the mouse submaxillary gland (Bhoola, Dorey & Jones, 1973). Changes in the activity of chymotrypsin- and trypsin-like enzymes and renin correlated closely with variations in the granule population of the secretory tubules of the mouse gland. In contrast, the estero-protease kallikrein and secretory organelles in the acinar cells showed no such dependence on androgens. Consequently, experiments were designed to determine whether kallikrein activity and the granule population in acinar cells of the mouse and hamster are influenced by oestrogens. No such relationship has been demonstrated for ovarian hormones previously, even though the hamster shows a sialomucin sex-hormone linked dimorphism (Shackleford & Klapper, 1961). In the present communication we report our findings in the hamster.

Estero-protease activity in the hamster submaxillary gland can be ascribed mainly to kallikrein; it was measured on benzoyl L-arginine ethyl ester (BAEe) and expressed as specific activity ($\Delta_{E_{366}}$/min)/mg protein, $n = 8$. The kallikrein activity (BAEe) increased post-natally from 2.91 in the male and 0.83 in the female (18-22 days old) to 9.88 in the male and 14.83 in the female (88-92 days old). Ovariectomy resulted in a fall in