

REFERENCES

- GILMORE, N. J., VANE, J. R. & WYLLIE, J. H. (1969). Prostaglandin release by the spleen in response to infusions of particles. In *Prostaglandins, Peptides and Amines*, ed. Mantegazza, P. & Horton, E. W., pp. 21-20. London: Academic Press.
- LINDSEY, H. E. & WYLLIE, J. H. (1970). Release of prostaglandins from embolized lungs. In the Press.
- PIPER, PRISCILLA J. & VANE, J. R. (1969). Release of additional factors in anaphylaxis and its antagonism by anti-inflammatory drugs. *Nature, Lond.*, **223**, 29-35.
- THOMAS, D. P., STEIN, M., TANABE, G., REGE, V. & WESSLER, S. (1964). Mechanism of bronchoconstriction produced by thromboemboli in dogs. *Am. J. Physiol.*, **206**, 1207-1212.

A comparison of the effects of betamethasone and tetracosactrin on hypothalamo-pituitary-adrenal activity in the rat

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Hypothalamo-pituitary-adrenal function may be impaired after therapy with corticosteroids or corticotrophin (ACTH). Hypothalamo-pituitary-adrenal activity was studied in male albino Sprague-Dawley rats which had been given prolonged treatment with betamethasone [Betnesol, Glaxo (40 μ g/100 g)/24 h for 2 weeks] in the drinking water, or with tetracosactrin (Cortrosyn Depot, Organon 10 μ g/100 g injected subcutaneously once a day).

The growth rate of the rats was impaired less by tetracosactrin than by betamethasone. The normal circadian rhythm and the stress-induced rise in plasma corticosterone concentration were absent following treatment with either the steroid or tetracosactrin. Betamethasone-treated rats showed adrenal atrophy and insensitivity to exogenous corticotrophin, in contrast to tetracosactrin-treated animals, in which there was adrenal hypertrophy and an exaggerated plasma corticosterone rise in response to exogenous ACTH.

Both tetracosactrin and betamethasone cause impairment of hypothalamo-pituitary-adrenal function. The effect of betamethasone is due both to insensitivity of the adrenals to ACTH and to an inability of the hypothalamo-pituitary complex to mobilize endogenous corticotrophin. Tetracosactrin, however, leaves adrenal sensitivity unaffected but inhibits ACTH secretion markedly. The findings suggest that the clinical use of ACTH to aid withdrawal of corticosteroids may be contra-indicated.

The relationship between ascorbic acid concentrations and cortisol production during the development of scurvy in the guinea-pig

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Male guinea-pigs weighing 400 g were fed on an ascorbic acid deficient diet for two weeks with a daily oral supplement of 50 mg of vitamin C, before being given the diet without the supplement for a period of 27 days. Ascorbic acid and cortisol

estimations were carried out on the blood and tissues of six animals at intervals while the scorbutic diet was being administered, and changes in tissue and body weight were recorded. On the 27th day animals were spontaneously dying and showed morphological evidence of scurvy. The body weight increased until the twelfth day on the scorbutic diet in the same way as in control and hypervitaminotic animals (Odumosu & Wilson, 1970). Thereafter it decreased, and was 8.5% less than the initial weight on the 27th day ($P < 0.05$). The adrenal weights increased consistently from the sixth day and finally were 65% above the initial weights. The adrenal cortisol concentration remained constant until the sixth day. It had fallen to 75% of its initial level by the eighteenth day, but the decrease then stopped until the end of the experiment. From the first day of vitamin C deprivation the plasma cortisol increased, and on the 27th day it was 27 times its initial value. Values for the biliary cortisol increased in a comparable fashion. Like the adrenal cortisol, the adrenal ascorbic acid concentration did not alter during the first 6 days of the scorbutic diet. Thereafter adrenal ascorbic acid diminished rapidly. 87% of the ascorbic acid had disappeared by the eighteenth day, and ultimately 99.5% had been lost. Plasma ascorbic acid increased during the first 6 days and then fell consistently to almost zero on the 27th day. Leucocyte ascorbic acid did not decrease until after the sixth day. By the eighteenth day 40% had been lost, but thereafter leucocyte ascorbic acid fell significantly more slowly than plasma ascorbic acid as shown by the change in angle of the regression lines relating plasma and leucocyte values. During the development of scurvy the corticosteroid secretion increases on the sixth day at the same time as a change appears in the metabolic use of ascorbic acid. On the eighteenth day adrenal production of cortisol levelled out at the same time as the leucocytes began to conserve their stores of ascorbic acid. Throughout the experiment plasma ascorbic acid showed a more extensive range of variation than leucocyte ascorbic acid. We suggest that this indicates that plasma values give a measure of metabolic demands, and leucocyte values indicate storage capacity for ascorbic acid.

REFERENCE

- ODUMOSU, A. & WILSON, C. W. M. (1970). The growth maintaining activity and intestinal absorption of ascorbic acid in guinea-pigs. *Br. J. Pharmac.*, in the Press.

Isolation of dense-cored granules from the neurosecretory system of the vena cava of the small octopod, *Eledone cirrosa*

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A system of nerves associated with the vena cava of the cephalopod, *Eledone cirrosa*, has been proposed as having a neurosecretory function (Alexandrowicz, 1964). An extensive system of nerve terminations, containing numerous electron-dense granules, is closely associated with the inner wall of the blood vessel. A potent cardio-excitatory substance is associated with these nerve terminations (Berry & Cottrell, 1970). It is possible to scrape off this inner layer of nerve terminations. Such material provides a very suitable preparation for the isolation of the electron-dense granules.

The tissue was isolated in 1.1 M sucrose (a solution approximately isotonic with sea-water), homogenized, and prepared for centrifugation on a discontinuous sucrose