The regulatory role of vitamin C on the adrenal function and resistance to histamine aerosol in the scorbutic guinea-pig

SIR,—Numerous controversial reports concerning the effect of vitamin C on the functional state of the adrenal cortex in the scorbutic guinea-pig have appeared. Bacchus & Heiffer (1953) reported a decrease in the urinary corticoid excretion; Done, Ely, Heiselt & Kelley (1953) found increased adrenocortical activity, while Nadel & Schneider (1952) reported a decrease in the early stage and an increase in the late stage of scurvy. The adrenal function and its possible effect on the resistance to histamine aerosol in the scorbutic guinea-pig is here reported.

Guinea-pigs, 375–425 g, were put separately in metabolic cages and 24 hr urine specimens collected in bottles containing 50% sulphuric acid (1·5 ml). After collecting 3 or 4 normal samples, the diet was replaced by a scorbutic diet and the daily urine specimens were collected for 21 days. The fluorimetric technique of Silber, Busch & Oslapas (1958) for the estimation of 11-hydroxy-corticosteroids was applied using a sulphuric acid : ethanol mixture (75 : 25 v/v) for developing fluorescence. The fluorescence was measured after 15 min in an Aminco–Bowman spectrophotofluorimeter. The peak activation (470 mμ) and fluorescence (530 mμ) wavelengths of all urine samples coincided with those of the hydrocortisone standard. Recovery of hydrocortisone from the urine samples ranged from 94 to 105%. Twenty-four hr after bilateral adrenalectomy the residual non-specific fluorescence amounted to 2·5 to 3·6 μg/day. The amount of 11-hydroxycorticosteroids excreted was dependent on diuresis and therefore the daily water intake was regulated. The average urinary daily corticoid excretion was 98 μg. On the 3rd day of scurvy there was a significant but transient rise in corticoid excretion, possibly due to the rise in urine volume. On the 12th day the average daily excretion was 54 μg. Oral treatment of the scorbutic animals with 50 mg vitamin C daily for 5 days raised the lowered urinary corticoids to normal. If the guinea-pigs were left till the late stage of scurvy, there was a gradual increase in the corticoid excretion till on the 21st day it reached 2·5 times the normal level. Treatment with 50 mg of vitamin C orally for 7 days lowered the elevated corticoid excretion to normal.

The relation between adrenal function and resistance to histamine aerosol was striking. The drop in the resistance of the guinea-pig to histamine aerosol on the 12th day of scurvy and the marked rise on the 21st day (Guirgis, 1965) coincided with the stages of adrenal insufficiency and adrenal hyperfunction respectively. Vitamin C treatment at both stages restored to normal not only the impaired adrenal function but also the resistance to histamine aerosol. The disturbance in histamine metabolism in the scorbutic guinea-pig as reported by Dawson & West (1965) may also have some effect on the resistance of the animal to histamine aerosol.

The mechanism of the anti-anaphylactic effect of vitamin C in the normal guinea-pig is still uncertain. Vitamin C injected in a dose of 100 mg, 20 min before challenge did not protect the guinea-pig from histamine aerosol. Such treatment, however, increased 2·9 times the mean preconvulsion time of sensitized guinea-pigs subjected to antigen aerosol. In this connection Goadby & Smith (1964) reported an increase of 2·1 times with hydrocortisone hemi-succinate.

It is concluded that the functional state of the adrenal cortex in the scorbutic guinea-pig determines the resistance of the animal to histamine aerosol. The

effect of vitamin C on anaphylaxis in the normal guinea-pig is worthy of further investigation.

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The pharmacology of amygdaloid neurones

SIR,—The amygdala contains several potential neurotransmitter substances together with their enzymes of synthesis, for example, 5-hydroxytryptamine, noradrenaline (Vogt, 1954; Kuntzmann, Shore, Bogdanski & Brodie, 1961) and acetylcholine (Hebb & Silver, 1956). However, the direct response of single cells in the amygdala to these substances is unknown. This letter describes the response of amygdaloid neurones to various biogenic substances introduced into their environment by microelectrophoresis.

Four cats anaesthetized with chloralose or diallylbarbituric acid and urethane were used. The skull was opened on one side and the structures overlying the amygdala aspirated. The exposed area of brain was then covered with 3% agar in Ringer's solution to prevent drying. Using the stereotaxic co-ordinates of Jasper & Ajmone-Marsan (1960) the surface of the agar was now marked in several places overlying different areas of the amygdala. Five barrelled glass micropipettes (tip diameter 4 to 8μ) were now inserted through the marks in the agar to the required depths in the amygdala. At the end of the experiments the position of the micropipette tracks was checked histologically in celloidin sections. Eleven out of the fourteen tracks were in the amygdala.

The technique for preparing and using the micropipettes for microelectrophoresis was essentially that described by Krnjević & Phillis (1963). The four outer barrels contained aqueous solutions of the various drugs to be tested, whose pH was adjusted to give maximal ionisation compatible with stability. Drug ions were expelled from the tip of the pipette by appropriate currents. Extracellular spike responses from single cells were recorded simultaneously through the saline-filled central barrel of the pipette. After amplification these spikes were displayed on an oscilloscope and counted on a ratemeter. The ratemeter output was then displayed on a penwriter.

One hundred and thirteen cells were studied; two thirds of these were in the lateral or basomedial complex of the amygdaloid nucleus, the rest in the amygdaloid area. Some cells were firing spontaneously, or could be evoked synaptically through stimulation of the olfactory bulb. Otherwise quiescent cells were