'free' tryptophan concentrations were increased by 50% (2·12 ± 0·12 μg ml^{-1} to 0·38 ± 0·38 μg ml^{-1}), total serum tryptophan concentrations were unchanged and brain tryptophan concentrations were increased by 14% (1·22 ± 0·05 to 1·39 ± 0·05 μg g^{-1}). There was no change in the endogenous concentrations of 5-HT, but brain 5-HIAA concentrations were increased by 20% (267 ± 9 ng g^{-1} to 321 ± 12 ng g^{-1}).

The activity of liver tryptophan pyrrolase was reduced by 60% 3 h after the injection of allopurinol (20 mg kg^{-1}). Total serum tryptophan concentrations were simultaneously reduced by 60% and serum 'free' tryptophan concentrations by 53%. The concentrations of tryptophan in the brain were not significantly altered.

The results confirm the findings of Curzon & Green (1969) that liver tryptohan pyrrolase activity is increased by hydrocortisone. However, instead of the predicted decrease of 5-HT turnover, there was a significant increase in serum 'free' tryptophan and brain tryptophan concentrations. The fact that these increased concentrations were associated with an increase in brain 5-HIAA concentrations suggests an increased turnover of 5-HT in the brain. Similarly, although the decrease in tryptophan pyrrolase activity produced by allopurinol confirms the findings of Curzon & Green (1969), in our experiments this decrease was associated with a decrease rather than an increase in serum tryptophan levels.

The reasons for the increase in brain 5-HT turnover following hydrocortisone injection are not known, but the results of these experiments suggest that the action of corticosteroids in increasing tryptophan pyrrolase activity does not play a significant part in the regulation of brain 5-HT metabolism.

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An examination of the possible contribution of circulating corticosterone to the changes in brain monoamine metabolism during the oestrous cycle, pregnancy and the post-partum period in mice

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Greengrass and Tonge have shown that changes in brain monoamine concentrations occur during the oestrous cycle (1971), the post-partum period (1972a) and pregnancy (in press) and have attributed these changes to fluctuations in the levels of female sex hormones at these times. They have also shown that there are interactions between female sex hormones and psychotropic drugs (1972b) and have suggested that the relatively high incidence of mental disturbances at times when oestrogen and progesterone levels are fluctuating indicates an involvement of these hormones in the regulation of the mental state. Alterations in circulating levels of corticosterone have been shown to accompany some affective disorders (Coppen, 1967) and it is therefore possible that some of the disturbances of brain monoamine metabolism that are believed to exist in the affective disorders may result from the effects of corticosterone rather than sex hormones.

Plasma corticosterone levels have been measured during the oestrous cycle, pregnancy and the post-partum period to see whether any obvious correlation between these levels and alterations in brain monoamine metabolism could be detected. Corticosterone was measured by the method of Zenker & Bernstein (1957); blood was collected from the carotid artery and jugular vein after decapitation of the mice. There were no statistically significant differences in corticosterone levels at the oestrus and dioestrus stages of the cycle, but a marked increase at proestrus; the fluctuation did not appear to correlate with changes in brain monoamine metabolism previously described (Greengrass & Tonge, 1971). There was a gradual increase in corticosterone concentrations during pregnancy, with an acceleration

of the rate of increase in the later stages. Plasma concentrations of corticosterone in mice during early pregnancy were not significantly different from those of dioestrous mice. No clear interrelations between circulating corticosterone levels and changes in brain monoamine concentrations was apparent. Corticosterone concentrations during the postpartum period were considerably increased in mice allowed to suckle their litters, but not in those from which the litters were removed immediately after parturition: this suggests a relation between lactation and corticosterone levels. It is concluded that changes in corticosterone concentrations may contribute to the production of changes in brain monoamine metabolism, but that a much clearer relation can be seen between oestrogen/progesterone concentrations and alterations in monoamines.

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The labilization of lecithin liposomes by steroidal anaesthetics: a correlation with anaesthetic activity

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A large and rapidly increasing corpus of published work on phospholipid spherular bilayers (liposomes) is leading to a general acceptance that such systems provide realistic and valuable models for biological membranes, particularly in studies of pharmacological action. We have demonstrated the membrane disordering effect of a series of steroidal anaesthetics related to, and including, 3α-hydroxy-5α-pregnane-11,20-dione (Alphaxalone) by measuring the increases in the release rate of sequestered sodium ions from sonicated egg lecithin liposomes together with decreases in the gel-liquid crystal transition temperature of sonicated 1,2-dipalmitoyl-L-phosphatidylcholine liposomes. Flame photometry was used to measure the release rates of sodium from 5% liposome dispersions containing purified egg lecithin, cholesterol and dicetylphosphate (70:10:20 mole ratios) and D.S.C. measurements on the pure synthetic lecithin (transition temperature, 41°) were carried out on a 10% liposome dispersion with a Perkin-Elmer D.S.C. Model IB, at a scanning rate of 8° min^{-1}. Steroid was added both as a solid and in solution in ethanol in the sodium release experiments. For the D.S.C. work, steroid was added as a solid to give a suspension containing 2% concentration of steroid.

Steroids possessing high anaesthetic activity, as measured intravenously in mice, generally showed the largest effect on the liposomes both in increasing sodium release rates (20–35% enhancement) and in decreasing the transition temperature of dipalmitoyl phosphatidylcholine by as much as 8°. Little or no effect was shown by anaesthetically inactive steroids or steroids of low activity whilst steroids of intermediate anaesthetic potency had correspondingly intermediate effects on the liposomes. Hydrocortisone, which, in common with several other corticosteroids, has been reported as having membrane stabilizing properties (Bangham, Standish & Watkins, 1965) had no effect on cation release or transition temperature. The steroid, 5α-pregnane-3,11,20-trione, which is not an anaesthetic but is a convulsant, had no effect on transition temperature but showed inhibition (2–3%) rather than enhancement of sodium release.

Thus, although the total effect of an anaesthetic on the cns is almost certainly a complex summation of many different factors, it appears probable, at least for steroidal anaesthetics, that membrane labilization is an essential step in their *modus operandi.*

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