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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