Plasma corticosterone levels during pregnancy in the mouse

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Plasma corticosteroid levels are elevated during pregnancy in the human as a result of both an increase in secretion and an alteration in metabolism of these hormones (Diczfalusy & Troen, 1961) but whether they are of adrenal, ovarian or placental origin is not yet clear. In the rhesus monkey (Wolf & Bowman, 1966) and the macaque (Diczfalusy, 1972) however, no increases in plasma or urinary corticosteroids have been found during pregnancy and in rodents, apart from an isolated report of elevated corticosterone levels in ' grossly ' pregnant mice (Brain & Nowell, 1970) there has been no systematic investigation of plasma corticosterone levels during pregnancy. The present study, part of a wider investigation of the effects of stress on pregnancy, was undertaken to ascertain normal resting levels of corticosterone throughout pregnancy in the mouse.

Blood was taken by cardiac puncture from non-stressed, unanaesthetized mice, animals being killed at approximately 3 day intervals throughout pregnancy. Plasma corticosterone was measured using a fluorescence microassay after separation by thin layer chromatography to eliminate interfering fluorescent steroids such as oestradiol and pregnanediol, present in high concentrations during pregnancy. Individual values were obtained for each mouse, all samples being assayed in duplicate.

Non-pregnant female mice had a resting corticosterone level of $2{\cdot}3 \pm 0{\cdot}9$ μg/100 ml plasma (mean, S.E. of mean, n=5). During the first half of pregnancy plasma corticosterone levels gradually increased, reaching $15{\cdot}2 \pm 2{\cdot}4$ μg/100 ml (n=6) by day 10 of pregnancy. During the second half of pregnancy plasma corticosterone levels increased markedly to reach a peak on day 16 of $138{\cdot}3 \pm 30{\cdot}4$ μg/100 ml (n=8), around 60 times the non-pregnant resting level. Thereafter levels began to fall and by day 19 were down to $92{\cdot}9 \pm 13{\cdot}0$ μg/100 ml (n=10). Following parturition during the night of day 19, plasma corticosterone levels had dropped by the next morning to $18{\cdot}3 \pm 6{\cdot}4$ μg/100 ml (n=6), which is close to the physiological stress levels observed in the strain of mice used. Protein binding studies on pooled plasma taken from mice on day 16 of pregnancy indicated that 2% of the total corticosterone present was unbound hormone.

The sharp increase in plasma corticosterone levels following placentation on day 10 of pregnancy and the abnormally low corticosterone levels found during the second half of 3 pregnancies in which there were only 2 or 3 foetuses per mother together suggested that the placenta might be the major source of the corticosteroid. Subsequent studies have shown that the maternal adrenal glands are the major source of the corticosterone.

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Does stimulation of Na^+-K^+-Mg^{2+}-activated ATP-ase inhibit acetylcholine release from nerve terminals?

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Paton, Vizi & Zar (1971) and Vizi (1972) presented evidence that conditions known to inhibit membrane ATP-ase enhanced acetylcholine (ACh) release. It has been shown (Vizi, 1972) that Ca^{2+} ions are not essential in those cases where membrane ATP-ase

inhibitors were used to release ACh. This fact indicated that the activity of membrane ATP-ase might have a role in the release mechanism. It was suggested that, under physiological conditions, calcium might act by inhibiting the membrane ATP-ase and thereby promoting release of ACh.

Recent work on ACh release from eserinized (2 μg/ml) longitudinal muscle strips of guinea-pig ileum suggests that conditions which stimulate membrane ATP-ase reduce the volley output of ACh.

When 5·9 mM potassium was added to tissues which had been suspended in potassium-free Krebs' solution for 1 h the output/volley of ACh at 0·1 Hz stimulation was reduced from $49{\cdot}5 \pm 3{\cdot}8$ to $3{\cdot}1 \pm 0{\cdot}5$ (pmol/g)/volley ($n=3$; $p<0{\cdot}01$). However, the output during stimulation at 10 Hz for 1 min was only slightly reduced; outputs being $7{\cdot}5 \pm 0{\cdot}4$ and $5{\cdot}9 \pm 0{\cdot}6$ (pmol/g)/volley, respectively. The impairment of ACh output in response to stimulation at 0·1 Hz on adding of 5·9 mM potassium lasted not more than 10–15 min and the output recovered slowly. The resting output during the control period, (252 (pmol/g)/min) was enhanced when potassium was withdrawn (403·5 (pmol/g)/min) and reduced on adding 5·9 mM potassium (82·5 (pmol/g)/min). This is a result which was not expected on the basis of the Nerst equation for a potassium electrode.

Both magnesium-excess (9·3 mM) and noradrenaline (10^{-6} M) influenced the output of ACh: a reduction was observed at low (0·1 Hz), but not at high (10 Hz) frequencies of sustained stimulation.

Since potassium, excess magnesium and noradrenaline, all stimulated (Na^+-K^+-Mg^{2+})-activated ATP-ase and were capable of reducing output of acetylcholine it is suggested that the actual activity of membrane ATP-ase may control the release of ACh. It is not unreasonable to assume that the higher the activity of membrane ATP-ase and the more stabilized the membrane, the less the ACh is released. This might also explain why the output/volley is low when high frequency stimulation is applied as this is also known to stimulate membrane ATP-ase (Ritchie & Straub, 1957).

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Impaired performance of delayed matching in monkeys by heptabarbitone, pentobarbitone sodium and quinalbarbitone sodium

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The ability of monkeys to match stimuli separated by short intervals of time has been used by several workers to study the effect of drugs. Roberts & Bradley (1967) found that chlorpromazine and pentobarbitone sodium impaired performance on a delayed matching task and they suggested that, though chlorpromazine acted as a sedative, pentobarbitone sodium may have had a specific effect on recent memory. In view of the sedative properties of both drugs and their depressive effect on motor responsiveness, Glick, Goldfarb, Robustelli, Geller and Jarvik (1969) carried out further studies using a delayed matching to sample task which involved responses over a 16 h period after administration of the drug. They agreed with the findings of Roberts & Bradley (1967) on chlorpromazine, but were unable to support the suggestion that pentobarbitone sodium specifically impaired short term memory.

We have re-examined this because of the importance of the possible neurological effects of hypnotics used by persons engaged in skilled activity. A delayed matching task similar to that described by Roberts & Bradley (1967) was used. The stimuli were white illuminated patterns (cross or square) on dark backgrounds and were displayed on