Short communications

Hydrocortisone and the concentration of choline in the plasma of rodents

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Cortisone has been reported to reduce significantly the plasma choline concentration in dogs within 30 min after its injection. However, in the present experiments hydrocortisone had no effect on the plasma choline concentration of mice, guinea-pigs and rabbits. The protective effect of hydrocortisone against the toxic effects of hemicholinium in mice which was described previously cannot, therefore, be attributed to changes in the concentration of plasma choline.

The toxicity of hemicholinium no. 3 (HC-3) has been attributed to a failure in acetylcholine synthesis due to an inhibition of choline transport to the intracellular sites where it is acetylated (MacIntosh, Birks & Sastry, 1958; Gardiner, 1961). Choline has also been shown to antagonize specifically the toxic effects of HC-3 (Schueler, 1955; Reitzel & Long, 1959). Collier & MacIntosh (1969) recently established that the plasma choline is 'the ultimate source from which acetylcholine is manufactured'. Drugs or procedures which can produce changes in the plasma choline concentration might therefore be expected to modify the toxicity of HC-3. Thus Angeles, Schueler, Lim & Sotto (1964) have shown that a choline deficient diet, which is known to lower the plasma choline concentration (Bligh, 1953), potentiated the toxicity of HC-3 in mice.

Since cortisone has been reported to lower the plasma concentration of choline by 60–80% in the dog within 30 min after the injection, steroids might be expected to enhance the toxicity of HC-3. However Gwee & Lim (1971) found that hydrocortisone in fact protected mice to a small extent against the toxic effects of HC-3 and its paraterphenyl analogue. We have therefore studied the effects of hydrocortisone on the plasma choline concentrations of mice, guinea-pigs and rabbits.

Methods.—Animals of either sex were used. All species received 10 mg hydrocortisone/kg body weight, and the controls received the equivalent volume of a 0·9% solution of sodium chloride (saline).

Albino mice (16–24 g) were given hydrocortisone intraperitoneally (i.p.); 1 h later the mice were anaesthetized with diethyl ether and a deep cut was made through the axilla region of the mouse. As much blood as possible was sucked from the wound into a teat pipette which had previously been rinsed with saline containing heparin (100 units/ml). Guinea-pigs (400–600 g) were anaesthetized with sodium pentobarbitone (35 mg/kg i.p.) followed by heparin (200 units/kg i.v.). Two control samples (0·5 ml each) of arterial blood were

TABLE 1. *The effect of hydrocortisone on the plasma choline concentration of rodents. Hydrocortisone (10 mg/kg) or 0·9% sodium chloride was injected intraperitoneally in mice and intravenously in guinea-pigs and rabbits*

		Plasma choline concentrations (nmol/ml)				
		Controls (saline injected)		Hydrocortisone injected		
		Guinea-pig No.				
Time (min)		I	II	III	IV	V
Before injection	mean:	32	14	35	19	13
0 and 15	range:	(30–35)	(14–15)	(34–36)	(19)	(13–14)
After injection	mean:	27	15	38	19	16
30 and 60	range:	(26–28)	(13–17)	(36–40)	(17–22)	(16–17)
		Rabbit No.				
		I	II	III	IV	V
Before injection	mean:	11	6	9	17	8
0, 5, 10 and 15	range:	(9–12)	(6–7)	(8–9)	(14–18)	(8–9)
After injection: every	mean:	12	7	8	17	9
15 min up to 180 min	range:	(10–15)	(5–11)	(6–11)	(14–21)	(7–12)
		Mice				
60 min after injection	mean±S.E.*	32±0·6			33±0·5	

*n=12.

withdrawn from a cannula in the carotid artery at 15 min intervals. Hydrocortisone was then injected intravenously and arterial blood samples were taken 30 and 60 min later.

Rabbits (1·3–1·6 kg) were anaesthetized with sodium pentobarbitone (50 mg kg i.v.) followed by heparin (200 units/kg i.v.). Four control samples (0·5 ml each) were withdrawn from a cannula in the femoral artery at 5 min intervals. Hydrocortisone was then injected intravenously and arterial blood samples were taken at 15 min intervals during the following 3 hours.

All blood samples were centrifuged at 1,000 × *g* for 10 min. The choline contained in 0·2 ml of plasma was acetylated by the procedure described by Gardiner & Domer (1968). The acetylated product was bioassayed for acetylcholine on the longitudinal muscle of the guinea-pig ileum as described by Rang (1964).

Results.—The results given in Table 1 show that the plasma choline concentration of rabbits is lower than that of mice and guinea-pigs. Individual variations were large in guinea-pigs and rabbits; however, in any individual animal the plasma choline remained steady throughout each experiment. This is consistent with the finding of Bligh (1952) that the plasma choline concentration of various animal species remains fairly constant over prolonged periods.

Application of the *t* test showed no significant difference ($P=0{\cdot}1-0{\cdot}15$) between the mean plasma choline concentration of control and hydrocortisone-treated mice (see Table 1). Similarly Table 1 shows that hydrocortisone did not produce any appreciable changes in the plasma choline concentration throughout the duration of each experiment in the guinea-pigs and rabbits.

Discussion.—Our results show that hydrocortisone has no effect on the plasma choline concentrations of mice, guinea-pigs and rabbits. This was surprising because cortisone (10 mg/kg, i.m.) has been reported to reduce significantly the plasma choline concentration within 30 min after its injection into dogs (MacIntosh, 1963).

The lack of effect of hydrocortisone on the plasma choline concentrations of rodents indicates that the protective effect of hydrocortisone against the toxic effects of hemicholinium in mice (Gwee & Lim, 1971) cannot be attributed to changes in the concentration of plasma choline.

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