activity of brucine is altered three days after a single dose of GABA, but whether GABA or a metabolite is responsible for this effect remains to be determined.

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Anti-anaphylactic action of water-soluble glucocorticoids

SIR,—Natural and synthetic glucocorticoids have proved to be highly active in clinical practice for the treatment of various allergic conditions and the prevention of surgical shock. But in animal experiments most authors have shown steroid treatment to be ineffective in experimental anaphylactic shock (Herxheimer & Rosa, 1952; Goadby & Smith, 1964).

We have now compared, using the intravenous route, a new water-soluble steroid Depersolon (11,17-dihydroxy-21-(4-methylpiperazin-l-yl)-pregna-1,4-diene-3,20-dione hydrochloride) (Tóth, Tuba & Szporny, 1961; Görög & Szporny, 1963) with the water-soluble prednisolone sodium hemisuccinate and dexamethasone-21-phosphate for their capacity to confer protection on guinea-pigs in shock induced by an albumin aerosol.

Anaphylactic shock was produced by the micro-shock method of Herxheimer (1952). Guinea-pigs of 250–400 g were sensitised with 5% commercial crystalline albumin solution, 75 mg per animal, injected intraperitoneally. After three weeks the animals were placed in a plastic box and 5% egg albumin aerosol was introdced into the chamber The point when the animal exhibited signs of severe dyspnoea, lying down on its side and turning its head to right and left, was taken as the preconvulsion time. If aerosol treatment is discontinued at this juncture, the animals can be saved from certain death by oxygen insufflation as recommended by Smith (1961).

Preconvulsion time was assessed initially on the 21st day after sensitisation and then twice more at weekly intervals. The average of the two latter values was taken as control. On the fourth occasion the drug was injected into the jugular vein of unanaesthetised guinea-pigs at various times before giving the albumin aerosol. The control group was given physiological saline under similar conditions.

The measure of protection was represented by the quotient of post-treatment and control preconvulsion times (Ratio = R). Protection was considered as maximal when R was 10.

The findings in Table 1 show that the new steroid exerted a strong protective influence against anaphylactic shock, the effect reaching a peak 10 min after

administration, and the protective action beginning to wane within 30 min. Prednisolone hemisuccinate on the other hand, even in massive doses, did not give any marked protection until 30 or as much as 90 min after administration.

Dexamethasone, in doses corresponding in anti-inflammatory activity to prednisolone, did not display any protection against shock.

It is worth-while to compare our results with those of Goadby & Smith (1964) who found a weak protection after subcutaneous administration from water-soluble hydrocortisone only, prednisolone proving to be completely ineffective. By the subcutaneous route Depersolon also did not avert shock.

TABLE 1. EFFECT OF WATER-SOLUBLE GLUCOCORTICOIDS ON ANAPHYLACTIC SHOCK ELICITED IN GUINEA-PIGS

Substance	Dose mg/kg i.v.	Min before shock	Protection ratio (R)	No. of animals protected of total used
Control	—	—	1·25	0/25
Depersolon	10	10	9·03	7/8
	10	30	7·60	5/8
	30	30	9·13	7/8
	60 s.c.	30	1·63	0/8
Prednisolone hemisuccinate	30	10	2·20	0/8
	30	30	5·70	4/9
	30	90	6·30	5/8
Dexamethasone phosphate ..	5	30	1·01	0/8
	5	90	1·26	0/8
	5	180	1·85	0/8

Our findings provide further evidence that solubility in water and intravenous injection bring about an essential alteration of pharmacological action, presumably by changing steroid metabolism. Applied intravenously, prednisolone hemisuccinate shows a marked protective action against shock, though its effect is much weaker and less acute than that of Depersolon. Both compounds have prednisolone structure, but the absence of the hydroxy group at position 21 and its substitution by methylpiperazine make an essential difference in the effect of Depersolon.

Our findings indicate that the shock-preventing effect of glucocorticoids can be demonstrated in animal experiments; they furthermore emphasise the importance of the metabolism of the applied steroids in the development of this effect.

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