with these LD50 determinations, mice from the same source and of similar weight range were used in biochemical determinations of brain and liver MAO activity. Both phenelzine and tranylcypromine, at each dose level and after 4 and 16 hr pretreatment produced 85 to 100% inhibition of liver MAO activity, and 90 to 100% inhibition of brain MAO activity.

Conclusions. Both fencamfamin and amphetamine antagonise reserpine-induced depression in mice, fencamfamin having about one-third the potency of amphetamine in this test. However, the toxicity of fencamfamin, unlike that of amphetamine, is not markedly enhanced by previous administration of MAO inhibitors. It seems probable, therefore, that the main cause of the increased toxicity of amphetamine in animals previously treated with MAO inhibitors is due to an enhancement of its peripheral sympathomimetic effects. The toxicity of fencamfamin was increased only by high doses of phenelzine or tranylcypromine. It is difficult to attribute this increase to a specific drug effect and it is probably due to summation of the central and peripheral toxic effects of the two drugs.

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Effect of adrenalectomy on the response of rat skin to an intradermal injection of histamine and 5-hydroxytryptamine

SIR,—The immediate oedema produced in the ears of haematoporphyrine-treated rats by illumination with a small dose of visible light is greater in adrenalectomised rats maintained on saline than in intact animals and is mediated by 5-hydroxytryptamine (5-HT) to a greater extent than by histamine (Ashford, 1963). This fact prompted an investigation into the effect of histamine and 5-HT on capillary permeability in the skin of adrenalectomised and intact rats.

Female albino Wistar rats (140 and 180 g) were bilaterally adrenalectomised through a dorsal incision under ether anaesthesia. Sham-operated and non-operated control animals were included. The room temperature was 27° and adrenalectomised animals drank saline instead of tap water. Histamine acid phosphate and 5-hydroxytryptamine creatinine sulphate were made up in isotonic saline and were injected intradermally into the dorsal, and in some instances abdominal, skin in a volume of 0·1 ml immediately after an intravenous injection of pontamine sky blue (0·1 ml 2%/100 g). Intradermal injections were made on either side, and well clear of the mid-line. The rats were killed 15 min later, and the diameter of the wheals was measured on the underside of the skin by means of calipers. The results (Table 1) show that neither saline nor histamine were more effective whealing agents in adrenalectomised than in intact rats with

TABLE 1. THE MEAN DIAMETER OF WHEALS INDUCED BY AN INTRADERMAL INJECTION OF SALINE, HISTAMINE AND 5HT IN INTACT AND ADRENALECTOMISED RATS

Treatment	No. days after surgery	No. rats/ group	Mean diameter of wheals ± s.e.				
			Saline 0·1 ml	Histamine 0·5 μg	Histamine 1·0 μg	5-HT 0·05 μg	5-HT 0·01 μg
Dorsal skin							
Adrenalectomised	7	8	—	9·0±0·4	11·1±1·1	11·1±0·6	13·1±0·7
Sham-operated	7	8	—	9·3±0·5	11·6±1·1	9·8±0·7	12·1±0·5
Adrenalectomised	8	3	8·3±1·0	—	—	9·7±1·2	15·3±0·4
Sham-operated	8	3	8·8±0·7		—	10·3±0·4	13·0±0·8
Adrenalectomised	10	8	9·4±1·0†	10·8±0·4	12·4±1·0	11·6±0·5	13·3±0·7
Sham-operated	10	8	9·4±1·1†	10·9±0·6	11·4±0·5	10·5±0·5	13·8±0·3
Non-operated	10	8	9·3±0·8†	11·1±0·5	11·3±0·6	10·5±0·9	13·1±0·6
Adrenalectomised	13	9	8·6±0·8	—	—	9·1±0·6	15·3±0·5***
Sham-operated	13	11	8·6±0·7	—	—	8·8±0·4	12·5±0·6
Adrenalectomised	13	7	10·1±1·2†	10·9±0·4	11·7±0·8	11·4±0·6	13·3±0·4
Sham-operated	13	7	9·8±0·3†	11·5±0·5	11·6±0·2	12·6±0·5	13·9±0·8
Non-operated	13	7	9·4±0·6†	11·4±0·4	11·8±0·4	12·6±0·4	13·9±0·2
Abdominal skin							
Adrenalectomised	3	10	—	10·7±0·4	15·9±0·5*	—	—
Sham-operated	3	10	—	10·0±0·5	13·9±0·7	—	—
Adrenalectomised	13	7	5·1±1·9	10·4±0·8	11·2±0·4	11·9±0·6	14·9±0·4**
Sham-operated	13	7	3·5±1·7	12·2±0·5	11·9±0·6	11·8±0·2	14·1±0·4
Non-operated	13	7	2·4±1·5	9·6±1·0	10·1±0·6	10·8±0·3	13·1±0·6

* $P < 0.05$
** $P < 0.05$—compared with non-operated controls.
*** $P < 0.01$.
†These groups contained 1 rat less than the stated number.

the exception of one experiment in abdominal skin in which 1·0 μg of histamine induced a larger wheal in the adrenalectomised group ($P < 0.05$). However, the low dose of histamine was not more active in these animals. A slight increase in the effectiveness of 5-HT was seen 13 days after adrenalectomy in dorsal skin ($P < 0.01$) in one experiment and in abdominal skin in another ($P < 0.05$). However, the potentiation in dorsal skin was not confirmed and in abdominal skin it was apparent only in relation to non-operated controls there being no difference between adrenalectomised and sham-operated animals.

The increased susceptibility of photosensitised rats to light after adrenalectomy may be due to, either, the release of an increased amount of histamine and 5-HT from storage sites in the skin, or, a lowered ability of skin to inactivate and remove the released amines, or, an increase in sensitivity of the skin capillaries to histamine and 5-HT (Spencer & West, 1962).

From the present results increased sensitivity to light is unlikely to be wholly due to a greater effect of histamine and 5-HT on skin capillaries and may be mainly due to an increase in the amount of histamine and 5-HT available for release and possibly to a reduction in the rate of inactivation of 5-HT in skin.

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