was no difference between control (1·54 ± 0·29) and *o,p'*-DDD-treated (1·33 ± 0·36) adrenals. This lack of effect on baseline steroid production was also indicated in results from nonsuppressed dogs (3·43 ± 0·30 and 2·83 ± 0·85) and in the combined steroid production results of all experiments, suppressed or not (2·37 ± 0·26 and 1·72 ± 0·32).

On the other hand, it is quite obvious that 2 hr of *o,p'*-DDD treatment *in vivo* completely blocked ACTH-induced steroidogenesis in dog adrenal slices. This can be seen very clearly in all of the graphs on the right side of Fig. 2.

The data presented here show that *o,p'*-DDD does not affect baseline steroid production at a time when ACTH-induced steroidogenesis is completely blocked. These findings suggest that *o,p'*-DDD interferes with the mechanism by which ACTH stimulates steroidogenesis, i.e. the activation of the conversion of cholesterol to pregnenolone.

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Effects of α-methylnoradrenaline on cardiac metabolism

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IT HAS been suggested that α-methylnoradrenaline (α-MNA) mediates the hypotensive action of α-methyldopa by acting as a false transmitter of less potency than the natural transmitter, noradrenaline.[1] More recently, it has been proposed that, although α-MNA may be less potent than noradrenaline on autonomic α-receptors, it may be at least equipotent to, or more potent than, noradrenaline on autonomic β-receptors.[2,3] A difference in affinity between α-MNA and noradrenaline for α- and β-receptors may well explain the hypotensive properties of α-methyldopa. A greater affinity of α-MNA for vascular β-receptors and a lesser affinity for vascular α-receptors would both decrease the hypertensive properties of α-MNA.

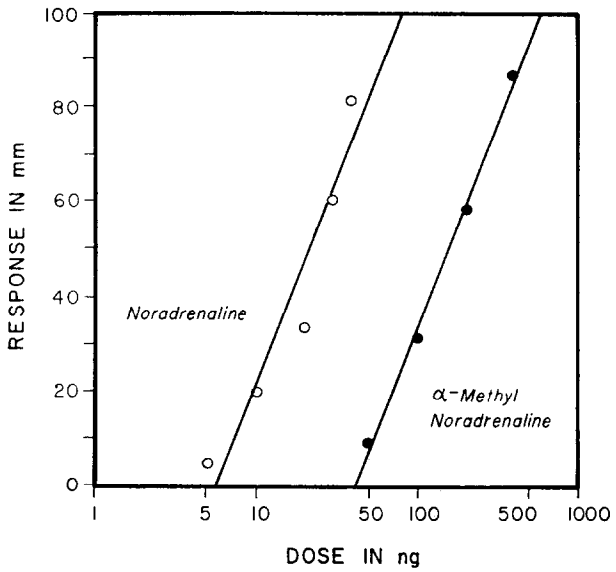

FIG. 1. A comparison of the potencies of α-MNA and noradrenaline on the perfusion pressure of the isolated perfused central artery of the rabbit ear. The ordinate is the response in millimeters of mercury; the abcissa is the dose in nanograms.

Cardiac muscle has mainly autonomic β-receptors, the stimulation of which produces carbohydrate utilization and lipolysis in addition to an increased force of contraction.[4] The actions of α-MNA have been compared with those of noradrenaline and adrenaline on metabolism and contraction in the isolated rat heart in order to determine whether α-MNA has qualitative and quantitative actions similar to adrenaline and noradrenaline. This has provided a comparison of the potencies of the three amines on cardiac β-receptors. The potencies of α-MNA and noradrenaline have also been compared on the perfusion pressure of an isolated perfused arterial segment of the rabbit ear. This has enabled a composite study of the potencies of α-MNA and noradrenaline on both the cardiac and peripheral components of the cardiovascular system.

The isolated, perfused hearts of rats of the Sprague–Dawley strain were used in this study.

Methods for preparation and perfusion of hearts and arterial segments, metabolic analyses and measurements of contraction are described elsewhere.[4,5]

l-adrenaline tartrate was obtained from Burroughs Wellcome and Co. Ltd. (Australia). *l*-noradrenaline bitartrate and *l*-α-methylnoradrenaline HCl were obtained from Winthrop Laboratories (Australia).

Studies of the effects of equal doses of adrenaline, noradrenaline and α-MNA can be seen in Table 1, which shows that a marked depletion of the glycogen store occurred with noradrenaline and α-MNA as well as with adrenaline. The three catecholamines accelerated the rate of glucose uptake; noradrenaline was slightly less potent than adrenaline in this action. Adrenaline, noradrenaline and α-MNA all caused a 3-fold increase in lactate production.

Table 1 shows that adrenaline causes a liberation of free-fatty acid (FFA) from endogenous sources including triglyceride and possibly phospholipid. α-MNA and noradrenaline also liberate FFA, their potencies being almost identical in this action.

It is therefore demonstrated that α-MNA has effects which are qualitatively and quantitatively similar to those of the naturally occurring catecholamines on metabolism in perfused rat heart.

Since the three catecholamines exhibit equal potency with respect to metabolic effects, it may be expected that equal potency would also be shown for their effects on amplitude of contraction, a well known β-receptor action. That this is so is shown in Table 1.

The three catecholamines are therefore equipotent with respect to the parameters of metabolism examined and the amplitude of contraction in perfused rat heart. It is, therefore, apparent that if α-methyldopa has a hypotensive action due to the lesser potency of its catecholamine metabolite on the cardiovascular system, then this action must be on the peripheral vasculature rather than on the heart itself. In order to test this hypothesis the potencies of α-MNA and noradrenaline were compared on the perfusion pressure of the isolated perfused rabbit ear artery segment. Noradrenaline was

TABLE 1. A COMPARISON OF THE EFFECTS OF ADRENALINE, NORADRENALINE AND α-METHYLNORADRENALINE ON PERFUSED RAT HEARTS

	Final glycogen content (glucose equivalents) (μM/g)	Glucose uptake from medium (μM/g)	Lactate production (μM/g)	FFA (μM/g)	Triglyceride (FFA equiv.) (μM/g)	Maximum size of contraction after drug / Size of contraction before drug
Control	21·1 ± 1·5 (9)	14·2 ± 2·1 (9)	14·4 ± 0·9 (9)	1·14 ± 0·10 (9)	1·72 ± 0·15 (3)	
l-Adrenaline tartrate 0·5 μg/ml	11·3 ± 1·2† (20)	28·8 ± 3·7* (23)	41·5 ± 4·6† (10)	2·06 ± 0·33* (8)	1·65 ± 0·14 (8)	3·06 ± 0·16 (10)
l-Noradrenaline bitartrate 0·5 μg/ml	8·5 ± 0·7† (7)	22·2 ± 3·9 (8)	38·8 ± 6·3† (7)	2·28 ± 0·44 (4)		2·76 ± 0·34 (7)
l-α-Methylnoradrenaline HCl 0·5 μg/ml	7·9 ± 0·6† (11)	33·3 ± 3·8 (13)	40·3 ± 2·3† (11)	2·23 ± 0·36 (4)		2·99 ± 0·35 (9)

Number of animals in the group in brackets.
* $P < 0.05$ against control.
† $P < 0.001$ against control.

found on average to be 8·3 times more potent than α-MNA. Log dose/response curves are plotted for one experiment (see Fig. 1). This result is in agreement with the findings of other workers. Day and Rand[1] have shown that noradrenaline is 8·5 times more potent than α-MNA on rabbit blood pressure and recently Malik and Muscholl[6] demonstrated that noradrenaline has three times the pressor potency of α-MNA on a rat mesenteric artery preparation.

The finding that α-MNA is equipotent with noradrenaline on cardiac β-receptors yet considerably less potent than noradrenaline on perfused artery preparations supports the idea that the site of the hypotensive action of α-methyldopa is the peripheral vasculature rather than the heart. It is likely that α-MNA is less potent at this site than noradrenaline due to a lesser affinity for α-receptors, the stimulation of which promotes vasal constriction and raises blood pressure.

Substitution on the α-carbon of the phenylethylamine structure such as occurs in α-MNA may diminish its ability to stimulate the α-receptor; this is well known to occur with alkyl substitution on the adjacent amine group.

It must be born in mind that whilst it is valid to compare the effects of α-MNA on α- and β-receptors by perfusion techniques such as are described in the present communication, therapeutically its effect depends upon its liberation at the sympathetic nerve ending.

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Quantitative studies of the release of purine compounds following stimulation of non-adrenergic inhibitory nerves in the stomach

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FOR MANY years it has been assumed that inhibition of intestinal smooth muscle in mammals is mediated solely via the release of noradrenaline from sympathetic neurones. However, since 1964, pharmacological and electrophysiological evidence has been presented of a neurone type in the gut wall which is neither adrenergic nor cholinergic,[1,2] yet causes inhibition of the gut. This neurone is located in Auerbach's plexus; it is the post ganglionic element in a vagal parasympathetic pathway to the