heart was removed with the great vessels cut close to the heart, and the organ weighed. The weights of each embryo and its heart are seen tabulated in Fig. 1.

The largest embryos were seen at 37·5° C. The hearts from the group at 32·5° C were largest, even though the embryos bearing these hearts were smaller than those at the normal temperature. On gross examination we saw that the increase in size at 32·5° C consisted of enlargement of the chambers of the heart as well as thickening of their walls. On microscopic section the increased heart tissue mass was found to be composed of heart muscle and supporting tissues, not of an inflammatory exudate or œdema.

Two other gross changes were consistently present. In the low-temperature groups the intra-abdominal veins of the embryos as well as veins of the extra-embryonic membranes were distended. Also the kidneys were enlarged—both the mesonephric and metanephric kidneys.

To see whether the variation in the size of heart resulting from the difference in temperature of incubation would be observed in heart fragments transplanted to the chorioallantoic membrane, we removed the hearts of several 8-day-old embryos, pooled them, cut them into 1-mm explants in Hanks's balanced salt solution, and transplanted them to the chorioallantoic membranes of one hundred 8-day-old embryos. These were incubated at the normal temperature, 37·5° C, for 3 days. On the eleventh day of incubation 95 eggs were alive. Eleven were fixed for histological examination. The remainder, 84 embryos, were divided into three groups, and incubated at the three test temperatures.

The largest transplants obtained after one week were in the group at 37·5° C. On microscopic examination these were found to be well vascularized, with abundant heart muscle tissue. The smaller transplants, at 32·5° C, contained heart muscle tissue similar in appearance to that seen at 37·5° C. The smallest transplants, found at 42·5° C, showed many foci of calcification and degeneration, although areas of histologically normal heart muscle were also seen.

We think that the influence of environmental temperature on the size of the intact heart is not a direct reaction of heart tissue to the alteration in temperature of incubation, but results from other causes. Perhaps it is a hæmodynamic response to congestive failure or arterial hypertension, a response which may require an intact nervous innervation.

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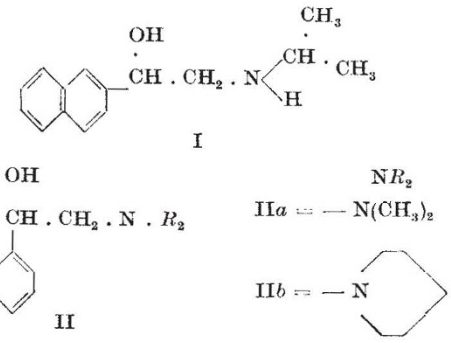
PHARMACOLOGY

Local Anæsthetic Activity of the β-Receptor Antagonist, Pronethalol

IN 1962 it was reported that pronethalol (I) (formerly 'Nethalide'), a derivative of isoprenaline in which the catechol ring is replaced by naphthalene, was able to antagonize the β-responses to sympathetic stimulation or sympathomimetic drugs[1]. It was afterwards shown[2] that pronethalol approximately doubled the lethal dose of ouabain, completely prevented the onset of ventricular fibrillation during intoxication by cardiac glycosides, and restored a regular rhythm to guinea pig hearts which had already been made to fibrillate by an overdose of ouabain. Experiments on isolated rabbit atria[3], from which action potentials were recorded with intracellular micro-electrodes, indicated that pronethalol was an anti-arrhythmic agent approximately twice as potent as quinidine, and with a similar mode of action. Since many anti-arrhythmic agents are also local anaesthetics, it was of interest



to discover whether pronethalol also could produce local anæsthesia.

Guinea pigs were lightly anæsthetized with sodium pentobarbitone (30 mg/kg intraperitoneally) and local anæsthetic potency determined by the intradermal weal method of Bülbring and Wajda[4]. It was found that pronethalol is 1·8 times as active as procaine (log $R = 0·270 \pm 0·05$). Pronethalol is very closely related to a series of compounds studied as local anæsthetics by MacIntosh and Work[5]. They found that the compounds II*a* and II*b* were 0·5 and 1·5 times as active, respectively, as procaine. Pronethalol and isoprenaline both have the same side-chain structure, but work on the sympathomimetic amines has shown that it is unwise to draw analogies between phenolic and non-phenolic amines.

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Interaction of Oxytocin and Vasopressin with β-Adrenergic Receptors in the Kidney

THERE is evidence which suggests that oxytocin and vasopressin can interact with β-adrenergic receptors in various tissues of several species. For example, the depressor effect of oxytocin in the chicken is blocked by dichloroisoprenaline (DCI) (ref. 1) and that of vasopressin by pronethalol[2], a pure β-blocking agent[3]. In the dog, the vasodilator action of adrenaline is abolished and the depressor effect of ethylnoradrenaline reversed by large doses of vasopressin[4].

A recent investigation by Lees and Lockett[5] of renal function in the rat has revealed the existence of receptors in the kidney termed β-receptors as they are activated preferentially by low doses of isoprenaline and blocked by pronethalol. It was suggested that there are two groups of β-receptors involved in the renal response to isoprenaline: those associated with the "postganglionic sympathetic innervation of the proximal tubules" and those associated with "sympathetic vasodilator fibres".

Both oxytocin and vasopressin have effects on renal tubular function and, in suitable doses, on the renal vasculature. The work recorded here was undertaken to determine to what extent, if any, the diuretic or antidiuretic actions of oxytocin and vasopressin in rats are mediated through β-adrenergic receptors.

Preliminary experiments were carried out with oxytocin using the water-loaded rat under ethyl alcohol anæsthesia with continuous monitoring of blood pressure[6]. Pronethalol given intravenously in a dose as low as 0·1 mg/kg caused no significant change in blood pressure or urine flow but reduced or abolished the antidiuretic effect of oxytocin. This is illustrated in Fig. 1. Evidence for the blockade of β-receptors was provided by the finding that