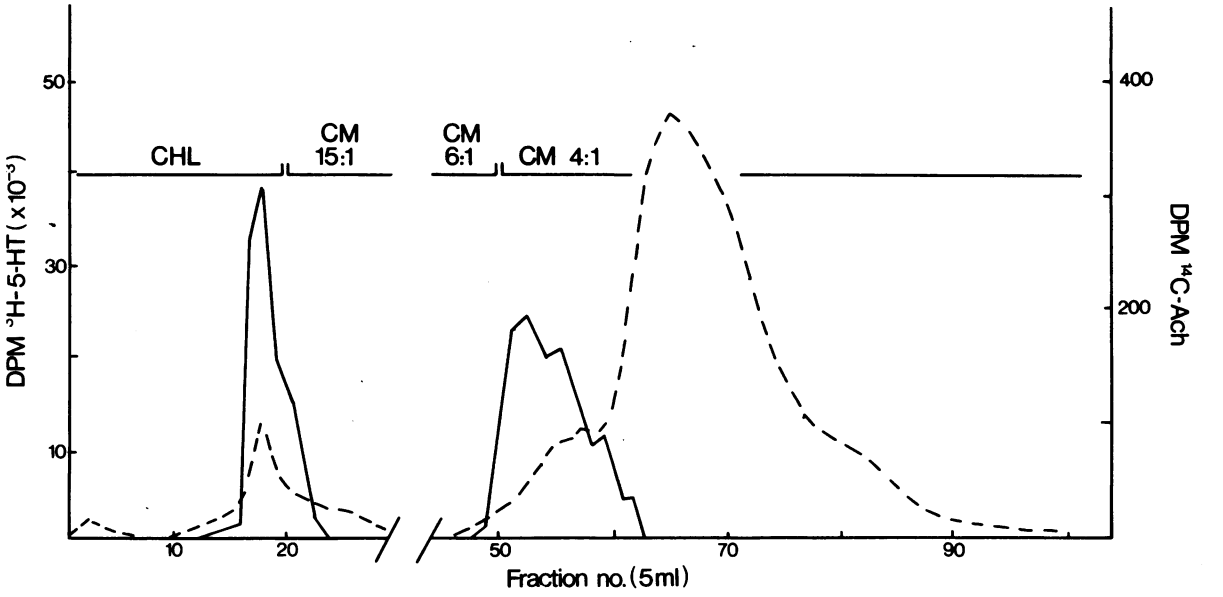

Figure 1 Double-label (—— = ^{3}H-5-HT), —— = ^{14}C-Ach) binding to butanol extract of rat brain and elution on an LH20 Sephadex column (2.6 x 32 cm) using 100 ml Chl, 50 ml each of CM 15 : 1, CM 10 : 1, CM 6 : 1, and then 300 ml CM 4 : 1.

ACh-binding increase notwithstanding). No binding of ^{3}H-5-HT was observed, the ^{3}H-label appearing in the region where free ^{3}H-5-HT is known to elute.

Further drug studies designed to examine the specificity of these interactions are in progress.

S.G. is an M.R.C. Scholar.

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Effect of propranolol treatment on the development of DOCA/saline hypertension in rats

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The mechanism whereby propranolol lowers arterial blood pressure in man is uncertain and attempts to reproduce this action in laboratory animals have produced conflicting results. In rats with established DOCA/saline hypertension neither Farmer & Levy (1968) nor Conway (1974) detected any antihypertensive effect of β-adrenoceptor blocking doses of propranolol, whilst Dusting & Rand (1974) reported a marked fall in blood pressure in their experiments using low twice daily doses (0.2 mg kg^{-1} day^{-1}) of propranolol. Similarly, inconsistent results have been published concerning the influence of β-adrenoceptor blockade on the development of hypertension in rats. Weiss, Lundgren & Folkow (1974) reported that both propranolol and the cardioselective β-adrenoceptor blocker H93/26 markedly reduced the development of hypertension in spontaneously hypertensive rats (SHR) and Conway (1974) has made a similar observation with propranolol and ICI 66082 in SHR and DOCA/saline hypertensive rats. However, Lundgren (1974) found that propranolol did not influence the development of renal (unilateral renal artery constriction) hypertension in rats and Frohlich (1974) observed a similar lack of effect of sotalol treatment on the development of hypertension in SHR.

The present study was designed to test the effects of a range of propranolol doses on the development of DOCA/saline hypertension in rats. Male Wistar rats (60-90 g) were made hypertensive by implanting a 25 mg DOCA pellet subcutaneously, left nephrectomy and substitution of 1% saline for drinking water for the 14 days following the operation. Systolic blood pressures were measured by the tail cuff method, twice weekly, for the first eight weeks after operation and thereafter weekly. Propranolol treatment was started two days after operation and continued for five weeks. Daily intraperitoneal doses of propranolol used were 25, 10, 2, 0.2 and 0.02 (mg $kg^{-1}day^{-1}$).

In untreated DOCA/saline rats the systolic blood pressure rose steeply during the first one to two weeks following operation from average values of 125 mm Hg to 160 mm Hg. Thereafter the blood pressure rose much more gradually reaching a level of 190-200 mm Hg by week 12. None of the dose-regimens of propranolol used produced any marked effect on the initial rapidly developing phase of the hypertension but at each dose level the secondary slowly developing phase was markedly reduced. The 10 mg $kg^{-1}day^{-1}$ regimen of propranolol was slightly more effective than the 25 mg $kg^{-1}day^{-1}$ dose level but the three lower dose levels each produced a similar reduction in the development of hypertension as did the 10 mg $kg^{-1}day^{-1}$ level. When the propranolol treatments were discontinued the blood pressure of each group of treated animals remained at or only slightly above the treatment levels for the next seven weeks.

Parallel experiments were performed using either α-methyldopa (100 mg $kg^{-1}day^{-1}$ i.p.) or pargyline (10 mg $kg^{-1}day^{-1}$ i.p.) instead of propranolol. Both treatments markedly reduced the development of hypertension both in the rapid early and slow secondary phase of the disease.

The results suggest that propranolol can markedly reduce the development of hypertension in DOCA/saline treated rats. Previously reported failures to do this may possibly be accounted for by too high doses of propranolol and/or too short a period of treatment. α-Methyldopa and pargyline produced a similar effect to propranolol on the slow secondary phase of the hypertension and in addition markedly reduced the rapidly developing phase.

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Cyclic adenosine-3′,5′-monophosphate in cerebrospinal fluid

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Recently Dascombe & Milton (1975) have reported raised levels of cyclic adenosine-3′,5′-monophosphate (cAMP) in the cerebrospinal fluid (c.s.f.) of the unanaesthetized cat during bacterial pyrogen fever. In the present work experiments have been conducted to determine the effects of heat and cold stress on c.s.f. levels of cAMP, the effects of intravenous cAMP on body temperature, and the passage of intravenous cAMP across the blood/c.s.f. barrier.

The method described by Feldberg, Gupta, Milton & Wendlandt (1973) was used to obtain samples of c.s.f. from the unanaesthetized cat. The cAMP content of the c.s.f. was measured after ethanol deproteinization by competitive binding assay (Brown, Albano, Ekins, Sgherzi & Tampion, 1971; Gilman, 1970). The animals were individually caged and unrestrained, rectal temperature was monitored continuously.

Animals were cold stressed by exposure to an