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

ambient temperature of $0 \pm 2^{\circ}$C for three hours. During exposure to cold, body temperature increased and was associated with vasoconstriction, a crouched posture and shivering. Levels of cAMP in c.s.f. removed during and after this period were not significantly different ($P > 0.2$) from control levels (ambient temperature $25 \pm 1^{\circ}$C).

Exposure to an ambient temperature of $45 \pm 1^{\circ}$C for 3.5 h caused the body temperature of the cats to rise $2.45 \pm 0.30^{\circ}$C and was associated with vasodilatation, panting and stretching out. Upon cessation of heat exposure body temperature fell rapidly to control levels. Levels of cAMP in c.s.f. during and after heat stress were not significantly different ($P > 0.1$) from control.

cAMP (0.1-10 mg/kg) injected intravenously in cats at an ambient temperature of $22 \pm 2^{\circ}$C caused a dose-related, rapid increase in the amount of cAMP assayed in c.s.f. High doses (5 mg and 10 mg/kg) of cAMP, but not lower doses (0.1 mg and 1 mg/kg), produced a significant ($P < 0.01$) fall in rectal temperature, which began 2-3 min after injection and reached a maximum in about 18 minutes. The hypothermia was associated with ear skin vasodilatation, and in one animal in response to cAMP 10 mg/kg, polypnoea and sweating from the paw pads.

Intravenous injections of ^{3}H-cAMP were followed by a rapid rise in ^{3}H-cAMP levels in the c.s.f. showing that the exogenous nucleotide was passing from the blood into the c.s.f.

The level of cAMP in c.s.f. may therefore be raised as a result of increased levels of cAMP in the blood; as these results show, the nucleotide rapidly enters c.s.f. from the blood. The raised levels of cAMP recently reported following i.v. bacterial pyrogen could possibly result from raised levels of cAMP released peripherally by the pyrogen. The raised levels of cAMP reported during bacterial pyrogen-induced fever are not, however, considered a consequence of either raised body temperature or active thermoregulatory processes.

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Cyclic AMP in developing chick brain: changes with ischaemia and catecholamine administration

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Cyclic AMP has been implicated in the functioning of the central nervous system, and there is evidence indicating that cyclic nucleotides are involved in the control of cell growth and differentiation (for review, see Drummond, 1973). The concentration of cyclic AMP in rat brain has been reported to increase throughout development (Schmidt, Palmer, Dettbaru & Robison, 1970; Ebadi, Weiss & Costa, 1971), but the method of sacrifice used in these studies does not eliminate rapid post-mortem changes in the nucleotide (Nahorski & Rogers, 1973).

We have measured the concentration of cyclic AMP in the cerebral hemispheres of chicks during their neonatal development using a method whereby brain tissue is removed and frozen by a freeze-blowing technique which largely eliminates post-mortem changes (Nahorski & Rogers, 1973). Cyclic AMP was assayed by the protein binding saturation method of Brown, Albano, Ekins, Sgherzi & Tampion (1971). The cyclic AMP content of freeze blown chick cerebral hemispheres was found to decrease during neonatal development, from 12.5 ± 0.8 p moles/mg protein in one day old chicks to 3.0 ± 0.01 p moles/mg protein in 28 day old chickens. However, in chicks killed by decapitation there was a rapid increase in cerebral cyclic AMP. This post-mortem rise in the