intravenously 18 hr and 1·5 hr previously), dopamine (0·1 μ-mole) now elicited sleep within 10 min of infusion and lowered temperature 3° C for 5 to 6 hr. The effects of isoprenaline and noradrenaline were prevented by pretreatment with phenoxybenzamine (10 μ-mole/100 g intravenously 1·5 hr to 2 hr previously) but not with propranolol (0·5 to 1 μ-mole/100 g., 30 min previously). These or smaller doses of antagonist abolished the peripheral cardiovascular effects of these amines.

Noradrenaline, which acts peripherally on α-receptors for catecholamines, and isoprenaline, which acts mainly on β-receptors, had only central depressant actions when infused into the hypothalamus of chickens. These results imply that there are receptors in the hypothalamus similar to peripheral α-receptors, because the effects were prevented by phenoxybenzamine but not by propranolol. Noradrenaline, α-methylnoradrenaline and isoprenaline had similar actions in young chickens on behaviour, electrocortical activity, temperature and oxygen consumption whether given into the hypothalamus or intravenously, indicating that their effects when given intravenously were likely to be due to the drugs penetrating to the brain. Dopamine is deaminated more rapidly than the other catecholamines tested (Blaschko, 1952), which could account for its inactivity when given intracerebrally unless the chicken had been pretreated with a monoamine oxidase inhibitor. Its depressant action after monoamine oxidase inhibition suggests that dopamine is a central depressant in the fowl and not a central excitant as proposed for mammalian species.

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Hypothermia due to α-methylnoradrenaline in young chickens

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In newborn mammals noradrenaline acts on brown fat (Dawkins & Hull, 1964) to produce hyperthermia and increased oxygen consumption unaccompanied by shivering (Taylor, 1960; Moore & Underwood, 1963). In young chicks, noradrenaline does not cause lipolysis (Carlson, Liljedahl, Verdy & Wirsén, 1954) and brown fat is not present (Freeman, 1967); indeed, body temperature and oxygen consumption are lowered by catecholamines given intravenously (Allen & Marley, 1967) or micro-infused into the hypothalamus (Marley & Stephenson, 1968).

The present experiments were made in unanaesthetized 1–21 day old chicks to determine how intravenous α-methylnoradrenaline elicited these effects. Tempera-

ture and oxygen consumption were recorded at environmental temperatures of 31° C (thermoneutrality) and 16° C (below thermoneutrality) as previously described (Allen & Marley, 1967). Blood pressure was recorded; a quantitative measure of muscle activity was obtained from continuously integrated electromyograms.

At thermoneutrality, α-methylnoradrenaline (1 to 2 μ-mole/100 g intravenously) lowered body temperature by 1·5 to 4° C, reduced oxygen consumption 20 to 40% and substantially diminished electromyographic activity. However, at 16° C, although temperature was lowered further by α-methylnoradrenaline and the increased oxygen consumption halved, the substantial increase in electromyographic activity was only temporarily diminished. Thus lowering of temperature and oxygen consumption occurred despite increased heat production caused by shivering and diminished heat loss due to vasoconstriction evoked by α-methylnoradrenaline. Decrease in oxygen consumption followed the same time-course as the pressor response to α-methylnoradrenaline but was unlikely to be reflexly determined by this because equipressor doses of tyramine were ineffective.

Concentrations of blood glucose and non-esterified fatty acids (NEFA) were measured to determine whether α-methylnoradrenaline interfered with their production or utilization. At thermoneutrality and at 16° C, blood glucose was not significantly altered by hypothermic doses of α-methylnoradrenaline. NEFA were significantly lowered by α-methylnoradrenaline at thermoneutral environments but not at 16° C.

The evidence suggested a central rather than a peripheral mechanism for the fall in temperature and decrease in oxygen consumption caused by α-methylnoradrenaline. Favouring this idea, the hypothermic effects of α-methylnoradrenaline (1 or 2 μ-mole/100 g intravenously) were abolished in chickens with chronic transection of the brainstem posterior to the hypothalamus but anterior to the respiratory centre, so that respiration continued unassisted. The effects were unlikely to be due to depression of hypothalamic metabolism because oxygen consumption of brain-slices of diencephalon was unaltered by α-methylnoradrenaline (0·01, 0·05, 0·1, 0·5 or 1·0 μ-mole). Inhibition of release of thyrotrophic hormone was also considered because this follows injection of adrenaline into the mamillary bodies of rabbits (Harrison, 1961). Preliminary results suggest that this mechanism is not crucial since similar hypothermic effects were obtained with α-methylnoradrenaline 7 to 11 days after the removal of both thyroid glands, although the half-lives of thyroxine and tri-iodothyronine are 22·5±1 hr in chickens (Tata & Shellabarger, 1959).

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The effects of pempidine and hexamethonium on release of antidiuretic hormone by nicotine and osmotic stimuli in the cat

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The synapses at the supraoptic nuclei are thought to be cholinergic (Pickford, 1939, 1947) and pharmacologically may resemble autonomic ganglia (Walker, 1957). Bisset & Walker (1957) showed in rats that nicotine releases both antidiuretic hormone (ADH) and oxytocin and release is not diminished by hexamethonium. In contrast reflex release of oxytocin to suckling is abolished by pentolinium (Chaudhury, 1961).

In these experiments using cats anaesthetized with chloralose, 4 ml. blood samples were collected 5 min before and 2 and 40 min after intracarotid injection of nicotine hydrogen tartrate (40 μg nicotine base/kg) or 1 ml. M sodium chloride solution. Following intravenous pempidine tartrate (5 mg/kg) or hexamethonium bromide (5 mg/kg) the stimulus was repeated and blood samples taken as before. The blood was extracted according to the method of Bisset, Hilton & Poisner (1967) and assayed for antidiuretic activity on alcohol anaesthetized rats (Bisset, 1962).

Experiments showed that nicotine released ADH even when carotid chemoreceptors had been denervated. The results summarized in Table 1 demonstrate that the release of ADH by nicotine is prevented by pempidine but not by hexamethonium. In contrast, pempidine does not block release of ADH by osmotic stimulation. Table 1 also shows that the concentration of ADH in the blood increased after pempidine but not after hexamethonium.

The effect of pempidine on ADH release by nicotine may result from blockade of central synapses which are not reached by hexamethonium. The failure of

TABLE 1. *Effects of intravenous pempidine* (5 *mg/kg*) (*P*) *and hexamethonium* (5 *mg/kg*) (C_6) *on release of ADH by intracarotid nicotine* (40 μg/*kg*) (*N*) *and sodium chloride solution* (1 *ml.* M) *NaCl*

Time of blood sample (min)	ADH (μ-u./ml. blood)							
	−5	0 Stimulus	+2	+40	Blocking agent	−5	0 Stimulus	+2	+40
		↓N					↓N		
	<5		18	7·5	P	22		12·5	<5
	5		18·5	8·5	P	15		3·5	<2
	<2		5	2	P	11		10	<2
	<5		8	<5	P	400		15	<5
		↓N					↓N		
	9·5		30	15	C_6	34		48	20
	<3		7	3·5	C_6	3		7·4	4
	17		34	7	C_6	6		17	11
		↓NaCl					↓NaC		
	9·4		25	9·4	P	31		50	12·5
	12·5		45	12·5	P	100		400	100
	6		36	16	P	23		100	90