behavioural response from the pups. The antagonists were given i.v. after 60–90 min, i.e. after the occurrence of 5–8 milk ejections. In this control period, and after saline treatment, milk ejections were observed at regular intervals of 6.5 ± 2.3 min (s.d.).

The α-adrenergic blocking drug phentolamine (0.4 mg/kg) caused a three-fold increase in the interval to the first milk ejection following its administration. Higher doses were more effective, and at 1.6 mg/kg this milk ejection interval increased to about 120 minute. By contrast, the β-adrenergic antagonist propranolol (5 mg/kg) failed to block the reflex. Haloperidol, pimozide and metoclopramide, all considered as dopamine antagonists, also prevented milk ejection. Haloperidol and pimozide were equi-effective, causing a three-fold increase in the latency at 1.5 mg/kg, whereas 7.0 mg/kg metoclopramide was required for the same result. A six-fold increase in latency (i.e. 39 min) was obtained with 4.0 mg/kg haloperidol, 4.5 mg/kg pimozide and 12 mg/kg metoclopramide; the period of antagonism was related linearly to the dose. Partial responses, associated with the release of small pulses of hormone, were rarely observed. Further, the milk-ejection intervals which followed the initial delay were within the control range. A direct action of the drugs on the neurohypophysis or mammary glands was unlikely, since the milk-ejection responses to exogenous oxytocin and electrical stimulation of the neurohypophysis were not decreased. Hexamethonium (2 mg/kg) did not inhibit milk ejection, though it caused a similar reduction in blood pressure to that observed with the antagonists.

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The effects of prostaglandins E_1 and E_2 on heart rate responses to cervical sympathetic nerve stimulation and ganglion stimulant drugs in the anaesthetized mouse

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Prostaglandins E_1 and E_2 inhibit the bradycardia caused by vagal stimulation in anaesthetized mice (Feniuk & Large, 1975). Their effect has now been studied on the tachycardia produced by either cervical sympathetic nerve stimulation (Large, 1975) or administration of drugs.

Anaesthetized mice were prepared as described by Feniuk & Large (1975). Following section of the left cervical sympathetic and both vagi, the intact right cervical sympathetic nerve was stimulated through bipolar electrodes (rectangular pulses; 0.5 ms duration; supramaximum voltage). Prostaglandins were injected i.v. when the tachycardia to a given frequency of stimulation had levelled and % changes were measured. In assessing the reduction of drug-induced tachycardia, prostaglandins were given 30–60 s prior to the third successive injection of the stimulant drug.

Initial mean arterial pressure was 52 ± 3 mm Hg and heart rate was 430 ± 9 bts/minute. Frequency-dependent tachycardia occurred with nerve stimulation, the maximum usually at 10 Hz ($\Delta HR = 208 \pm 11$ bts/min). Prostaglandins E_1 and E_2 caused dose-dependent inhibition of the tachycardia which seemed more pronounced at the lower frequencies of stimulation. There was also marked inhibition by the prostaglandins of the tachycardia produced by the muscarinic stimulant McN-A-343 (4-(*m*-chlorophenylcarbamoyloxy)-2-butynyltri methyl ammonium chloride), but virtually no modi fication of the responses elicited by either DMPP (1,1 dimethyl-4-phenyl piperazinium) or by noradrenaline (Table 1). Similar results were obtained with the prostaglandins when nerve stimulation or DMPP injection was made in the presence of atropine (0.5 mg/kg) or when McN-A-343 injection was made after hexamethonium (2.5 mg/kg).

Although the results demonstrate that the prostaglandins can modify sympathetic transmission to the heart *in vivo*, their site of action is still unknown.

Table 1 The effect of i.v. prostaglandins E_1(PGE_1) and E_2(PGE_2) on the tachycardia induced by either sympathetic nerve stimulation or various drugs in the anaesthetized mouse

	Control response mean hr beats/min	*% Control Responses*					
		Dose PGE_1			*Dose PGE_2*		
		10 μg/kg	*20 μg/kg*	*40 μg/kg*	*10 μg/kg*	*20 μg/kg*	*40 μg/kg*
0.5 Hz	92 ± 7(30)	83 ± 2(4)	53 ± 9(5)	25 ± 7(3)	85 ± 5(7)	58 ± 10(7)	42 ± 5(4)
1 Hz	121 ± 5(29)	84 ± 3(4)	52 ± 6(5)	43 ± 4(3)	88 ± 2(6)	62 ± 2(5)	55 ± 8(6)
2 Hz	139 ± 7(29)	88 ± 2(5)	67 ± 5(6)	55 ± 5(4)	84 ± 8(5)	68 ± 7(5)	58 ± 14(4)
5 Hz	183 ± 7(25)	88 ± 5(5)	82 ± 7(4)	79 ± 10(4)	98 ± 1(4)	95 ± 2(4)	90 ± 2(5)
NA (1–2 μg/kg)	71 ± 5(19)	115 ± 8(4)	112 ± 9(3)	—	106 ± 9(4)	97 ± 4(6)	95 (2)
DMPP (100–300 μg/kg)	97 ± 10(9)	—	—	90 ± 11(3)	—	—	102 ± 8(6)
McN-A-343 (60–200 μg/kg)	93 ± 5(10)	—	—	11 ± 6(4)	—	—	22 ± 7(6)

Figures in parentheses indicate number of observations. All values are means ± s.e. mean. All doses of the stimulant drugs produced submaximal tachycardia.

Antagonism of noradrenaline's direct action on the effector organ is unlikely. Alternatively an effect on postganglionic neurones is possible because the prostaglandins can inhibit both responses to McN-A-343, which are mediated via muscarinic receptors on this structure (present paper), and noradrenaline release from electrically stimulated postganglionic nerves (e.g. Hedqvist & Wennmalm, 1971). However, an additional inhibition by prostaglandins of preganglionic acetylcholine release should be considered, since the prostaglandins failed to reduce the tachycardia caused by DMPP's stimulation of nicotinic receptors in the ganglia. This lack of an effect by the prostaglandins might be merely a function of dose or because DMPP-induced tachycardia relies heavily on amines released from the adrenals. Experiments are being conducted to investigate these possibilities.

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Interaction between the release of SRS-A and of prostaglandins

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Walker (1973) found in human chopped lung that treatment with indomethacin potentiated the release of SRS-A and suggested that prostaglandins inhibit its release. We investigated the effects of three non-steroid anti-inflammatory drugs on the release of SRS-A and histamine from sensitized guinea-pig lungs during challenge.

Lungs were removed from guinea-pigs previously sensitized to ovalbumen and rapidly perfused via the pulmonary artery with oxygenated Tyrode (37°C) at 5 ml/minute. Lungs were challenged by intra-arterial (i.a.) injection of ovalbumen (Sigma, grade III). The effluent was collected on ice for 10 minutes. The SRS-A content was estimated by immediately assaying aliquots of effluent on a strip of smooth muscle from guinea-pig ileum (blocked with mepyramine and hyoscine) against a laboratory standard preparation of