Emulsions of triolein (20 mM) at pH 6·3 in sodium taurodeoxycholate were prepared at 20° C; the system also contained 0·5 mM labelled diethylstilboestrol. The aqueous phase was separated by centrifugation and the partition of the drug between oil and aqueous-micellar phase (M/O) calculated (Freeman, 1969). An increase in the concentration of bile salt over a range 3–20 mM resulted in a proportional increase in the partition ratio (M/O) of diethylstilboestrol.

Diethylstilboestrol, therefore, is soluble in micellar solutions of sodium taurodeoxycholate and in mixed intestinal content will be distributed partly in any oil present and partly in aqueous micellar solution. The drug does not behave like non-polar solutes such as the sterols, which show enhanced solubility in mixed monoglyceride-bile salt micelles.

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Effects of circulating oestrogen on function of the cholinergic dilator nerves supplying the guinea-pig uterine artery

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Recent published evidence has been advanced to indicate that the extrinsic uterine arterial supply of the guinea-pig is innervated by cholinergic vasodilator nerves. These nerves are functional only during the last half of pregnancy, and it has been suggested that their existence is concerned with the production of uterine hyperaemia of pregnancy (Bell, 1968, 1969). In the present study, release of acetylcholine (ACh) from the vasodilator nerves in response to nervous stimulation was examined in tissues taken from guinea-pigs in different hormonal states. The arteries were cleared of surrounding tissues and mounted at *in vivo* length in a 2·5 ml bath of Krebs solution (37° C) containing physostigmine (2×10^{-5} M). Trains of 3,000 pulses at 5 Hz and 25 Hz were delivered with platinum electrodes at either end of the bath. The bathing fluid was collected 10 min after commencement of a stimulation period, diluted 10 : 4 with distilled water and assayed on the dorsal muscle of the leech.

Arteries from dioestrous virgin animals released $0{\cdot}48 \pm 0{\cdot}11$ (mean $\pm$ standard error, six arteries) and $0{\cdot}5 \pm 0{\cdot}11$ ng (ten arteries) ACh/artery per train at 5 Hz and 25 Hz respectively. During oestrus these rose to $2{\cdot}6 \pm 0{\cdot}36$ (eight arteries) and $4{\cdot}0 \pm 0{\cdot}64$ ng (eight arteries) ACh/artery per train. Values obtained in tissues from animals in mid to late pregnancy were still high in comparison to those obtained in dioestrus, but lower than those in oestrus ($1{\cdot}1 \pm 0{\cdot}14$ (twelve arteries) and $1{\cdot}8 \pm 0{\cdot}31$ ng (twelve arteries) ACh/artery per train). This disparity might be attributable to lessened diffusion of ACh out of the hypertrophied pregnant tissues.

It has been shown previously that sensitivity to ACh of the arterial muscle is low during both oestrus and dioestrus, although it becomes high during the course of pregnancy (Bell, 1968). The effect of chronic treatment of virgin animals with high doses of oestrogen (0·5 mg oestradiol i.m. per day) on responses of isolated perfused arteries to ACh was therefore investigated. It was found that following oestrogen treatment for 14 days or longer, the sensitivity of the arterial muscle to ACh was significantly increased.

It is concluded that the functionality of both pre- and postsynaptic components of this vasomotor system is determined by the levels of circulating oestrogenic hormones. The results emphasize the complex interaction which may exist between hormonal and nervous control of the female reproductive tract, as previously remarked for the adrenergic nervous system by Sjöberg (1968a, b).

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A new muscarinic agent: 1,4,5,6-tetrahydro-5-phenoxypyrimidine (AH 6405)

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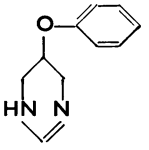
Oral administration of 1,4,5,6-tetrahydro-5-phenoxy-pyrimidine (AH 6405) to rodents caused overt parasympathomimetic effects—for example, profuse lacrimation, salivation and urination. Intravenous injection of AH 6405 (0·01–1·0 mg/kg) into anaesthetized cats and dogs caused similar effects but unlike most other parasympathomimetic agents also caused a secondary pressor response after the initial vasodepression. Since there is evidence (Roszkowski, 1961; Franko, 1963) that certain muscarinic agents may produce a vasopressor response by stimulation of sympathetic ganglia, experiments were undertaken to investigate the possibility that AH 6405 possessed stimulant activity on autonomic ganglia.



AH 6405

In cats anaesthetized with chloralose, close-arterial injections of AH 6405 (2–10 μg/kg) to the superior cervical ganglion via the lingual artery caused dose-dependent contractions of the ipsilateral nictitating membrane. This action was not affected by pentolinium (1 mg/kg intravenously), but was abolished by section of the post-ganglionic sympathetic nerves or by previous close-arterial injection of atropine (0·1 μg/kg) or cocaine (0·1 mg/kg). Large intra-arterial doses of nicotine (0·1 mg/kg) had a biphasic effect on the response to AH 6405. Initially it blocked the action of AH 6405, but the response to AH 6405 soon returned even when the ganglion was