The *in vitro* rat cervix

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It has been suggested on the basis of histological studies in the human (Danforth, 1947) and mechanical studies in the rat (Harkness & Harkness, 1959) that the physical properties of the cervix are determined more by the connective tissue than by the smooth muscle. However, the isolated human cervix has been shown to exhibit spontaneous contractility and to respond to drugs (Najak, Hillier & Karim, 1970).

Isolated rat cervices or uterine horns (from ovariectomized animals pre-treated daily for seven days with 17β oestradiol, 5 μg/kg s.c.) were perfused intraluminally with Krebs solution at $37 \pm 0.5^{\circ}$C at constant flow (1.5 ml/minute). Drugs were either injected into the perfusing Krebs or added to the reservoir. Contractions were recorded as increases in perfusion pressure. The magnitude of responses were measured as either the maximum pressure produced or the integrated pressure, above atmospheric, in the 5 min period after drug injection.

Methacholine (5×10^{-9} to 1.2×10^{-6} mol; $n = 8$) and oxytocin (5×10^{-2} to 4×10^{-4} i.u.; $n = 5$) produced cervical contractions. Oxytocin (1×10^{-2}: i.u./ml), added to the Krebs, produced regular contractions which were inhibited by isoprenaline (1×10^{-12} to 7.2×10^{-10} mol; $n = 6$) and phenylephrine (1×10^{-8} to 2.7×10^{-7} mol; $n = 6$). Phenylephrine (up to 2.7×10^{-7} mol; $n = 6$) did not contract the cervix.

Transmural stimulation of the cervix produced single contractions; the magnitude of which were frequency related between 1 and 64 Hz. These contractions were markedly reduced by hyoscine hydrobromide (2.5×10^{-8} M; $n = 6$) and tetrodotoxin (3.1×10^{-7} M; $n = 6$). The former abolished responses to methacholine (4.5×10^{-8} mol). The responses to oxytocin (4×10^{-2} i.u.) were unaffected by either agent.

Histochemical studies showed the presence of a denser network of acetylcholinesterase-staining fibres in the cranial end of the cervix than in the uterine born and a sparse cervical nor-adrenergic innervation.

In most qualitative and quantitative aspects the cervix responded in a similar manner to the uterine horn. These studies therefore provide no evidence for any cervical sphincteric function. The cervix possesses a cholinergic and nor-adrenergic innervation. The rat cervix can respond to drugs and so has smooth muscle with possible functional roles.

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Effects of quazodine on cat fast- and slow-contracting skeletal muscles

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Quazodine (6,7-dimethoxy-4-ethylquinazoline) relaxes smooth muscle and enhances the contractility of cardiac muscle (Lish, Cox, Dungan & Robbins, 1964; Aviado, Folle & Pisanty, 1967; Parratt & Winslow, 1972). In isolated skeletal muscle preparations quazodine enhances indirectly- and directly-evoked contractions (Nott & Winslow, 1973). The effects of quazodine on fast- and slow-contracting skeletal muscles in chloralose anaesthetized cats are now reported.

Quazodine (0.5-4 mg/kg i.a.) enhanced the tension of maximal twitches of the fast-contracting flexor hallucis longus (FHL) muscle. The highest dose produced increases in peak tension ranging from 10 to 16%. Onset of action occurred within 10 s; peak effect occurred within 30 s and the effect lasted from 2 to 6 minutes. The increase in tension was associated with an increase in the time to peak tension and overall duration of this twitch. Quazodine enhanced the tension of incomplete (24-32 Hz) and maximal (120 Hz) tetanic contractions of the FHL, the effect upon incomplete tetani (up to 114%) being more marked as a consequence of prolongation of the units of contractions.

The initial effects of quazodine (0.5-4 mg/kg i.a.) in the slow-contracting soleus muscle were

similar to those seen in the FHL muscle. The highest dose of quazodine increased the peak tension of maximal twitches by 8 to 15%. Incomplete (8-10 Hz) and maximal (100 Hz) tetanic contractions were also enhanced but, unlike the effects in the FHL muscle, incomplete tetani were no more responsive than maximal tetani. The time course of enhanced contractility was similar to that observed in the FHL muscle. Following the period of enhancement of contractility of the soleus muscle, twitch tension and submaximal tetanic tension were reduced. No such effect was seen in maximal tetani. The depressant effect on incomplete tetanic tension was more marked (up to 30%) than the effect on twitches (up to 12%). It reached a peak within 5 min of injection of quazodine and was associated with defusion of the contractions. All effects in the FHL and soleus muscle were observed both in fully curarized, directly stimulated muscles and in indirectly stimulated muscles, indicating that they were not a result of actions of quazodine on neuromuscular transmission (Nott & Winslow, 1973).

The enhancing effect of quazodine on contractions of the FHL and soleus muscles was similar to that observed with theophylline (2-20 mg/kg i.a.) and as with the methylxanthines (Sandow, 1965), probably involves mobilization of calcium ions. The secondary phase in the soleus was similar to the depression seen following treatment with β-adrenoceptor agonists (Bowman & Nott, 1970), and in the present experiments was reduced or abolished by prior treatment with (±) propranolol (100-200 μg/kg i.v.).

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The relationship of ascorbic acid to leptazol-induced convulsions in guinea-pigs

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Hepatic ascorbic acid (AA) is reduced to about 9% (Hurley, Jones & Hughes, 1972; Odumosu & Wilson, 1973a), and adrenal AA to almost zero (Odumosu & Wilson, 1970), in scorbutic guinea-pigs. In contrast, brain AA is only reduced to 48% of normal (Hurley, Jones & Hughes, 1972). Supplementary AA disappears more slowly from the brain than from other tissues (Hornig, Weber & Wais, 1972). The function of ascorbic acid in the brain is unknown, although it may be involved in olfaction (Ash, 1969), taste (Loh & Wilson, 1973) and in the production of anorexia arising from fenfluramine (Odumosu & Wilson, 1973b, c). Clonic and tonic convulsions are produced in normal guinea-pigs by administration of leptazol, 60 mg/kg i.p., resulting in 100% mortality, whereas 40 mg/kg produces clonic seizures in only 50%. At the time of death, brain AA is significantly reduced to 56-70% of normal, and plasma AA is elevated to 142% of normal by 60 mg/kg leptazol. In guinea-pigs receiving 40 mg/kg leptazol, brain AA falls to 83% of normal, but plasma AA is unaltered, indicating that brain AA is being catabolized. The incidence, and time preceding onset, of convulsions is related to the concentration of brain AA. A second dose of 40 mg/kg of leptazol was administered over 60 min to animals which had not developed convulsions, and to convulsing animals 15 min after the last tonus. All developed clonic convulsions in 12 minutes. Brain AA was reduced to 54% and plasma AA was raised to 130% of control values.

AA administration (200 mg/kg i.p.) 1 h before leptazol 60 mg/kg results in a lower incidence of tonic convulsions after a prolonged latent period, but brain AA decreases to the same level as in unsupplemented animals. The incidence is increased and the latent period of convulsions is shortened by leptazol in scorbutic guinea-pigs. Their brain AA is reduced to 37% of normal, and AA is released into the plasma during the convulsions. AA concentrations fall to 63% in the mid-brain and 91% in the fore-brain, of normal