observation is consistent with the results reported by Fitzsimons and Setler (1971) in the rat.

Fitzsimons & Setler (1971) proposed that central catecholaminergic mechanisms were involved in angiotensin-induced drinking since the response was abolished after pretreatment with 6-hydroxydopamine centrally. We have found that bethanidine (400 μg) caused a significant reduction in drinking in each of 5 cats whilst a dose of 600 μg abolished drinking in three animals and reduced the response in two others. Phentolamine (250 μg) abolished drinking but tolazoline (600 μg) another α-adrenoceptor blocker, had no effect. The drinking response to angiotensin was abolished by propranolol (450 μg) and significantly reduced by practolol (400 μg).

These results indicate that angiotensin-induced drinking in the cat involves central adrenergic mechanisms.

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Tetanic and single twitch responses of skeletal muscle during repeated injections of suxamethonium in man

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The effect of repeated I.V. injections of suxamethonium in man was studied by measuring simultaneously single twitch and tetanic contraction responses of the thumbs (Gissen & Katz, 1969). The investigation was carried out during Helmstein's treatment (Helmstein, 1966) for carcinoma of the bladder, a procedure which lasts for 6 hours.

Eleven patients were studied after informed consent had been obtained on the previous day. Without premedication, anaesthesia was induced with halothane, nitrous oxide and oxygen. In some patients pentazocine supplements instead of halothane were used for maintenance. Respiration was controlled or assisted in order to maintain the pH within normal limits. Statham force transducers, Model UC with hand grips, were mounted one on each hand to measure the force of the thumb adduction. The ulnar nerves were stimulated at the wrists ; a single square wave pulse of 200 μs duration was applied to one nerve every 12 s and a tetanic stimulus of 30 Hz for 1 s was used every 12 s on the other. The force of the thumb adduction was recorded on a Brush-Clevite recorder with a slow speed of 5 mm/min and on a Mingograf recorder at a fast speed of 5 mm/s.

After an initial control period, repeated injections of suxamethonium (0·1–0·2 mg/kg) were given at 15 min intervals. In most patients the first dose of suxamethonium caused complete block of the tetanic contraction and partial block of the single twitch contraction. With the single twitch response tachyphylaxis developed progressively with successive injections and this trend continued until virtually no depression was seen. With the tetanic response the initial depression became less, the initial stage of recovery developed earlier but complete recovery occurred more slowly with successive injections.

In five patients edrophonium (0·1 mg/kg) I.V. was given at the 50% recovery point of the tetanic contraction after the first injection of suxamethonium and caused a potentiation of the block but this potentiation was less obvious when edrophonium was repeated after subsequent injections of suxamethonium and ultimately towards the end of each study edrophonium reversed the block by suxamethonium.

These studies have shown that the single twitch and the tetanic contraction respond

differently to repeated injections of suxamethonium and that each type of response itself differs with time. These gradually changing patterns in response probably reflect a change in the mode of action of suxamethonium and this interpretation is supported by the observation that edrophonium at first enhances and later antagonizes suxamethonium block.

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Possible mechanisms of action for the influence of ketamine on uterine tone

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Ketamine hydrochloride [2-(o-chorphenyl-2-(methylamino) cyclohexanone HCl] causes contractions of pregnant human uterus (Galloon, 1973). Our attention was drawn to this by gynaecologists in our hospital, who noticed that there was a decrease in uterine bleeding during ketamine anaesthesia for vaginal termination of pregnancy. There are a number of ways in which ketamine could increase tone, for example Bovill, Clarke, Davis & Dundee (1971) found an increase in plasma noradrenaline after ketamine. Noradrenaline has been shown to cause uterine contractions in pregnant women (Garrett, 1964). We have investigated other possible mechanisms.

(a) Strips from the main body of the uterus removed at hysterectomy (premenopausal, n=6), hysterotomy (one at 16 weeks) and Caesarean section (n=2), were set up in an isolated organ bath in Krebs–bicarbonate solution aerated with 95% O_2/5% CO_2. Spontaneous activity was recorded on a kymograph. Every strip tested responded to noradrenaline (100 ng–1 μg/ml) either by contraction or by an increase in the frequency of the spontaneous activity. No sample tested responded to ketamine (1 μg–100 μg/ml).
(b) Radioimmunoassay of oxytocin levels in plasma was carried out by the method of Chard, Boyd, Forsling, McNeilly & Landon (1970) on blood samples collected during anaesthesia for vaginal terminations of pregnancy, using either diazepam (10–20 mg)/ketamine (induction dose 2 mg/kg, maintenance 1 mg/kg) or conventional thiopentone 5 mg/kg), nitrous-oxide-oxygen-trilene sequence (control group). Samples were also assayed for vasopressin using the bioassay method of Forsling, Jones & Lee (1968). This technique was modified to include an extraction procedure which increased the specificity of the estimation (Forsling, 1971). Blood samples were taken postpremedication and also at timed intervals during anaesthesia (3–6 samples from each patient). At no time during either combination did the oxytocin levels rise to a detectable level in the plasma (limit of detection 1 μU/ml). The vasopressin levels showed some inconsistent changes; the range for vasopressin in 15 patients receiving ketamine was $<0{\cdot}5$ μU/ml–15 μU/ml and that for the two controls $<0{\cdot}5$ μU/ml–7 μU/ml.

It is unlikely that the effect of ketamine on uterine tone is due solely to a direct action on the uterus or to the action of released vasopressin or oxytocin.

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