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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