after 200 ms (ileum) or 2 s (uterus). These values of the current were used to plot the current-voltage relationship. Currents required to hyperpolarize the membrane were constant after the capacitive transient.

The current-voltage characteristics of the additional conductance appearing in the presence of carbachol were derived from the current-voltage plots obtained in the absence and in the presence of carbachol ($10^{-7}$ to $10^{-5}$ g/ml), (Ginsborg, 1967). This conductance was constant for small deviations from the resting membrane potential but with large deviations it apparently increased. The current through this conductance reversed in direction at a point somewhat negative to the peak of the evoked spike. The position of this point, the equilibrium potential, was in good agreement with previous predictions (Bolton. 1972).

A further series of experiments were done using ramp commands (Fishman, 1970), since large rectangular command pulses may produce appreciable shifts in ion concentrations. Ramps have the additional advantage that if a suitable rate of rise is chosen, one or two applications of the ramp can yield the whole current-voltage curve. Using such ramps, the carbachol dependent conductance was found to change much less with large perturbations from the resting membrane potential.

Experiments have also been done on a short 'closed cable' preparation of smooth muscle using intracellular recording of membrane potential with microelectrodes. This 'closed cable' preparation was polarized uniformly by current passed into it from an external electrode. The preparation thus avoids the difficulties encountered in measuring the current-voltage characteristics of the usual 'infinite cable' preparation (Tomita, 1966) which arise due to the spatial decrement of polarization with distance from the current passing electrode.

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## The effect of the dissociative anaesthetic, ketamine, on transmembrane potentials of Purkinjé fibres of the pig heart

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Several investigators have reported effects on the heart of the dissociative anaesthetic ketamine including depression (Goldberg, Keane & Phear, 1970), stimulation (Traber, Wilson & Priano, 1968) and antiarrhythmic activity (Goldberg *et al.*, 1970; Dowdy & Kaya, 1968). In this laboratory we have demonstrated that ketamine potentiates and then depresses the isolated rat diaphragm preparation (Hamilton, Jones, Kiraly & Parker, 1972) and that this was a direct effect upon the muscle, as both potentiation and blockade of the directly stimulated muscle were produced in the presence of tubocurarine. It was concluded that the initial stimulant actions were possibly veratrine-like in nature.

In the present investigation the actions of ketamine have been further studied on the Purkinjé conduction system of the mammalian heart. Intracellular recordings have been made from isolated spontaneously active and electrically-driven cells of the septomarginal trabecula (moderator band) of the pig.

Domestic pigs weighing between 4.5 and 9.0 kg were stunned with a captive bolt pistol, exsanguinated and the heart was rapidly removed. The moderator band was dissected out and placed in cold, oxygenated Krebs-Henseleit solution, and then transferred to an organ bath, held firmly by two threads placed over the pieces of myocardium at the ends of the band, and totally immersed in a continuous flow of pre-warmed ($37^{\circ} \pm 1^{\circ}$C) Krebs-Henseleit solution gassed with 95% oxygen, 5% carbon dioxide.

The preparation was then rested for a period of

1 to 2 h during which time it usually developed spontaneous activity. In some experiments it was stimulated orthodromically with a bipolar electrode inserted into the intraventricular musculature using pulses of 0.5 ms duration and up to 5 V amplitude at source, delivered from a Grass S8 stimulator.

The Purkinjé fibres were impaled with glass floating microelectrodes containing 3 M KCl (resistances between 10 and 30 megohms) and the electrical activity amplified with either a W.P.M. 4 electrometer probe or a Mentor N950 intracellular probe system. The action potentials were displayed on an oscilloscope and recorded simultaneously on a Grass Model 7 Polygraph, a Mingograph spray pen galvanometer and a tape recorder.

Ketamine hydrochloride altered the transmembrane potentials in a dose-related and reversible manner. Concentrations of $1 \times 10^{-5}$ M were subthreshold whereas $5 \times 10^{-5}$ M and $1 \times 10^{-4}$ M slowed the frequency and increased the action potential duration of spontaneous preparations, actions consistent with an antiarrhythmic effect. Higher concentrations of $5 \times 10^{-4}$ M ketamine initially led to a shortening of the action potential duration then failure of the original spontaneous activity. During recovery pacemaker-like activity developed associated with a loss of resting membrane potential. In electrically-driven preparations $5 \times 10^{-4}$ M ketamine significantly shortened the duration of the action potentials, allowed the appearance of spontaneous potentials between evoked potentials and markedly augmented the response to adrenaline, actions consistent with an arrhythmogenic effect. These findings suggest a basis for isolated reports of cardiac side effects and interactions (e.g. Koplan & Cooperman, 1971) and as the concentrations administered in clinical practice are higher than those employed in the present experiments, cardiac side effects should not be unexpected.

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## Some observations on electrically-inexcitable cells (neuroglia?) in rat sympathetic ganglia

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During the course of some recent experiments using intracellular recording methods in isolated rat superior cervical ganglia (Adams & Brown, 1973) we frequently impaled cells which had high initial membrane potentials (80-90 mV) but low input resistances (<5 MΩ) and which responded passively to depolarizing current pulses. These resemble the 'inexcitable' cells in guinea-pig sympathetic chain ganglia described by Blackman, Crowcroft, Devine, Holman & Yonemura (1969) and by Blackman & Purves (1969), and tentatively identified by them as capsular (oligodendroglial) cells. In our experiments the frequency with which these cells were impaled was quite high (several times in each experiment), but their resting potential usually discharged rather rapidly. However, on a few occasions the membrane potential was sustained at a reasonably elevated level (50-75 mV) for sufficient time to note some of their properties. The experimental methods used have been described previously (Adams & Brown, 1973).

No action potential could be elicited in these cells either by (i) direct stimulation using depolarizing current passed through the recording microelectrode or (ii) orthodromic stimulation of the preganglionic trunk using parameters sufficient to elicit a synaptically-mediated response of normal ganglion neurones. However, single orthodromic