occurs (Fig. 1). We conclude that an electrogenic sodium pump is operating which requires extracellular K^+ to activate it. Cs^+ is much less effective than K^+ in stimulating the pump as has been shown for the rat superior cervical ganglion by Brown, Brownstein & Scholfield (1969).

By the sucrose-gap method, the mechanism underlying the production of the drug-induced hyperpolarization is compared with the hyperpolarization of ganglion cells evoked by orthodromic excitation, the P wave or slow IPSP. Unlike the drug-induced hyperpolarization, the P wave has a component whose amplitude increases in potassium-free solution (Kosterlitz *et al.*, 1968). Furthermore, in confirmation of the findings of Kobayashi & Libet (1968) and Libet & Kobayashi (1969), the amplitude of the *P* wave is not readily diminished by ouabain.

This work was supported by U.S. Public Health Service Grant NB 03026 from the National Institute of Neurological Diseases and Stroke.

†Present address: Department of Physiology, University College, Cardiff.

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The effects of morphine-like substances and their antagonists on transmission at the neuro-effector junction of the myenteric plexus-longitudinal muscle preparation of the guinea-pig ileum.

A. LOUISE COWIE, H. W. KOSTERLITZ, R. J. LYDON and ANGELA A. WATERFIELD, *Section of Pharmacology, Department of Therapeutics & Pharmacology, University of Aberdeen.*

It has been shown (Gyang & Kosterlitz, 1966; Kosterlitz & Watt, 1968) that, in the guinea-pig ileum, narcotic analgesic drugs have both agonist and antagonist properties and that the pharmacological effects depend on the ratio of agonist to antagonist potency. There are only a few compounds which are pure antagonists devoid of agonist activity, for example, naloxone. The order of agonist and antagonist potencies as determined on the guinea-pig ileum are in good agreement with observations made in man. This fact has made it possible to use the guinea-pig ileum for the prediction of agonist and antagonist activities of new compounds (Kosterlitz & Watt, personal communication).

Since this method depends on the effects of the narcotic analgesic drugs on impulse transmission at the myenteric plexus-longitudinal muscle junction, it was of interest to investigate more fully the factors which influence the release of acetylcholine and the response of the longitudinal muscle to the transmitter. It has been shown (Paton & Zar, 1968; Cowie, Kosterlitz & Watt, 1968) that morphine in low concentrations depresses the acetylcholine output when the myenteric plexus-longitudinal muscle

preparation is stimulated at low frequencies (0·1–1 Hz). Thus, in the presence of morphine, the evoked output per volley is low and almost constant at frequencies between 0·1 and 10 Hz, whereas without morphine the output per volley is usually much higher at low frequencies of stimulation and falls with increasing rates of excitation. When trains of 2–16 pulses, with intervals of 20–500 ms between pulses, are repeated at intervals of 10 s between trains, the output of acetylcholine caused by the later pulses in a group is lower than that due to the earlier pulses.

While there is so far no unequivocal evidence that morphine reduces the acetylcholine release evoked by the earlier pulses more than that induced by the later pulses, electrophysiological experiments are in favour of such an interpretation. When a single rectangular current pulse is applied to the myenteric plexus-longitudinal muscle preparation, a nerve action potential is obtained which, after a junctional delay of about 200 ms, is followed by a complex of spikes due to activity in the muscle cells (Kosterlitz & Lydon, 1969). Morphine (0·06–0·4 μM) depresses the muscle action potential without affecting the nerve action potential. The depressant action of morphine is less with trains of 16 pulses than with shorter trains or single pulses; this observation is in agreement with the assumption that the acetylcholine release evoked by the later pulses in a train is not affected by the depressant action of morphine.

This work was supported by U.S. Public Health Service Grant NB 03026 from the National Institute of Neurological Diseases and Stroke.

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A further method of eliminating interfering compounds in the gas chromatographic determination of urinary methylimidazoleacetic acids.

A. S. KELVIN (introduced by P. B. MARSHALL), *Department of Pharmacology, University of Dundee.*

Estimation of the histamine metabolite 1-methylimidazole-4-acetic acid (1-MeIm4-AA) and its isomer 1-methylimidazole-5-acetic acid (1-MeIm5-AA) in urine by the method of Tham (1966) has presented difficulties in this laboratory due to the presence of interfering peaks on the gas chromatograms. A method of eliminating these has been described (Kelvin, 1968). We now describe an alternative procedure involving elution of urinary methylimidazoleacetic acids from Dowex 1 with a 0·1 M acetate buffer instead of the 0·5 M acetic acid previously used. This simple modification substantially improves the gas chromatograms (Fig. 1).