the rat Notley (1968) observed both afferent and efferent fibres and an apparent absence of ganglia, perhaps indicating that the ureter is innervated only by sympathetic fibres.

Methods of investigation have included *in vivo* and *in vitro* techniques where results have been obtained by direct observation, recording intraluminal pressure, measurement of isotonic muscle contraction, ureteral electromyography and forms of ureteral radiography. Each method, however, suffers from disadvantages which could seriously influence the results obtained or severely limit the scope of investigation.

The method demonstrated here allows measurement of the peristaltic rate and the flow of a perfusing solution along the ureter. Peristaltic rate is measured by recording the action potential of each peristaltic wave using a flexible-tipped glass microelectrode inserted into the outer muscle coat. This has the advantage that mechanical stimulation and damage to the ureter is minimal.

The microelectrodes are pulled mechanically from soda glass tubing (1·0 mm external diameter, 0·75 mm internal diameter) to have a shank length of 15–20 mm and a tip diameter of approximately 4 μm. These dimensions have been found to give the tip the flexibility which is required for the measurement of action potentials from a tissue as mobile as the ureter. The electrodes are filled under vacuum with 3 M KCl and those having a resistance of less than 10 MΩ are accepted for use. The microelectrode is linked to the pre-amplifier via an agar-KCl bridge and Ag/AgCl electrode.

By tying off both the renal artery and renal vein urine production is prevented and perfusion of the ureter is carried out through a fine needle inserted into the pelvis of the kidney. The flow of the perfusion fluid is measured photoelectrically, while the incorporation of 0·002% w/v Evans's blue in the perfusion solution facilitates visual observation.

This method allows investigation of the effects of renal pelvic pressure, autonomic drugs and, with some modification, autonomic nerve stimulation on the rat ureter.

D.M.J. was supported by the M.R.C.

REFERENCES

GRUBER, C. M. (1933). The autonomic innervation of the genito-urinary system. *Physiol. Rev.*, **13**, 497–609.
LAPIDES, J. (1948). The physiology of the intact human ureter. *J. Urol.*, **59**, 501–537.
NOTLEY, R. G. (1968). Electronmicroscopy of the upper ureter and pelvic ureteric junction, M.S. Thesis, London University.
WHARTON, L. R. (1932). Innervation of the ureter with respect to denervation. *J. Urol.*, **28**, 639–673.

A method for studying release of prostaglandins from superfused strips of isolated spleen.

A. L. WILLIS (introduced by J. R. VANE), *Department of Pharmacology, Institute of Basic Medical Sciences, Royal College of Surgeons of England, London, W.C.2.*

In response to nerve stimulation or adrenaline, dog spleens contract and release prostaglandins (E_2 and $F_{2\alpha}$) into the venous effluent; these effects are blocked by phenoxybenzamine (Ferreira & Vane, 1967; Davies, Horton & Withrington, 1968; Gilmore, Vane & Wyllie, 1968). This effect has now been investigated by a simple *in vitro* method.

Prostaglandin release from superfused strips of rabbit spleen was detected by isolated tissues suspended in cascade below the spleen (Fig. 1). Selectivity of these assay tissues was enhanced by infusing a mixture of antagonists at point B. On infusion of a

stimulating substance (for example, adrenaline) at point A, the spleen strip contracted and prostaglandins were released. The concentration of prostaglandins released was estimated (in terms of E_2) by infusions of prostaglandins E_2 at point B. These were made in the presence of the same concentration of the substances used to excite the spleen, also infused at point B.

Adrenaline (20–1,300 ng/ml) contracted the spleen and induced an output of prostaglandin activity which was highest during the early part of the infusion. This output increased from 1–25 ng/ml (estimated as E_2) with the concentration of adrenaline. Splenic contraction and release of prostaglandins was blocked by phenoxybenzamine (0·1–1 μg/ml). The prostaglandin-like activity could be extracted into ethyl acetate at pH 3. Simultaneous parallel assay of these extracts (Willis, 1969) suggested that their activity was due to E-type prostaglandins, a result supported by chromatography; similar results have been obtained with noradrenaline.

Acetylcholine (0·2–20 μg/ml) induced non-sustained contractions of the spleen and an output of prostaglandins. Although contractions induced by acetylcholine were not

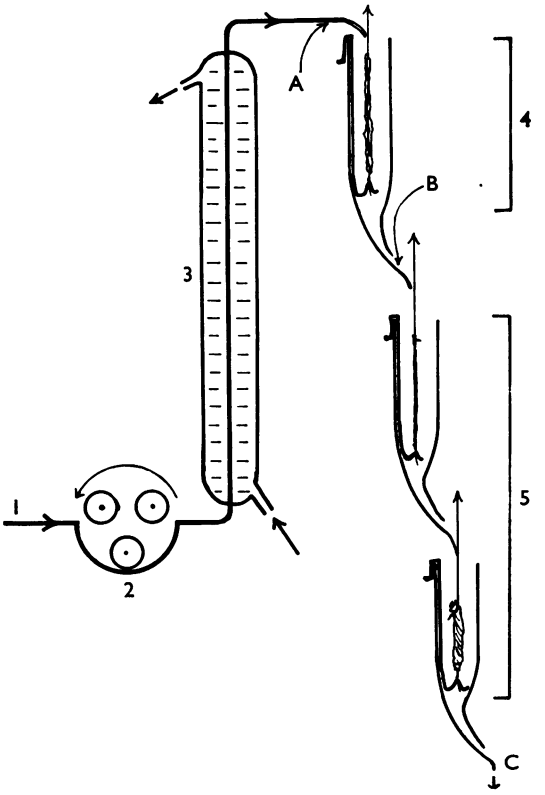

FIG. 1. Experimental details. Krebs solution, gassed with 95% oxygen and 5% carbon dioxide (1) was delivered at 5 ml/min by a roller pump (2) and after heating to 37°C by a warming jacket (3) was passed over the spleen strip (4) and assay tissues (5). The assay tissues were chosen from a rat stomach strip, a rat colon, chick rectum and gerbil colon. Changes in length of the spleen strip and assay tissues were recorded on a kymograph or with isotonic transducers and a Watanabe (Type WTR 281) pen recorder. Antagonists infused at point B were: phenoxybenzamine (100–200 ng/ml), propranolol (2–4 μg/ml), mepyramine (100–200 ng/ml) and methysergide (20–400 ng/ml). Concentration of hyoscine was usually 100–200 ng/ml, although it was increased to 1 μg/ml when high doses of acetylcholine were used. At point C effluent from the cascade ran to waste or was collected for extraction.

antagonized by hyoscine (0·1–1 μg/ml) they were inhibited by phenoxybenzamine or phentolamine (100 ng/ml) in parallel with those to adrenaline, suggesting that contractions to acetylcholine may be mediated via catecholamine release.

This work was supported by the M.R.C.

REFERENCES

DAVIES, B. N., HORTON, E. W. & WITHRINGTON, P. G. (1968). The occurrence of prostaglandin E_2 in splenic venous blood of the dog following splenic nerve stimulation. *Br. J. Pharmac. Chemother.*, **32**, 127–135.

FERREIRA, S. H. & VANE, J. R. (1967). Prostaglandins: their disappearance from and release into the circulation. *Nature, Lond.*, **216**, 868–873.

GILMORE, N., VANE, J. R. & WYLLIE, J. H. (1968). Prostaglandins released from the spleen. *Nature, Lond.*, **218**, 1135–1140.

WILLIS, A. L. (1969). Parallel assay of prostaglandin-like activity in rat inflammatory exudate by means of cascade superfusion. *J. Pharm. Pharmac.*, **21**, 126–128.

Drug-induced pilomotion: an easily demonstrated α-effect of sympathomimetic drugs.

A. HERXHEIMER and A. TOTHILL, *Department of Pharmacology and Therapeutics, The London Hospital Medical College.*

It may be difficult to demonstrate α-receptor activity of sympathomimetic amines convincingly, especially when a drug also has prominent β-effects. Pilomotion, a purely α-receptor effect, substantially changes the appearance of the animal and can conveniently be used for this purpose in various laboratory species, for example, mice and guinea-pigs.

Illustrations of three groups of mice were shown, injected subcutaneously with phenoxybenzamine (1·0 mg/kg), propranolol (10 mg/kg) and saline respectively. Isoprenaline (1·0 mg/kg), orciprenaline (20 mg/kg) or salbutamol (20 mg/kg) were subsequently injected by the same routes.

Pilomotion was also elicited locally by injecting α-receptor stimulants intradermally. This enabled both different concentrations to be injected into different sites in the same animal and different drugs to be compared directly. Such a procedure might be suitable for screening drugs for α-receptor stimulant activity.