

in Krebs solution containing half the normal concentration of Ca^{++} , equilibrated with 5% carbon dioxide in oxygen and maintained at 35° C. *In vivo* experiments were carried out on cockerels anaesthetized with halothane and decerebrated; after an interval of 60–90 min contractions of the oesophagus to stimulation of the vagus and descending oesophageal nerves were recorded by a balloon-tambour system (Hassan, 1967). In both *in vitro* and *in vivo* experiments the nerves were stimulated with square wave pulses (width 10 msec, frequency 20 c/s and intensity 5V) the duration of stimulation being 5–15 sec applied every 2–15 min.

Exposure of the isolated oesophagus to hyoscine (1–100 $\mu\text{g}/\text{ml}$.) for 30 min abolished the contraction produced by stimulation of either nerve if the duration of stimulation was less than 5 sec; however, prolonged stimulation produced a delayed contraction which was not antagonized by hyoscine (100 $\mu\text{g}/\text{ml}$.) although cocaine (50 $\mu\text{g}/\text{ml}$.) abolished it (Bartlet & Hassan, 1968b). The hyoscine-resistant contraction was abolished by cutting the nerves, but mepyramine, methysergide or bretylium had no effect on it. Physostigmine (5 $\mu\text{g}/\text{ml}$.) did not have a significant effect on the hyoscine-resistant contraction and physostigmine (50 $\mu\text{g}/\text{ml}$.) antagonized it ($P < 0.05$). In six experiments tubocurarine (50 $\mu\text{g}/\text{ml}$.) reduced the height of the hyoscine-resistant contraction by a mean (\pm S.E. of mean) of 21% (± 8 , $P < 0.05$) and hexamethonium (100 $\mu\text{g}/\text{ml}$.) reduced it by a mean of 59% (± 14 , $n=3$, $P < 0.05$).

In previous experiments with pentobarbitone-anaesthetized chickens, the contraction of the oesophagus *in vivo* produced by stimulation of the vagus and descending oesophageal nerves was abolished by intravenous hyoscine (Hassan, 1967). Decerebrate preparations have now been used to find out whether the pentobarbitone had blocked a hyoscine-resistant response of the oesophagus to nerve stimulation. Hyoscine (100 $\mu\text{g}/\text{kg}$ intravenously) abolished the contractions of the oesophagus produced by prolonged stimulation of the vagus and descending oesophageal nerves.

The *in vivo* experiments suggest that the vagus and descending oesophageal nerves are cholinergic, but the *in vitro* experiments suggest that these nerves release acetylcholine which acts on receptors inaccessible to hyoscine added to the organ bath.

REFERENCES

- BARTLET, A. L. & HASSAN, T. (1968a). Some actions of histamine and 5-hydroxytryptamine on isolated chicken oesophagus. *Br. J. Pharmac. Chemother.*, **32**, 156–163.
 BARTLET, A. L. & HASSAN, T. (1968b). The action of physostigmine and the distribution of cholinesterases in the chicken oesophagus. *Br. J. Pharmac. Chemother.*, in the Press.
 HASSAN, T. (1967). Effects of stimulation of the cervical vagus and descending oesophageal nerves on the alimentary tract of the domestic fowl. *Zentbl. Vet. Med. A.*, **14**, 854–861.

Study of the effects of progesterone therapy on the oestrogen-induced sensitivity of rat uterus

I. KHAN* and N. AHMED, *Department of Pharmacology and Therapeutics, Jinnah Post-graduate Medical Centre, Karachi, Pakistan*

Khan & Qureshi (1967) observed that reserpine therapy prevented the marked increase in the sensitivity of rat isolated uteri to oxytocic drugs by stilboestrol. They considered this to be due to excessive release of progesterone from the corpora lutea. This effect of reserpine disappeared in ovariectomized (Ansary, 1965) and hypophysectomized rats (Khan & Shariff, 1967).

The effect of progesterone on the isolated uterine sensitivity both in ovariectomized and intact animals was determined in eighty-eight rats. Progesterone was administered

to ovariectomized rats on the first and third day of dioestrous in doses ranging from 4 to 100 mg/kg. Intact animals received fixed doses of progesterone (50 mg/kg). Both groups of animals received a single dose of stilboestrol (100 µg/kg), on the fourth day of dioestrous 18 hr before killing.

Vaginal smears were taken and the sensitivity to oxytocic drugs—namely acetylcholine, oxytocin and 5-hydroxytryptamine—was studied after suspending the isolated uterine horns in a 5 ml. bath containing De-Jalon solution at 30° C. A 3 point assay method was used comparing oxytocin and 5-hydroxytryptamine to acetylcholine; the results were expressed as equipotent molar ratios.

Vaginal smears of all rats treated with progesterone (50 mg/kg) showed abundant leucocytes indicating absence of stilboestrol effect. Progesterone therapy in ovariectomized animals increased the sensitivity of the uterus to oxytocic drugs. The maximum increase in sensitivity was observed with progesterone (50 mg/kg) where the sensitivity to acetylcholine, oxytocin and 5-hydroxytryptamine was increased by 4, 11 and 3 times respectively as compared with the control rats in induced oestrous. In intact animals, on the other hand, progesterone (50 mg/kg) therapy decreased the sensitivity to acetylcholine, oxytocin and 5-hydroxytryptamine by 2, 1.4 and 17.7 times respectively. In these experiments progesterone therefore desensitizes the uterus to the effect of stilboestrol only in normal rats. This shows that the ovary is essential for the desensitizing effect of progesterone similar to reserpine. The probable mechanism of release of yet another chemical substance from the ovary is put forward.

REFERENCES

- ANSARY, H. R. (1965). Investigation of the role of ovaries in the mechanism of action of reserpine on the genital system of rat. M.Sc. thesis, University of Karachi, Pakistan.
- KHAN, I. & QURESHI, Z. (1967). Effects of reserpine on the sensitivity of rat isolated uterine preparations to oxytocic drugs. *J. Pharm. Pharmac.*, **19**, 815.
- KHAN, I. & SHARIFF, S. H. (1967). Investigation into the effects of reserpine on isolated uterine preparation of hypophysectomized female rats. *Life Sci.*, **6**, 2469.

Pharmacological activity in polyvinyl chloride (PVC) tubing

N. G. BOWERY* and G. P. LEWIS, *CIBA Laboratories, Horsham, Sussex.*

In searching for pharmacological activity in lymph and plasma after injury it was discovered that when stored in "Portex" polyvinyl chloride (PVC) tubing these fluids contained activity which they did not possess when freshly collected. Plasma stored in the tubing contracted the guinea-pig isolated ileum slowly and usually increased the spontaneous activity of the tissue. In addition, the plasma inhibited non-specifically the contractions of the rat uterus to many stimulating substances.

The amount of both activities leaching out of the tubing depended on the time during which the fluid remained in the tubing. After 3 min contact, only traces of activity appeared in the plasma, after 10 min a considerable amount had leached out, while in 60 min the concentration reached a maximum. But when the plasma was removed and replaced by fresh plasma the leaching process occurred again as before, and this procedure could be repeated many times with a similar result. The leaching still occurred after washing the tubing either with water or organic solvent.

The amount of activity leached out was also dependent on the concentration of the protein in the fluid. Lymph, which contains about a third of the plasma protein concen-