J. Pharm. Pharmac., 1969, **21**, 47

LETTERS TO THE EDITOR

An improved cannula suitable for chronic implantation into a lateral cerebral ventricle of the rat

A cannula suitable for chronic implantation into a lateral cerebral ventricle of the rat should be simple and inexpensive. It should also be easy to accurately manipulate into the ventricle, rigidly attached to the skull and subsequently facilitate the passage of an injection needle. Several cannulae have been described for this purpose (Wagner & de Groot, 1963; Decima & George, 1964; Feldberg & Lotti, 1967; Khavari, Feider & others, 1967; Myers, Casaday & Holman, 1967), but only that of Hayden, Johnson & Maickel (1966) appeared to meet all these criteria. Experience with this cannula, however, revealed disadvantages in its design and several modifications have now been evolved which greatly improve its implantation, patency and efficiency during the injection of drugs. The modified cannula is illustrated in Fig. 1.

The trochar hole in the original cannula was superfluous, as implantation into a lateral cerebral ventricle is readily carried out visually using fixed co-ordinates (1·4 mm caudal to the bregma and 1·3 mm lateral to the mid-line). Moreover, as the Perspex base was bulky and of an awkward shape for the implantation procedure, a ledge was cut into its two sides, and the central turret so formed was rounded off. A notch was cut into the posterior wing of the cannula to accommodate a bone screw in the region of thick bone just rostral to lamda. This screw together with two other bone screws, sited just lateral and rostral to the cannula respectively, were used as anchoring points for Surgical Simplex C which firmly secured the cannula to the skull. The modified cannula has the advantage that the wings are easily covered with Surgical Simplex C and the skin can be neatly sutured around the turret. A dummy needle was also incorporated into the assembly as the guide needle of the original cannula tended to become blocked by tissue particles and debris.

The modified cannula may be adapted for injecting small quantities of drugs into other discrete areas of the brain by varying the length of the guide needle.

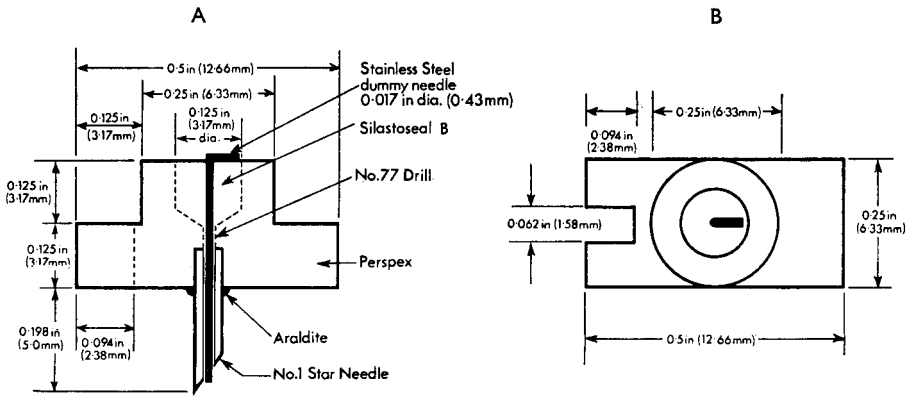

FIG. 1. Side (A) and top (B) view of a modified cannula suitable for implantation into a lateral cerebral ventricle of the rat.

Thanks are due to S. W. Smith for technical assistance and to R. B. Murdoch who acted as a personal assistant while on a sandwich course from Bath University of Technology.

Department of Pharmacology,
Allen & Hanburys Ltd.,
Ware,
Herts, England.

S. I. ANKIER

October 24, 1968

Silastoseal B is obtainable from Midland Silicones Ltd., Barry, Glamorgan.

Bone screws—nickel silver cheese head 16 BA × 1/8 inch obtainable from Laubscher Brothers, London, E.C.1.

Surgical Simplex C is an autopolymerizing acrylic resin obtainable from North Hill Plastics Ltd., London, N.16.

REFERENCES

FELDBERG, W. & LOTTI, V. J. (1967). *Br. J. Pharmac. Chemother.*, **31**, 152–161.

DECIMA, E. & GEORGE, R. (1964). *Electroenceph. clin. Neurophysiol.*, **17**, 438–439.

HAYDEN, J. F., JOHNSON, L. R. & MAICKEL, R. P. (1966). *Life Sci.*, **5**, 1509–1515.

KHAVARI, K. A., FEIDER, A. J., WARBURTON, D. M. & MARTIN, R. A. (1967). *Ibid.*, **6**, 235–240.

MYERS, R. D., CASADAY, G. & Holman, R. B. (1967). *Physiol. Behav.*, **2**, 87–88.

WAGNER, J. W. & DE GROOT, J. (1963). *Electroenceph. clin. Neurophysiol.*, **15**, 125–126.

Effect of chelating agents on copper content and tyramine response of the rat heart

Of the three enzymes involved in the conversion of tyrosine to noradrenaline, two have been shown to be metalloproteins. Tyrosine hydroxylase, which converts tyrosine to dopa in what is generally considered to be the rate-limiting step, contains iron (Udenfriend, 1966) and dopamine-β-hydroxylase, which converts dopamine to noradrenaline, contains copper (Friedman & Kaufman, 1965). Pharmacological inhibition of either of these two enzymes or of dopa decarboxylase, which converts dopa to dopamine, has been shown to lower catecholamine levels in guinea-pig heart to varying degrees (Spector, 1966). Among the substances which have been shown to inhibit dopamine-β-hydroxylase *in vitro* are various chelating agents (Goldstein, Lauber & McKereghan, 1964). *In vivo*, the acute administration of chelating agents has led to decreased levels of noradrenaline in the rat heart (Collins, 1965; Carlsson, Linqvist & others, 1966).

While studying the effect of chronic administration of three chelating agents on the copper levels of various tissues in rats, the response to tyramine of atria isolated from these rats was determined. An apparent relation between the copper levels of the heart tissue and the chronotropic response of the atria to tyramine was observed. The three chelating agents were: γ-thujaplicin (5-isopropyltropolone) (Bryant & Fernelius 1954), plicatic acid (Bock, L. H., personal communication; Gardner, Swan & others, 1966) and penicillamine (Walshe, 1960). The dosages of drugs in Table 1 are shown as equimolar quantities calculated as the sodium salt of γ-thujaplicin (GT), the potassium salt of plicatic acid (P) and free penicillamine (PA).