Cation dependence of metaraminol retention by rat uterus

SIR,—The ability of adrenergically innervated organs to retain exogenous noradrenaline is markedly cation dependent; sodium (Iversen & Kravitz, 1966; Gillis & Paton, 1966, 1967), calcium (Titus & Dengler, 1966; Gillis & Paton, 1966, 1967) and potassium (Gillis & Paton, 1966, 1967) are all necessary for optimal retention. However, whether the absence of these cations reduces retention by preventing the uptake of amine across the axonal membrane or by impairing the subsequent binding to intraneuronal granules, or by both mechanisms, has not been definitely established. Certainly the efflux of [^{3}H]noradrenaline from prelabelled tissues is increased in calcium-free (Taylor & Nash, 1966), in potassium-free (Gillis & Paton, 1967), and in low sodium media (Keen, 1967). The ability of peripheral organs to accumulate exogenous [^{3}H]metaraminol is now reported.

Uterine horns from virgin immature Wistar rats (35–55 g body weight) were incubated at 37° and gassed with oxygen 95% and carbon dioxide 5%. One horn from each rat served as a control and was incubated in Krebs Ringer medium; the other horn was used as the test organ and was incubated in either low sodium (22 mM) or potassium-free Krebs Ringer medium. After 30 min pre-incubation, [^{3}H]metaraminol was added to achieve a final concentration of 13·2 ng of the salt per ml and the incubation was continued for a further 45 min. The amine was then extracted from the tissue and measured as described previously for [^{3}H]noradrenaline (Gillis & Paton, 1967). Retention of [^{3}H]metaraminol was expressed as a ratio (R) calculated by dividing the [^{3}H] counts/min/g of uterine horn by [^{3}H] counts/min/ml of medium. Chromatographically pure (±)-metaraminol-7-[^{3}H]-hydrochloride with a specific activity of 6·7 c/mmole was obtained from the New England Nuclear Corporation.

The results obtained are presented in Table 1. Both low sodium and potassium-free Krebs Ringer medium markedly reduced the retention of [^{3}H]metaraminol.

TABLE 1. INFLUENCE OF SODIUM AND POTASSIUM ON THE RETENTION OF [^{3}H]METARAMINOL BY RAT UTERINE HORNS

Medium used	No. of horns in each group	R value mean ± s.e.		*t* test
		Control horns	Test horns	
Low Na^+	8	8·67 ± 0·42	2·78 ± 0·13	$P < 0.001$
K^+-free	9	8·47 ± 0·56	4·28 ± 0·82	$P < 0.01$

Metaraminol appears to be accumulated by adrenergically innervated organs in a manner essentially similar to noradrenaline; however, unlike noradrenaline, it is not a substrate for either monoamine oxidase or catechol-*O*-methyl-transferase (Giachetti & Shore, 1966). The retention by isolated organs of noradrenaline, but not of metaraminol, is much reduced by reserpine pretreatment; to explain these findings Giachetti & Shore (1966) have proposed that reserpine blocks only the intracellular binding of both amines without altering their passage through the axonal membrane. Consequently amines become exposed to degradation by monoamine oxidase in reserpine-pretreated tissues. Since metaraminol is not a substrate for monoamine oxidase, this amine can still accumulate in reserpine-treated organs (Giachetti & Shore, 1966). Consequently, these authors have suggested that any substance inhibiting the accumulation

of metaraminol *in vitro* may be presumed to act on the membrane "pump" (i.e. the uptake phase of retention) and not to be acting by impairing intraneuronal binding (Giachetti & Shore, 1966). Thus the results of the present investigations, using [^{3}H]metaraminol, strongly suggest that both sodium and potassium are required for the optimal functioning of the membrane "pump" or carrier system, which is responsible for the initial uptake of noradrenaline and related amines into adrenergic nerves.

Acknowledgements. This investigation was supported by a grant from the Alberta Heart Foundation and a fellowship from the Canadian Heart Foundation.

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July 17, 1967

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Complexation of penicillins and penicilloic acids by cupric ion

SIR,—We wish to correct two errors in a paper by Cressman, Sugita & others (1966) with the above title. These are: (1) the values given for the logarithmic association constants for penicilloic G and V acids were transposed. The values should read:

penicilloic V acid	$\log K = 4{\cdot}50 \pm 0{\cdot}02$
penicilloic G acid	$\log K = 4{\cdot}20 \pm 0{\cdot}5$

and (2) the value for the logarithmic association constant for penicillin V and cupric ion should be corrected to read:

penicillin V	$\log K = 2{\cdot}24$ (in the absence of ionic strength control)
penicillin V	$\log K = 2{\cdot}09$ (at ionic strength of 0·01 molar).

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August 12, 1967

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