The methylester hydrochloride of (±)-α-methyl tyrosine (H 44/68) is an efficient inhibitor of tyrosine hydroxylase (Corrodi & Hanson, 1966), an enzyme involved in the rate limiting step of biosynthesis of noradrenaline.

In rats pretreated with H 44/68 (250 mg/kg I.P., 6–12 hr, beforehand) and pargyline (75 mg/kg I.P., 1 hr beforehand), amphetamine failed to elicit contraction of the eyelid. In the same animals or similarly treated animals, tyramine still elicited a marked response while the response to nerve stimulation was not affected. The results indicate that an appreciable proportion of noradrenaline released by the indirectly acting sympathomimetic amines are metabolized by intraneuronal mono-amine oxidase and provide evidence which strongly suggests that the stores from which adrenergic nerve stimulation, tyramine or amphetamine releases noradrenaline may be different.

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Histochemical studies on the uptake of noradrenaline in the perfused rat heart

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Iversen has defined two different uptake mechanisms for noradrenaline in rat heart. One ($Uptake_1$) works at low amine concentrations (10–1,000 ng/ml.) and is inhibited by cocaine and desipramine, while the other ($Uptake_2$) works at much higher concentrations (1–40 μg/ml.) and is inhibited by normetanephrine.

We have studied the cellular localization of noradrenaline and also of α-methyl-noradrenaline taken up in the rat heart during perfusion with different concentrations of the amines, using the fluorescence method of Falck and Hillarp. The hearts of adult female albino rats (Sprague-Dawley) were perfused by the method of Langendorff. The amine was added to the perfusion solution.

When hearts from normal or reserpine-pretreated rats (10 mg/kg reserpine I.P. 16 hr beforehand) were perfused with low concentrations of noradrenaline or α-methyl-noradrenaline (0.02–0.2 μg/ml.) no evidence for an extra-neuronal binding of the catecholamines was found. In the hearts from the reserpine-pretreated animals, however, where the endogenous noradrenaline had been depleted, an accumulation of catecholamines into the adrenergic nerves could be found. The accumulation was prevented when desipramine (10^{-6} M) was added to the perfusion medium, but not when normetanephrine (10^{-4} M) was added. These results support the view of Iversen (1965) that the $Uptake_1$ in the rat heart is localized in the adrenergic nerves and are consistent with the results obtained from the adrenergic nerves in the rat iris (Malmfors, 1965).

When the hearts were perfused with high concentrations of noradrenaline or α-methyl-noradrenaline (20 μg/ml.) there was a markedly increased background fluorescence in the muscle cells due to the presence of catecholamines. Furthermore, small non-neuronal cells with a strong specific green to yellow-green fluorescence could be found, mainly in the connective tissue. These cells were only found in large numbers in the atria. The increase of the specific fluorescence in the muscle cells was objectively measured by means of microspectrophotofluorometry. Addition of desipramine (10^{-4} M) to the perfusion medium prevented the neuronal but not the extraneuronal accumulation, while addition

of normetanephrine (10^{-4} M) had no effect on the neuronal accumulation but completely prevented the accumulation in the small non-neuronal cells.

These findings strongly indicate that not all the noradrenaline or α-methyl-noradrenaline present in the heart immediately after the perfusion with high concentrations of the amine (that is, $Uptake_2$) is located in the adrenergic nerves, but that it is also accumulated extraneuronally, most evidently in the muscle cells and in small non-neuronal cells.

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A new programmed interval timer for use with automatic assay apparatus

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The apparatus is designed to give accurate programmed intervals from 1 to 1,000 sec. An electronic pulse generator provides the basic frequency, which is divided by dekatron tubes into tens and units to give the required time intervals. The cathodes of the dekatrons are brought to switches, two for each channel, and the circuit (called a coincidence circuit) is so arranged that a signal from the pulse generator is made available to both of the switches when the required ten and unit selected is reached.

Each channel has a bistable circuit which controls its own output relay. If a channel is live, the coincidence pulse from the generator will switch it off, and automatically the circuit will then return the dekatron to the zero position and the new count will start.

The front panel of the apparatus has plugs so that a programme of any sequence can be selected. The "off" pulse of any one bistable circuit is used to trigger the "on" position of the next bistable circuit, which is switched off by its selected time pulse, and so on. "Hold" and "cancel" controls are fitted on each channel. An important feature is the time multiplier which allows the apparatus to be infinitely variable up to a thousand seconds in each individual channel and therefore for any number of operations the machine is required to perform. Spare bistable circuits are available so that sequences of operations may be repeated within a programme.

The machine can be used to produce an infinitely variable programme. It can be used to control, say, a 90 sec cycle for use with acetylcholine-like compounds on the guinea-pig ileum or a frog rectus preparation for the assay of nicotine-like compounds in which the time cycle is 30 min.

The apparatus will drive standard G.P.O. relays and can also be used to control solenoid valves.

The use of intracerebral pyretogenins in testing for antipyretic activity in conscious mice

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The injection of pyretogenins into the cerebral ventricles of conscious mice produces a pyresis of short duration, which can be antagonized by prior administration of antipyretic drugs at doses approximating those used clinically.

Temperatures are measured at 15 min intervals for 1 hr with a thermistor (Standard Telephones and Cables Ltd., Type F15) inserted 1 cm into the rectum of each mouse.