The radioactive content of tracheal homogenates was separated by ion exchange chromatography (Dowex 50W-X4, 200–400, Na^+ form) into fractions representing deaminated metabolites and noradrenaline. At a substrate concentration of 50 pmol/ml only 40% of the radioactivity in the homogenate was noradrenaline: as substrate concentration increased this fraction declined.

The ionic and metabolic dependence of the uptake of radioactivity into the slowly exchanging compartment from H^3-L-noradrenaline (50 pmol/ml, 15 min) is shown by the results in Table 1.

Effect of the monoamine oxidase inhibitor pargyline on the uptake of labelled noradrenaline by the cat's spleen

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We have recently reported that the monoamine oxidase inhibitor, pargyline, increases the overflow of transmitter from the cat spleen. Whilst such an increase could be accounted for by the inhibition of monoamine oxidase there was no correlation in our experiments between the increase in overflow and the inhibition of monoamine oxidase as determined by the method of Otsuka & Kobayashi (1964). Inhibition of uptake could produce the increased overflow of transmitter. Some inhibitors of monoamine oxidase reduce noradrenaline uptake although pargyline does not do so in the rat heart (Iversen, 1966).

We have carried out experiments to determine whether pargyline affects noradrenaline uptake in the cat spleen.

First, 1 μg of ^{3}H-L-noradrenaline (5·8 mCi/μmol in 0·5 ml saline) was injected over a period of 5 s close arterially into the blood perfusing the spleen (Blakeley, Brown, Dearnaley & Woods, 1969). The venous blood containing the overflowing noradrenaline was collected during the subsequent 3 minutes. Thirty minutes later this procedure was repeated using the same amount of ^{14}C-L-noradrenaline (57 μCi/μmol). Overflowing labelled noradrenaline was separated from its metabolites by thin layer chromatography and measured by liquid scintillation counting.

In the experiments with pargyline the inhibitor was added to the blood 20 min before the second injection to give a concentration of 5×10^{-4} M.

The amounts of labelled noradrenaline collected in the venous blood after the first and second collection periods were not significantly different. The amounts were 49·03 $\pm$7·53% S.E. of mean (n=11) of ^{3}H-noradrenaline following the first injection and 58·03$\pm$7·54% (n=4) of ^{14}C-noradrenaline following the second. Pargyline significantly reduced the amount of noradrenaline collected to 27·12$\pm$7·46% (n=7) ($P<0·02$) indicating an increased uptake of noradrenaline by the spleen.

The inhibitor also affected the amount of labelled metabolites produced by the spleen following the injection of labelled noradrenaline. In control experiments 5·89$\pm$0·96% (n=11) of the injected noradrenaline appeared in the venous blood as metabolites. This fell to 2·06$\pm$0·60% (n=7) after pargyline (P of difference$<$0·01).

The previously observed increase in transmitter overflow due to pargyline cannot be explained in terms of an inhibition of uptake.

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Attempt to assess the selectivity of β-adrenoceptive blocking agents towards the effects of electrical stimulation of the spinal cord on different organs

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In the pithed guinea-pig, propranolol was reported to block the effectiveness of cord stimulation in reducing bronchoconstriction at lower doses than those blocking tachycardia, whereas practolol reduced both effects at the same doses (Burden, Parkes & Gardiner, 1971). Selectivity of blocking agents towards the consequences of sympathetic nerve stimulation of different organs may reflect not only their effectiveness in blocking the neurotransmitter at the respective sites, but also differences in innervation, and the effectiveness of stimulation, which determine the amounts of neurotransmitter involved.

In this study, we compared the effectiveness of cord stimulation for β-adrenoceptive responses in different organs with that of injected catecholamines, as reference. This was necessary since the parameters of the responses studied did not permit direct comparison.

Heart rate and air overflow were measured in the pithed guinea-pig, bronchoconstriction being produced by methacholine; heart rate and the tone of a loop of

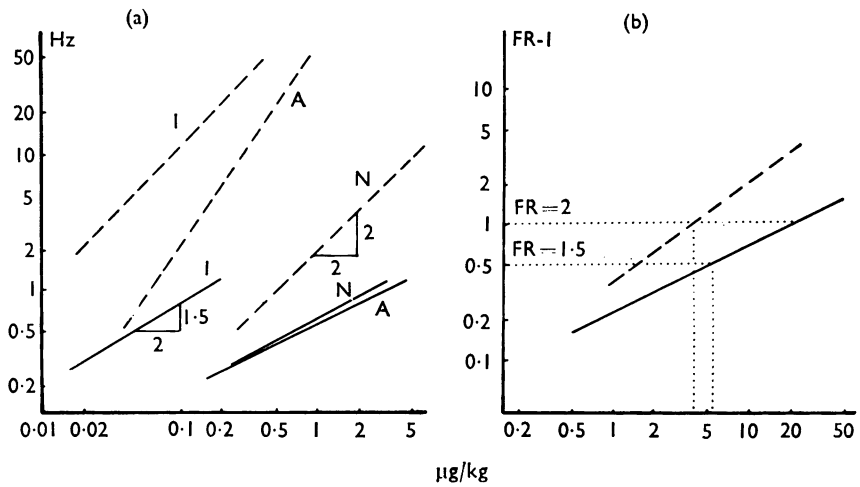

FIG. 1. (a) Relationship between the frequency (80V) of stimulation of the spinal cord of the pithed guinea-pig for 20 s and the intravenous dose of catecholamines for equal effect on —— heart rate; - - - - air overflow (log-log plots derived from computed regression lines). N-noradrenaline; A-adrenaline; I-isoprenaline, DR=dose ratio; FR=frequency ratio.

(b) Relationship between intravenous dose of propranolol and frequency ratio for effects of cord stimulation on —— heart rate; - - - - air overflow, in the pithed guinea-pig (log-log plots of dose against FR-1).