For a given increase in $\dot{V}$, SDC was more effective than nikethamide in lowering P_{a,CO_2}. This would be expected of a drug acting on tidal volume rather than respiratory rate.

The response to SDC was sustained during infusions lasting 30 minutes.

We conclude that SDC may have advantages over centrally acting drugs for the replacement of hypoxic drive, making it possible for pure oxygen to be breathed in respiratory depression.

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Evidence for an active uptake of noradrenaline in the guinea-pig isolated trachea

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Tracheae were incubated for 15 min in Krebs solution at 37·5°C containing ^{14}C-sorbitol (16 nmol/ml) or H^3-L-noradrenaline (50 or 6,400 pmol/ml.) After transfer to a washing solution which was changed at intervals over 60 min the tissue radioactivity showed a double exponential decay. The first decay corresponded with the loss from a rapidly exchanging compartment which was virtually cleared within 30 minutes. The second decay corresponded with the loss from a slowly exchanging compartment.

Tracheae were incubated for 3·75 or 7·5 min with H^3-L-noradrenaline (20–10,000 pmol/ml) and washed for 30 minutes. The concentration of radioactive material in the tissue was measured and used to estimate the initial velocity of uptake into the slowly exchanging compartment. This uptake was attributable to a saturable and a non-saturable mechanism. The saturable mechanism predominated at substrate concentrations of 20–500 pmol/ml, obeyed Michaelis-Menten kinetics and showed a K_m similar to that seen in other tissues ($0{\cdot}53 \times 10^{-6}$ M) but a very low V_{max} (70 (pmol/g)/min). The non-saturable mechanism predominated at substrate concentrations of 1,600 to 10,000 pmol/ml.

TABLE 1. *Effect of modifications of the incubation medium on the concentration of radioactive material in the trachea after exposure for 15 min to 50 pmol/ml H^3-L-noradrenaline and 30 min of washing*

Incubation medium	Concentration mean ± S.E.M. (pmol/g)	*n*	*P* Two-tailed
Krebs solution	65·0 ± 4·4	13	—
Low Na^+ solution (63 mEq/l)†	54·0 ± 4·1	10	≃0·1
Low Na^+ solution (25 mEq/l)†	30·0 ± 0·7	10	<0·001
K^+-free solution	47·5 ± 1·5	5	<0·005
Ouabain (10^{-4} M)	9·6 ± 0·6	5	<0·001
2,4-Dinitrophenol (10^{-3} M)	72·4 ± 5·9	5	>0·1
Bubbled with 95% N_2/5% CO_2	85·4 ± 13·9	4	>0·1
Glucose-free solution	60·4 ± 6·8	4	>0·1
Glucose-free solution bubbled with 95% N_2/5% CO_2	13·4 ± 1·0	4	<0·001
NaF (2×10^{-2} M)	25·3 ± 3·7	5	<0·001

Most preincubations were for 1 h but glucose-free conditions were maintained for 3 h and bubbling with N_2/CO_2 for 30 min: preincubation conditions were maintained during exposure to radioactive material and during washing. †Tonicity maintained with sucrose.

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.