from the animal house (22–24° C) and placed in individual compartments without restraint. Rectal temperatures were measured using a thermistor probe inserted to a depth of 1 cm. Hexamethonium bromide was injected at zero time and measurements of rectal temperature taken at 15 min intervals for the following hour. Rectal temperatures were also taken 15 min before the injection of the hexamethonium or saline.

At T_A 23 ± 1° C hexamethonium bromide (10 mg/kg I.P.) had no significant effect, but 40 mg/kg caused a marked fall in rectal temperature which attained its maximum value after 30 min. At T_A 5 ± 1° C, however, hexamethonium bromide (10 mg/kg) caused a fall in rectal temperature which reached its maximum after 15 min. At T_A 34 ± 1° C, hexamethonium bromide (10 mg/kg) produced a rise in rectal temperature which was significant only after 45 min and which had not decreased after 1 hr.

Other mice made hypothermic with reserpine (4 mg/kg) 20 hr before the experiment showed a response to hexamethonium which was different from that of normal mice. At T_A 23 ± 1° C the rectal temperatures of the reserpinized mice were rising. Whereas hexamethonium bromide (10 mg/kg) had no effect on the rate of rise of rectal temperature, 40 mg/kg decreased it. At T_A 5 ± 1° C the rectal temperatures of the reserpinized mice were falling and hexamethonium bromide (10 mg/kg) increased the rate of fall. The degree of hypothermia of reserpinized mice at T_A 34 ± 1° C was less than that at T_A 23° C. The rectal temperatures at T_A 34° C continued to rise throughout the experimen al period and were not affected by hexamethonium bromide (40 mg/kg).

The results show that in normal mice, hexamethonium can cause a rise or fall of rectal temperature. These effects may be due to a blockade of vasoconstriction causing a redistribution of blood to the skin at low T_A and to the core at high T_A, in the former case heat conservation being blocked and in the latter, heat transfer from core to periphery being prevented.

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Nicotine uptake by isolated rat ganglia

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The cat superior cervical ganglion retains a higher concentration of nicotine than the adjacent nodose (afferent vagal) ganglion after close-arterial injection of nicotine to the two ganglia *in vivo* (Appelgren, Hansson & Schmiterlow, 1963; Brown, Hoffmann & Roth, 1969). Since only the superior cervical ganglion responds to nicotine (Langley & Dickinson, 1889; Brown *et al.*, 1969), this suggests that the neuronal uptake of nicotine might be related to the amount of depolarization.

In the present experiments, the uptake of ^{3}H-nicotine by isolated rat superior cervical sympathetic and nodose ganglia has been studied. Ganglia were incubated in Krebs solution at room temperature (19°–24° C), bubbled with 95% oxygen/5%

carbon dioxide (pH 7·4), and containing ^{3}H-nicotine. Tritium was extracted by dissolving the ganglia in methanolic KOH solution and counted: ^{3}H-nicotine was not metabolized by isolated ganglia. Ganglionic water content was determined from the wet and dry weights, and extracellular space measured using ^{3}H-mannitol. Ganglion depolarization was measured using the moving-fluid electrode technique (Pascoe, 1956).

After 30 min incubation in ^{3}H-nicotine (5 μg/ml.), the intracellular/extracellular fluid concentration ratios (means ± S.E. of means) in the ganglia were: sympathetic, 7·8 ± 0·22; nodose, 6·1 ± 0·13. The intracellular concentration in the sympathetic ganglion was 30 ± 4% greater than that in the nodose ganglion, in reasonable agreement with previous *in vivo* observations (Brown *et al.*, 1969).

A full blocking concentration of hexamethonium (1 mg/ml.) reduced the uptake of nicotine by the sympathetic ganglion by up to 19%, without modifying nicotine uptake by the nodose ganglion. This effect of hexamethonium was only seen when strongly-depolarizing concentrations of nicotine were used. This suggests that depolarization can augment the uptake of nicotine by sympathetic ganglion cells.

Measurement of the partition of a weak acid, ^{14}C-5,5-dimethyl-2,4-oxazolidinedione (DMO, Waddell & Butler, 1959) between intra and extracellular fluids indicated that the overall intracellular pH in the sympathetic ganglion was reduced by 0·16 ± 0·01 pH units during application of nicotine (5 μg/ml.), with no significant change of nodose ganglion cell or bath fluid pH. Since nicotine probably penetrates cell membranes as the unionized base (Weiss, 1966), this reduction of intracellular pH may play a part in increasing cellular uptake of nicotine, by increasing the degree of ionization. However, the pH gradient between extra and intracellular fluids in the absence of ganglion cell depolarization (0·003 pH units) is not sufficient to account for the high intracellular nicotine concentrations in non-depolarized ganglia.

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On the nature of the drug-induced after-hyperpolarization in isolated rat ganglia

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The depolarization of isolated rat or rabbit superior cervical ganglia produced by acetylcholine or carbachol is followed, on washing out the depolarizing agent, by a