terial pressure and renal resistance in 2 of 3 experiments. A second injection of "Isuprel" resulted in hypotension, tachycardia and decreased renal resistance which were greater in extent and duration than the effects observed before injection of Et_4N. In the anesthetized dog, the vasodepressor effect of "Isuprel" is shown to be increased by injection of Et_4N. The augmentation is demonstrable at 5 but not at 30 minutes after injection of Et_4N. The reactive pressor effect of "Isuprel" after injection of Et_4N was observed in other experiments on anesthetized dogs.

Comment and Summary. The increased pressor responsiveness to adrenaline caused by injection of Et_4N is shown to be associated with an increase in renal vasoconstriction. The depressor response to injection of "Isuprel," the N-isopropyl homologue of adrenaline, is shown to be associated with renal vasodilation. The depressor, cardioaccelerator and renal vasodilator effects of injection of "Isuprel" are augmented by prior injection of tetraethylammonium. On the assumption that the effects of tetraethylammonium are due to blocking of autonomic ganglia,[4] we conclude that inhibition of these ganglia increases vascular responsiveness to typical vasoconstrictor and vasodilator sympatheticomimetics.

We acknowledge the donation of "Isuprel" hydrochloride by Dr. Earl Burbidge, Frederick Stearns Co., Inc.; of tetraethylammonium chloride ("Eatmon") by Dr. E. C. Vonder Heide, Parke, Davis and Co., Inc.; of *p*-aminohippurate by Drs. Karl Beyer and W. Boger, Sharp and Dohme, Inc., and the skillful assistance of William West.

[4] Acheson, G. H., and Moe, G. K., *J. Pharm. Exp. Therap.*, 1945, **84**, 189.

16014 P

Pharmacology of Dibenzyl-β-Chloroethylamine Hydrochloride (Dibenamine).*

G. R. DE VLEESCHHOUWER. (Introduced by C. Heymans).

From the J. F. Heymans Institute of Pharmacology, University of Ghent, Belgium.

Recently Nickerson, Goodman and Smith,[1,2,3] Raab and Humphreys,[4] Acheson and co-workers,[5] Haimovici[6] reported their experiments with dibenzyl-β-chloroethylamine hydrochloride (dibenamine).

We wished to investigate further the pharmacology of dibenamine and the mechanism of transmission of sympathetic nerve impulses.

Methods. The experiments have been carried out on dogs under chloralosane anesthesia. The blood pressure was registered from a femoral artery. In some experiments the peripheral vasomotor reactions were recorded by means of the 3-manometers-method.[7]

Results. I. *Effects of Dibenamine on blood pressure and heart rate.* Dibenamine, from 1 to 5 mg/kg, does not induce a noticeable change in blood pressure, nor any variations of heart rate. Doses of 10 to 15 mg/kg produce a slight and transient hypotension, but no direct change of heart rate. Subsequent injections of dibenamine do not produce the some hypotension. A primary, slight increase

* This investigation was made with the assistance of grants from the Ella Sachs Plotz Foundation, New York.

[1] Nickerson, M., and Goodman, L. S., *Fed. Proc.*, 1946, **5**, 194.

[2] Nickerson, M., Smith, S. M., and Goodman, L. S., *Fed. Proc.*, 1946, **5**, 195.

[3] Nickerson, M., and Goodman, L. S., *J. Pharm. Exp. Therap.*, 1947, **89**, 167.

[4] Raab, W., and Humphreys, R. J., *J. Pharm. Exp. Therap.*, 1946, **88**, 268.

[5] Acheson, G. H., and co-workers, *Fed. Proc.*, 1947, **6**, 305.

[6] Haimovici, H., PROC. SOC. EXP. BIOL. AND MED., 1947, **64**, 486.

[7] Nolf, P., *Bull. Acad. Roy. Belg.*, 1902, p. 895.

of blood pressure has been recorded in some experiments.

II. *Localization of the hypotensive action of dibenamine.* No noticeable changes in blood pressure have been observed after injection of dibenamine into the carotid artery (to control a possible central action), while small quantities of dibenamine injected into the peripheral circulation produced an immediate local vasodilatation.

III. *Effects of Dibenamine upon the carotid sinus vasomotor reflexes.* Dibenamine (0.5 to 15 mg/kg) does not produce a marked change of the pressor and depressor carotid sinus reflexes on the arterial blood pressure; same doses, however, reverse the pressor action of epinephrine into a vasodepressor one. Only 60 to 90 minutes after the injection of high doses of dibenamine, a depression, but not a reversal of the carotid sinus vasopressor reflexes could be observed.

IV. *Effects of Dibenamine on hypertensive substances.* Reversal of the vasopressor action of epinephrine appears after administration of at least 10 mg/kg dibenamine. But dibenamine does not suppress or reverse the epinephrine tachycardia. Small quantities of dibenamine, injected into the circulation of the leg, induce a strictly localized reversal of the vasoconstrictor effect of epinephrine.

Ten to 15 mg/kg dibenamine do not reverse the hypertensive action of nicotine in the atropinized dog. Larger quantities decrease slightly, but never reverse, the vasopressor effects of nicotine.

In atropinized dogs, with normal adrenal glands, 10 to 15 mg/kg dibenamine convert the vasopressor action of acetylcholine into a vasodilator response.

The vasoconstrictor effects of ephedrine and pituitrin are scarcely altered by dibenamine.

Ten to 15 mg/kg dibenamine convert the asphyxia hypertension into an hypotension.

V. *Effect of Dibenamine on sympathetic nerve stimulation.* In dogs, with adrenal glands, after injection of 10 to 15 mg/kg dibenamine, the hypertensive response of splanchnic nerve stimulation is converted into a vasodilatation, after an initial rise of the blood pressure.

In dibenamine-treated dogs, after adrenalectomy, the stimulation of the splanchnic nerve produces a monophasic or no rise of the blood pressure; no reversal of this neurovasopressor effect has been observed.

After injection of dibenamine, the general reflex vasoconstrictor response, induced by stimulation of the central end of the vagus, is not converted into a vasodilatation.

Summary. Experiments on dogs showed that dibenamine:

1. Induces a slight fall of arterial pressure; this hypotension depends mainly on a peripheral vasodilator action.

2. Has no direct effect upon the heart rate.

3. Produces no lasting decrease of the carotid sinus vasopressor reflexes; it never induces a reversal of these reflexes, while the same dose reverses completely the action of epinephrine on blood pressure and blood vessels.

4. Does not affect the tachycardic action of epinephrine.

5. Has no marked effect upon the hypertensive properties of nicotine, ephedrine and pituitrin.

6. Produces a reversal of the asphyxia hypertension.

7. Induces, in atropinized dogs, a reversal of the vasopressor action of acetylcholine.

8. May decrease, but does not produce a reversal of the vasomotor responses of sympathetic origin.

9. Is primarily a powerful adrenolytic, but a weak sympathicolytic agent.