

lowing atropinization, pilocarpine even in doses of 10 to 50 mg. produced no typical effects in the presence of physostigmine. Pilocarpine, unlike physostigmine, did not elicit pressor effects from small doses of acetylcholine in atropinized animals.

The mechanism of pilocarpine action is fundamentally different from that of physostigmine.

8981 P

Further Studies on Physostigmine-Nicotine Antagonism.

CHARLES R. LINEGAR, ROBERT P. HERWICK AND THEODORE
KOPPANYI.

From the Department of Pharmacology and Materia Medica, Georgetown University School of Medicine, Washington, D. C.

It has been reported by several authors¹⁻⁴ that large doses of nicotine (30 to 60 mg. per kg.) prevented the pressor effects of acetylcholine (1 to 5 mg. per kg.) in atropinized animals.

The drugs used in these experiments were all given intravenously and the doses expressed in milligrams per kg. In 6 dogs and 6 cats anesthetized with barbiturates and treated with 2 mg. atropine sulphate and 1 mg. of physostigmine salicylate, pressor effects were elicited in every case following the injection of 0.05 to 0.1 mg. of acetylcholine. The administration of paralytic doses of nicotine salicylate (3 to 6 mg.) in addition to the above drugs changed the effects of acetylcholine injections to uniformly vasodilator responses. Nicotine thus caused a reversal of the hemodynamic action of acetylcholine under the above conditions. In 5 cats and 5 dogs, it was further found that paralytic doses of nicotine are not necessary to obtain this reversal. Doses of nicotine from 0.25 to 2 mg. always diminished and often reversed the hemodynamic effect of acetylcholine. Further doses of physostigmine salicylate again reversed the acetylcholine vasodepressor effects into pressor responses. The administration of nicotine again changed these pressor responses of acetylcholine into depressor effects. This mutual antagonism between physostigmine and nicotine in reversing the acetylcholine blood pressure effects can be demonstrated several times in the same animal.

¹ Dale, H. H., *J. Pharm. and Exp. Therap.*, 1914, **6**, 147.

² Hunt, R., *Am. J. Physiol.*, 1918, **45**, 231.

³ Fuehner, H., *Biochem. Z.*, 1916, **76**, 232.

⁴ Feldberg, W., and Minz, B., *Arch. Exp. Path. and Pharm.*, 1931, **163**, 66.