tionship of ascorbic acid to the metabolic activity of folic acid is discussed.

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Procaine and Autonomic Innervation. (17807)

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Hunt(1) reported that procaine may counteract the influence of acetylcholine on blood pressure and heart rate. Hazard, Corteggiani and Cheymol(2) showed that intravenous injection of procaine paralyzes the cardiac vagus innervation and suppresses the bradycardia by acetylcholine(3), physostigmine(4) and nicotine(5), while the hypotensive effects of acetylcholine are maintained. The hypertensive effect of acetylcholine in atropinized animals may be changed to a hypotensive by procaine. Harvey(6) and Dutta(7) stated that procaine may block conduction in the first cervical sympathetic ganglion. Laqua (8) showed that procaine protects the guinea pig against physostigmine intoxication. Conway *et al.*(9) reported that physostigmine and di-isopropylfluorophosphate(DFP) protect mice against procaine intoxication, while neostigmine and carbamic acid, N,N-dimethyl- 4 -dimethylamino-3-isopropylphenyl ester, methiodide (DIP) lower the LD50 of procaine.

Experiments have been performed on 24 dogs anaesthetized with chloralosane to investigate the mechanism of action of procaine on autonomic innervation.

The observations may be summarized as follows: 1. Small doses of procaine (10-40 mg/kg) given intravenously to 11 atropinized dogs decrease acetylcholine (60-240 γ/kg) hyperpnea and change the hypertensive effect to an arterial hypotension, while the vasopressor reflexes of carotid sinus origin are unaltered.

2. High doses of procaine in 15 normal dogs (40-300 mg/kg) curarize first intercostal respiratory muscles, then the diaphragm and finally the skeletal muscles, and suppress bradycardia induced by vagus stimulation or by nicotine. Small doses of acetylcholine (30-60 γ/kg) provoke arterial hypotension, without bradycardia. Higher doses of acetylcholine still induce bradycardia, which is in turn suppressed by higher doses of procaine. Vasopressor reflexes of carotid sinus origin or induced by central vagus nerve stimulation are first depressed and then blocked by high doses of procaine. Vasomotor synaptic stimu-

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lation by nicotine is decreased by low doses and suppressed by higher doses of procaine.

3. Procaine (40-100 mg/kg) protects against physostigmine (0, 1-0, 3 mg/kg) and di-isopropylfluorophosphate (DFP) (10-40 mg/kg) bradycardia, bronchospasm, salivation, muscular fasciculations and convulsions.

4. After injection of doses of physostigmine, dimethyl-carbamate of hydroxyphenyl-benzyl-trimethylammonium (Nu 683) or DFP inducing bradycardia, bronchospasm, muscular fasciculations and convulsions, injection of procaine (40-100 mg/kg) suppresses these symptoms, although marked cholinergic reactions may still be induced by injection of acetylcholine. Procaine thus acts against physostigmine and DFP intoxication in the same way as tetra-ethyl-ammonium, diethyl-aminoethyl-ester of phenyl-cyclopentane-carboxylic acid (Parpanit) and diethylamino-ethyl-pheno-thiazine (Diparcol) (10-13).

5. After injection of doses of procaine blocking the heart vagus innervation, suppressing the nicotinic and muscarinic action of acetylcholine on the heart and suppressing the nicotinic action of acetylcholine on sympathetic vasomotor synapses, injection of physostigmine (0.3-0.5 mg/kg) or DFP (5-10 mg/kg) deblocks the heart vagus innervation and restores the nicotinic and muscarinic effects of acetylcholine on the heart and on the vasomotor synapses. This antagonistic effect of physostigmine and DFP occurs when serum cholinesterase (pseudo-cholinesterase) is completely inactivated only, while acetyl-choline-esterase (true-cholinesterase) of erythrocytes is only inhibited to 15-20% of normal values. The titropotentiometric method of Delaunois and Casier (14) has been used for determinations of cholinesterases activity.

After deblocking the effects of procaine by physostigmine or DFP, one may induce again the paralyzing effects of procaine by injection of higher doses of the drug, and in turn deblock these procaine blocking effects by new injections of physostigmine or DFP.

Conclusions. Procaine paralyzes first the parasympathetic and later the sympathetic synapses. Procaine suppresses the nicotinic and muscarinic effects of acetylcholine on the heart, but not the muscarinic effect of acetylcholine on the blood vessels. Procaine curarizes first the intercostal respiratory muscles, then the diaphragm and finally the skeletal muscles. Physostigmine, dimethyl-carbamate of hydroxy-phenylbenzyl-trimethylammonium (Nu-683) or di-isopropylfluorophosphate (DFP) suppress the paralyzing effects of procaine on synapses, on postsynaptic cardiac innervation and on neuro-muscular junctions, while procaine protects against most symptoms of intoxication induced by physostigmine, Nu-683 or DFP.

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