TABLE I.
The Urinary Ascorbic Acid Following Ether Anesthesia.

Date	Urine Volume cc.	Ascorbic Acid mg. per 100 cc.	Ascorbic Acid mg. per 24 hr.	Remarks
6/ 5/35	994	3.2	31.7	Control
6/ 6/35	635	3.9	24.5	"
6/ 7/35	1610	11.8	190.0	Two hours ether anesthesia
6/ 8/35	810	2.6	22.0	
6/ 9/35	830	3.2	26.5	
6/14/35	500	6.1	31.3	Control
6/15/35	2385	11.1	266.0	Two hours ether anesthesia
6/16/35	300	3.6	10.9	
6/17/35	610	3.6	22.2	
6/20/35	850	3.8	29.6	Control
6/21/35	1571	16.2	255.0	Two hours ether anesthesia
6/22/35	1090	2.7	29.2	
6/23/35	710	4.8	34.2	

pigs, the urinary excretion of the l-ascorbic acid was increased. Other experiments are in progress dealing with the metabolism of ascorbic acid in the dog and also experiments attempting to explain the action of ether anesthesia in causing the increased urinary excretion.

8403 P

New Pharmacological Actions of Physostigmine.

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While investigating the peripheral action of barbiturates it was observed that in all experimental animals where the cardiac vagus response to weak faradic stimulation had been abolished by large doses of most barbiturates, and by moderate doses of amytal and pernoston, the administration of physostigmine salicylate in doses from 0.2 to 0.35 mg. per kilo by vein, caused usually no detectable spontaneous effect upon the heart rate or blood pressure. The injection of comparable doses of acetylcholine and pilocarpine produced in the same animals a marked fall in blood pressure which in many cases was accompanied by a slowing of the heart.[1] If 2 or 3 minutes were allowed to elapse after the intravenous administration of physostigmine and then the peripheral vagus was stimulated elec-

[1] Koppanyi, Linegar and Dille, *Science*, 1935, **82**, 228.

trically, profound cardiac slowing and fall in blood pressure was produced in 6 dogs, 4 cats and 6 rabbits. In 7 experiments these vagus effects outlasted for several minutes the actual stimulation of the nerve. This physostigmine sensitization of the vagus to stimulation of the preganglionic fibers lasted for about a half hour and was antagonized in ten animals by further doses of barbiturates. Since barbiturates abolished the cardiac vagus response to faradic stimulation but not to pilocarpine, it was postulated that their vagus-impairing effects are due to ganglionic depression (see also Kobacker and Rigler,[2] and Garry.[3]) We have, therefore, employed nicotine and curare, drugs known to produce ganglionic paralysis. After sufficient doses of nicotine (2 to 10 mg. per kilo) or curare (3 to 6 mg. per kilo) had been given intravenously to abolish the peripheral vagus effects in 2 dogs, 3 rabbits and 3 cats, 0.2 to 0.3 mg. of physostigmine salicylate per kilo was injected intravenously. In every case within a few minutes following injection of physostigmine faradic stimulation of the peripheral vagus produced marked cardiac inhibition. Pilocarpine had no such effects. Therefore physostigmine antagonized the synaptic paralysis produced by nicotine and curare.

Since physostigmine abolished the block in parasympathetic synapses it was investigated whether it would act in a similar manner on sympathetic synapses. Nicotine and curare were employed intravenously, in the same doses as above, to abolish the eye effects (dilatation of the pupil, exophthalmos, withdrawal of the nictitating membrane and widening of the palpebral fissure) and the blood pressure responses which follow stimulation of the preganglionic fibers of the cervical sympathetic nerve. After sufficient doses of nicotine or curare were given to produce paralysis in the superior cervical ganglion, 0.2 to 0.3 mg. of physostigmine salicylate per kilo were injected intravenously in 3 cats and 2 rabbits. A few minutes after the injection, the preganglionic fibers of the cervical sympathetic were again stimulated and this was now followed by the characteristic ocular and vascular responses to sympathetic stimulation. Physostigmine, therefore, opposed the synaptic paralysis due to nicotine or curare in the sympathetic as well as the parasympathetic division.

Physostigmine does not sensitize the cardiac vagus to electrical stimulation if its excitability has been abolished by atropine (2 mg. per kilo).

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[2] Kobacker and Rigler, *J. Pharm. and Exp. Therap.*, 1930, **37**, 129.

[3] Garry, *J. Pharm. and Exp. Therap.*, 1930, **39**, 129.

It is possible that this newly discovered action of physostigmine might be due to inhibition of the esterase which is responsible for the destruction of acetylcholine and that in the final analysis the substance producing the ganglionic effect is acetylcholine. This interpretation of the effect on the sympathetic synapse seems to be in harmony with the view that the transmission through the sympathetic synapse is cholinergic (Feldberg and Gaddum[4]).

8404 C

Procedure for Quantitative Extraction of Sex Hormones from Urine.

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The excretion of sex hormones in the urine has been the subject of a voluminous literature. Attempts have been made to relate the amount of these substances excreted to various pathological conditions with the hope that new information of clinical value would be made available. Unfortunately most of this effort is valueless because certain fundamental facts are completely ignored. Thus it is known from the researches of Zondek, Cohen and Marrian,[1, 2, 3] and others that some fraction of the estrogenic substance in urine is conjugated so that it is either not extractable, biologically inert, or both. Conversion to the active form, therefore, must be an essential feature of any method for assaying the urine for total content of female hormone. Further it is immediately evident that a unit expressed solely in terms of a biological response is almost useless for the purpose under discussion. The only unit acceptable is a definite quantity of substance. Such a standard for the female hormone has been available for several years and recently a standard has been designated for the male hormone. Unfortunately, few workers have used these or indeed any standards. Only by the use of such standards can the values obtained by a given individual and by different laboratories be accurately compared, for without a standard it is impossible to detect change in sensitivity of the test

[4] Feldberg and Gaddum, *J. Physiol.*, 1934, **81**, 305.

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[1] Zondek, Bernhard, *Nature*, 1934, **133**, 209.

[2] Zondek, Bernhard, *Ark. Kemi., Min. o. Geol.*, 1934, part 3, paper 24.

[3] Cohen, S. L., and Marrian, Guy F., *Biochem. J.*, 1934, **28**, 1603.