to give consistent results and close agreement between duplicate determinations. The amount of phosphoarginine (preparation I) injected was sufficient, if totally converted, to yield 1.2 mg. of creatine (as creatinine) per gram of mouse. This would represent an increase of 90% over the basal creatine-creatinine level. Any appreciable hydrolysis of the phosphoarginine would also be reflected by significant increases in urea, because of the rapid metabolism of arginine. With preparation II of phosphoarginine, 30% increases in total creatinine would be the maximum attainable.

The results presented in Table I demonstrate that under the conditions of these experiments phosphoarginine failed to undergo conversion into phosphocreatine, creatine or creatinine. They do not support the hypothesis that arginine or phosphoarginine is the mother-substance of creatine.

6054

Influence of Digitalis on the Sensitivity of the Cardiac Vagus Endings.

W. DOCK AND M. L. TAINTER.

From the Departments of Medicine and of Pharmacology, Stanford University School of Medicine, San Francisco.

The work of Heymans[1, 2] on the mechanism of the bradycardia of digitalis seems to dispose of the older theory that this drug stimulates the vagal centers directly. It supports Straub's[3] suggestion that the slowing is due to a direct myocardial action, the sinus pacemaker becoming more responsive to vagal tone. In support of this viewpoint, Rothberger and Winterberg[4] have claimed that digitalis lowers the threshold to electrical stimulation of the vagus trunks, and Weger has observed[5] that it makes the parasympathetic endings in the intestine more irritable to stimulation by pilocarpine. However, Weiss[6] regards the slowing after digitalis as due to reflexes originating in the viscera innervated by the vagus. In order to obtain data regarding the validity of the first of these theories,

[1] Heymans, J. F., and Heymans, C., *J. Pharm. Exp. Therap.*, 1926, **29**, 203.
[2] Heymans, C., *Ergeb. der Physiol.*, 1929, **28**, 300.
[3] Straub, W., *Heffter's Handb. der Exp. Pharmakol.*, **2**, 1422.
[4] Rothberger and Winterberg, *Arch. f. Physiol.*, 1910, **132**, 233.
[5] Weger, P., *C. R. Soc. Biol.*, 1927, **96**, 803.
[6] Weiss, S., *Med. Clinics of N. Amer.*, 1932, **15**, 963.

we have attempted to demonstrate the presence or absence of an altered vagus sensitivity after digitalis, by comparing the responses in pulse rate to parasympathetic stimulants before and after administration of this drug.

The slowing caused by choline or acetyl choline in 6 anesthetized and unanesthetized dogs and cats, including one dog in which the adrenals were removed and the stellate ganglia and upper thoracic sympathetic trunks destroyed, was so slight that these drugs seemed of no value as tests for vagus sensitivity. We, therefore, selected physostigmine as a stimulant of the vagus endings. In 3 dogs, the vagi were cut aseptically, and after a 24-hour recovery period, 0.3 mg. per kilo of physostigmine was injected intravenously and the pulse rate changes recorded. The next day, 20 mg. digitalis per kilo, as the dilution of an active tincture, was given intravenously, and 2 hours later physostigmine was reinjected in the same dosage. The maximum slowing of the control physostigmine-action was 18, 16, and 28% of the control rates. After the digitalis, the slowing was 24, 19, and 14%, respectively, of the rates after the digitalis. There was thus no definite increase in the pulse rate response to the physostigmine after digitalization. The influence of digitalis on the minimum dose of physostigmine required to cause slowing in a vagotomized dog was also studied. Digitalization did not alter this threshold dose.

Both types of experiments failed to provide any definite evidence that digitalis sensitized the vagus endings in the heart to direct parasympathetic stimulation. Therefore, these results lend additional weight to the view that digitalis-bradycardia, like digitalis-emesis,[7] is due to reflexes originating in the viscera.

[7] Hanzlik, P. J., and Wood, D. A., *J. Pharm. Exp. Therap.*, 1929, **37**, 67. Dresbach, M., and Waddell, K. C., *J. Pharm. Exp. Therap.*, 1928, **34**, 43.