Effect of Digitoxin on Latent Period of Frog Gastrocnemius Muscle. (17769)

FREDERICK R. FRANKE. (Introduced by Campbell Moses.)

From the Addison H. Gibson Laboratory, University of Pittsburgh School of Medicine, Pittsburgh, Pa.

The accepted action of digitalis on heart muscle according to Sollman(1) is the production of a "lowered threshold of irritability, more powerful and more prolonged contraction with corresponding lengthening of the refractory period." Early workers, Bradenburg(2) and Gies(3) working with isolated frog heart preparations demonstrated this prolongation as seen by an increased duration of contraction period. Little work has been done recently on this particular phase of digitalis action. The present paper is a report of the action of digitoxin on the latent period of isolated frog gastrocnemius muscle. In these experiments the latent period may be defined as "the period of apparent inactivity between the application of an effective stimulus and the earliest evidence of tissue response(4)." It is not to be confused with the electrocardiographic P-R interval which represents the period between electrical depolarization of auricle and that of ventricle.

Materials and methods. Frog gastrocnemius muscles were mounted immediately after isolation to a myograph consisting of a fixed point and writing lever connected with a suitable tissue bath for immersing the muscle in digitoxin and the control solution of 0.7% sodium chloride. The myograph was mounted to a kymograph modified for high speed work using a tuning fork timer with an automatic drum key for applying break stimuli from a Porter induction coil after the design and method of Guthrie(4,5). By this method latent periods were graphically recorded on a smoked drum from the muscle contraction obtained by the direct application of maximal stimuli. Duration of the latent period was measured from the time of recorded stimulation to the onset of muscular contraction using the recorded tuning fork vibrations for time intervals. Control latent periods were determined with the preparation constantly immersed in 0.7% sodium chloride solution in 9 experiments. Latent periods were also determined with the muscle immersed in digitoxin solution following a single saline control determination in 12 experiments. Digitoxin* was freshly prepared in 0.7% sodium chloride solution and dilutions of 1:25,000, 1:50,000 and 1:100,000 were used.

Results. Control latent periods have been repeatedly determined on 9 preparations of isolated frog gastrocnemius muscle after immersion in 0.7% sodium chloride solution after being mounted on the myograph for a total time interval of 124.4 minutes. The results which are summarized in Table I demon-

TABLE I.
Control Latent Period (0.7% NaCl).

	Latent period (milliseconds)			
Frog	1	2	3	4
B	10	10	10	10
F	11	11	11	11
K	11	11	11	11
P	9	9	10	9
Q	10	11	11	12
R	11	11	10	12
S	13	13	13	13
T	11	12	12	14
U	11	11	11	—
Mean value	10.7	11	11	11.5
Mean time (min.) after immersion	29.8	63.9	92.4	124.4

1. Sollman, T., A Manual of Pharmacology, 7th Ed., W. B. Saunders Co., Philadelphia, 1948, p. 454.

2. Bradenburg, K., *Arch. f. Anat. V. Entwcklngsgesch*, Leipsig, 1904, 384.

3. Gies, K., *Z. f. Biol.*, 1927, v86, 427.

4. Guthrie, C. C., Laboratory Directions in Experimental Physiology, 2nd Ed., Edwards Bros., Ann Arbor, 1947.

5. Guthrie, C. C., Contributions to Practical Physiology and Pharmacology, published by the author, 1915.

* Digitoxin was supplied through the courtesy of Dr. G. E. Farrar, Jr., of Wyeth, Inc.

TABLE II.
Latent Period After Digitoxin.

Frog	Control latent period	Strength digitoxin × 1000	Latent periods (milliseconds) 1	2	3	4	5	6	7
A	12	1:100	12	12	15				
C	13	"	10	11	14	18			
D	5	"	7	14	14	15			
E	11	"	11	11	11	16	17		
G	10	1:50	11	12	14	13	17		
M	9	"	12	13	13	13	14	17	
N	11	"	12	12					
O	9	"	12	13	13	13	14	17	
H	10	1:25	11	13	14	14	15		
I	11	"	11	11	10	11	12	15	17
J	10	"	10	10	10	12			
L	9	"	10	12	13	12	14		
Mean value	10		10.7	12	12.8	13.7	14.7	16.3	17
Mean time (min.) after immersion	29.8	33.4	59.9	81.7	107.3	126.5	137.2	140.	155.

strate that the latent periods remained constant both when compared with each other and over the total time period. Table II summarizes the results of the determinations of latent periods of 12 similar isolated gastrocnemius preparations in which digitoxin of varying strengths was used as a bath material immediately following a preliminary control latent period determination. Following immersion in the saline bath the preliminary latent period determinations were made after a mean time of 29.8 minutes and the muscle was immersed in digitoxin solution at a mean time of 33.4 minutes. The mean value of the preliminary latent period control of 10.0 milliseconds in this group compares favorably with that of 10.7 milliseconds for the initial latent period of the saline control series presented in Table I. The prolongation of the latent periods of isolated frog gastrocnemius muscles immersed in digitoxin solution can be seen in Table II in which the mean latent period values progressively increase with time from the first mean value after addition of digitoxin of 10.7 milliseconds to the final 17.0 milliseconds. From this data it is evident that after digitoxin was added the duration of latent period increased while that of the control remained relatively constant.

Summary. Digitoxin solution applied by immersion technic prolongs the latent period of isolated frog gastrocnemius muscle.

Received February 28, 1950. P.S.E.B.M., 1950, v73.

Anatomy of the Thoracic Vagus in the Dog and a Technic for Its Interruption.* (17770)

JOHN R. HILSABECK AND FREDERICK C. HILL

From the Departments of Experimental Surgery and Physiology, Creighton University School of Medicine, Omaha, Nebr.

Preparatory to observing the role of the vagus nerve in the genesis of peptic ulcer produced experimentally in dogs by cincophen(1), it was mandatory to have a procedure which would free the stomach from vagus nerve supply. It has been established(2) that the

1. Hilsabeck, J. R., and Hill, F. C., PROC. SOC. EXP. BIOL. AND MED., 1947, v66, 155.

2. Hartzell, J. B., *Am. J. Physiol.*, 1929, v91, 161.