TABLE I.
Clinical Data and Results of Exercise Tolerance Tests.

Subject	Sex	Age	Diagnosis	No. of trips performed	
				1st trial	2nd trial
A.L.	M	55	Arteriosclerosis, hypertension, enlarged heart, dilated aorta. ECG: Prolonged A-V conduction	24 (S)*	27 (C)†
J.G.	M	63	Arteriosclerosis, enlarged heart, coronary sclerosis. ECG: Ventricular premature contractions	12 (S)	11 (C)
J.M.	M	66	Arteriosclerosis, myocardial fibrosis, sclerotic aorta. Myocardial infarction in 1940. Diabetes mellitus	11 (S) 18 (C)	11 (C) 16 (S)
S.K.	F	66	Arteriosclerosis, hypertension, enlarged heart, myocardial fibrosis. ECG: Bundle branch block	16 (S)	17 (C)
S.S.	M	65	Arteriosclerosis, enlarged heart, myocardial fibrosis, dilated aorta. ECG: Myocardial damage	29 (C) 48 (S)	42 (S) 49 (C)
M.W.	M	70	Arteriosclerosis, enlarged heart, dilated aorta, myocardial, fibrosis. ECG: Myocardial damage. Myocardial infarction, 1938	30 (S)	11 (C)
F.P.	F	58	Arteriosclerosis, hypertension, enlarged heart, myocardial fibrosis. ECG: Myocardial damage	22 (S) 38 (C)	22 (C) 36 (S)
M.F.	M	47	Arteriosclerosis, myocardial fibrosis, aortic sclerosis. ECG: Myocardial damage. Myocardial infarction, 1942	26 (S) 39 (C)	22 (C) 39 (S)

* (S) Physiological saline.
† (C) Cytochrome C.

up or utilized by the tissues within 5 minutes. However, we were unable to demonstrate any increase in the capacity for effort without pain in patients with angina of effort following intravenous injections of 50 mg of Cytochrome C as compared with placebo injections of physiological saline solution.

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The Delay in the Action of Digitalis Glycoside (Lanatoside C.)*

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Since the studies of Clark[1] were published, it has been believed[2] that after the administration of digitalis glycosides, a latent period occurs before a cardiac effect is produced.

In our previous studies however, concerning the effect of different concentrations of Lanatoside C upon the embryonic duck heart, we observed that although the above described latent period did exist, nevertheless, its duration appeared to vary inversely with the

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1 Clark, A. J., *Proc. Roy. Soc. Med.*, 1912, **5**, 181.

2 Gold, H., Cattell, M., Modell, W., Kurt, N. T., and Kramer, M. L., *Proc.*, 1943, **2**, 80.

TABLE I.
Relationship Between Concentration of Digitalis Glycoside and Time of Occurrence of "Digitalis Effect" in Embryonic Duck Hearts.

Digitalis glycoside (mg/cc)	Diameter embryonic sinus (Mm)	Hearts (No.)	Onset: "digitalis effect" (Min.)
.00005	30	15	39
.0001	28	19	22
.0005	32	18	15
.001	33	39	7
.002	30	4	4
.005	30	8	3
.01	30	7	1.75
.05	31	5	0.50
.10	30	10	0.25

concentration of glycoside in contact with the heart. In these same studies however some delay in cardiac response was observed even at the greatest concentration of digitalis glycoside employed (0.001 mg per cc). It seemed important then to discover the effect, at higher concentrations of glycoside, upon the described latent period. The embryonic duck heart lent itself admirably for the purpose because of its relative paucity of tissue which allowed a possible opportunity for changing rapidly, the milieu of the cardiac cells.

Methods. The duck hearts were obtained as previously described[3,4] from embryos having a vascular sinus of 25-35 mm in diameter. The temperature of the fluid bathing the embryonic heart, was maintained at 35 C which caused more rapid beating than observed in previous studies. Consequently the appearance of A-V block or missing beats also occurred earlier. Either of these two latter abnormalities in rhythm were considered indicators of a "digitalis effect." Lanatoside C, varying in concentration from 0.00005 to 0.10 mg per cc of Tyrode's solution was employed in all experiments.

Results. As Table I indicates, the delay in "digitalis effect" varied inversely with the concentration of digitalis glycoside in contact with the embryonic hearts. For example, 18 hearts exposed to a concentration of 0.00005 mg of Lanatoside C per cc, beat for an average period of 39 minutes before exhibiting A-V block. On the other hand, hearts exposed to concentrations of 0.002 mg per cc or higher, almost immediately exhibited the acceleration of beating previously noted[3] in hearts affected by glycoside and exhibited A-V block much sooner. As a matter of fact, the embryonic hearts, exposed to 0.10 mg of glycoside per cc exhibited A-V block in 15 seconds or less. It is possible that the so-called latent period observed in previous studies may be explained as delay attendant to the penetration of digitalis glycoside into the cells of the adult heart.

Conclusion. The evidence obtained from the actions of Lanatoside C upon the embryonic duck heart indicated that such a heart exhibits a "digitalis effect" with no fixed latent period as described in previous studies. It would appear that if a sufficient quantity of digitalis glycoside is present, a "digitalis effect" may be expected almost immediately.

[3] Friedman, M., and Bine, R., Jr., PROC. SOC. EXP. BIOL. AND MED., 1947, **64**, 162.

[4] Friedman, M., and Bine, R., Jr., *Am. J. Med. Sci.*, 1947, **214**, 633.