STUDIES ON THE ELECTRICAL SYSTOLE ("*Q-T*" INTERVAL) OF THE HEART

IV. The Effect of Digitalis on Its Duration in Cardiac Failure

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Though digitalis has been known in medicine since 1785 and its beneficial effects have been intensively studied, its action on the heart muscle is still far from fully understood. Numerous studies have been made on animals, but very little is known of its action on the dynamics of the human heart. Many theories have been proposed to explain the beneficial results of its use in disease, but to a large extent these have been based on animal experimentation or inferred from clinical observation. The work here reported was undertaken in the hope of obtaining information concerning the mechanism of the action of digitalis on the human myocardium in disease. At the same time a better understanding of this process might be expected to throw important light on the mechanism of heart failure.

In a previous study it was found that the electrical systole ("*Q-T*" interval of the electrocardiogram) varies with the cycle length in a way which can be expressed sufficiently accurately by the formula, $S = K\sqrt{C}$, in which "S" is the "*Q-T*" interval, "C" the "*R-R*" interval of the electrocardiogram, and "K" has the value of 0.374 ± 0.0012 for normal Chinese men and 0.388 ± 0.0015 for normal Chinese women (1). It has also been shown that in patients with heart failure the "*Q-T*" interval is prolonged in relation to cycle length, so that "K" in the formula just given was increased in average value to 0.432 ± 0.0023 for 121 men and 0.432 ± 0.0027 for 100 women in our series of patients with myocardial insufficiency (2). It would seem that this finding constitutes an important factor in the dynamic disturbance under discussion.

For the present study [1] a large number of patients with heart failure have been observed. They have all been under our clinical direction. The cases presented were not in any way selected. Electrocardiograms were taken and measured by one of us under conditions described in the previous papers. Measurements were made from lead II with a few exceptions in which the "T" wave of lead II was indistinct (but the same

[1] A preliminary report of this work was published in 1931 (3), at which time the work was completed. Subsequently the article of Berliner (4) appeared.

TABLE 1

Electrocardiographic measurements showing the effect of digitalis on "R-R" and "Q-T" intervals

E.K.G. number 2662. Female, age 14. Active rheumatic heart disease, mitral and aortic disease, pericarditis; heart failure IV

Date and hour	"P-R" interval	"T" 2	"R-R" interval	"Q-T" interval	"K"*	Digitalis.† Remarks	Calculated "Q-T" interval‡	Calculated duration systole‡	Actual duration systole
	seconds	*mm.*	*seconds*	*seconds*		*grams*	*seconds*	*seconds per minute*	*seconds per minute*
January 20									
9 a.m.	.16	3.5	.540	.330	.449	None. Weight 29 kgm.	.285	31.6	36.6
2 p.m.	.16	3.5	.535	.335	.450	None			
5 p.m.	.16	4.0	.530	.325	.447	0.3 at 5 and 8 p.m.	.283	31.9	36.8
January 21									
9 a.m.	.18	3.5	.635	.290	.364	0.6 at 8 a.m.	.309	29.2	27.4
2 p.m.	.24	3.0	.680	.280	.339	0.5 at 10 a.m.			
5 p.m.	.20	2.0	.640	.255	.319	0.2 at 1 p.m.			
January 22									
9 a.m.	.20	3.0	.590	.240	.318	Total 1.9	.298	30.3	24.4
2 p.m.	.24	0	.936	.278	.287	Occasional 2:1 block			
5 p.m.	.24	2.5	.970	.315	.319				
January 23									
9 a.m.	.24	2.5	.695	.230	.276	Occasional 2:1 block	.322	27.9	20.0
2 p.m.	.24	2.0	.690	.274	.330	Occasional 2:1 block			
5 p.m.	.26	2.0	.690	.250	.301				
January 24									
9 a.m.	.24	2.0	.710	.240	.280		.327	27.6	20.2
3 p.m.	.20	2.5	.645	.250	.311				
5 p.m.	.18	3.0	.625	.250	.316				
January 26	.20	3.0	.620	.245	.311		.305	29.5	23.7
January 29	.20	3.5	.630	.270	.340	Weight 26 kgm.	.308	29.3	25.8
February 4	.16	4.0	.650	.300	.372		.313	28.8	27.6
February 12	.16	5.0	.635	.325	.408		.309	29.1	30.7
March 2	.16	5.0	.520	.320	.443		.280	32.3	36.9
March 9	.16	5.5	.540	.320	.435		.285	31.6	35.5

* "K" = "Q-T" interval: $\sqrt{\text{"R-R" interval.}}$ Its average value for normal female Chinese is 0.388 ± 0.0015; for males 0.374 ± 0.0012 (1).

† Digitalis was given by mouth in the form of compressed powdered leaves, assayed 92 ± 5.2 mgm. per cat unit.

‡ The "Q-T" interval calculated for the actual rate by using the average normal value of "K". Using the value obtained the duration of systole per minute is calculated for comparison with the actual duration.

lead was always used in a given patient). A few instances of auricular fibrillation were included; in these cases an average of 16 "*R-R*" and "*Q-T*" measurements was calculated. Special attention was given to one or more records taken before the patient received digitalis, except in some cases included because observations were subsequently made after digitalis had been discontinued for a long period. Digitalis was given by mouth as compressed powdered leaves, assayed to have a value of 92 ± 5.2 mgm. per cat unit. No very precise rule for dosage was followed, but the majority of the patients were "digitalized" in 36 to 48 hours. The usual clinical observations were carefully made, but are not presented as they are of no special interest. In most of the patients the heart size was measured in teleoroentgenograms according to the method of Hodges and Eyster (5).

RESULTS

In selected cases serial records were made for several days at the same hours before and after digitalis treatment which was pushed to the point at which a clinical effect was clearly seen. Five such cases are summarized in Tables 1 to 5. The results in 45 males and 28 females studied in less

TABLE 2

The effect of digitalis on "R-R" and "Q-T" intervals

E.K.G. number 3053. Male, age 21. Active rheumatic heart disease, mitral and aortic disease, pericarditis, heart failure III

Date and hour	"P-R" interval	"T" 2	"R-R" interval	"Q-T" interval	"K" *	Digitalis.* Remarks
	seconds	*mm.*	*seconds*	*seconds*		*grams*
November 19						
9.30 a.m.	.16	3.8	.585	.360	.470	None. Weight 44 kgm.
2.30 p.m.	.16	4.0	.555	.330	.443	None
5.30 p.m.	.16	4.0	.545	.335	.454	None
November 20						
9.30 a.m.	.16	4.0	.590	.320	.417	1.4 in 15 hours
2.30 p.m.	.16	3.0	.605	.305	.392	2.2 in 20 hours
5.30 p.m.	.16	3.0	.610	.310	.397	2.2 in 23 hours
November 21						
9.30 a.m.	.16	3.0	.600	.280	.361	2.8 in 39 hours
2.30 p.m.	.16	2.0	.475	.240	.348	3.2 in 44 hours
5.30 p.m.	.17	3.0	.520	.250	.342	No more
November 22						
9.30 a.m.	.18	3.0	.665	.242	.297	
2.30 p.m.	.20	4.0	.615	.240	.306	
5.30 p.m.	.18	4.0	.580	.240	.316	
November 24	.16	4.0	.530	.265	.364	Weight 40 kgm.

* See footnotes to Table 1.

detail are given in Tables 6 and 7. We have continued to use the value of "K" (the ratio of systole to the square root of cycle length) as a convenient means of comparison.

TABLE 3

The effect of digitalis on "R-R" and "Q-T" intervals

E.K.G. number 3056. Male, age 61. Syphilis of cardiovascular system, aortic regurgitation, aneurysm of ascending aorta; heart failure, IIb

Date and hour	"P-R" interval	"T" 2	"R-R" interval	"Q-T" interval	"K" *	Digitalis.* Remarks
	seconds	*mm.*	*seconds*	*seconds*		*grams*
November 18	.16	3.0	.890	.420	.445	None. Weight 48 kgm.
November 25	.16	3.0	.815	.395	.438	None.
November 26						
10 a.m.	.16	3.0	.900	.375	.395	None
2 p.m.	.16	3.2	.640	.345	.432	None
5 p.m.	.16	3.0	.728	.364	.428	0.5 at 6 and 10 p.m.
November 27						
9.30 a.m.	.16	3.0	.977	.425	.431	0.5 at 9 a.m.
2 p.m.	.16	3.0	.900	.420	.444	0.3 at 1 p.m.
5 p.m.	.16	3.0	.880	.423	.451	0.2 at 8 p.m.
November 28						
9 a.m.	.16	3.0	.995	.395	.396	0.2 at 6 a.m.
2 p.m.	.16	3.0	.785	.325	.367	0.2 at 10 a.m. and 1 p.m.
5 p.m.	.16	3.0	.770	.349	.397	0.3 at 9 p.m.
November 29						
9 a.m.	.16	3.0	.940	.360	.372	Total 2.9
2 p.m.	.16	3.0	.965	.385	.392	
5 p.m.	.16	3.0	.955	.378	.384	
December 1	.16	3.0	.835	.345	.378	Weight 43 kgm.
January 8	.16	3.0	.940	.320	.330	
January 23	.15	3.0	.940	.360	.371	

* See footnotes to Table 1.

Digitalis was found to shorten the relative length of the "*Q-T*" interval with remarkable consistency. The same finding has been reported by Berliner (4). We have previously reported the same result in normal persons (6). The shortening occurs at least as early as any other known effect of digitalis. It takes place simultaneously with the lowering of the "T" wave (7) and precedes a change of "T" to a diphasic or negative form and a sagging of the "*Q-T*" level (cf. Tables 1 and 2). In some cases "T" remains unchanged, although systole is relatively shortened (cf. Table 3). Some time after withdrawal of digitalis systole

returns to approximately its previous relative value, usually in parallel with the return of "T" to its former height, but occasionally "T" remains depressed for a longer period.

That the amount of digitalis effective in producing the relative shortening of systole does not always follow the body weight is shown in

TABLE 4

The effect of digitalis on "R-R" on "Q-T" intervals

E.K.G. number 3011. Male, age 41. Syphilis of cardiovascular system, aortic regurgitation; heart failure III.

Date and hours	"P-R" interval	"R-R" interval	"Q-T" interval	"K"*	Digitalis.* Remarks
	seconds	*seconds*	*seconds*		*grams*
November 4					
10 a.m.	.12	.505	.288	.405	None. Weight 62 kgm.
2.30 p.m.	.16	.526	.288	.397	None
5 p.m.	.14	.524	.300	.415	0.5 at 5.30 p.m.; 0.4 at 9.30 p.m.
November 5					
9.30 a.m.	.16	.530	.295	.405	0.4 at 8 a.m.
2.30 p.m.	.12	.505	.280	.399	0.4 at noon
5.30 p.m.	.14	.508	.255	.358	0.4 at 4 and 6 p.m.
November 6					
8.30 a.m.	.20	.456	.196	.290	0.4 at 4 and 8 a.m.
2.30 p.m.	.20	.483	.188	.270	Total 3.3
5.30 p.m.	?	.570	?	?	Auricular fibrillation
November 7					
9.30 a.m.	?	.554	.253	.340	Auricular fibrillation
3.30 p.m.	.20	.570	.251	.332	Normal mechanism
November 8	.28	.585	?	?	Normal mechanism

* See footnotes to Table 1.

Table 5A (data from Tables 1 to 5). In the cases shown in Tables 4 and 5 digitalis was pushed to a point at which auricular fibrillation occurred, as also happened with some of the cases in Tables 6 and 7. In these and in other instances of excessive digitalis administration the ratio of systole to the square root of cycle length ("K") was lowered often far below the usual normal value. In the cases of Tables 4 and 5 "K" was 0.270 and 0.326 just before fibrillation set in. It is our impression that reduction of "K" to or below 0.330 indicates the beginning of a toxic as opposed to a therapeutic effect. This may sometimes happen with a truly small dose as in Case 3478, Table 7, in which after 0.8 gram digitalis, "K" was 0.298, the pulse 50, and the "*P-R*" interval 0.40 second. It should be noted that the original value of "K" in this case was only 0.366. The value of "K" has also appeared to furnish a guide to the dose of digitalis necessary to maintain a patient in his optimal condition, for which the usual clinical criteria are sometimes slow in developing and difficult to interpret.

TABLE 5

The effect of digitalis on "R-R" and "Q-T" intervals

E.K.G. number 3069. Female, age 30. Rheumatic heart disease; mitral stenosis; heart failure IIb

Date and hour	"P-R" interval	"T" 2	"R-R" interval	"Q-T" interval	"K"*	Digitalis.* Remarks
	seconds	*mm.*	*seconds*	*seconds*		*grams*
December 3						
9.30 a.m.	.16	2.0	.510	.260	.365	None. Weight 56 kgm.
2 p.m.	.16	2.0	.525	.270	.374	None
5 p.m.	.16	2.0	.528	.280	.386	0.5 at 6 and 10 p.m.
December 4						
9.30 a.m.	.16	2.0	.580	.275	.363	0.5 at 8 a.m. and noon
2 p.m.	.16	2.0	.550	.245	.331	
5 p.m.	.16	2.0	.555	.235	.318	
December 5						
9.30 a.m.	.16	2.5	.660	.253	.314	0.2 at 6 a.m.; 0.4 at 10 a.m.
2 p.m.	.16	2.5	.765	.304	.350	
5 p.m.	?	3.0	.608	.258	.334	Auricular fibrillation
December 6						
9 a.m.	?	2.0	.597	.230	.300	Auricular fibrillation
2 p.m.	.16	2.0	.580	.264	.334	Normal mechanism
5 p.m.	.16	2.0	.605	.250	.324	Weight 50 kgm.
December 11	.16	2.0	.620	.275	.352	
December 15	.16	2.5	.645	.305	.381	Weight 44 kgm.

* See footnotes to Table 1.

The tables contain several examples of patients in whom the effect of digitalis on the relative length of systole was repeatedly brought out by alternating periods of withdrawal and administration of the drug. In some cases it appeared that a smaller dose was effective on a second or later occasion than was necessary at first. In Case 2677 (Table 6) digitalis 1.4 gram in 3 days brought the value of "K" from 0.416 to 0.403 and later after an interval of four weeks without digitalis, 1.5 gram in 3 days re-

TABLE 5A

Comparison of body weight and effective dose of digitalis

E.K.G. number	Age	Sex	Weight	Effective dose digitalis		Time elapsed
	years		*kgm.*	*grams*	*grams per kgm.*	*hours*
2662	14	F	26	1.2	0.046	16
3053	21	M	40	1.8	0.045	17
3056	61	M	43	2.2	0.051	28
3069	30	F	43	1.5	0.035	15
3011	41	M	62	1.3	0.021	18

TABLE 6

Effect of digitalis on the duration of the "Q-T" interval in 45 male Chinese with heart failure

ABBREVIATIONS

A.D. = aortic disease (stenosis and regurgitation).
A.F. = auricular fibrillation.
A.R. = aortic regurgitation.
Ac.Neph. = acute nephritis.
Chr.Neph. = chronic nephritis.
Cor.Ob. = coronary obstruction.
G.A. = general arteriosclerosis.
H. = hypertension.
M.D. = mitral disease (stenosis and regurgitation).
P.T.b. = pulmonary tuberculosis.
S. = syphilis.

E.K.G. number	Age	Clinical diagnosis	Date	Weight	"P-R" interval	Heart rate	"K"*	Digitalis†
	years			*kgm.*	*seconds*			*grams*
A. Rheumatic heart disease								
2019	26	M.D.	August 18	63	.17	102	.384	1.0 in 24 hours
			August 21		.16	97	.367	1.8 in 5 days
2201	33	M.D., S.	March 4		.16	111	.436	None
			March 11	58	.20	86	.396	1.5 in 7 days
2244	22	M.D.	January 14		.17	93	.402	None
			January 21	49	.16	100	.374	1.5 in 5 days
			February 22		.20	105	.369	4.2 in 25 days
			March 11		.20	48	.301	4.9 in 32 days
2340	22	A.D.	March 29		.20	76	.402	None
			April 1	55	.20	72	.395	0.7 in 4 days
			April 5		.20	73	.390	1.5 in 8 days
			April 14		.20	63	.375	3.2 in 17 days
			June 4		.20	81	.431	None for 1 month
2344	30	M.D.	March 30		.16	80	.447	None
			April 1		.18	78	.409	0.6 in 2 days
2717	28	M.D.	March 20		.13	123	.414	None
			March 24	47	.16	87	.380	1.7 in 5 days
2780	23	M.D., A.D.	May 2		.20	63	.408	None
			July 25	46	.20	65	.335	4.3 in 39 days
2865	41	M.D., A.D.	July 11		.28	95	.438	None
			July 14	46	.28	90	.427	1.4 in 4 days
			November 12		.32	98	.421	None for 1 month
			November 22		.24	92	.398	0.8 in 12 hours
			December 6		.32	75	.380	3.0 in 16 days
2903	21	M.D., A.D.	July 25		.16	115	.441	None
			July 30	58	.16	99	.360	2.0 in 6 days
			August 5		.20	86	.346	2.6 in 12 days
			August 21		.20	87	.385	None for 12 days

TABLE 6 (*continued*)

E.K.G. number	Age	Clinical diagnosis	Date	Weight	"P-R" interval	Heart rate	"K"*	Digitalis†
	years			*kgm.*	*seconds*			*grams*
2909	36	M.D.	August 5		.18	107	.428	None
			August 8	46	.24	81	.382	1.6 in 4 days
			August 16		.27	56	.320	2.8 in 12 days
			September 26		.20	101	.415	None for 21 days
			October 6		.25	81	.366	1.9 in 10 days
			October 20		.24	87	.349	3.2 in 23 days
3162	38	M.D.	March 2		.18	110	.409	None
			March 6		.19	102	.390	1.5 in 4 days
			March 13		.22	82	.357	2.3 in 11 days
			March 23		.24	78	.360	3.5 in 20 days
			March 27		.20	87	.372	3.9 in 24 days
3293	17	M.D., P.T.b.	June 15		.16	98	.423	None
			June 22		.16	84	.331	1.0 in 24 hours
			June 25	30	.16	78	.320	1.4 in 48 hours
B. Syphilitic heart disease								
2033	45	S., Tabes, H.	March 28	54	.16	83	.412	None
			April 3		.16	81	.395	1.2 in 7 days
			July 18		.16	87	.379	0.1 q.d.
2054	38	S., A.R.	September 17	68	.19	114	.373	1.5 in 2 days
			September 21	59	.20	96	.370	1.9 in 6 days
			October 3		.19	100	.411	None for 5 days
2055	60	S., A.R.	September 17		.16	80	.360	1.7 in 10 days
			October 1		.17	80	.353	0.1 q.d.
			November 19		.16	80	.480	None for 14 days
			December 18		.16	68	.434	0.1 q.d.
			April 22		.16	59	.369	2.0 in 7 days
			May 18		.18	64	.497	None for 4 months
			June 18		.16	77	.378	2.6 in 19 days
2306	25	S., A.R.	September 6		.16	84	.474	None
			March 10		.16	78	.370	1.2 in 4 days
2501	27	S., A.R.	September 14	77	.17	81	.432	1.3 in 2 days
			September 19	71	.16	89	.403	1.9 in 7 days
			September 27		.16	102	.369	3.4 in 15 days
			October 11	74	.16	99	.354	5.8 in 29 days
2539	46	S., A.R., P.T.b.	October 25		.16	82	.425	None
			October 28		.16	82	.375	0.9 in 3 days
			November 1	57	.16	78	.362	1.5 in 6 days
			November 6		.18	93	.314	3.2 in 12 days
			November 16		.16	85	.362	0.1 q.d.
2583	38	S., Aortitis	December 17	54	.16	111	.443	None
			December 18		.16	111	.392	1.6 in 2 days

TABLE 6 (*continued*)

E.K.G. number	Age	Clinical diagnosis	Date	Weight	"P-R" interval	Heart rate	"K"*	Digitalis†
	years			*kgm.*	*seconds*			*grams*
2618	54	S., A.R.	January 11	55	.20	82	.427	1.0 in 24 hours
			March 14	52	.22	82	.414	0.1 q.d.
			March 21		.24	80	.394	1.0 in 7 days
2655	60	S., A.R.	February 11	65	.16	81	.413	None
			March 10		.14	78	.365	1.0 in 4 days
			March 14	59	.16	78	.361	1.7 in 7 days
			August 20	62	.16	70	.407	None for 1 month
2677	44	S., A.R., G.A.	February 28	79	.16	98	.416	0.8 in 6 hours
			March 1		.17	100	.403	1.4 in 3 days
			March 8	66	.16	97	.386	2.1 in 10 days
			July 4		.18	108	.431	None for 4 weeks
			July 7		.18	92	.347	1.5 in 3 days
			July 15	59	.16	91	.363	0.1 q.d.
			August 4		.20	113	.396	0.1 q.d.
			September 1		.16	82	.333	0.1 q.d.
2709	40	S., A.R.	March 17	46	.16	107	.419	None
			March 18		.16	87	.391	1.2 in 24 hours
			March 20	44	.17	83	.359	1.6 in 4 days
			March 23		.17	72	.390	None for 1 week
2776	41	S., A.R.	April 29	62	.15	95	.451	None
			April 30		.16	92	.389	1.9 in 24 hours
			May 5	59	.17	94	.375	2.6 in 7 days
2819	50	S., A.R., G.A.	May 6		.16	82	.421	None
			May 19		.16	78	.370	1.0 in 3 days
2831	56	S., A.R.	May 29	71	.16	90	.428	None
			July 28		.14	100	.388	0.1 q.d.
			August 1	65	.16	91	.345	1.2 in 3 days
			August 20				.402	None for 2 weeks
2855	44	S., A.R. A.F.	June 17	80	.17	69	.343	? Outside
			June 19		?	53	.329	1.5 in 2 days
			June 24	78	.16	83	.376	None for 5 days
2879	45	S., A.R.	July 4	72	.13	101	.416	None
			July 14		.16	88	.386	1.2 in 3 days
			July 21		.16	86	.341	2.1 in 10 days
3017	46	S., A.R.	November 7		.15	70	.450	None
			December 15	49	.13	63	.352	1.2 in 3 days
			June 16		.13	56	.424	None for 2 months
			June 19		.16	57	.365	0.6 in 3 days

TABLE 6 (*continued*)

E.K.G. number	Age	Clinical diagnosis	Date	Weight	"P-R" interval	Heart rate	"K"*	Digitalis†
	years			*kgm.*	*seconds*			*grams*
3305	26	S., A.R.	June 22	49	.16	99	.437	None
			June 26		.16	103	.387	1.2 in 4 days
			July 3		.16	98	.403	2.0 in 12 days
3497	50	S., Aortitis	October 22	56	.16	56	.410	None
			October 23		.17	66	.430	0.8 in 2 days
			November 17	49	.18	86	.412	4.6 in 27 days
C. Hypertensive and arteriosclerotic heart disease								
1441	58	H., G.A., S.	August 9	49	.17	88	.378	1.8 in 8 days
			August 15	46	.18	81	.351	2.4 in 14 days
			October 11	52	.17	86	.468	None for 3 months
1649	28	H., Chr. Neph.	December 14	54	.14	138	.428	None
			December 22		.16	75	.406	2.2 in 8 days
2010	36	H., G.A., Emphysema	August 7	63	.16	90	.406	None
			August 14	59	.16	87	.388	1.8 in 7 days
			August 31	55	.16	92	.399	4.6 in 25 days
2221	61	H., G.A.	January 2	75	.16	105	.437	None
			February 25	70	.16	95	.397	2.1 in 21 days
			March 25		.16	105	.439	None for 10 days
			June 3	61	.18	92	.398	8.4 in 78 days
			March 10		.16	100	.451	None for 1+ month
			June 9		.16	111	.381	7.4 in 61 days
2422	59	H., G.A., Cor.Ob.	March 18		.16	120	.424	None
			March 19	59	.16	110	.425	0.8 in 24 hours
			March 20		.20	108	.375	1.2 in 3 days
			March 25		.20	100	.369	2.0 in 7 days
			April 1	57	.16	90	.397	2.8 in 15 days
2440	51	H., G.A., Chr. Neph.	June 21	70	.13	102	.482	None
			June 22		.13	100	.408	1.3 in 24 hours
			June 24		.14	98	.404	1.5 in 3 days
			July 27	68	.16	86	.366	2.8 in 16 days
			August 19		.15	93	.428	None for 14 days
			August 23		.16	83	.424	1.1 in 5 days
			August 30		.16	80	.401	0.1 q.d.
			September 5		.13	89	.435	0.1 q.d.
			October 25		.13	100	.412	0.1 q.d. +1.0 in 5 days
			November 6		.16	92	.335	0.1 q.d. +1.6 in 6 days
			November 26	73	.16	86	.372	0.1 q.d.
2545	36	H., Chr. Neph.	November 27	66	.16	66	.458	None for 14 days
			December 24	63	.16	70	.387	0.9 in 24 hours
			January 3		.16	64	.378	1.8 in 10 days
			January 13		.16	98	.401	0.1 q.d.
			January 17		.16	81	.376	1.4 in 5 days

TABLE 6 (*continued*)

E.K.G. number	Age	Clinical diagnosis	Date	Weight	"P-R" interval	Heart rate	"K"*	Digitalis†
	years			*kgm.*	*seconds*			*grams*
2638	48	H., G.A.	January 31		.19	83	.495	None
			February 3		.20	86	.456	0.8 in 3 days
			February 14	80	.20	79	.419	2.7 in 14 days
2648	53	H., G.A., Chr. Neph.	February 10	70	.16	95	.460	None
			February 28		.19	91	.400	2.4 in 28 days
			March 11	65	.18	59	.388	0.1 q.d.
2694	70	G.A., Emphysema, P.T.b.	March 7	58	.16	106	.446	None
			March 8		.18	87	.319	1.3 in 24 hours
			March 10		.18	91	.308	1.7 in 3 days
			March 14	56	.16	94	.356	2.2 in 6 days
2695	70	G.A., Hemiplegia	March 7		.16	61	.421	None
			March 10		.16	62	.396	1.0 in 4 days
			March 17		.16	58	.391	1.7 in 11 days
2836	62	H., Cor. Ob., Angina	May 30	54	.28	65	.394	None
			June 9		.36	79	.367	1.6 in 11 days
2921	53	H., G.A., Chr. Neph., Bronchial Pneumonia	August 14		.16	105	.523	None
			August 15		.16	110	.358	1.2 in 20 hours
			August 16		.16	110	.336	1.6 in 3 days
			August 18		.16	118	.352	2.1 in 5 days
			August 23		.20–.40	70	?	2.7 in 10 days
3256	64	H., G.A., Aortic Dilatation, A.F.	October 17		.16	77	.373	0.1 q.d.
			October 19	60	?	72	.307	1.5 in 2 days
			October 20		?	68	.311	No more
			October 31		.16	63	.327	0.8 in 8 days
			November 14		.17	81	.406	2.2 in 22 days

* "K" = "Q-T" interval: $\sqrt{\text{"R-R" interval}}$. Its average value for normal male Chinese is 0.374 ± 0.0012 (1).

† See footnote to Table 1.

duced the value of "K" from 0.431 to 0.347. In spite of the length of the interval in these cases, it would appear that this change is due to subliminal amounts of the drug remaining in the body. Case 2440 (Table 6) is instructive with regard to the maintenance of digitalis effect.

We have not extensively investigated the relation between the change in the relative length of systole produced by digitalis and the size of the heart. Cohn and Stewart (8) have shown that digitalis reduces the size of the heart in dogs and Stewart (9, 10) has extended the observa-

TABLE 7

Effect of digitalis on the duration of the "Q-T" interval in 28 female Chinese with heart failure

(Abbreviations as in Table 6)

E.K.G. number	Age	Clinical diagnosis	Date	Weight	"P-R" interval	Heart rate	"K"*	Digitalis†
	years			*kgm.*	*seconds*			*grams*
A. Rheumatic heart disease								
2095	35	M.D.	October 19		.17	91	.430	None
			October 26		.20	65	.342	2.2 in 7 days
			November 7		.20	67	.359	3.4 in 19 days
2160	12	M.D. (active) A.F.	December 3	29	.20	92	.378	0.6 in 3 days
			December 5		.24	71	.303	1.9 in 6 days
			December 7		?	53	.343	2.1 in 8 days
			December 10		.20	72	.306	No more
2312	36	M.D., A.D.	March 20		.16	70	.433	None
			March 25		.15	74	.356	1.3 in 5 days
2427	26	M.D.	June 10	43	.20	82	.420	None
			June 14		.18	88	.389	1.6 in 3 days
			November 6		.20	78	.429	None for 2 months
			November 11	42	.20	63	.382	1.2 in 4 days
2549	22	M.D., A.D.	November 8		.15	78	.411	None
			November 11	53	.17	73	.398	1.2 in 4 days
2553	24	M.D.	November 13	45	.20	100	.455	None
			November 14		.16	102	.417	0.6 in 2 days
			November 16		.16	98	.412	1.0 in 3 days
			November 19		.16	95	.405	1.7 in 6 days
			November 21		.17	108	.376	2.0 in 8 days
2656	39	M.D., Pregnancy	February 12	59	.14	95	.401	None
			February 15		.13	64	.387	1.1 in 2 days
			February 18	57	.15	57	.354	1.7 in 6 days
2662	10	M.D.	July 4	34	.16	120	.465	None
			July 5		.16	118	.490	None
			July 7	33	.16	111	.463	None
			July 9		.16	111	.428	0.4 in 10 hours
			July 10		.16	94	.400	1.0 in 24 hours
			July 12		.16	74	.377	1.5 in 3 days
			July 15		.16	93	.409	0.1 q.d.
			July 21	27	.20	86	.370	0.1 q.d.
			October 20		.16	110	.490	None for 1 month
			October 25		.24	100	.405	1.5 in 5 days
2663	42	M.D., A.D.	February 17	40	.16	74	.394	None
			March 7		.16	81	.354	1.2 in 4 days

TABLE 7 (*continued*)

E.K.G. number	Age	Clinical diagnosis	Date	Weight	"P-R" interval	Heart rate	"K"*	Digitalis†
	years			*kgm.*	*seconds*			*grams*
2734	26	M.D., A.D.	April 3	52	.17	97	.411	None
			April 8		.20	94	.375	1.6 in 6 days
			May 16		.18	97	.417	None for 14 days
			May 19		.16	97	.355	1.0 in 4 days
			May 27		.20	105	.344	1.4 in 11 days
2744	31	M.D.	May 22	52	.16	94	.411	None for 2 months
			June 19		.20	61	.388	4.7 in 30 days
2799	22	M.D.	May 8	38	.15	100	.411	None
			May 12		.12	98	.320	1.8 in 5 days
			May 23	34	.20	51	.384	3.2 in 16 days
2918	24	M.D.	August 13	53	.28	87	.432	None
			August 14		.32	74	.439	1.1 in 2 days
			August 16		.32	73	.420	1.3 in 4 days
			August 21	44	.32	75	.396	2.0 in 10 days
			August 26		.32	70	.374	2.6 in 14 days
			September 16		.28	76	.353	5.8 in 34 days
2931	37	M.D.	August 30	40	.16	84	.423	None
			October 13		.12	103	.394	4.0 in 44 days
			November 30		.16	106	.381	0.1 q.d.
			December 1		.13	90	.367	0.1 q.d.
3015	25	M.D., Pregnancy A.F.	March 7		.18	102	.416	None
			March 14		.20	120	.396	1.8 in 7 days
			February 2	46	.25	88	.314	2.3 in 8 days
			March 4		?	165	.331	1.2 in 2 days
			March 13		.20	106	.375	No more
			May 25		.20	87	.433	No more
3232	28	M.D.	April 28	46	.18	103	.380	? Outside
			April 29		.24	86	.304	1.2 in 24 hours
		A.F.	May 1		?	78	.273	0.1 q.d.
			May 4	41	.20	71	.333	0.1 q.d.
3280	20	M.D., A.D. (active)	June 8	50	.17	98	.410	None
			June 9		.20	71	.343	1.2 in 24 hours
			June 10		.20–.39	63	.317	1.5 in 2 days
			June 11		.32	66	.294	1.6 in 3 days
3349	9	Acute Carditis	August 1	24	.16	130	.361	None
			August 3		.16	107	.334	0.6 in 2 days
			August 5		.20	118	.322	0.9 in 5 days
3354	30	M.D.	August 6	42	.16	85	.415	None
			August 18		.16	60	.345	1.5 in 6 days
3478	21	M.D., A.D. (active)	October 15		.16	79	.366	? Outside
			October 28		.40	50	.298	0.8 in 24 hours
			October 29	38	.24	39	.313	No more
			October 30		.20	56	.345	No more
			November 9		.22	54	.378	1.2 in 14 days

TABLE 7 (*continued*)

E.K.G. number	Age	Clinical diagnosis	Date	Weight	"P-R" interval	Heart rate	"K"*	Digitalis†
	years			*kgm.*	*seconds*			*grams*
B. Syphilitic heart disease								
3364	39	S., A.R.	August 13	49	.12	55	.405	0.6 in 24 hours
			August 20		.13	49	.396	1.2 in 7 days
C. Hypertensive and arteriosclerotic heart disease								
1777	51	H., G.A.	February 2		.15	91	.448	None
			February 8		.16	80	.430	1.6 in 7 days
1785	39	H., S.	February 14	60	.20	86	.424	None
			March 10		.20	68	.348	3.8 in 25 days
1890	48	H., G.A.	December 5		.15	75	.407	None
			December 7		.15	60	.402	1.2 in 2 days
1983	23	H., Ac. Neph.	July 19		.12	120	.401	None
			July 23	51	.15	94	.316	1.8 in 4 days
2343	43	H., G.A.	March 30	52	.16	82	.440	None
			April 15		.16	68	.417	1.1 in 3 days
2643	43	H., G.A., Chr. Neph., S.	March 15	40	.16	95	.477	None
			March 17		.16	82	.415	1.2 in 2 days
			March 24	34	.18	73	.398	2.6 in 9 days
			April 1		.18	60	.362	4.1 in 17 days
			April 7	30	.20	61	.382	0.1 q.d.
2666	37	H., Chr. Neph.	February 19	54	.16	109	.484	None
			February 28		.16	105	.409	1.2 in 24 hours
			March 3		.16	104	.384	1.7 in 5 days
			March 8	48	.16	86	.365	2.3 in 10 days
			March 17	44	.17	93	.346	4.0 in 20 days

* "K" = "Q-T" interval: $\sqrt{\text{"R-R" interval.}}$ Its average value for normal female Chinese is 0.388 ± 0.0015 (1).

† See footnote to Table 1.

tion to normal persons and to patients with heart failure. In general our data (not presented here) agree with these results. Under various circumstances there are exceptions and it must be noted that in some of these the relative duration of systole is decreased, although the heart size remains the same or is increased; in a few instances the reverse combination occurs (see Table 8). These exceptional cases are for the most part among patients with an actively progressive infection of the heart. There has so far not been demonstrated any constant relation between heart size, aside from heart failure, and relative length of systole, but this question is of such importance as to demand further careful study.

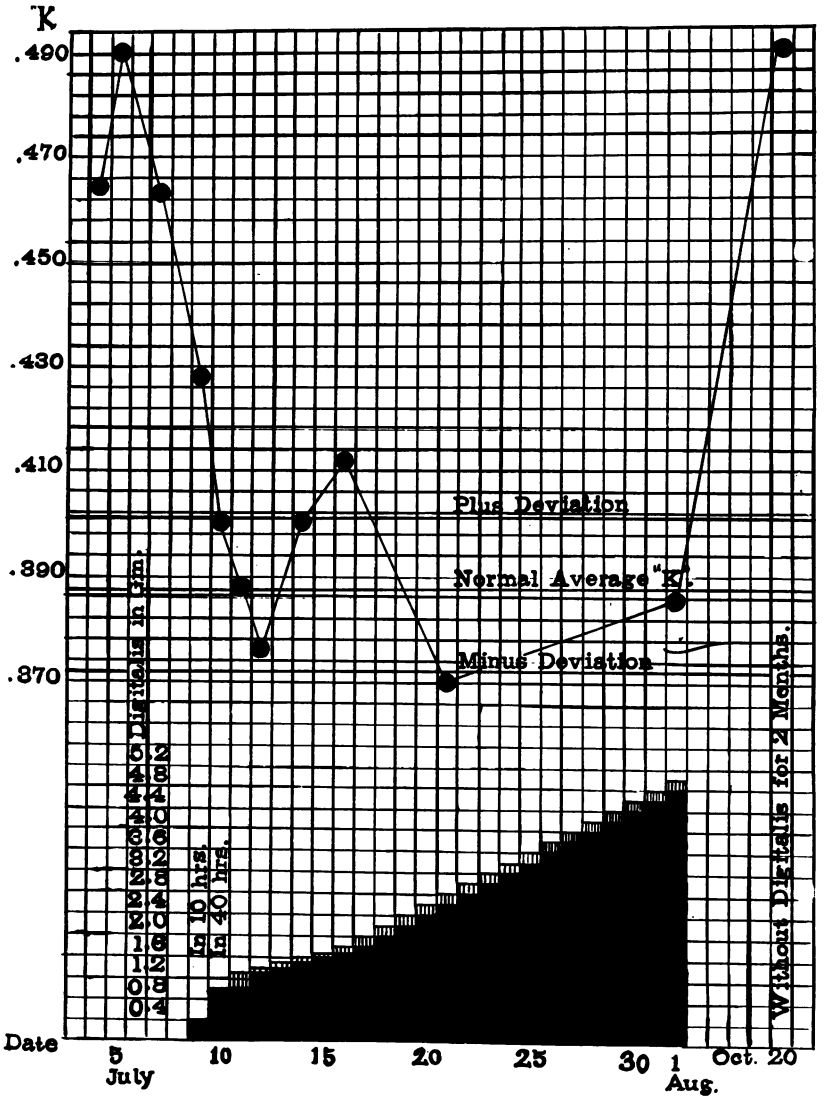

FIG. 1. E. K. G. NUMBER 2662, TABLES 1 AND 7

After 1.3 gram of digitalis the value of "K" (see text) rapidly falls to within normal limits. With 0.1 gram a day the value rises above normal (July 16) but with 0.2 gram a day it remains normal. After two months without digitalis "K" is far above normal.

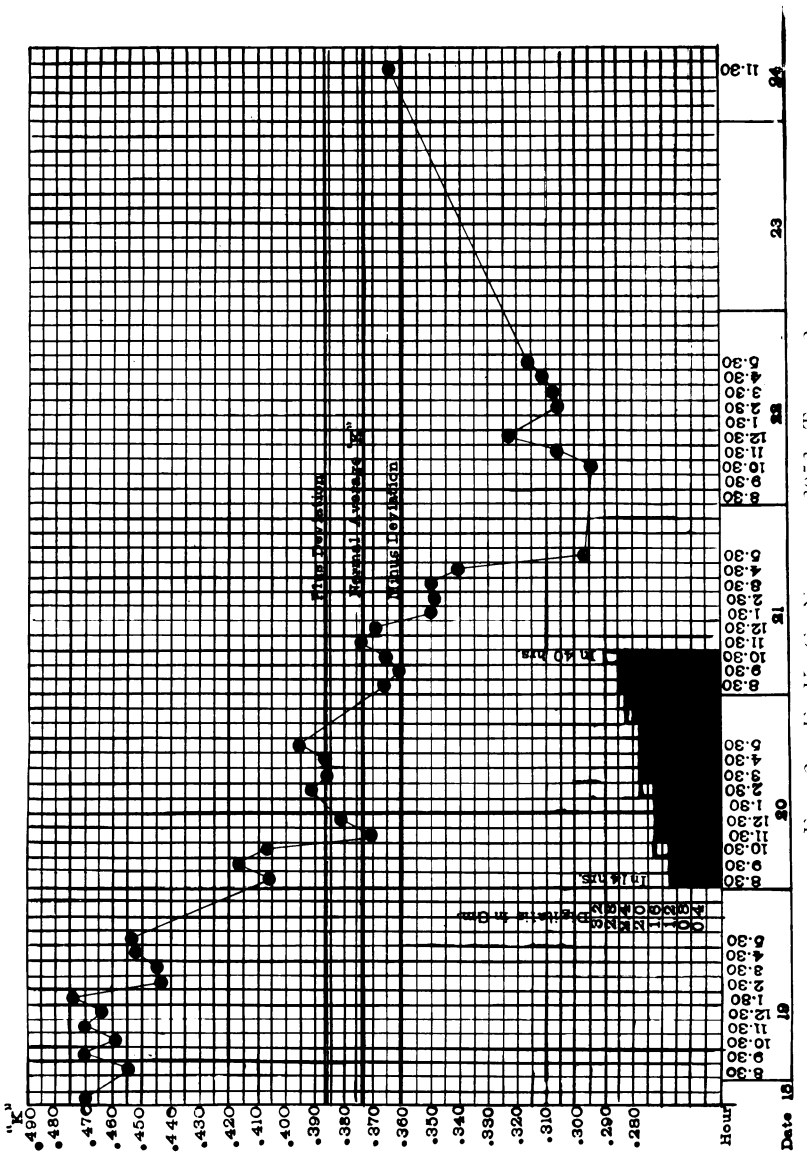

FIG. 2. E. K. G. NUMBER 3053, TABLE 2

The value of "K" (see text) is rapidly reduced to within normal limits and after a large dose of digitalis (3.2 grams) falls below normal.

TABLE 8

Changes in heart size and relative length of systole during digitalis therapy

E.K.G. number	Sex and age	Clinical diagnosis	Date	Weight	Heart failure*	Heart rate	"K"†	Digitalis†	Heart oversize
	years			*kgm.*				*grams*	*sq. cm.*
1886	M, 19	M.D. (active)	May 15	47.5	I	88	.406	None	+ 6
			June 4	41.7	0	75	.348	3.3 in 17 days	+50
			June 18	41.7	0	70	.350	3.8 in 24 days	+16
3053	M, 21	M.D., A.D.	November 18	44	III	102	.470	None	+51
			November 21	42	IIa	94	.260	3.2 in 3 days	+47
3100	M, 27	M.D.	May 13	85.2	IIb	97	.405	None	+53
			May 19	56.6	I	80	.368	3.0 in 4 days	+37
			May 27	52	I	79	.367	0.1 q.d.	+36
			June 2	56	I	93	.372	0.1 q.d.	+42
			October 16	55	I	92	.432	None for 3 months	+25
2662	F, 11	M.D., A.D. (active)	July 18	26	IIa	93	.409	1.8 in 8 days	+44
			October 24	26	I	100	.405	1.5 in 4 days	+22
			January 16	28	IIb	120	.460	None	+63
			March 2	26	I	115	.443	39 days after 1.9 in 19 hours	+35
			June 8	31	I	99	.463	None for 2 months	+25
			November 26	35	I	103	.428	None for 2 months	+30

* Classified according to the criteria of the New York Tuberculosis and Health Association.

† See footnotes to Tables 1 and 2.

DISCUSSION

It is still impossible to measure satisfactorily the work done by the human heart. One factor which must enter into a consideration of this problem is the duration of systole. We have shown that this is increased in heart failure out of proportion to the rise in heart rate. Heart rate is another factor of importance and in failure is usually elevated to some degree.

The results of the heart's work are shown in the blood pressure, which, except in the case of auricular fibrillation, is usually well maintained, and in the cardiac output per minute, which is usually decreased in failure. In spite of the fall in mass movement of blood, it would seem as if the work of the heart was not decreased, but rather is inefficiently performed. Calculation of the time occupied by systole in our cases shows that it may be increased to twice the average normal length. The known changes in the direction of increased efficiency brought about by digitalis are first slowing of the heart and second relatively greater shortening of systole. Not infrequently the second result may be obtained without the first.

With regard to the mass movement of blood, the work of Cohn and Stewart shows that in recovery from heart failure the significant change is toward more efficient emptying of the ventricles, for in spite of decreases in heart size and rate, the cardiac output per minute increases. As we have already suggested one would expect in this connection some relation between heart size and contraction time.

There are many reasons for believing that the effect of digitalis under discussion is chiefly exerted directly upon the myocardium. Vascular changes cannot be excluded, but would seem to be secondary. In congestive failure there is always an increase of venous pressure (11), which is apparently a reflection of the decreased mass movement of blood. The fall in venous pressure which accompanies improvement in the circulation (12) must go hand in hand with decreased diastolic volume of the heart and may be related to the shortening of systolic time.

It is desirable to emphasize the fact that the various aspects of the efficiency of the circulation cannot be considered separately, but are intimately interrelated. There is always danger of serious error in starting with one factor and arguing that various changes "result" from its operation. Nor should we be too quick to apply the normal laws of physiology to pathological conditions. In spite of the importance of ventricular filling under normal conditions, it does not seem that this factor operates toward the decreased cardiac output per minute in heart failure, for the ventricles are apparently filled to an abnormal extent.

The duration of systole in relation to cycle length would appear to be a valuable guide to digitalis therapy. Reference to a chart such as that presented in our previous article (2), immediately shows the relation of the values obtained to the normal limits. The changes are much more delicate than those in the "*P-R*" interval and often much clearer than those in the "T" wave. Our experience has led us to believe that excessive use of digitalis is no more desirable than insufficient use and the relative length of systole has proved a delicate guide to the danger of overdosage.

SUMMARY

An electrocardiographic study was made of the action of digitalis on the "*R-R*" and "*Q-T*" intervals of patients with heart failure. A consistent decrease was found in the length of the "*Q-T*" interval in relation to the "*R-R*" interval, which was often decreased. This reduction was not always paralleled by a decrease in heart size. It is apparently an important index of the greater efficiency of the myocardium in recovery from heart failure, and is interpreted as the result of a direct action of digitalis on the myocardium. The relative length of systole is a good guide to digitalis therapy.

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