

THE EFFECT OF DIGITALIS ON THE NORMAL HUMAN
ELECTROCARDIOGRAM, WITH ESPECIAL
REFERENCE TO A-V CONDUCTION.

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PLATES 91 TO 94.

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A study of the effect of digitalis on the normal human electrocardiogram was undertaken by us through a desire to throw more light on the significance of the various grades of heart block not infrequently produced in patients by only moderate amounts of digitalis. Little attention has hitherto been paid to the careful electrocardiographic study of the influence of digitalis on A-V conduction in the normal human heart.

Cohn and Fraser¹ in 1913 reported the study with the string galvanometer of twelve patients with normal cardiac rhythm, four of them without heart lesion. Digitalis in doses equivalent to 2 to 4 gm. of the leaves produced changes in A-V conduction in all the patients. A partial or complete return to the original conduction time was always produced by atropine. In 1914 Cohn² reported an investigation with digitalis of patients having an early stage of heart disease with normal mechanism. He concludes that "An effect on conduction may be set down as a usual effect of giving the drug, apart from specific preexisting injury." In our experiment with normal active young adults we have come to the same conclusion and have evidence to show that this defect in conduction is practically entirely due to increased tone and irritability of the vagus.

In this investigation five healthy young male adults were studied by us electrocardiographically. The Cambridge model of the Ein-

¹ Cohn, A. E., and Fraser, F. R., *Jour. Pharm. and Exper. Therap.*, 1913-14, v, 512.

² Cohn, A. E., *Jour. Am. Med. Assn.*, 1915, lxiv, 463.

TABLE I.
Table of Measurements of Case I, Age 29 Years.

	Date.	Electrocardiogram.										Blood pressure.		Subjective sensations.
		Intervals (sec.).			Amplitudes (10 ⁻³ volt).						Heart rate.	Systolic.	Diastolic.	
		P-R	R+S	R to end of T	P ₁	R ₂	S ₃	T ₁	T ₂	T ₃				
1915	Nov. 8	0.164	0.065	0.312	0.1	0.8	0.05	0.15	0.15	0	76	118	78	
Normal (before digitalis).....	" 10				0.1	0.85	0.05	0.2	0.15	0	71			
After 0.3 gm. digitalis.....	" 11				0.1	0.85	0.05	0.1	0.15	-Tr.	68	112	64	
" 0.6 " ".....	" 12				0.1	0.8	Tr.	0.1	0.15	-Tr.	68			
" 0.9 " ".....	" 13				0.1	0.85	"	0.1	0.1	0	64	124	72	Headache, anorexia.
" 1.2 " ".....	" 14	0.164			0.1	0.85	"	0.1	0.15	-0.05	69			
" 1.5 " ".....	" 15	0.187			0.1	0.8	0.05	0.1	0.15	-Tr.	64	122	72	
" 1.8 " ".....	" 16	0.186			0.1	0.85	Tr.	-Tr.	0.05	-Tr.	64			Palpitation.
" 2.1 " ".....	" 17	0.186			0.05	0.8	0	+0.05	0.05	+Tr.	71	130	70	"
" 2.4 " ".....	" 18	0.203			0.05	0.85	0	+0.05	0.05	+Tr.	70			" and anorexia.
" 2.7 " ".....	" 19	0.205	0.069	0.317	0.1	0.8	+Tr.	-Tr.	-0.05	-0.05	77	124	70	Palpitation and nausea.
" 3.0 " ".....	" 20	0.222	0.072		0.1	0.9	"	+Tr.	0.1	+Tr.	69			Arrhythmia, nausea.
1 day after stopping digitalis.....	" 21	0.185			0.1	0.85	0	-0.05	0.1	Tr.	80			Bigeminy at night.
2 days " ".....								+Tr.						

TABLE II.
Table of Measurements of Case 2, Age 27 Years.

Date.	Electrocardiogram.												Blood pressure.		Subjective sensations.			
	Intervals (sec.).						Amplitudes (10 ⁻³ volt).						Heart rate	Systolic.		Diastolic.		
	P-Q	Q+R+S	O to end of T	P ₂	Q ₂	R ₂	S ₂	T ₂	T ₁	T ₊								
1915																		
Normal (before digitalis).....	Nov. 8	0.161	0.078	0.344	0.15	0.1	1.45	Tr.	0.3	0.15	0.15	0.15	67	130	70			
After 0.3 gm. digitalis.....	" 10				0.15	0.05	1.35	"	0.3	0.2	0.1	0.1	75					
" 0.6 "	" 11				0.15	0.05	1.35	"	0.25	0.15	0.1	0.1	72	122	70			
" 0.9 "	" 12				0.1	0.1	1.35	"	0.15	0.05	0.1	0.1	79				Palpitation.	
" 1.2 "	" 13				0.15	0.1	1.45	"	0.1	Tr.				87	116	82		Malaise.
" 1.5 "	" 14	0.161			0.1	0.1	1.4	"	0.1	0.05	0.05	0.05	75					
" 1.8 "	" 15	0.173			0.1	0.05	1.3	"	0.05	0.1			80	102	70			Headache, malaise.
" 2.1 "	" 16	0.166			0.15	0.1	1.4	"	0.1	0.1			73					Malaise.
" 2.4 "	" 17	0.170			0.1	0.05	1.35	"	-Tr.	0.1			64	112	70			Headache.
" 2.5 "	" 18	0.172	0.078	0.310	0.1	0.05	1.35	"	-Tr.	0.05			66	106	70			"
1 day after stopping digitalis...	" 19	0.167			0.15	0.05	1.2	0.05	0.1	0.05			84					
3 days "	" 21	0.167			0.1	0.05	1.35	Tr.	0.15	0.1			75					
5 "	" 23	0.172			0.15	0.05	1.4	0	0.2	0.15			62					
8 "	" 26	0.162			0.1	0.05	1.4	Tr.	0.2	0.1			75					

12 days after stopping digitalis.	Nov. 30																			
19 " " " "	Dec. 7																			
After 2.5 gm. digitalis.																				
{ 1 min. after exercise.....	Nov. 18	0.183	0.082	?		0.2	0.1	1.3-1.6	0.15	Tr.		0.35	0.2	0.15	118					
{ 45 " " atropine.....	"	180.144	0.081	0.259		0.15	0.1	1.4	Tr.			{ -0.1	0.1	120						
Normal.	1916																			
{ 1 min. after exercise.....	Jan. 10	0.152				0.2	0.2	1.6+	0.1			0.55		136						
{ 45 " " atropine.....	"	100.137				0.15	0.1	1.5	0.1			0.2	0.15	Tr. 128						
Normal control.....	"	100.157											0.1	0.1						
" " " " " " " " " "	"	180.155																		
" " " " " " " " " "	1915																			
" " " " " " " " " "	May 10	0.170																		

thoven string galvanometer was used with non-polarizable electrodes. Photographic plates containing the three leads of Einthoven were taken before the administration of the drug, at approximately 24 hour intervals during the administration and at intervals of a day or two after the drug was stopped until the electrocardiograms had returned to normal. We have used Caesar and Loretz digitalis leaf in amounts ranging from 2 to 3 gm. at the rate of 0.3 gm. daily. Different amounts of digitalis were used in order to compare the durations of the drug effects. The effects of atropine (0.002 gm. subcutaneously) and exercise (a fast run of about one-quarter of a mile) on the normal and on the digitalized electrocardiograms were studied. Several control records were taken in order to determine the normal range of A-V conduction time in the individuals tested.

Measurements were made by projecting the images on the photographic plates upon a glass screen at a magnification of twenty-five diameters. For this purpose a microphotographic apparatus was used. The electrocardiographic intervals were measured off by calipers on a scale of one-sixtieth of an inch and compared with the measurements of the time intervals. Our maximum error is below 0.01 second. Time intervals of 0.2 second were used instead of smaller intervals, such as 0.04 second, because of the greater accuracy of measurement. In work which one of us did with Lewis³ on the measurement of P-R intervals in experimental curves it was found that the upstrokes of deflections so often fell upon and were obscured by the time lines separating intervals of 0.04 second that these small intervals were given up and 0.2 second time intervals adopted. Three beats were measured on each plate and their average was recorded in the final tables (Tables I to V).

In addition to the determination of the A-V conduction time as obtained from the P-R or P-Q interval (the latter if a Q is present), the Q-end of S and Q-end of T intervals before and after digitalis have been measured; the digitalis effects on the amplitudes of the electrocardiographic deflections, on the heart rates, on the blood pressures, and on the subjective sensations have been studied. On account of the fact that the tension of the string was not always

³ Lewis, T., and White, P. D., *Heart*, 1914, v, 335.

accurately adjusted allowance for errors has been made in calculating the curves.

Tables I to V contain the measurements of the A-V conduction times as expressed by the P-Q or P-R intervals, the measurements of the Q-end of S and the Q-end of T intervals, the amplitudes of the deflections, the heart rates, the blood pressures, and the subjective sensations. Table VI contains the effects of exercise on A-V conduction in the normal electrocardiogram. Figs. 1 and 2 show the control electrocardiograms of the five subjects and those taken at the end of the digitalis administration. Fig. 3 shows the atropine and exercise effects on the digitalized electrocardiograms. Figs. 4 and 5 illustrate the phenomenon resulting from digitalis in one of the subjects.

DISCUSSION.

A-V Conduction.

Digitalis caused a delay in A-V conduction in four of our five subjects. In three the lengthening was but slight and hardly greater than the normal range of conduction time in these same individuals (Tables II, III, and IV). In none of these three did the P-R interval equal or exceed 0.2 second. In the first subject (Table I) prolongation of conduction time up to 0.3 second occurred after 3.0 gm. of digitalis, but in no one of the five did the P-R interval increase to as much as 0.2 second after the ingestion of 2.5 gm. or less of digitalis. In every instance after digitalis even when the delay in conduction amounted to more than 0.05 second atropine reduced the P-R interval to less than its original value. The increased vagal action occurring with the rapidly slowing pulse after exercise added to the defect already present after digitalis. Normally we have found that immediately after exercise the A-V conduction time is markedly decreased, more even than it is decreased normally by atropine, 0.002 gm. subcutaneously (Tables I, II, and VI). Our maximum shortening was from 0.158 to 0.112 second. Shortening of the P-R interval after exercise was found by Lewis and Cotton⁴ in 1913.

⁴ Lewis, T., and Cotton, T. J., *Jour. Physiol.*, 1913, xlvi, p. lx.

TABLE III.
Table of Measurements of Case 3, Age 28 Years.

Date.	Electrocardiogram.											Blood pressure.		Subjective sensations.				
	Intervals (sec.).			Amplitudes (10 ⁻³ volt).								Heart rate.	Systolic.		Diastolic.			
	P-Q	Q+R+S	Q to end of T	P ₂	Q ₂	R ₂	S ₂	T ₂	T ₁	T ₂								
1915																		
Normal (before digitalis).....	Nov. 8	0.135	0.104	0.379	0.05	0	1.1-1.25	0.3	0.2	0.25	0.25	0.25	0.25	0.25	68	122	70*	
After 0.3 gm. digitalis.....	" 10				0.1	Tr.	1.25	0.35	0.2	0.25	0.25	0.25	0.25	0.25	60			
" 0.6 " ".....	" 11				0.15	0.05	1.45	0.35	0.1	0.25	0.25	0.25	0.25	0.25	73	125	68	
" 0.9 " ".....	" 12				0.1	Tr.+	1.3	0.35	{-Tr. +0.05	0.15	0.15	0.15	0.15	0.15	73			
" 1.2 " ".....	" 13	0.134			0.05	0.05	1.3±	0.35±	0.1	0.15	0.15	0.15	0.15	0.15	70	134	78	
" 1.5 " ".....	" 14	0.149			0.1	0.05	1.4±	0.35±	{-0.05 +0.1	0.15	0.15	0.15	0.15	0.15	63			
" 1.8 " ".....	" 15	0.154			0.1	0.05	1.3±	0.3	{-0.05+ +0.05	0.15	0.15	0.15	0.15	0.15	64	140	62	
" 2.1 " ".....	" 16	0.152			0.1	Tr.	1.35±	0.3	{-0.05 +0.1	0.15	0.15	0.15	0.15	0.15	70			
" 2.3 " ".....	" 17	0.156	0.108	0.367	0.05	"	1.3±	0.3	{-0.05 +0.05	0.15	0.15	0.15	0.15	0.15	57	126	64	Slight nausea.
1 day after stopping digitalis....	" 18	0.150			0.1	0.05	1.35±	0.35	{-0.1 +0.05	0.15	0.15	0.15	0.15	0.15	63			

3 days after stopping digitalis....	Nov. 20	0.149	0.1	Tr.	1.4±	0.35	{ -0.05 +0.1	0.2	-0.2	75		
5 " " " " " " " " " " " "	"	22	0.154	0.1	0	1.3±	0.35±	{ -0.05 +0.1	0.15	67		
7 " " " " " " " " " " " "	"	24	0.148	0.1	0	1.25-	0.35±	{ -Tr. +0.1	0.2	{ -0.15 +Tr. 66		
9 " " " " " " " " " " " "	"	26	0.159	0.1±	Tr.	1.2	0.35±	{ -Tr. +0.1	0.2	-0.15 74		
12 " " " " " " " " " " " "	"	29	0.135	0.05	0	1.25	0.35±	0.2-	0.25	{ -0.05 +Tr. 59		
14 " " " " " " " " " " " "	Dec. 1			0.05	0	1.2	0.3	0.15	0.2	-0.1 64		
After 2.3 gm. digitalis.												
{ 1 min. after exercise.....	Nov. 17	0.151	0.100	0.290	0.25	0.05	1.0-1.3	0.3-0.45	0.3	0.15	{ -0.05 +0.1 113	
{ 45 " " atropine.....	"	17	0.144	0.087	0.314?	0.2	0.1	1.3+	0.3	{ -0.1 +0.05	0.1	-0.2 116
Normal control.....	Dec. 6	0.144			0.1	0	1.4	0.4-	0.15+	0.25	{ -0.05+ +Tr. 65	
" " " " " " " " " " " "	"	8			0.1	Tr.	1.3±	0.3-0.35	0.2	0.3	{ -0.05 +Tr. 55	
" " " " " " " " " " " "	1916 Jan. 10	0.141			0.1	0	1.3±	0.35±	0.2	0.25	{ -0.05 +Tr. 75	

* Blood pressure estimation made Nov. 9, 1915, after 0.1 gm. digitalis.

The U deflection in this subject is unusually pronounced but is unaffected by digitalis. As the T wave flattens it becomes at length level with the U wave.

From the effect of digitalis on A-V conduction in normal hearts it seems to us reasonable to conclude that there is either an abnormal irritability of the vagus or a damage to the conduction tissue itself, if heart block, even a delay in conduction beyond a P-R interval of 0.2 second, occurs in patients after small or moderate amounts of an active preparation of digitalis (for example 1.0 to 2.0 gm. of Caesar and Loretz standardized leaves in 4 to 7 days). If, however, this drug is continued up to and beyond 3.0 gm., a slight defect in A-V conduction then appearing for the first time may be reasonably ascribed to the digitalis and no blame be placed on the conducting tissue.

Arrhythmia.

The greater action, or at least the less balanced action, of the vagus at night slowed the heart rate in two of the subjects (Cases 3 and 1) below the usual rate, in one the pulse falling as low as 48 to the minute; in the other subject the vagal activity was still further evidenced by the occurrence of blocked auricular premature beats—a phenomenon dependent on delay in conduction time (Figs. 4 and 5). This arrhythmia, the only one produced in any of the subjects, began to appear after 3.0 gm. of digitalis had been taken. As far as we are aware it is the first recorded observation of such a result from digitalis. It consisted of an interruption of the normal rhythm by premature ectopic auricular contractions (almost isoelectric in the electrocardiogram) without ventricular response. Polygrams and electrocardiograms of the phenomenon were obtained with considerable difficulty because of the fact that the irregularity almost always occurred late at night, apparently when the influence of the vagus was greatest and tended to disappear if an attempt was made to obtain graphic records. At times it occurred so often as to produce a bigeminy—two normal beats followed by a premature auricular contraction during and after which there was a pause in the pulse. This irregularity first appeared when the influence of digitalis was at its maximum, as shown by the P-R interval (0.222 second) 1 day after stopping digitalis. It occurred off and on for the following 8 days and nights, but since the 9th day after stopping digitalis (3 months ago) it has not once occurred. The subject had never had premature beats so far as known prior to the ingestion of the

TABLE IV.
Table of Measurements of Case 4, Age 24 Years.

Date.	Electrocardiogram.											Blood pressure.		Subjective sensations.				
	Intervals (sec.).			Amplitudes (10 ⁻³ volt).								Heart rate.	Systolic.		Diastolic.			
	P-Q	Q+R+S	Q to end of T	P ₂	Q ₂	R ₂	S ₂	T ₂	T ₁	T ₃								
1915																		
Nov.	Normal (before digitalis)	90	132	0.080	0.303	0.15	Tr.	0.95-1.0	0.35	0.3	0.2	0.1	85	140	100			
"	After 0.6 gm. digitalis	11			0.15	"	"	1.0	0.3-0.35	0.25	0.15-0.2	0.05±	80	144	100			
"	" 0.9 "	12			0.15	"	"	1.0-1.05	0.35±	0.2	0.15	0.05	83				Malaise.	
"	" 1.2 "	13			0.1	"	"	0.95	0.35	0.2	0.15	0.05	80	122	86		" and head-ache.	
"	" 1.5 "	14	0.133		0.15	"	"	1.05-1.1	0.25-0.3	0.2-	0.1+	0.05+	82				Palpitation.	
"	" 1.8 "	15	0.140		0.15	"	"	0.9-0.95	0.3-0.35	0.2-	0.15	0.05-	83	138	90		Dizziness and anorexia.	
"	" 2.0 "	16	0.150	0.075	0.301	0.15	"	1.0-1.05	0.35±	0.25	0.15	0.1	83	128	90			
"	1 day after stopping digitalis	17	0.147		0.1	0	0.95-1.0	0.3	0.2+	0.2	0.2	0.05	81					
"	3 days "	19	0.140		0.15	Tr.	0.95	0.3	0.2	0.2	0.15	0.05	76					
"	" "	21	0.142		0.15	"	"	1.1	0.35	0.25	0.2	0.1	88					
"	" "	23	0.134		0.15	"	"	1.05	0.35	0.2	0.1+	0.1-	86					
"	" "	27			0.15	"	"	1.05±	0.3	0.25	0.2	0.05	86					
"	" "	30			0.15	0	1.1±	0.3±	0.3	0.3	0.2	0.1±	75					
"	After 2.0 gm. digitalis.																	
"	{ 1 min. after exercise	160	155	0.090	0.273?	0.25±	0.05	1.0	0.65-0.8	0.7	0.2	0.4	140					
"	{ 20 " " atropine	160	124	0.082	0.263?	0.25	0	0.9-0.95	0.5	0.3	0.15	0.15	138					
"	Normal control	Dec. 3			0.1	Tr.	0.95-1.0	0.3	0.3	0.3	0.25	0.1	79					

TABLE V.
Table of Measurements of Case 5, Age 32 Years.

	Date.	Electrocardiogram.											Blood pressure.		Subjective sensations.		
		Intervals (sec.).			Amplitudes (10- μ volts).								Heart rate.	Systolic.		Diastolic.	
		P-Q	Q-R+S	Q to end of T	P ₂	Q ₂	R ₂	S ₂	T ₂	T ₁	T ₃						
1915	Nov. 8	0.138	0.081	0.322	0.2	0.1	1.65±	0.2	0.3+	0.1	0.25+	76	116	82			
	Normal (before digitalis).....																
	After 0.3 gm. digitalis.....																
	" 0.6 "																
	" 0.9 "																
	" 1.2 "																
	" 1.5 "																
	" 1.8 "																
	" 2.0 "																
		15	0.137	0.080	0.310	0.15	0.1	1.6-	0.15-0.2	0.1	0.15-0.2	0.1	0.05	78	122	70	Slight anorexia, nausea, dizziness. Slight anorexia, nausea, dizziness.

1 day after stopping digitalis...	Nov. 16	0.136																							
3 days " "	" "	18																							
5 " "	" "	20																							
7 " "	" "	22																							
9 " "	" "	24																							
11 " "	" "	26																							
14 " "	" "	29																							
After 2.0 gm. digitalis.																									
45 min. after atropine.....	"	15	0.123	0.081	?	0.2	0.2±	1.3±	0.2-0.25	{ -0.1+ +0.1- }	0.05	{ -0.2 +0.05 }	124												
Normal control.....	Dec. 1916	6	0.140										75												
" "	Jan. 1916	9	0.141										75												

drug. For these reasons and because of the fact that it was directly dependent on a certain degree of prolongation of the P-R interval (to 0.295–0.300 second) the arrhythmia can be ascribed to digitalis. The subjective sensations of the irregularity were interesting, for the pause following the ectopic auricular beat could always be foretold by the feeling of the premature auricular systole itself consisting of a wave of fulness rising in the neck and throat. The association of mechanical activity of the auricle with the abnormal deflection in the electrocardiogram is clearly shown in the jugular tracing (Fig. 5 b) taken by Dr. O. F. Rogers, Jr. The production of the premature auricular systole by a mechanical stimulus from the contracting ventricle would at present best explain the fact that the R-P interval is much shorter than the P-R interval just preceding and that it varies little if at all in length.

Amplitudes of Electrocardiographic Deflections.

T Wave.—Cohn and Fraser¹ reported in 1913 their observations that the T wave of the human electrocardiogram was inverted in many of their patients who were under the influence of digitalis. More recently Cohn, Fraser, and Jamieson⁵ have shown that digitalis given by mouth to patients began to cause a change in shape and amplitude of the T wave as early as 36 to 48 hours after the administration of the drug had begun, the change increasing as the digitalis was continued and persisting for from 5 to 22 days after the drug had been stopped. It is interesting to note that in all five of our entirely normal subjects, as a result of digitalis the T wave was decreased in amplitude in every lead. There seemed to be no direct connection between the effects of digitalis on the conduction time and on the T wave as indicated particularly well by one subject (Table V), who suffered no defect in A-V conduction but who did show a considerable decrease in the amplitude of T (Fig. 1). We have found that the first electrocardiographic evidence of digitalis and, for that matter, the first evidence, of any sort, of digitalis action is the decrease in the amplitude of the T deflection in the case of normal individuals.

⁵ Cohn, A. E., Fraser, F. R., and Jamieson, R. A., *Jour. Exper. Med.*, 1915, xxi, 593.

TABLE VI.

The Effect of Exercise on Normal Electrocardiograms of Cases 1 and 2.

		P-Q interval.	Heart rate.
Case 1.	Normal (before exercise).....	0.158	75
	$\frac{1}{2}$ min. after exercise.....	0.112	178
	1 " " "	0.128	160
	2 " " "	0.167	111
	8 " " "	0.176	95
Case 2.	Normal (before exercise).....	0.150±	90
	$\frac{1}{4}$ - $\frac{1}{2}$ min. after exercise.....	0.117	155
	$\frac{3}{4}$ " " "	0.132	145
	1 " " "	0.144	135
	2 " " "	0.150	115
	5 " " "	0.153	99
	10 " " "	0.149	102
30 " " "	0.156	86	

Effect of Exercise and Atropine on the Digitalized T Deflection.

The mechanism by which exercise acts on the heart temporarily removed the traces of the digitalis action on the T wave (Fig. 3), while atropine, 0.002 gm. subcutaneously, actually increased the digitalis effect on this deflection (Fig. 3) although the pulse rate was raised about equally by both procedures. Just the opposite action of these two tests was noted on the digitalized P-R interval.

P₂, Q₂, R₂, and S₂ Deflections.—These showed no clear-cut changes in amplitude as the result of the digitalis in our subjects.

SUMMARY.

Digitalis was given by mouth to five normal young male adults in amounts ranging from 2.0 to 3.0 gm. of standardized leaves in the course of 7 to 10 days. The As-Vs interval was prolonged in four of the five subjects, the greatest prolongation occurring in the case of the subject who received the most digitalis and none at all in one who received only 2.0 gm. There was no prolongation to so great an interval as 0.2 second until 2.7 gm. had been taken. The effects of the digitalis on conduction time began 5 to 6 days after the drug had been started and after 1.5 to 1.8 gm. had been taken. The

effects persisted for 1 to 2 weeks after the drug had been stopped. Atropine removed completely the effect of digitalis on A-V conduction. The slowing heart rate after exercise was accompanied by an enhancement of the defect in conduction. The change in conduction through digitalis was therefore almost entirely, if not entirely, due to increase of vagal tone and irritability.

Digitalis did not affect to an appreciable extent the Q-end of S and the Q-end of T intervals. Exercise and atropine both shortened the ventricular complex Q-end of T while the subject was under digitalis.

The amplitude of the T wave, especially in Lead II, was changed within 48 hours after digitalis had been started, a decrease then beginning which became greater as the drug was continued and which persisted until 10 to 19 days after the digitalis had been stopped. The change in the T deflection preceded by several days the change in conduction time. The T wave, therefore, in the normal subject as well as in the patient gives us the earliest indication of digitalis action.

The amplitudes of P, Q, R, and S were not materially influenced by the amounts of digitalis given.

The pulse rate in two subjects became lower than usual at night as the result of the digitalis; otherwise there was no evidence of vagal action on the sino-auricular node. Blood pressure was uninfluenced by the digitalis. Mild subjective sensations occurred in all the subjects during the administration of the drug.

A curious, hitherto undescribed, digitalis arrhythmia consisting of blocked auricular premature beats occurred in one subject after 3.0 gm. of digitalis had been taken.

Supplementary Note.—A second series of five healthy young male adults has recently (March, 1916) been studied by one of us electrocardiographically during a course of digitalis —2.6 to 3.3 gm. Caesar and Loretz leaf in 9 to 11 days. (The drug was weaker than that used in the previous investigation.) Three subjects showed slight prolongation of the P-R interval but no bradycardia; the other two subjects, who had no delay in A-V conduction, showed a marked total bradycardia after the digitalis (heart rate of 43 in each in the middle of the forenoon). The T_2 deflection of the electrocardiogram

was more or less flattened by the digitalis in all five subjects. Atropine given subcutaneously at the height of the digitalis action depressed the T wave still further in every instance.

EXPLANATION OF PLATES.

In all figures abscissæ equal 0.2 second and ordinates equal 10^{-4} volts.

Where the galvanometer string has been too slack or too tense, the error is seen in the control deflection. The proper correction in the amplitude has been made. Amplitudes have been estimated to 0.05 of a millivolt.

PLATE 91.

FIG. 1. Electrocardiograms (Lead II) of Case 5 (*A*), Case 4 (*B*), Case 3 (*C*), and Case 1 (*D*). The left hand column contains control records; right hand column contains records taken during full effect of digitalis. In the center below is a record of Lead II of Case 1 taken 1 day after digitalis had been stopped and showing the variation in the length of the P-R interval.

PLATE 92.

FIG. 2. The three electrocardiographic leads of Case 2 before and immediately after the course of 2.5 gm. of digitalis. The change in the T deflection in each lead is evident.

PLATE 93.

FIG. 3. Electrocardiograms (Lead II) of Case 4 (*A*), Case 3 (*B*), Case 2 (*C*) and Case 1 (*D*) after atropine (left hand column) and after exercise (right hand column) at the completion of digitalis. In the center below is the record of Lead II of Case 5 after atropine at the completion of 2.0 gm. of digitalis.

PLATE 94.

FIG. 4. Lead II of Case 1 showing blocked auricular premature beats following gradual prolongation of the P-R interval. Electrocardiogram taken 5 days after the completion of 3.0 gm. of digitalis.

FIG. 5. Radial pulse tracing (*a*) and polygram (*b*) of Case 1 taken by Dr. O. F. Rogers, Jr., showing arrhythmia produced by the auricular premature beats which occurred as the result of 3.0 gm. of digitalis. *a'*, evidence in jugular pulse of blocked auricular premature beat. Time interval, 0.2 second.

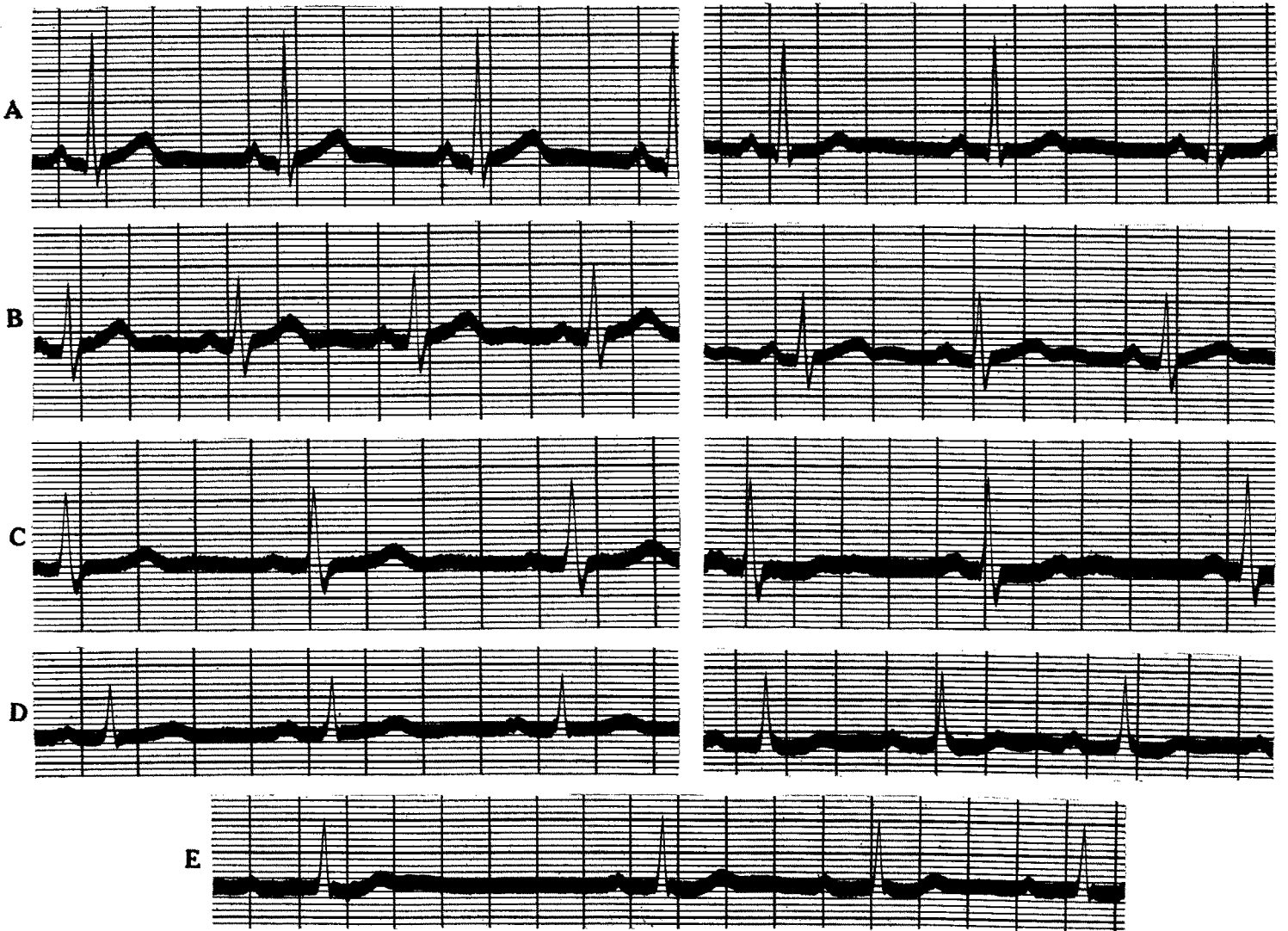


FIG. 1.

(White and Sattler: Effect of Digitalis on Human Electrocardiogram.)

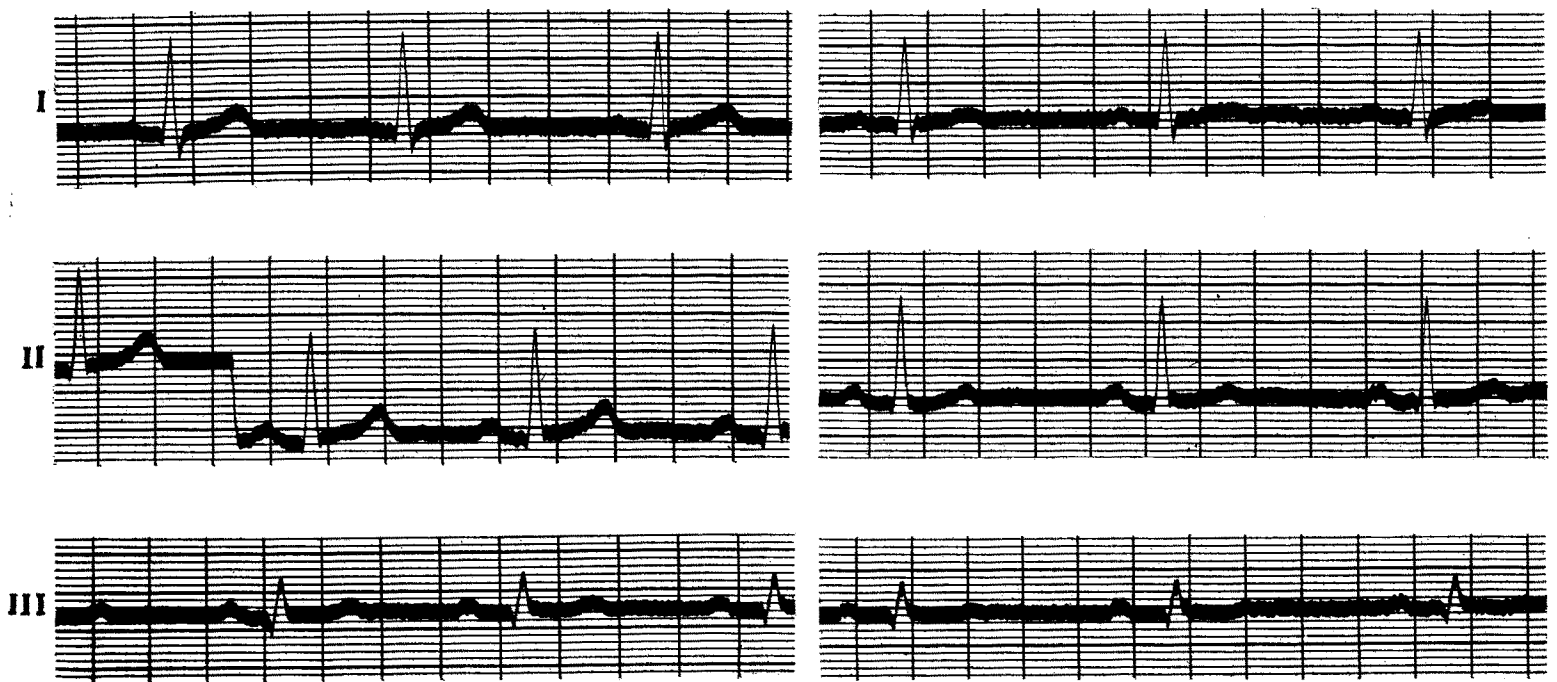


FIG. 2.

(White and Sattler: Effect of Digitalis on Human Electrocardiogram.)

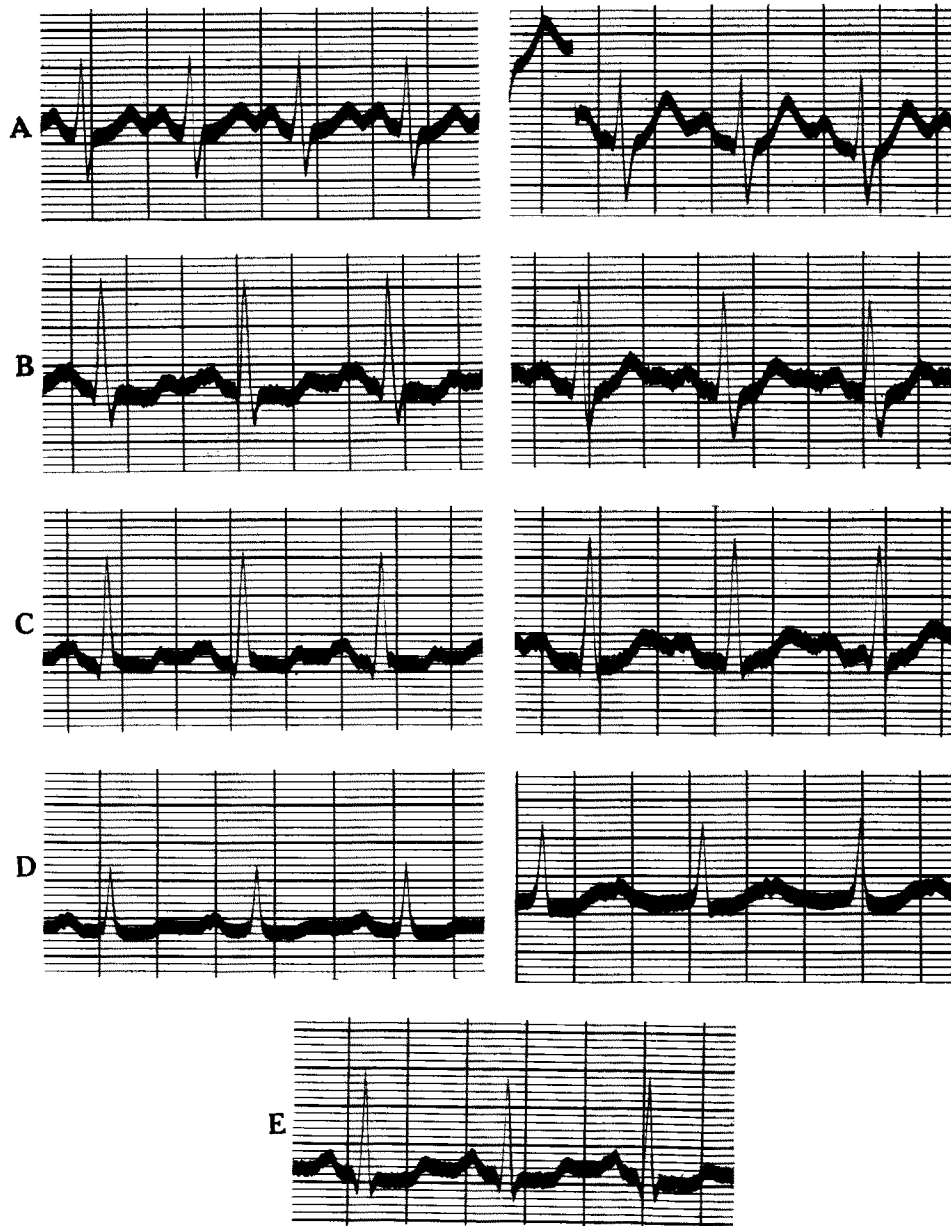


FIG. 3.

(White and Sattler: Effect of Digitalis on Human Electrocardiogram.)

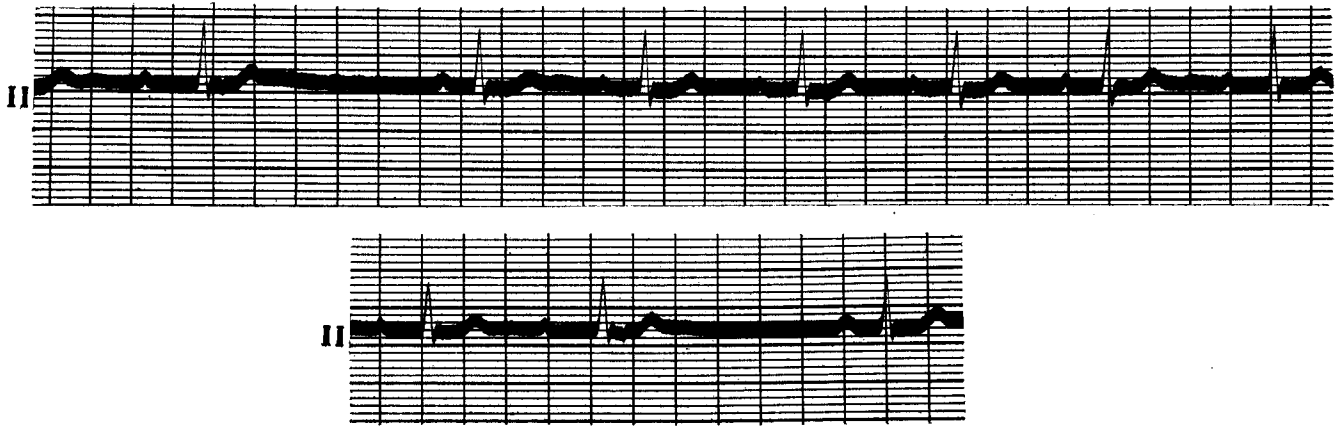


FIG. 4.

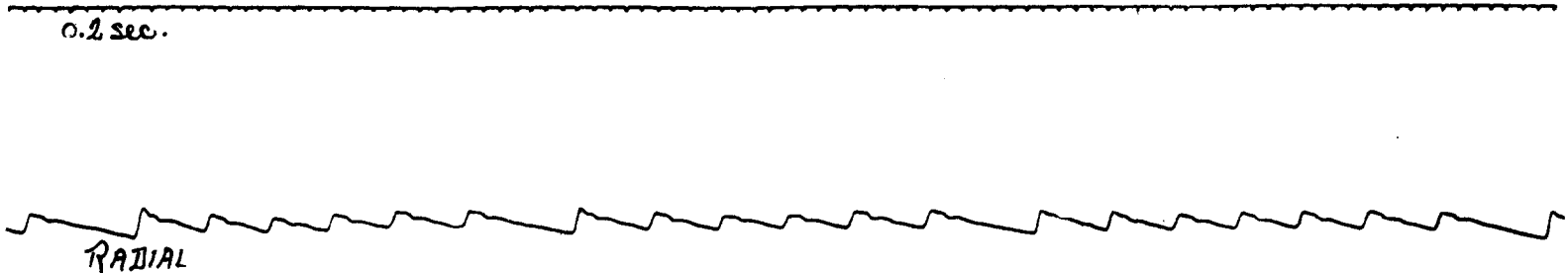


FIG. 5a.

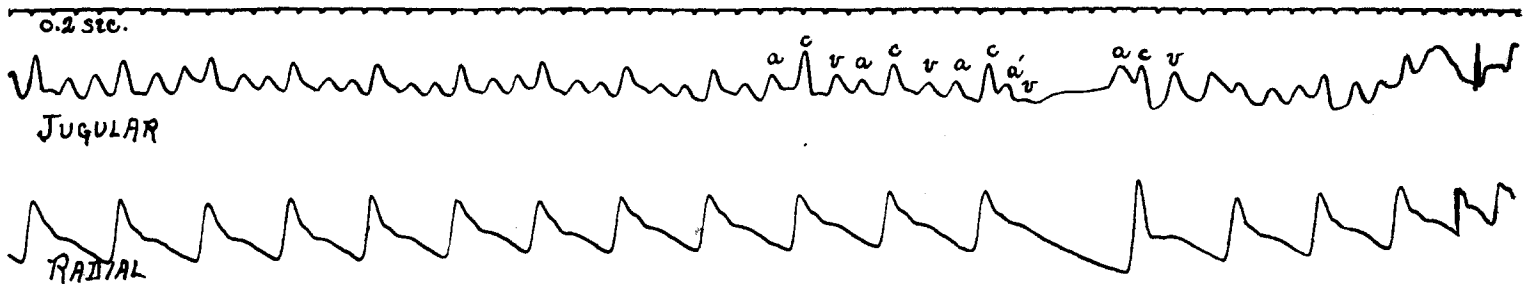


FIG. 5b.

(White and Sattler: Effect of Digitalis on Human Electrocardiogram.)