TABLE III. Effect of Simultaneous Administration of Thyroxin and Epinephrine on Organic-Bound I^{131} in the Blood.

Treatment	No. of animals	OBI, C/min.	Rat No.	Statistical significance
Exp. 1				
Thyroxin + epinephrine	5	91.8 ± 30.2*	1- 5	f = 38.91
Thyroxin	5	94.8 ± 28.2	6-10	p <.01
Epinephrine	5	132.0 ± 18.5	11-15	
Saline	3	152.0 ± 25.7	16-18	
Exp. 2				
Thyroxin + epinephrine	5	117.8 ± 10.6	1- 5	f = 9.37
Thyroxin	5	186.0 ± 46.5	6-10	p <.01
Epinephrine	5	196.0 ± 65.8	11-15	
Saline	3	299.7 ± 17.7	16-18	
Exp. 3				
Thyroxin + epinephrine	5	189.0 ± 33.0	1- 5	
Thyroxin	5	242.0 ± 82.0	6-10	
Epinephrine	5	246.0 ± 64.0	11-15	
Saline	1	318.0	16-18†	

* Mean ± stand. dev. † 2 samples lost.

Each animal inj. with 30 μc I^{131} 18 hr before sacrifice.

No. 1-10 inj. with 0.5 mg of thyroxin 2½ hr before sacrifice. No. 1-5 and 11-15 inj. with 0.1 mg epinephrine 2 hr before sacrifice. No. 16-18 inj. with a normal saline solution 2 hr before sacrifice.

thyroxin has been found to produce a lowering in the blood level of thyroid hormone (organic-bound I^{131}). This response to epinephrine is interpreted as being due to the increased utilization of circulating thyroid hormone caused by epinephrine. The significance of this finding is discussed.

The authors are indebted to Dr. G. L. Saiger for the statistical analysis of the data.

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Received March 29, 1954. P.S.E.B.M., 1954, v85.

The First Heart Sound in Ventricular Contractions Arising from the Apex and Base.* (20977)

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The first heart sound has been reported to be delayed in ectopic ventricular beats in humans(1,2) and in dogs(2). This delay was attributed to the mechanism of closure of the A-V valves. No attempt was made in these reports to differentiate between ectopic beats arising from the apex and those originating from the base. The mode of contraction may be different in beats arising from one or the other of these locations; therefore, variations in closure of the A-V valves and timing of the first sound might occur. The present study was undertaken to investigate this pos-

* Based on a thesis presented by Roy D. Schaefer in partial fulfillment of the requirements for the degree of M. S. in Physiology. This study supported by a grant from the Am. Heart Assn. and the Shamokin-Coal Township Heart Assn.

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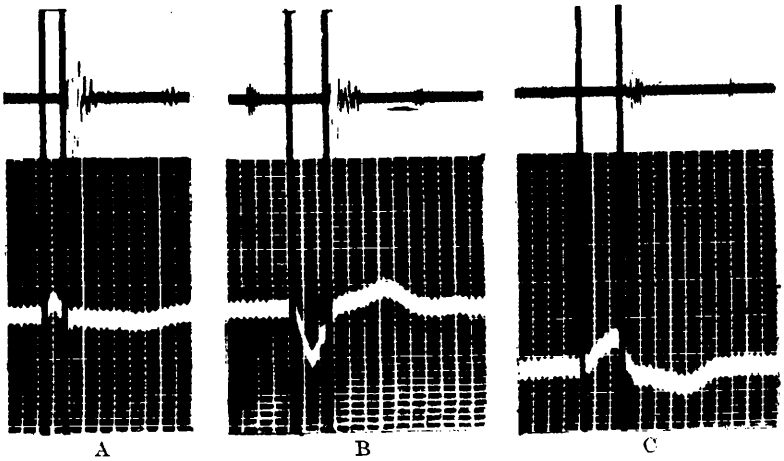

FIG. 1. Representative examples of a normal beat (A), an ectopic beat from the apex (B), and an ectopic beat from the base (C). Each is taken from the record of Patient III.

sibility and to explore further the effect of ventricular contractions on the timing of the first heart sound.

Method. Heart sounds were recorded from the exposed hearts of anesthetized dogs by the method of Little, *et al.*(2). Lead II of the electrocardiogram was simultaneously recorded with the sound tracing at a camera speed of 50 mm per second. No parallax existed between recording beams. Two small fish-hook electrodes were thrust into the myocardium one cm apart near the apex of the heart and 2 were similarly placed at the base of the pulmonary conus. Each pair of electrodes was connected to a Harvard inductorium. The heart was stopped by stimulation of the right vagus by means of a tetanizing current from a third inductorium. While the heart was stopped, single make and break induction shocks were used to produce ectopic ventricular contractions from the base or from the apex. Records of human cases of ectopic ventricular systoles were recorded with a Cambridge phonocardiograph at a camera speed of 50 mm per second. Lead II of the electrocardiogram was simultaneously recorded.

Results. Records from 5 dogs and 5 human subjects were suitable for analysis.‡ The sound records were free from artifacts, and the beginning of the first sound was not obscured by auricular sounds. The time interval between beginning of the QRS deflection and onset of the first sound was measured, by means of adequate magnification, to 0.005 second. This interval has been termed the "heart sound time"(2).

In ectopic ventricular beats, the QRS complex is broad, slurred, and notched, and the T wave extends in the opposite direction from the principal deflection of the QRS. In beats arising from an ectopic focus in the ventricular base the major deflection of the QRS complex is upright in all 3 standard electrocardiographic leads. If the beat originates in the apex the major deflection of the QRS is down in all 3 standard leads. Representative examples of a normal beat, an ectopic contraction from the base, and an ectopic contraction from the apex are shown in Fig. 1.

The mean heart sound times in dogs for normal beats, ectopic beats from the base, and ectopic beats from the apex are presented in Table I. In each animal the heart sound time for apical ectopic beats is longer than for normal beats, and the interval for ectopic contractions from the base is longer than for beats from the apex. The average of the means, or grand mean, is 0.048 second for the normal beats, 0.080 for the apical beats, and 0.093 second for beats from the base. Similar data from the human cases are presented in Table II. Only 2 of these patients had premature beats from both the base and

‡ Other observations on records of human subjects have been previously reported(2).

TABLE I. Mean Heart Sound Times in Dogs.

Dog	Origin of beats	No. of beats measured	Mean time in seconds	Stand. dev. (±)
I	Base	29	.087	.01769
	Apex	23	.077	.00985
	Normal	25	.044	.00878
II	Base	29	.105	.01020
	Apex	30	.089	.00894
	Normal	25	.055	.00877
III	Base	30	.092	.00548
	Apex	27	.078	.00854
	Normal	25	.043	.00480
IV	Base	22	.092	.01086
	Apex	29	.078	.01114
	Normal	25	.055	.00831
V	Base	29	.090	.00678
	Apex	30	.077	.00520
	Normal	25	.044	.00794

the apex. In these 2 cases the first heart sound was delayed in apical premature beats as compared with the normals, and was delayed to a greater extent in basal premature beats. In 2 patients with premature beats only from the apex, the mean heart sound times were longer in the case of the premature than in the normal beats. In the patient with premature beats arising only from the base, the mean heart sound time was markedly longer for the premature beats than for the normal beats. In the human cases the grand mean for the normal beats was 0.040 sec., that for apical premature beats was 0.088 sec., while the grand mean of the basal premature beats was 0.121 sec.

TABLE II. Mean Heart Sound Times in Human Subjects.

Patient	Origin of beats	No. of beats measured	Mean time in seconds	Stand. dev. (±)
I	Base	26	.136	.00866
	Normal	26	.044	.00300
II	Base	26	.128	.01456
	Apex	4	.106	.01109
	Normal	26	.039	.00469
III	Base	21	.099	.01510
	Apex	6	.083	.01536
	Normal	23	.056	.00906
IV	Apex	25	.073	.00985
	Normal	25	.029	.00574
V	Apex	16	.088	.01661
	Normal	16	.031	.00469

The probability of the occurrence of the observed time differences by chance alone in the dog experiments was computed by means of the T test, for normal beats as against apical ectopic beats, for normal beats as against basal ectopic beats, and for apical ectopic beats as compared with basal. These tests indicate that the time differences between apex and base in Dog 1 might be expected to occur by chance alone in 2 to 5% of similar experiments. For all of the remaining comparisons in all animals, the probability level is less than 0.1%.

A similar statistical analysis was carried out on the data obtained from the human records. This shows that the observed time differences between base and apex in Patient II would be expected to occur by chance alone in from 0.1 to 1% of a similar group of measurements. In Patient III the observed differences between ectopic beats initiated in base and apex might occur by chance alone in over 5% of a similar series of measurements. But in all of the other comparisons in patients the probability level is less than one in a thousand that chance alone would account for the measured time differences.

The method of sound recording used in this work was not adequate for accurate measurement of the intensity of the heart sounds. However, in many ectopic systoles the sound was of less intensity than that of normal beats. This would tend to refute the implication of Cossio *et al.*(1) that only the intensified extrasystolic first sounds are delayed. Our data indicate that the delay in the first sound occurs in all ectopic beats, regardless of the intensity of the sound.

Discussion. This study confirmed the observations(1,2) that the heart sound time is prolonged in ectopic ventricular contractions. Previous studies(2) on animals employed ventricular pressure curves to indicate the onset of ventricular contraction. This investigation utilized the electrocardiogram to indicate the onset of ventricular depolarization. As a result of the time difference between mechanical and electrical events, the heart sound times reported in animals are slightly longer than those found by previous authors. The relative increase in heart sound time in ectopic beats

is, however, of the same magnitude.

The reason for the greater delay of the first sound in basal as compared to apical ectopic beats remains speculative. When the ectopic focus is in the base of the ventricle, the impulse probably must proceed through the ventricular wall toward the apex and then through the wall of the other ventricle. However, if the ectopic focus is at the apex, it could travel simultaneously through both ventricular walls. In other words, the wave of depolarization would require a longer time to activate sufficient ventricular muscle mass to inaugurate contraction in basal ectopic beats. When auricular systole is absent the valves must be closed from the open position by ventricular contraction(3). The greater delay in the beginning of ventricular contraction in basal ectopic beats could thus explain the greater delay in onset of the first sound.

Summary. 1. Simultaneous electrocardiograms and phonocardiograms were recorded from 5 human subjects having ectopic ventricular systoles. Similar tracings were obtained from 5 dogs in which ectopic systoles were produced by induction shocks to the exposed heart during vagal arrest. The time interval between beginning of ventricular depolarization and onset of the first heart sound was measured for normal and for ectopic beats. The data were subjected to statistical analysis. 2. The beginning of the first heart sound was significantly delayed in ectopic ventricular contractions. The first sound occurred significantly later in ectopic beats arising from the ventricular base than in those from the apex. The probable reasons for these findings are discussed.

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Received March 29, 1954. P.S.E.B.M., 1954, v85.

Toxicity of Choline and Dimethylethanolamine in the Guinea Pig and the Rat.* (20978)

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The toxicity of choline in the rat has been established(1-3). The metabolism of choline in the liver is related to the activity of choline oxidase(4,5). This enzyme system has a very low activity or is entirely lacking in the liver of the guinea pig and thus choline deficiency cannot be produced by dietary means (6). Dimethylethanolamine, a precursor of choline(7), is not oxidized by liver choline oxidase(8). In view of these observations it was of interest to determine if there was a difference in the toxicity of choline or dimethylethanolamine in the guinea pig and rat.

Methods. Male albino rats (100-110 g) and guinea pigs (200-300 g) were divided into two groups. Group 1 received intraperitoneally 45 mg of dimethylethanolamine or choline (base) per 100 g of body weight in 1 cc and Group 2 received 60 mg. Animals which lived longer than 30 minutes in most cases survived.

Results. From the results in Table I it was apparent that there was no difference in the toxicity of choline in the guinea pig or

TABLE I. Toxicity of Choline and Dimethylethanolamine in the Guinea Pig and Rat.

mg (base) /100 g of body wt		Rats		Guinea pigs	
		No. of animals	% mortality	No. of animals	% mortality
45	Choline	14	29	45	20
	DME*	24	75	28	71
60	Choline	20	60	39	74
	DME	25	88	22	77

* Dimethylethanolamine.

* This investigation supported (in part) by a research grant from the Division of Research Grants and Fellowships of the National Institutes of Health, U. S. Public Health Service.