OBSERVATIONS UPON THE ELECTROCARDIOGRAM AND TENSION DEVELOPMENT IN ISOLATED, PERFUSED RABBIT HEARTS DURING CORONARY INSUFFICIENCY OR PROGRESSIVE REGIONAL ABLATION

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By

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This volume is respectfully dedicated

to my wife, Joanna

INTRODUCTION

The syncytial nature of the mammalian heart is still in debate. The present trend of thought is that the ventricles are not a syncytium, anatomically, but are a syncytium, electrically. That is, the ventricles are made up of many small muscle bundles. One or more of these bundles may be innervated by a Purkinje fiber, and the conducting fiber and its muscle bundle(s) constitute a motor unit. Upon stimulation a motor unit will respond according to the all-or-none law.

Summation and incomplete tetanus in the mammalian heart have been observed by many authors. The majority of the observations were recorded during nonphysiological states and led to much criticism. As a result summation and incomplete tetanus have come to be regarded as nonphysiological properties of the mammalian heart.

It is well known that the amplitude of contraction in heart muscle is not directly proportional to the amplitude of the electrical correlate. Few studies have considered the relationship between the electrical event and tension of contraction in the isolated, perfused mammalian heart. A dynamic, spontaneous vasomotion of the coronary arteries may have an effect on the varying amplitude of contraction in the isolated organ.

Most authors have utilized a simple bipolar lead to record the electrical events of the perfused mammalian heart. One author has mentioned electrical vectors in the excised mammalian heart. A good comparison and correlation between the electrocardiographic studies on the perfused mammalian heart and the direct and indirect electrocardiographic studies of previous investigators on the intact animal is lacking.

The primary intent of the present work is to show (a) the effect of coronary ligation, and ablation of anatomical regions, on the electrocardiogram and contraction tension of the excised, perfused rabbit heart; (b) a method of recording simultaneous electrical and mechanical events on the isolated heart; (c) the application of Einthoven's Law to the excised, perfused rabbit heart.

HISTORICAL SURVEY

Isolated Heart Perfusion

Early in the 19th century the French physiologist, Le Gallois (Experiénces sur le principe de la Vie, Paris, D'Hautel, 1812) prophesied that in the future man would be capable of extracting body organs, in toto, and maintain the life and function of those organs by circulating blood or artificial blood-like fluids through their interiors by way of the vessel networks (cited by Carrel & Lindbergh, 1938).

The mammalian heart was first isolated and perfused with blood in 1881 by Henry Newell Martin of Johns Hopkins (cited by Markowitz, 1959; and by Hoerr and Osol, 1956). Langendorff (1895) improved the perfusion technique by showing that a reverse perfusion in the aorta would maintain the heart adequately for cardiac studies. Locke and Rosenheim (1907) used the analytical blood studies of Abderhalden (1899) to prepare an isotonic solution containing the major salts of rabbit blood. They substituted this solution, warmed and well-oxygenated, for blood. Later, they found that the addition of glucose improved the preparation considerably.

Cardiac Interruption and Ablation

According to Ruch and Fulton (1960), in 1628 William Harvey ablated regions of an isolated heart and observed these

excised regions to beat spontaneously. Pieces of atrium had a higher inherent rate than pieces of ventricular muscle. In a study of asymmetrical recovery and T wave configuration on the dog ventricle, Orias et al. (1950) crushed the sinoatrial node to halt its activity. Hoffman and Cranefield (1960) perfused a portion of the intact, isolated rabbit heart, including the sinoatrial and atrioventricular nodes, interatrial septum, and part of the interventricular septum. Using microelectrodes they found that after excision of the sinoatrial node, the new stimulus was always initiated in the His bundle pacemaker and the pathway then traversed by excitation was the same as before.

Coronary Occlusion

Late in the 17th century, P. Chirac (De Motu Cordis, Adversaria Analytica, 1698) ligated a coronary artery in a dog and observed, soon after, the retarding and cessation of the heart beat. The first controlled coronary ligation study upon heart action began with John E. Ericksen (On the Influence of the Coronary Circulation on the Action of the Heart: The London Medical Gazette, 5:261-564, 1842). Twenty years after Ericksen's work, P. L. Panum (Experimentelle Beiträge zur Lehre von Emboli, Virchow's Archiv, 25:312, 1862) filled coronary arteries of a young dog by injecting from the truncus anonymous a mixture of tallow, wax, oil, and lampblack (cited by Porter, 1893).

Porter (1893) ligated various coronary arteries in dogs under ether anesthesia and studied the comparative survival rates, which he observed to be greatest in the occlusion of the anterior descending branch of the left coronary artery and least in the left circumflex branch. Smith (1918) studied effects of ligating various coronary vessel branches upon the ECG in dogs. He showed the ECG following surgery was highly variable with an increased S-T interval and lower voltage.

Pearcy et al. (1928) ligated coronary arteries of intact dogs and observed ventricular fibrillation after a few minutes in the majority of their experiments. In another study on intact dogs, Manning et al. (1947) observed that mortality due to coronary occlusion could be decreased by injection of ergot drugs or bilateral sympathectomy.

The Cardiac Syncytium

In 1949 Robb reconstructed saggital serial sections of human fetal heart muscle, which had been specifically stained for connective tissue, and observed that the organ was composed of small muscle bundles isolated by connective tissue sheaths. Schaefer (1949) and Rothschuh (1951) confirmed the small unit structure of the heart using very fine microelectrodes and electrocardiographic techniques. The unit size established by these methods was set at 1 to 2

millimeters diameter. Later, Kisch (1951) and Sjostrand (1958) reported that in their electron microscope photographs there was no syncytial connection of muscle fibrils.

Unit structure, as revealed by recent research, provides an anatomical explanation for the observations of Lewis (1925), in which he demonstrated that a premature beat did not pass along the surface of the heart, but penetrated to Purkinje tissue and later reached a distant surface electrode. Further evidence for lack of continuous passage of excitation along a parallel fibered surface was obtained by Katz and Feil (1923), Wiggers (1938), and Harris (1941). Their work suggests that a connective tissue sheath insulates each unit so that the activation of one can arouse another only through retrograde involvement of conducting tissue and subsequent peripheral spread over this tissue to other muscle islands.

Cardwell and Abramson (1934) described myocardial Purkinje fibers extending from the Purkinje system as far as the epicardial surface of the heart. They found fibers in the septum connecting the subendocardial system of the right ventricle with the left. Yet Robb and Robb (1936) showed no communication existed between the two systems. Abramson and Jochim (1937) found that the wave of excitation follows the Purkinje network and does not travel to the muscle itself for conduction.

Summation and Incomplete Tetanus

Between 1905 and 1920 six authors, Rohde (1905), Carlson (1906), Schultz (1906), Danielewsky (1906), Mines (1913), and Burridge (1920), reported summation in heart muscle. All of the authors utilized anesthetics, poisons, or extreme concentrations of salts to obtain their results.

In 1951 Dipalma and Mascatello, using a cat papillary muscle preparation, reported summation and incomplete tetanus at subphysiological temperatures and occasional delayed summation at higher temperatures (36°C.). Buchbinder and Katz (1949), studying intraventricular pressure curves, obtained records resembling summation curves in skeletal muscle. Finally, Robb (1952) perfused mammalian hearts which had empty chambers and obtained summation and incomplete tetanus at extreme temperatures in spontaneously beating hearts and in quiescent hearts, which were activated with stimulating electrodes.

Action Potential and Contraction

Wiggers (1938) showed that cardiac muscle contraction may be attenuated without a decrease in the action potential. In this respect, the action potential of cardiac muscle is not proportional to contraction force. Robb (1952) used direct bipolar leads and a force gauge in a study on the isolated,

perfused heart and observed the action potential was not proportional to contraction tension.

Electrocardiography

In an electrocardiograph study, Luisada, Weiss, and Hautman (1944) found the heart rate of the intact rabbit to be 200-220. The P wave was upright in all cases and 0.04 sec. in duration. The P-R interval was 0.06-0.07 sec. and the QRS complex lasted for 0.03 sec. Because of the rapid heart rate, the end of the T wave was followed immediately by the P wave of the succeeding contraction.

In intact rabbits, according to Lepeschkin (1951), the P wave is low or negative in lead I, but always positive in leads II and III. The duration of the P wave was 0.03-0.04 sec. The P-R interval was 0.05-0.10 sec. The QRS complex lasted 0.015-0.04 sec. with the Q-T interval being 0.12 sec. at a heart rate of 250. He further noted that the QRS vector of the excised rabbit heart rotated to the right.

By direct electrocardiography on the rabbit, Kisch, Graedel, and Borchardt (1952) found the P wave upright in all leads. The average heart rate was 130 and the average P-Q interval lasted 0.084 sec. The average QRS complex duration was 0.043 seconds and the average Q-T interval was 0.272 seconds. In the intact domestic rabbit, Spector (1956) shows

the normal P wave duration to be 0.04 sec., the P-R interval 0.06 sec., the QRS complex 0.03 sec. and the Q-T interval 0.28-0.36 sec. The average heart rate was 205.

In recording action potentials of myocardium, Hoffman and Cranefield (1960) showed the action potential amplitude to vary inversely with the size of the needle electrode, which may vary from one investigator to another. Dudel and Trautwein (1954), using ultramicroelectrodes, obtained an action potential of 28 mv. from cat papillary muscles. West (1955) showed the average action potential of rabbit heart muscle was 14 mv. Pae de Carvalho et al. (1959) observed the average action potential in rabbit myocardium was 18 mv.

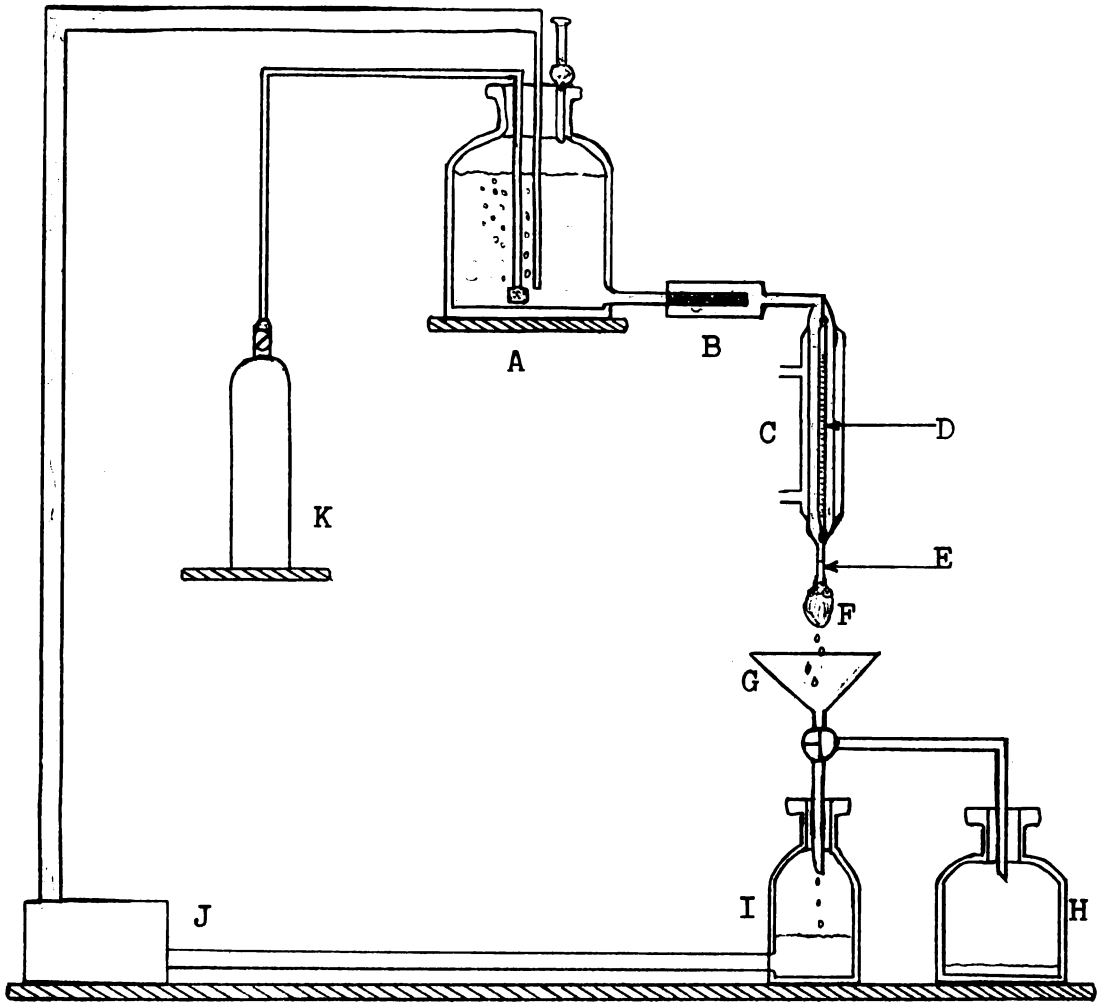
PROCEDURE AND MATERIALS

Perfusion Apparatus

A perfusion apparatus was constructed employing the basic techniques of Langendorff (1895), Locke (1907), and Anderson (1948). As shown in figure 1 a two-liter Pyrex[1] (A) with a bottom spout was the main perfusion bottle. A three-hole rubber stopper served as partial support for (1) a section of glass tubing, which extended to the bottom of the bottle with an air stone at its tip, connected to an oxygen tank (K) by rubber tubing, (2) a section of glass tubing from the circulating pump which extended to the bottom of the perfusion bottle, and (3) a gas filter filled with soda lime.[2]

The bottom spout of the perfusion bottle (A) was connected to a large, stainless steel, wire screen filter (B) containing forty wires to a centimeter. All fluid interconnections were made with Tygon[3] tubing.

The filter (B) was connected to the main perfusion column, a water condenser (C). The water jacket connections of the Pyrex condenser were connected to a water source, for temperature regulation, and a drain. A centigrade thermometer (D) was suspended by a silver wire in the perfusing column with its mercury tip at the lower end of the condenser. Perfusion fluid temperatures were read directly through the walls



A - Main perfusion bottle
B - Perfusate screen filter
C - Water condenser
D - Centigrade thermometer
E - Cannula
F - Heart
G - Funnel
H - Waste bottle
I - Used perfusate bottle
J - Sigmamotor pump (Model T-6)
K-- Oxygen pump

Fig. 1 Perfusion Apparatus

of the condenser. A glass cannula (E) connected the condenser with the aorta of the heart (F).

Directly below the heart was a Pyrex funnel (G) with a cone base diameter of ten inches. At the spout of the funnel was a three-way valve, which served to direct the perfusate into (1) a used perfusate bottle (I) or (2) a waste bottle (H). The used perfusate bottle (I) was connected by its bottom spout to a Sigmamotor pump[4] (J) (Model T-6). The Sigmamotor pump was connected to a short section of glass tubing which passed through the rubber stopper of the main perfusion bottle (A) and extended to the bottom of the bottle.

Perfusion Fluid

The following perfusion fluid of Locke and Rosenheim (1907) was employed in all experiments:

NaCl	9.000 gm.
KCl	0.420 gm.
$NaHCO_3$	0.200 gm.
$CaCl_2$	0.240 gm.
Glucose	1.000 gm.
H_2O (distilled) q.s. . . .	1000.00 cc.

Robb (1953, 1957) suggests that since the essential B complex vitamins are water-soluble, they may tend to wash out during the perfusion. To avoid possible deficiencies, ABDEC[5]

vitamin complex, 0.3 cc. per liter, was added to the perfusate. One liter of the perfusing fluid contains the following concentrations of the vitamins:

Vitamin A (0.75 mg.)	2500 units
Vitamin B_1 (thiamine hydrochloride)	0.5 mg.
Vitamin B_2 (riboflavin)	0.6 mg.
Vitamin B_6 (pyridoxine hydrochloride)	0.5 mg.
Vitamin C (ascorbic acid)	25.0 mg.
Vitamin D (viosterol), 12.5 mcg.	500 units
Nicotinamide	5.0 mg.
Pantothenic acid (as the sodium salt)	2.5 mg.

The perfusion fluid was placed in the main perfusion bottle, condenser, and three porcelain dishes. The fluid was circulated in the apparatus for fifteen minutes to ensure oxygen saturation and temperature adjustment to 37°C. The flow was about 25 cc. per minute approximating the average coronary output of the perfused rabbit heart. According to Locke (1907) the optimum perfusion pressure is 40 cm. of water.

Perfusion

Hearts from 20 New Zealand white rabbits, Lepus cuniculus (Palmer, 1949), were perfused. Each animal was rendered insensible with a blow retrocranially. Using a sharp surgical knife, a single incision along the entire side of the sternum

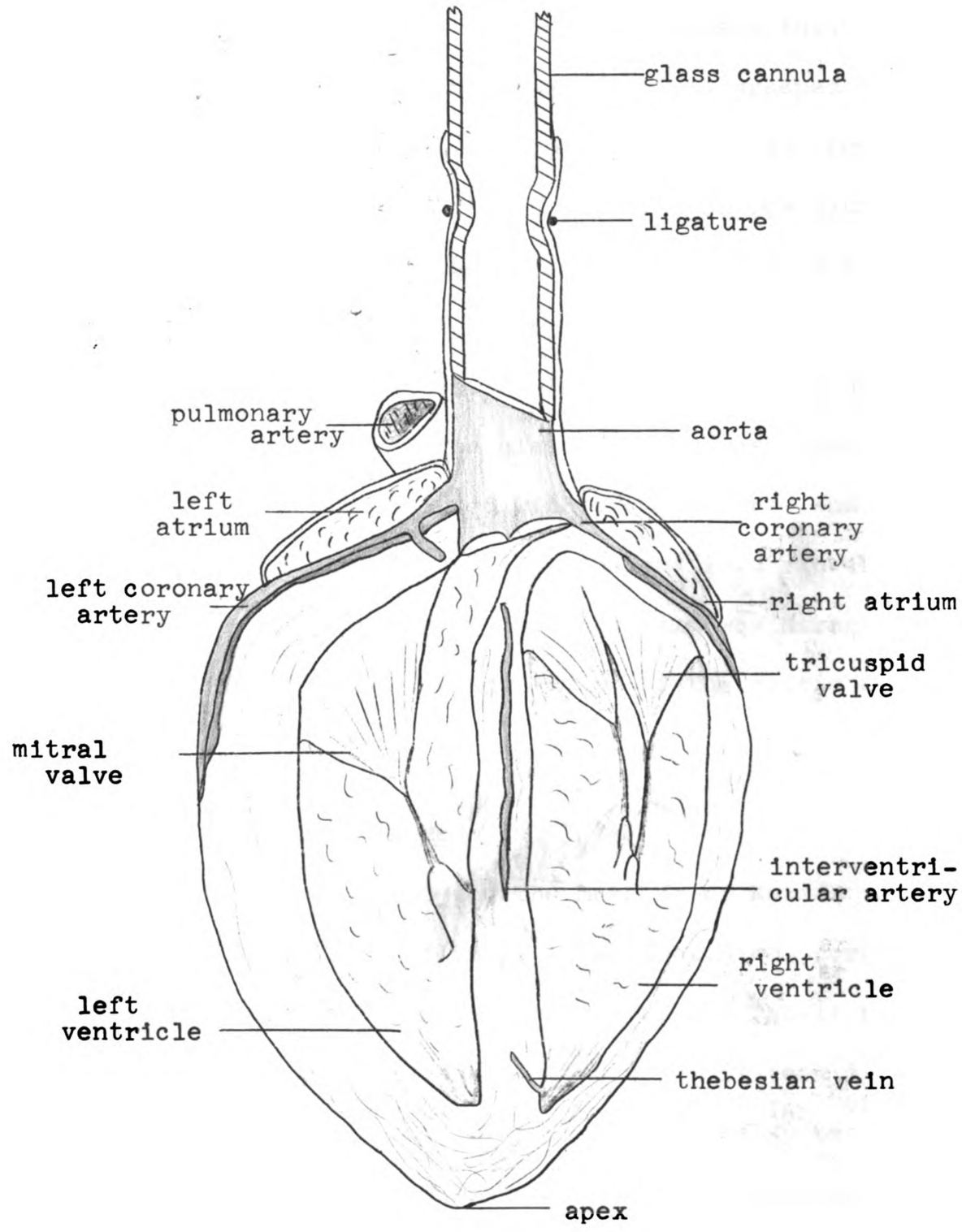


Fig. 2 **The Circulation of the Perfused Heart**

through the costal cartilage of the ribs exposed fully the entire pleural cavity. The beating heart was grasped between the fingers, retracted from its base, and cut away from the adjoining vessels. After slitting open the pericardium of the heart, the heart was rinsed through three dishes of the perfusing fluid, while gently being squeezed to force out the blood and prevent coagulation. A ligature was slipped over the isolated aortic stub. The glass cannula was inserted into the lumen of the aorta, secured with the ligature, and mounted in the perfusion apparatus. The perfusion fluid flowed from the condenser through the aortic cannula and was directed into the coronary arteries by the apposition of the aortic semilunar valves.

Coronary Arterial Network Model

Combining and modifying the methods of Kazzaz (1950), Tucker (1957), and Bilbey (1960), three anatomical corrosion models of the coronary arterial network of the rabbit heart were prepared. The hearts were perfused for fifteen minutes following a normal perfusion procedure. Ren epoxy resin[8] was mixed with its hardener and placed in a 50 cc. syringe. Another 50 cc. syringe was loaded with ethanol. After removing the heart from the perfusion apparatus and connecting the ethanol syringe to the cannula, the alcohol was forced through the vessel network to rinse out completely all perfusion fluid.

Fig. 3. Model of the Coronary Arterial Circulation in the Rabbit Heart--Ventral View (4X)

At this point ligatures were applied to all remaining open vessels. After dissembling the first syringe and attaching the second, resin was forced into the aorta by a strong, constant pressure on the plunger. Eventually, resin filled the coronary arteries, left ventricle, and left atrium. A ligature was applied to the aorta and the cannula withdrawn.

After allowing the resin to harden for twenty-four hours, the hearts were floated in a sulfuric acid-water mixture of a five to nine ratio for seventy-two hours. Following the digestion period, the corrosion specimens were rinsed for twenty-four hours in running water and allowed to air dry. The dried models were painted with enamel.

Because the more viscous resin was employed, filling of the very fine ramifications of the coronary vessel bed did not occur. This resin, however, did provide a sturdy, well-defined model of the desired major vessel network.

As shown in figure 3 the coronary arteries of the corrosion model envelope the case of the left ventricle. At the top of the model the right coronary artery emerges left from the aortic stub. From the right of the aortic stub, the larger left coronary artery arises. Where it turns posteriorly, the left coronary artery gives off a large interventricular branch, which descends left and into the interventricular septum. The major branch of the left coronary artery continues

descending around the heart posteriorly, giving off other large branches (Johnston, Davies, and Davies, 1958).

Recording

A four-channel Sanborn Poly-Viso recorder[6] (Model 67-1200) was used in the studies. Three channels were used for direct electrocardiography, while the fourth channel was a carrier amplifier for a force gauge.

Three leads recorded the action potential (ECG) of the perfused heart. The silver needle electrodes were inserted directly into the epicardium (figures 4 and 5) at the lateral wall of the left ventricle (LA) next to the left atrium, the lateral wall of the right ventricle (RA) next to the right atrium, and the apex (LL), respectively. A suture was placed through the apex and allowed to hang with both ends free. The ends of the suture were tied together, looped under a pully, and run laterally to a Statham force gauge[7] (Model GI-32.450). This force gauge has a maximum load capacity of almost 1 kg. and a sensitivity of a few milligrams.

The calibration of the electrocardiogram was 1 mv. per mm. The force gauge was calibrated at 1 gm. per 1 mm. by adding weights directly to a short loop of thread passed over the pulley. Paper speed of the recorder was 25 mm./sec.

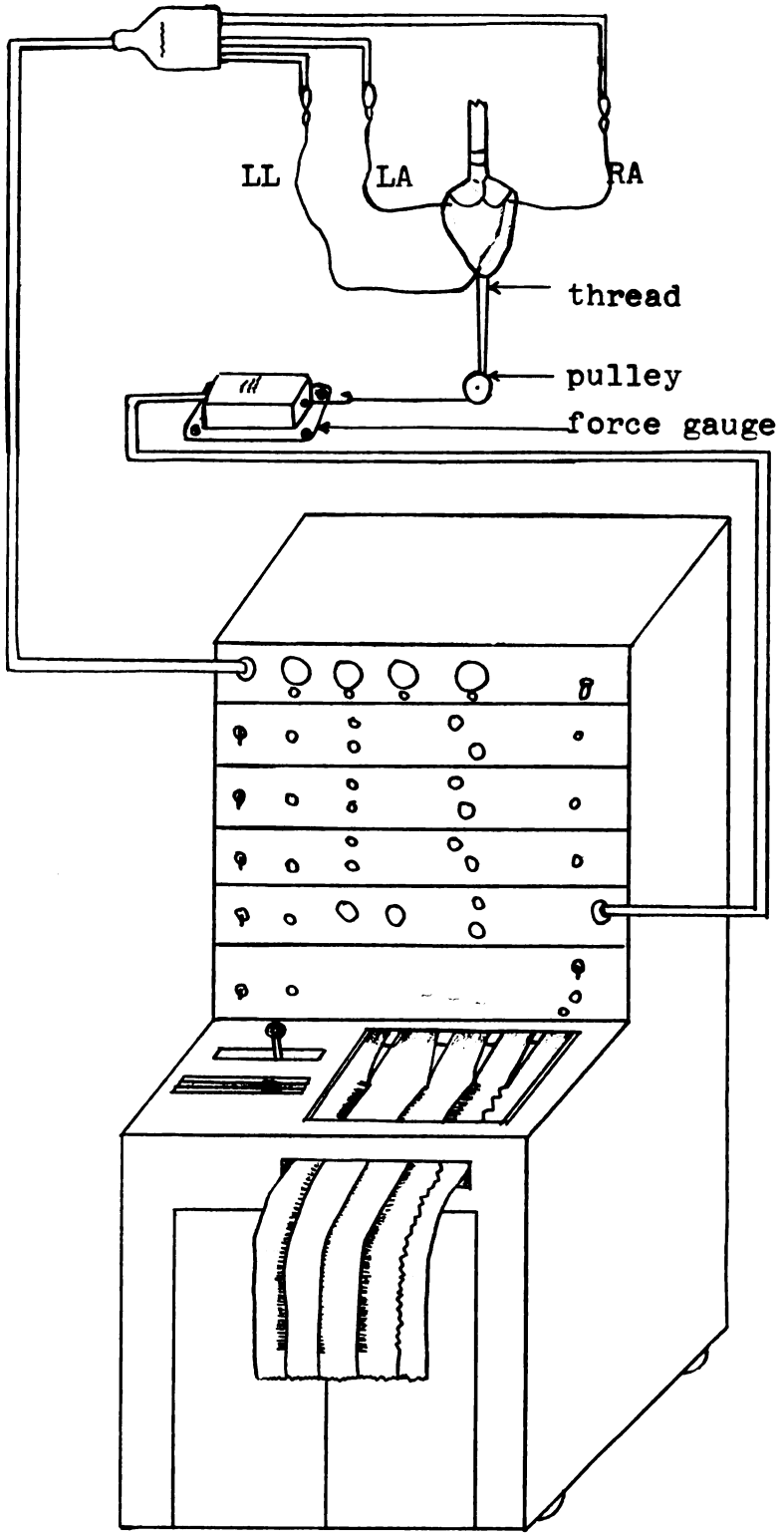


Fig. 4 Recording Apparatus

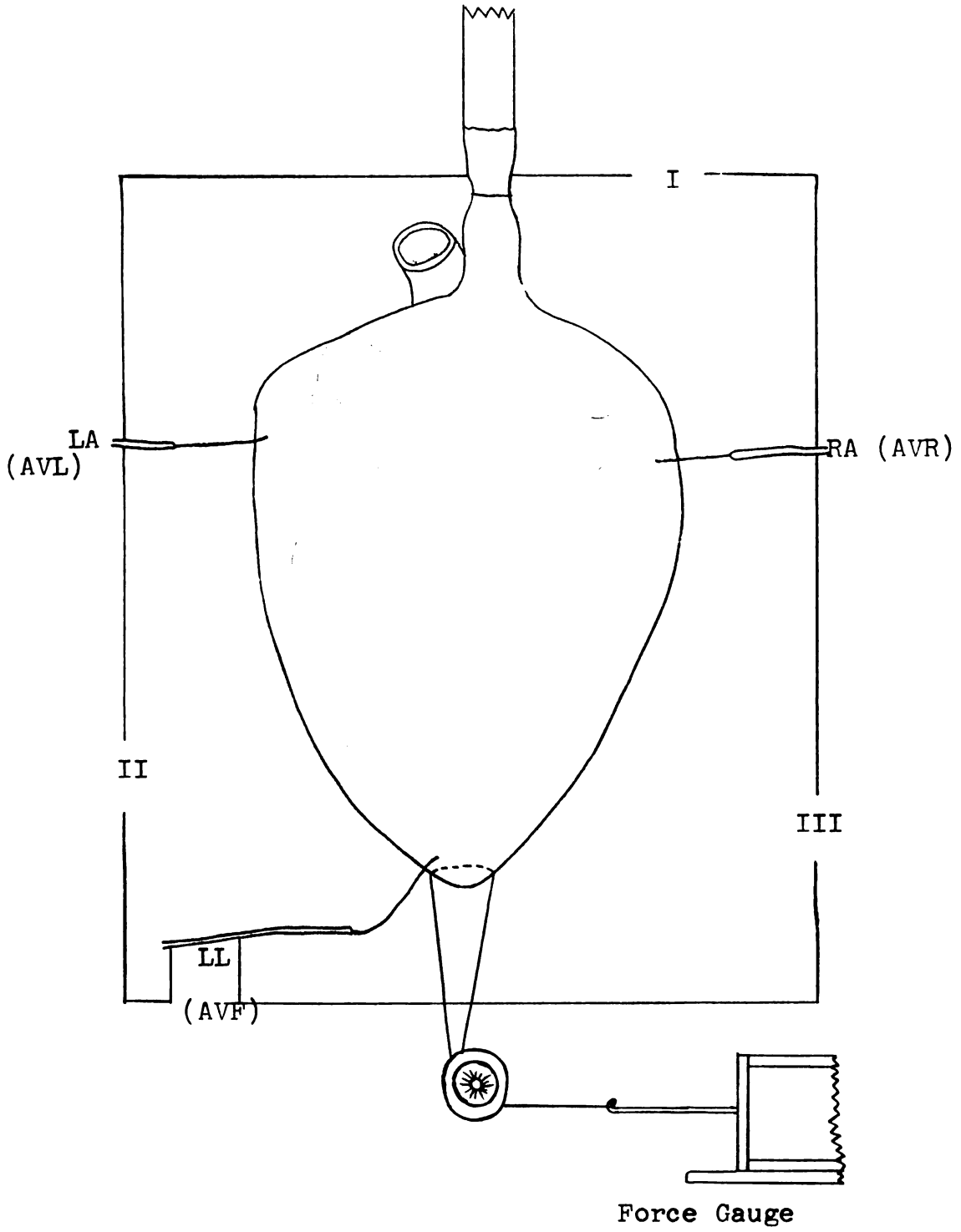


Fig. 5 Placement of Recording leads on the Heart

Ablation

All ablation procedures were done with forceps and scissors. In the first group the right atrium, left atrium, lateral wall of the right ventricle, and lateral wall of the left ventricle were removed in order. In the second group the left atrium, right atrium, lateral wall of the left ventricle, and lateral wall of the right ventricle were removed in order. Ligatures were applied to the coronary arteries in order of their incision.

Coronary Insufficiency

Ligatures on the coronary arteries were made with light weight thread following the pattern of the plastic corrosion model. Coronary vessels of all hearts in group one were ligated first on the right and later on the left. In the second group the vessels were ligated on the left and later on the right. The ligation of the left coronary artery was made below the ventral interventricular artery.

Fibrillation

As shown in figure 6, fibrillations of the perfused heart are readily correctable. Using a defibrillator set at an optimum of 20 volts, the plate electrodes were placed on opposite sides of the heart. The switch was thrown on and off as rapidly as possible. There was usually a pause of several seconds before the heart recovered and continued its rhythmic contractions.

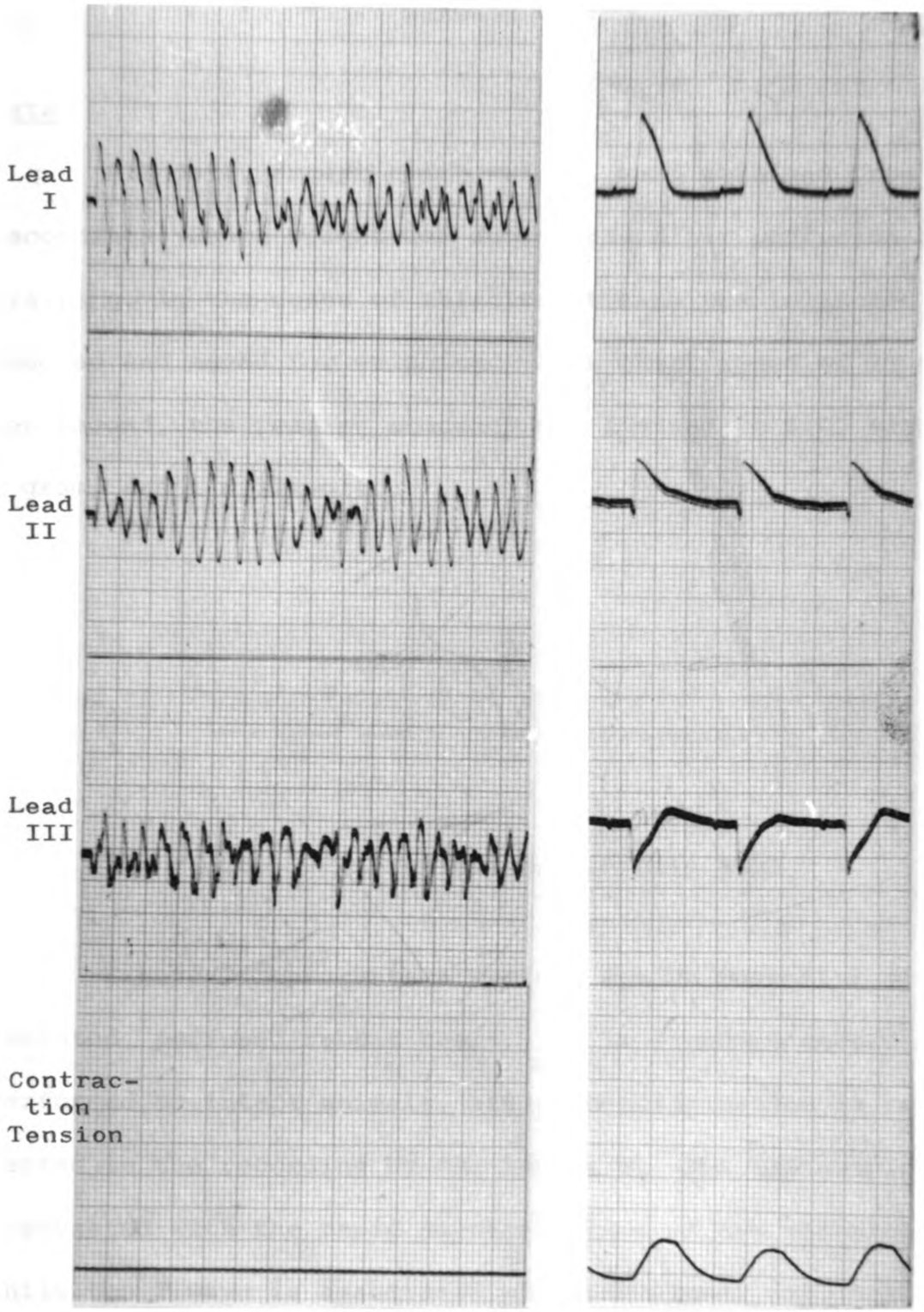


Figure 6. A typical record of fibrillation and recovery showing from top to bottom, lead I, II, III, and contraction tension. Note that no tension recording is obtained in the fibrillating isolated heart.

RESULTS

Data

All data, except heart weight, were obtained from the recordings. Heart weight was determined after perfusion and draining. In the cases of ablation, tissue was collected as removed and saved for weighing. At a chart speed of 25 mm. per second, the reading accuracy was limited to 0.02 seconds, 1 gram, and 1 millivolt.

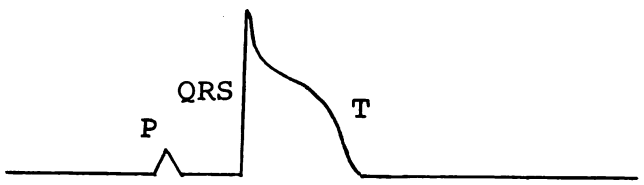


Figure 7 A Typical Action Potential

Figure 7 represents a typical action potential of the isolated, perfused rabbit heart. As in standard recordings performed on intact animals, atrial depolarization is represented in the recording by the letter P. The QRS complex is associated with the rapid depolarization of the ventricles, while the T wave is associated with the slower repolarization of the ventricles.

Statistics

The sample means of the controls and experimentals were compared using the small sample method for fewer than 30 observations. The unbiased estimate of the variance of the hypothetical common population is computed:

$$s_x^2 = \frac{\Sigma x_1^2 - \frac{(\Sigma x_1)^2}{n_1} + \Sigma x_2^2 - \frac{(\Sigma x_2)^2}{n_2}}{n_1 + n_2 - 2}.$$

Then, an unbiased estimate of the variance of the difference between the two sample means is computed:

$$s^2_{x_1 - x_2} = s_x^2 \left(\frac{1}{n_1} + \frac{1}{n_2}\right).$$

The formula,

$$t = \frac{\bar{x}_1 - \bar{x}_2}{\sqrt{s_x^2 \left(\frac{1}{n_1} + \frac{1}{n_2}\right)}}$$

follows the t distribution with $n_1 + n_2 - 2$ degrees of freedom.

TABLE I.

SYMBOLS

Weight	- Weight of the entire heart in grams
Rate	- Number of beats per minute
P-Q	- Time duration between beginning of P wave and beginning of Q wave in seconds
QRS	- Time duration of QRS complex in seconds
R-T	- Time duration between QRS complex and end of T wave in seconds
Q-C	- Time interval between beginning of QRS complex and beginning of ventricular contraction in seconds ("latent" period)
P-C	- Time interval between beginning of P wave and beginning of ventricular contraction in seconds
C.T.	- Ventricular contraction tension in grams
Lead I	- Average of QRS complex in millivolts
Lead II	- Average of QRS complex in millivolts
Lead III	- Average of QRS complex in millivolts
M.E.A.	- Mean electrical axis in degrees
Sys.	- Time duration of mechanical systole in seconds
Dias.	- Time duration of mechanical diastole in seconds
Dias.-Sys.	- Time duration between end of mechanical diastole and beginning of mechanical systole in seconds
T.C.D.	- Total cycle duration in seconds
AVR	- Average of QRS complex in millivolts
AVL	- Average of QRS complex in millivolts
AVF	- Average of QRS complex in millivolts

TABLE 2. INTACT HEART

	Weight	Rate	P-Q	QRS	R-T	Q-C	P-C	C.T.
1	8.1	100	.06	.02	.26	.06	.12	20
2	7.7	100	.08	.02	.22	.06	.14	16
3	12.2	136	.08	.02	.14	.06	.14	22
4	10.5	130	.08	.02	.22	.06	.14	6
5	11.1	88	.08	.02	.16	.06	.14	6
6	8.5	120	.06	.02	.12	.04	.12	14
7	6.0	83	.08	.04	.28	.06	.14	16
8	8.2	107	.06	.02	.16	.02	.08	31
9	8.1	120	.08	.04	.14	.04	.12	24
10	7.3	72	.08	.02	.16	.02	.10	8
11	7.1	167	.06	.02	.12	.02	.08	16
12	7.3	150	.06	.03	.12	.04	.10	20
13	6.8	187	.09	.02	.12	.04	.13	10
14	7.8	107	.06	.02	.20	.04	.10	15
15	9.7	100	.09	.03	.16	.06	.15	6
16	7.7	187	.06	.03	.12	.04	.10	21
17	9.0	94	.12	.04	.20	.08	.20	12
18	8.2	100	.08	.03	.20	.04	.12	16
19	9.0	79	.08	.04	.16	.06	.14	25
20	7.0	136	.08	.03	.16	.04	.12	20
Ave.	8.36	118	.076	.027	.171	.047	.124	16.2

TABLE 2 (continued) INTACT HEART

	Lead I	Lead II	Lead III	M.E.A.	AVR	AVL	AVF
1	5	-5	- 7	-46	-	-	-
2	5	-5	-11	-62	-	-	-
3	6	1	- 5	-20	-	-	-
4	1	7	5	80	-3	-3	6
5	-4	3	5	138	1	-4	4
6	3	5	7	73	1	-3	5
7	-3	-2	3	153	3	-4	-1
8	3	2	- 1	9	-1	0	1
9	-1	-2	2	120	-1	-3	9
10	-2	6	7	105	-3	-5	8
11	-2	0	2	152	2	-1	-1
12	5	-1	- 4	-15	1	-1	1
13	-3	-1	3	152	2	-2	1
14	-3	1	5	138	1	-4	3
15	-4	7	7	123	-1	-5	6
16	-4	-3	1	207	4	-2	-2
17	12	4	- 6	4	-6	9	-4
18	8	-5	-11	-43	0	9	-8
19	3	4	1	44	-3	-1	3
20	11	2	- 9	57	-4	8	-8
Ave.	1.8	0.9	-0.3	68.5	-.41	-.070	1.59

TABLE 2 (continued) INTACT HEART

	Sys.	Dias.	Dias.-Sys.	T.C.D.
1	.20	.28	.12	.60
2	.20	.32	.08	.60
3	.20	.22	.04	.46
4	.20	.24	.02	.46
5	.20	.28	.20	.68
6	.12	.16	.12	.40
7	.24	.24	.24	.72
8	.20	.28	.08	.56
9	.20	.24	.06	.50
10	.20	.20	.44	.84
11	.16	.16	.04	.36
12	.12	.24	.04	.40
13	.12	.18	.02	.32
14	.12	.24	.20	.56
15	.12	.28	.20	.60
16	.16	.12	.04	.32
17	.20	.40	.04	.64
18	.20	.36	.04	.60
19	.16	.36	.24	.76
20	.16	.12	.16	.44
Ave.	.174	.246	.121	.54

TABLE 3. HEART WITHOUT RIGHT ATRIUM

	Weight	Rate	P-Q	QRS	R-T	Q-C	P-C	C.T.
1	8.1	100	-	.02	.24	.08	-	14
2	7.7	54	-	.04	.16	.08	-	14
3	12.2	125	-	.02	.16	.06	-	16
4	10.5	40	-	.04	.16	.08	-	6
5	11.1	100	-	.04	.20	.08	-	2
Ave.	9.9	83	-	.032	.184	.076	-	10.4

	Lead I	Lead II	Lead III	M.E.A.	AVR	AVL	AVF
1	0	-3	- 3	-60	-	-	-
2	12	9	-11	-27	-	-	-
3	4	5	3	55	-	-	-
4	5	4	5	60	-6	5	5
5	-1	6	6	98	1	6	6
Ave.	4	4.2	0	25	-2.5	5.5	5.5

	Sys.	Dias.	Dias.-Sys.	T.D.C.
1	.24	.28	.08	.60
2	.20	.20	.72	1.12
3	.20	.20	.08	.48
4	.20	.24	1.04	1.48
5	.20	.24	.16	.60
Ave.	.208	.252	.416	.856

TABLE 4. HEART WITHOUT LEFT ATRIUM

	Weight	Rate	P-Q	QRS	R-T	Q-C	P-C	C.T.
6	8.5	158	.08	.02	.12	.06	.14	12
7	6.0	94	.08	.04	.16	.06	.14	19
8	8.2	125	.08	.02	.16	.04	.12	26
9	8.1	100	.08	.03	.18	.04	.12	15
10	7.3	68	.08	.02	.12	.04	.12	8
Ave.	7.6	109	.08	.026	.148	.058	.128	16.0

	Lead I	Lead II	Lead III	M.E.A.	AVR	AVL	AVF
6	12	-3	3	110	1	-4	6
7	-5	-2	4	165	3	-4	6
8	-1	2	5	101	0	-2	4
9	-3	4	5	125	1	-2	4
10	-4	6	7	120	-2	-3	6
Ave.	-3.2	2.6	5.8	124	0.6	-3	5.2

	Sys.	Dias.	Dias.-Sys.	T.D.C.
6	.16	.14	.08	.38
7	.28	.16	.20	.64
8	.16	.24	.08	.48
9	.16	.36	.08	.60
10	.20	.24	.44	.88
Ave.	.192	.228	.176	.598

TABLE 5. VENTRICLES ONLY

	Weight	Rate	P-Q	QRS	R-T	Q-C	P-C	C.T.
1	8.1	94	-	.02	.28	.08	-	14
2	7.7	37	-	.04	.20	.08	-	16
3	12.2	125	-	.02	.16	.06	-	16
4	10.5	25	-	.04	.18	.06	-	6
5	11.1	100	-	.04	.22	.08	-	2
6	8.5	68	-	.02	.12	.06	-	12
7	6.0	65	-	.04	.20	.06	-	17
8	8.2	79	-	.02	.16	.04	-	18
9	8.1	68	-	.03	.28	.04	-	18
10	7.3	42	-	.04	.12	.04	-	6
Ave.	8.8	70	-	.031	.192	.06	-	12.5

	Lead I	Lead II	Lead III	M.E.A.	AVR	AVL	AVF
1	-5	-2	4	162	-	-	-
2	11	8	-12	-33	-	-	-
3	6	2	- 5	-27	-	-	-
4	11	4	2	37	-7	6	3
5	1	6	6	82	-4	-4	6
6	-3	-1	2	169	-5	5	5
7	-6	0	6	152	4	-4	1
8	-1	1	3	108	-1	-2	2
9	-3	2	4	120	2	-2	3
10	-3	5	7	112	-1	-4	6
Ave.	0.8	2.5	1.7	88	-1.7	-0.7	3.7

TABLE 5 (continued) VENTRICLES ONLY

	Sys.	Dias.	Dias.-Sys.	T.C.D.
1	.24	.20	.08	.52
2	.24	.24	.96	1.44
3	.20	.20	.08	.48
4	.20	.28	1.88	2.36
5	.20	.24	.16	.60
6	.16	.12	.60	.88
7	.20	.28	.44	.92
8	.20	.28	.24	.72
9	.24	.40	.24	.88
10	.20	.24	1.00	1.44
Ave.	.208	.248	.568	1.024

TABLE 6. LEFT VENTRICLE ONLY

	Weight	Rate	P-Q	QRS	R-T	Q-C	P-C	C.T.
1	8.1	111	-	.02	.24	.08	-	10
2	7.7	60	-	.02	.20	.06	-	19
3	12.2	63	-	.02	.20	.08	-	10
4	10.5	83	-	.02	.18	.06	-	5
5	11.1	111	-	.02	.20	.08	-	3
Ave.	9.9	86	-	.02	.204	.072	-	9.4

	Lead I	Lead II	Lead III	M.E.A.	AVR	AVL	AVF
1	-12	-8	6	180	-	-	-
2	- 8	5	8	148	-	-	-
3	- 4	-1	4	150	-	-	-
4	- 5	0	5	147	0	-4	4
5	- 7	2	5	167	5	-6	2
Ave.	- 7.2	-0.4	5.6	158	2.5	-5	3

	Sys.	Dias.	Dias.-Sys.	T.C.D.
1	.24	.24	.08	.56
2	.24	.28	.48	1.00
3	.24	.36	.36	.96
4	.20	.24	.28	.72
5	.20	.28	.08	.56
Ave.	.224	.280	.256	.76

TABLE 7. RIGHT VENTRICLE ONLY

	Weight	Rate	P-Q	QRS	R-T	Q-C	P-C	C.T.
6	8.5	71	-	.02	.20	.08	-	4
7	6.0	65	-	.02	.22	.08	-	4
8	8.2	55	-	.02	.22	.06	-	4
9	8.1	40	-	.02	.32	.08	-	7
10	7.3	40	-	.02	.16	.04	-	5
Ave.	7.6	56	-	.02	.224	.068	-	5.6

	Lead I	Lead II	Lead III	M.E.A.	AVR	AVL	AVF
6	5	8	5	60	-5	3	10
7	9	9	-8	-28	-8	7	7
8	4	-2	-8	-60	-1	5	-4
9	6	4	-9	-49	-4	6	-3
10	-1	2	5	101	-2	-4	4
Ave.	4.6	4.2	-3	5	-4	3.4	2.8

	Sys.	Dias.	Dias.-Sys.	T.C.D.
6	.16	.26	.32	.74
7	.20	.40	.32	.92
8	.16	.48	.56	1.20
9	.24	.56	.40	1.20
10	.16	.36	1.00	1.52
Ave.	.184	.432	.52	1.116

TABLE 8. INTERVENTRICULAR SEPTUM ONLY

	Weight	Rate	P-Q	QRS	R-T	Q-C	P-C	C.T.
1	8.1	60	-	.02	.28	.09	-	2
2	7.7	43	-	.02	.24	.06	-	14
3	12.2	60	-	.02	.28	.08	-	7
4	10.5	67	-	.02	.20	.08	-	4
5	11.1	94	-	.02	.16	.08	-	2
6	8.5	48	-	.02	.24	.08	-	3
7	6.0	30	-	.04	.32	.16	-	3
8	8.2	27	-	.04	.36	.12	-	2
9	8.1	24	-	.02	.40	.10	-	4
10	7.3	100	-	.02	.24	.06	-	5
Ave.	8.8	55	-	.024	.276	.09	-	4.6

	Lead I	Lead II	Lead III	M.E.A.	AVR	AVL	AVF
1	12	7	-5	5	-	-	-
2	0	3	0	0	-	-	-
3	6	9	3	50	-	-	-
4	5	8	3	52	-7	1	5
5	-1	-1	0	180	3	2	1
6	-3	-1	2	168	1	-4	2
7	4	7	8	70	-5	-2	5
8	3	1	-4	-47	-2	3	-2
9	2	5	9	80	-2	-3	6
10	-2	-2	0	180	2	1	-1
Ave.	2.6	3.6	1.6	74	-1.4	-2.7	2.3

TABLE 8 (continued) INTERVENTRICULAR SEPTUM ONLY

	Sys.	Dias.	Dias.-Sys.	T.C.D.
1	.28	.24	.48	1.00
2	.32	.40	.68	1.40
3	.28	.44	.28	1.00
4	.18	.40	.32	.90
5	.12	.32	.20	.64
6	.24	.60	.40	1.24
7	.92	.52	.56	2.00
8	.32	1.08	.88	2.28
9	.36	1.40	.72	2.48
10	.16	.28	.16	.60
Ave.	.318	.568	.468	1.354

TABLE 9. WITH RIGHT CORONARY LIGATED

	Weight	Rate	P-Q	QRS	R-T	Q-C	P-C	C.T.
11	7.1	115	.06	.02	.20	.02	.08	18
12	7.3	136	.12	.02	.16	.04	.16	16
13	6.8	83	.08	.02	.16	.06	.14	13
14	7.8	88	.09	.04	.24	.04	.13	10
15	9.7	46	.18	.02	.20	.06	.24	4
Ave.	7.7	94	.106	.024	.192	.044	.120	12.2

	Lead I	Lead II	Lead III	M.E.A.	AVR	AVL	AVF
11	-2	-1	1	187	2	-1	-1
12	-2	-1	1	187	1	-1	1
13	-2	-1	1	187	1	-1	-1
14	-4	-1	5	148	2	-3	3
15	-3	6	7	114	-2	-4	5
Ave.	-2.6	0.4	3	165	0.8	-2	1.8

	Sys.	Dias.	Dias.-Sys.	T.C.D.
11	.20	.20	.12	.52
12	.20	.20	.04	.44
13	.16	.20	.36	.72
14	.18	.38	.12	.68
15	.20	.24	.88	1.32
Ave.	.188	.244	.304	.736

TABLE 10. WITH LEFT CORONARY LIGATED

	Weight	Rate	P-Q	QRS	R-T	Q-C	P-C	C.T.
16	7.7	107	.04	.02	.18	.06	.10	10
17	9.0	38	.08	.06	.28	.06	.14	11
18	8.2	79	.08	.04	.36	.08	.16	8
19	9.0	43	.06	.06	.32	.06	.12	7
20	7.0	136	.08	.04	.24	.06	.14	2
Ave.	8.2	80	.076	.044	.276	.064	.132	7.6

	Lead I	Lead II	Lead III	M.E.A.	AVR	AVL	AVF
16	4	1	-3	-2	-2	4	-1
17	7	8	-2	11	-7	4	4
18	8	4	-3	10	-6	6	2
19	4	2	-2	49	-3	3	-2
20	3	0	-3	-20	-1	3	-1
Ave.	5.2	3	-2.6	9.6	-3.8	4	0.4

	Sys.	Dias.	Dias.-Sys.	T.C.D.
16	.20	.28	.08	.56
17	.32	.84	.40	1.56
18	.20	.52	.04	.76
19	.24	.84	.32	1.40
20	.16	.20	.08	.44
Ave.	.224	.536	.184	.944

TABLE 11. AFTER 5 MINUTES WITH BOTH CORONARIES LIGATED

	Weight	Rate	P-Q	QRS	R-T	Q-C	P-C	C.T.
11	7.1	55	.08	.03	.32	.06	.14	17
12	7.3	94	.16	.04	.26	.08	.24	9
13	6.8	79	.08	.02	.36	.06	.14	13
14	7.8	19	.16	.04	.40	.08	.24	6
15	9.7	16	.20	.04	.28	.08	.28	4
16	7.7	107	.12	.06	.24	.06	.18	12
17	9.0	42	.09	.02	.28	.07	.16	12
18	8.2	27	.09	.04	.36	.09	.18	8
19	9.0	12	.20	.06	.40	.12	.32	6
20	7.0	115	.08	.05	.20	.09	.17	2
Ave.	8.0	57	.126	.040	.310	.079	.205	8.9

	Lead I	Lead II	Lead III	M.E.A.	AVR	AVL	AVF
11	-2	2	4	118	1	-2	3
12	6	1	-5	-18	-3	4	-2
13	3	-2	-1	13	-1	2	-2
14	-2	2	4	118	1	-3	3
15	2	8	6	75	-4	-3	6
16	7	2	-4	1	-4	6	-2
17	10	8	-3	15	-6	7	2
18	6	4	-3	3	-5	4	2
19	4	1	-3	-12	-2	4	-3
20	2	-2	-2	-24	2	1	-1
Ave.	3.6	2.4	-1.0	30	-2.1	2.0	0.6

TABLE 11 (continued) AFTER 5 MINUTES WITH BOTH CORONARIES LIGATED

	Sys.	Dias.	Dias.-Sys.	T.C.D.
11	.28	.64	.16	1.08
12	.24	.32	.08	.64
13	.24	.44	.08	.76
14	.40	1.92	.84	3.16
15	.24	1.08	2.40	3.72
16	.20	.32	.04	.56
17	.28	.72	.42	1.42
18	.40	.92	.84	2.26
19	.52	1.92	2.40	4.84
20	.20	.24	.08	.52
Ave.	.20	.852	.734	1.946

TABLE 12. AFTER 10 MINUTES WITH BOTH CORONARIES LIGATED

	Weight	Rate	P-Q	QRS	R-T	Q-C	P-C	C.T.
11	7.1	45	.08	.03	.36	.04	.12	18
12	7.3	107	.16	.02	.24	.08	.24	6
13	6.8	25	.14	.04	.44	.08	.22	10
14	7.8	16	.16	.04	144	108	.24	4
15	9.7	16	.10	.06	.44	.12	.22	4
16	7.7	10	.08	.02	.24	.06	.14	12
17	9.0	29	.14	.02	.36	.04	.18	15
18	8.2	47	.06	.04	.40	.08	.14	8
19	9.0	10	.20	.06	.40	.12	.32	4
20	7.0	70	.08	.06	.16	.08	.16	0.5
Ave.	8.0	37	.12	.039	.348	.078	.198	8.2

	Lead I	Lead II	Lead III	M.E.A.	AVR	AVL	AVF
11	-2	2	4	118	0	-2	3
12	-3	5	2	171	5	3	-4
13	4	1	-4	-22	-2	3	-1
14	-2	2	4	118	1	-2	2
15	2	7	5	73	-2	-1	5
16	5	2	-3	- 2	-3	4	-1
17	9	6	-3	13	-6	6	1
18	3	4	1	44	-3	2	1
19	4	1	-3	-15	-2	4	-3
20	3	-1	-2	- 7	-2	3	-2
Ave.	2.e	2.9	0.1	49.1	-1.4	2	0.1

TABLE 12 (Continued) AFTER 10 MINUTES WITH BOTH CORONARIES LIGATED

	Sys.	Dias.	Dias.-Sys.	T.C.D.
11	.36	.64	.32	1.32
12	.20	.36	.12	.68
13	.44	1.12	.84	2.40
14	.48	2.38	.84	3.70
15	.44	1.68	1.58	3.70
16	.20	.28	.12	.60
17	.32	1.16	.68	2.16
18	.40	.80	.08	1.28
19	.52	1.92	3.56	6.00
20	.24	.36	.16	.76
Ave.	.36	1.132	.83	2.26

TABLE 13 SUMMARY OF MEANS

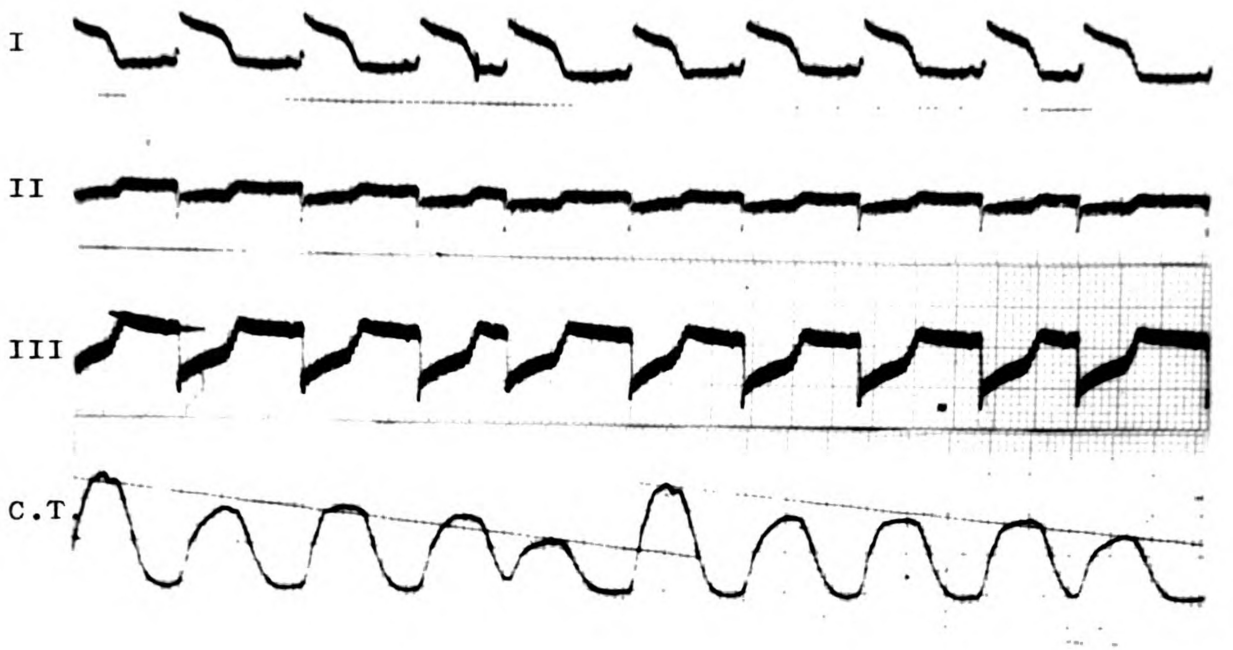
	Experimental Numbers	Rate	P-Q (sec.)	QRS (sec.)	R-T (sec.)
	(1-20)	118	.076	.027	.171
Intact	(1-5)	111	.076	.020	.200
Heart	(6-10)	100	.072	.028	.172
	(11-15)	142	.072	.024	.144
	(16-20)	119	.084	.034	.168
Without Right Atrium	(1-5)	83	-	.032	.184
Without Left Atrium	(6-10)	109	.080	.026	.148
Ventricles					
Only	(1-10)	70	-	.031	.192
	(1-5)	76	-	.032	.208
	(6-10)	64	-	.030	.176
Left Ventricle Only	(1-5)	86	-	.020	.204
Right Ventricle Only	(6-10)	56	-	.020	.224
Septum	(1-10)	55	-	.024	.272
Only	(1-5)	65	-	.020	.232
	(6-10)	46	-	.028	.312
Right Coronary Ligation	(11-15)	94	-	.024	.192
Left Coronary Ligation	(16-20)	80	.076	.044	.276
Both	(11-20)	57	.126	.040	.310
Coronary	(11-15)	53	.136	.034	.324
Ligations at 5 min.	(16-20)	61	.116	.046	.296
Both	(11-20)	37	.120	.039	.348
Coronary	(11-15)	42	.128	.038	.384
Ligations at 10 min.	(16-20)	32	.112	.040	.312

TABLE 13 (continued) SUMMARY OF MEANS

	Experimental Numbers	C.T. (gm.)	Syst. (sec.)	Dias. (sec.)	M.E.A. (deg.)
Intact	(1-20)	16.2	.174	.246	68.5
Heart	(1-5)	14.0	.200	.268	18.0
	(6-10)	18.6	.192	.224	92.0
	(11-15)	13.4	.128	.220	110.0
	(16-20)	18.8	.176	.272	53.8
Without Right Atrium	(1-5)	10.4	.208	.252	25.0
Without Left Atrium	(6-10)	16.0	.192	.228	124.0
Ventricles	(1-10)	12.5	.208	.248	88.2
Only	(1-5)	10.8	.216	.232	44.2
	(6-10)	14.2	.200	.264	132.2
Left Ventricle Only	(1-5)	9.4	.224	.280	158.0
Right Ventricle Only	(6-10)	5.6	.184	.432	5.0
Septum	(1-10)	4.6	.318	.568	73.8
Only	(1-5)	5.8	.236	.360	57.4
	(6-10)	3.4	.400	.776	90.2
Right Coronary Ligature	(11-15)	12.2	.188	.244	165.0
Left Coronary Ligature	(16-20)	7.6	.224	.536	9.6
Both	(11-20)	8.9	.200	.852	28.9
Coronary	(11-15)	9.8	.280	.880	61.2
Ligations at 5 min.	(16-20)	8.0	.320	.824	-3.4
Both	(11-20)	8.2	.360	1.132	49.1
Coronary	(11-15)	8.4	.384	1.360	91.6
Ligations at 10 min.	(16-20)	7.9	.336	.920	6.6

Contraction Recordings

Figures 8 through 17 are representative electrocardiograms and contraction tension records of the isolated, perfused rabbit heart in normal, ablated or anoxic states. The records are grouped in series of four channels, and labeled to the left of the recording. The first channel (top) is lead I or AvR; the second is lead II or AvL; the third is lead III or AvF; and the fourth (bottom) channel is the contraction tension record (C.T.). The larger blocks on the graph paper are 5 mm. square, whereas the smaller blocks are 1 mm. square. Calibration of the graph paper was 1 mv./mm. for the electrocardiograms and 1 gm./mm. for the contraction tension record. The chart speed was 25 mm./sec.



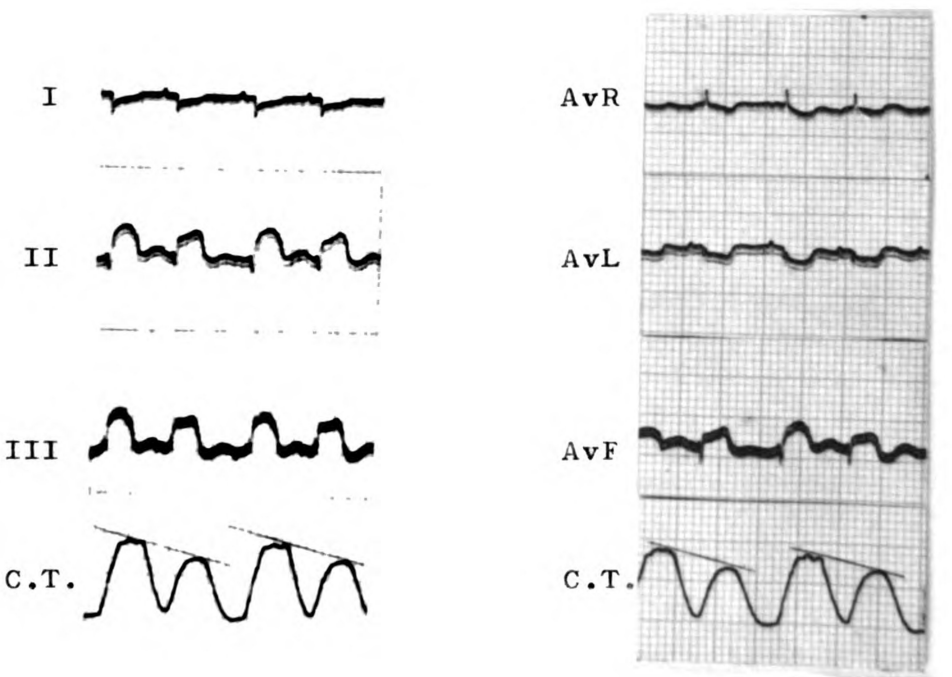
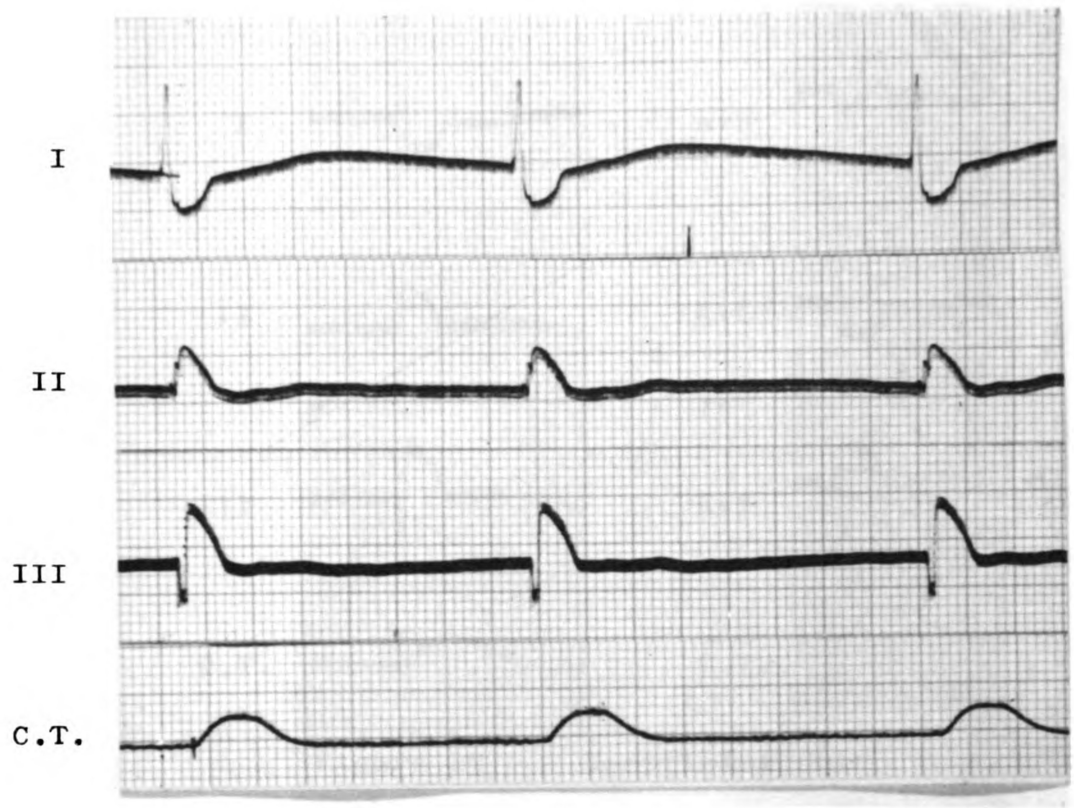


Figure 8 Intact Heart



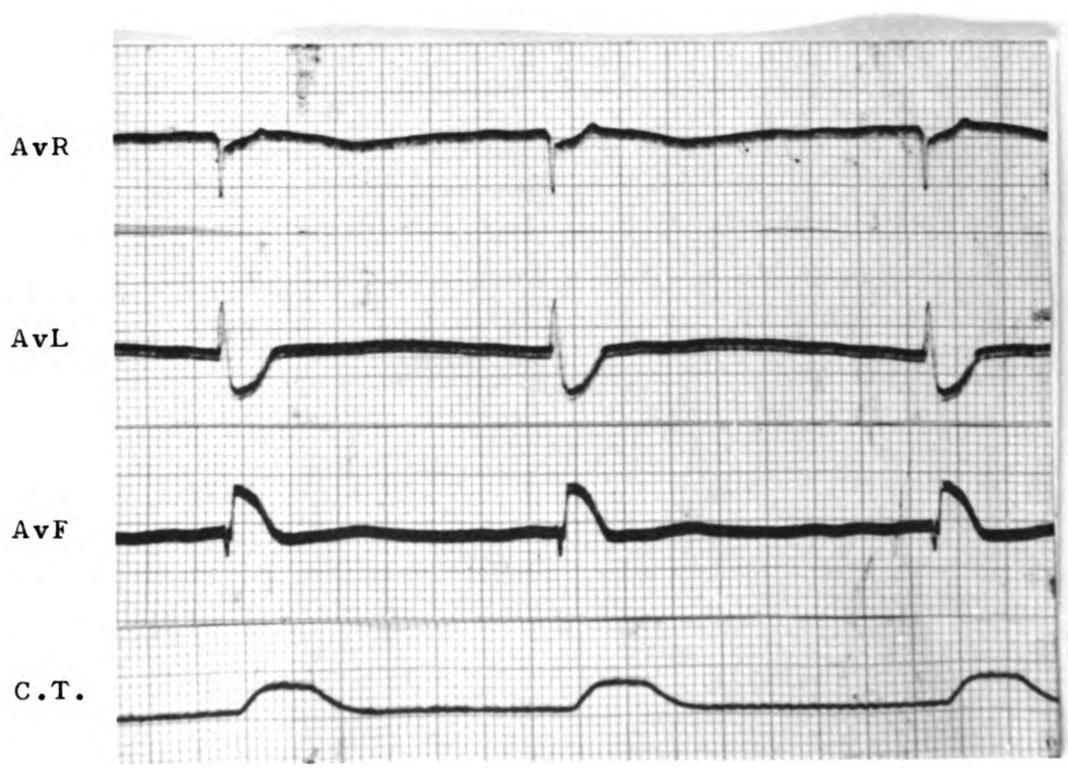


Figure 9 Heart Without Right Atrium

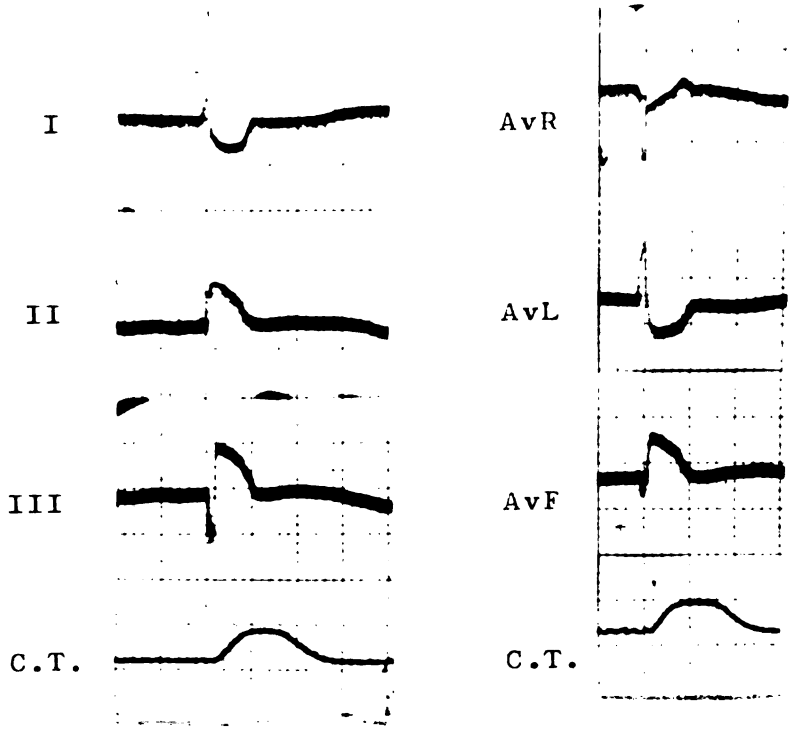


Figure 10 Ventricles Only

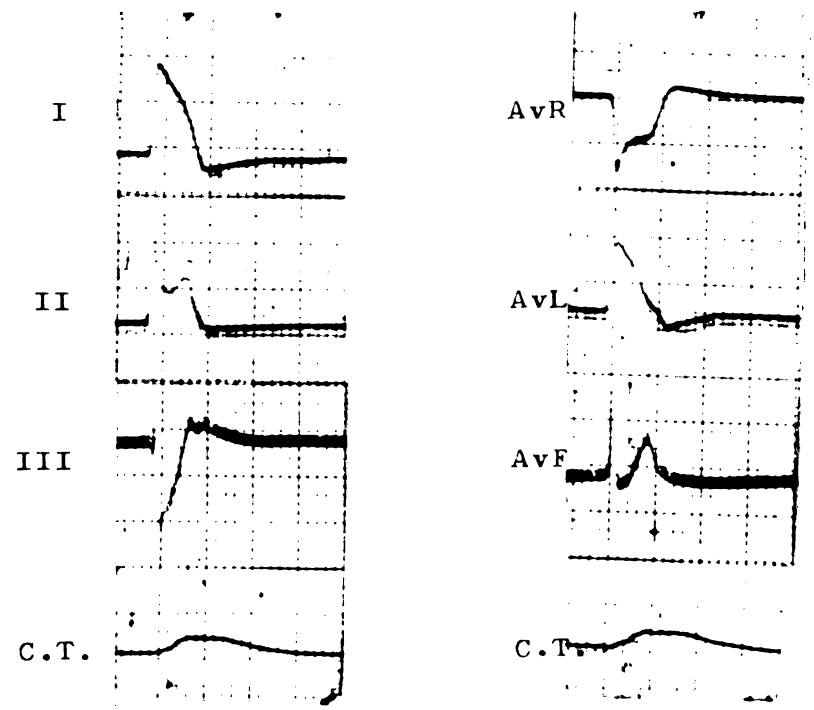


Figure 11 Right Ventricle Only

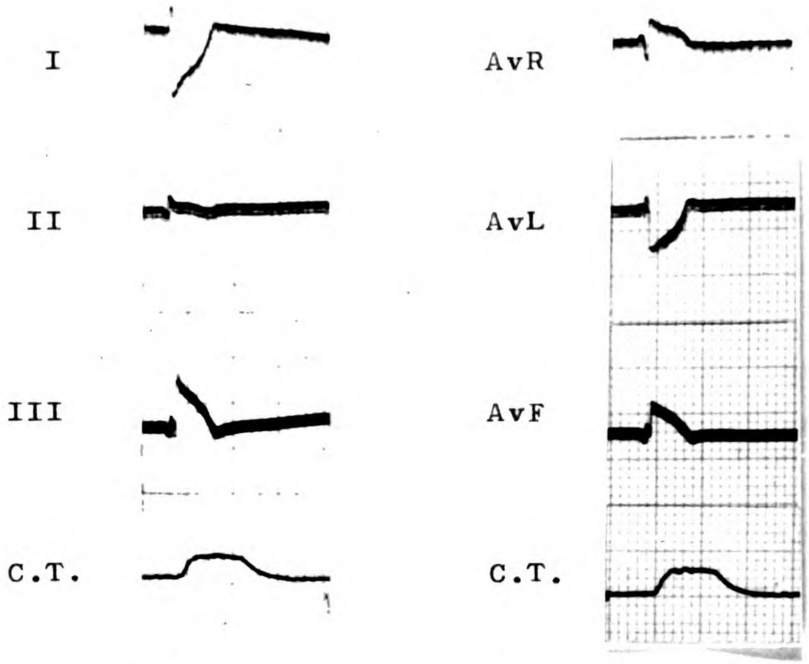


Figure 12 Left Ventricle Only

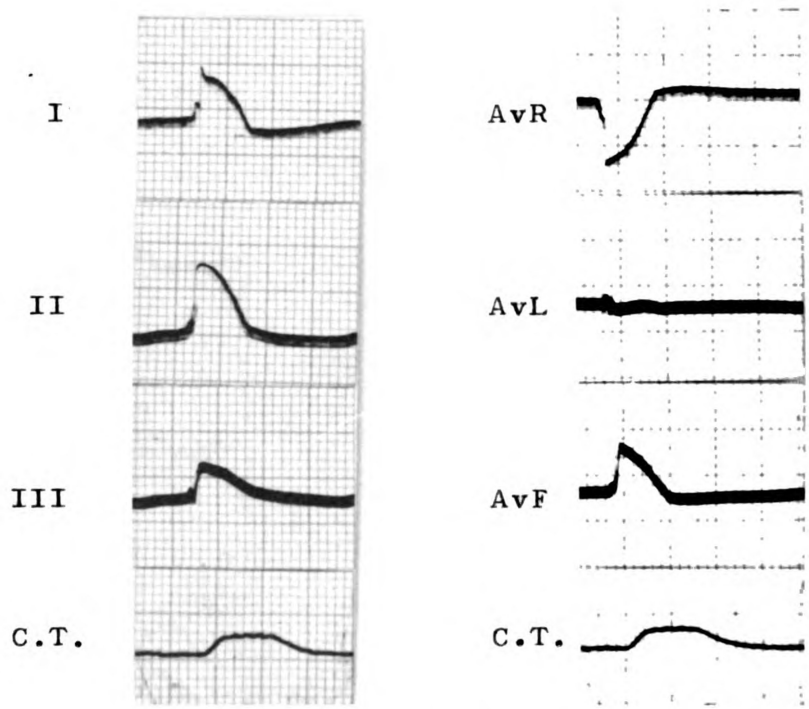


Figure 13 Septum Only

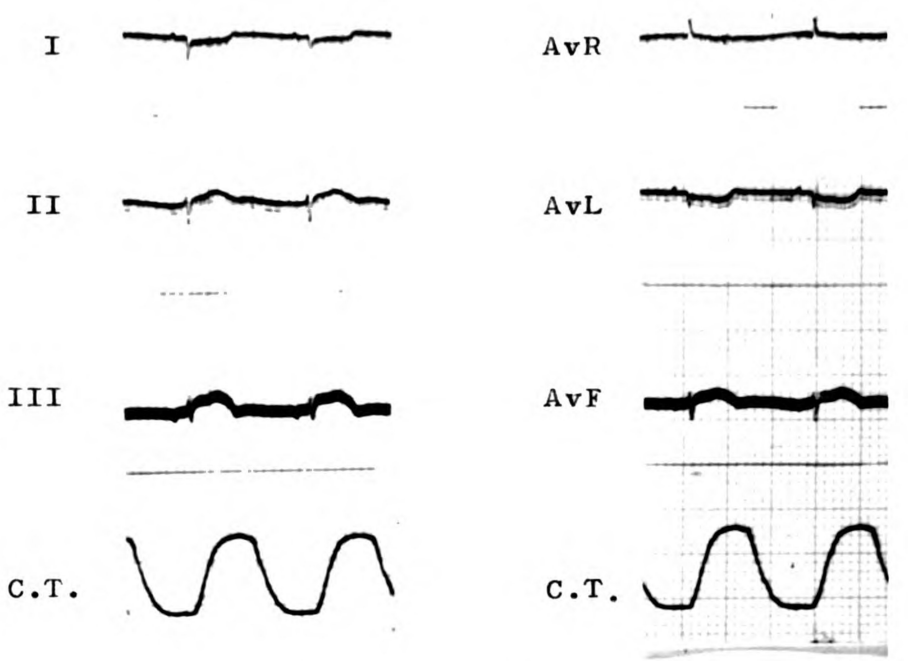


Figure 14 Right Coronary Ligation

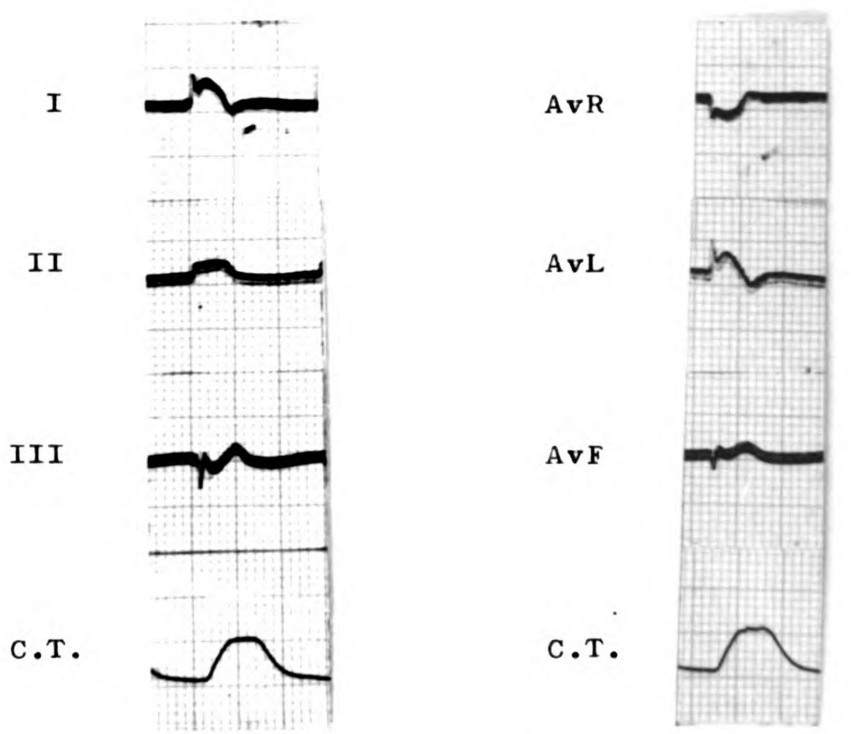


Figure 15 Left Coronary Ligation

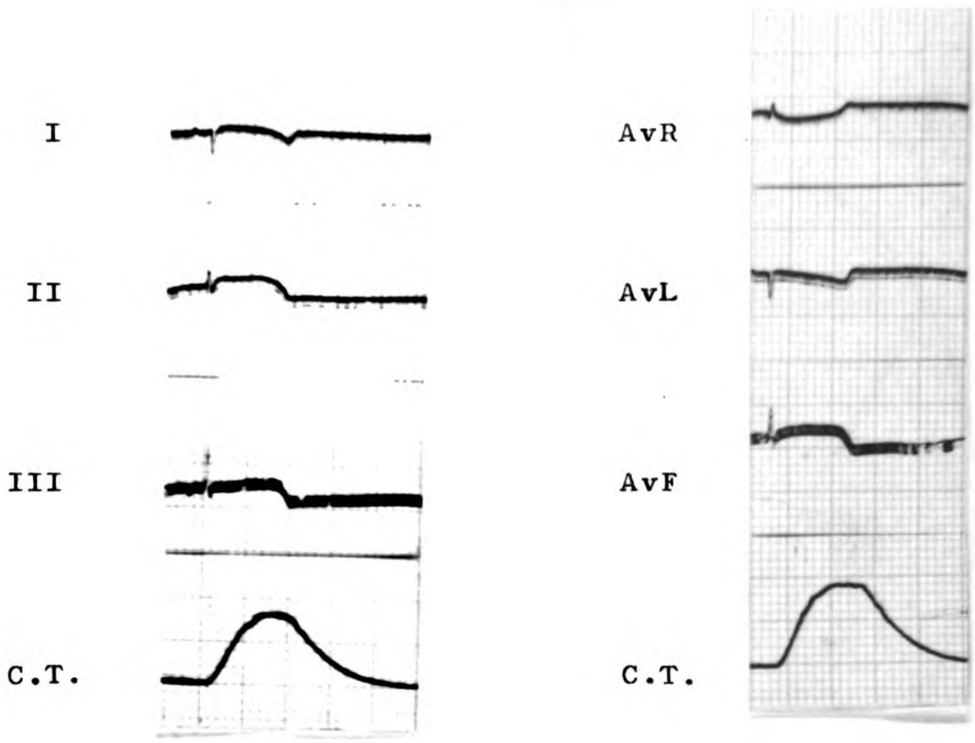


Figure 16 Both Coronary Ligations at 5 Minutes

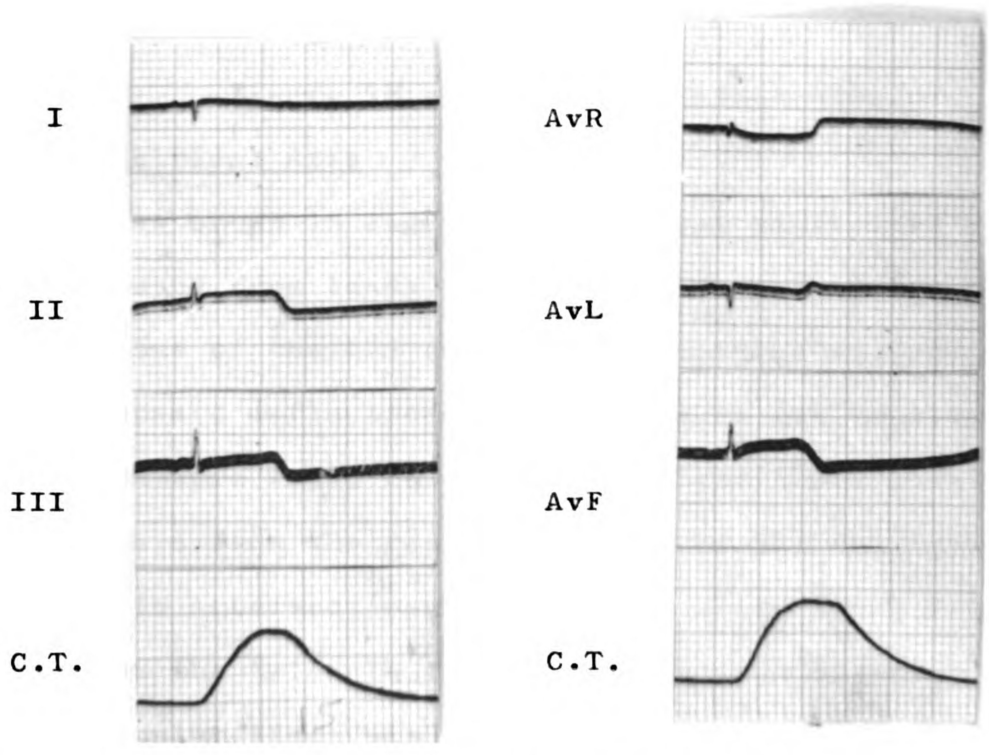


Figure 17 Both Coronary Ligations at 10 Minutes

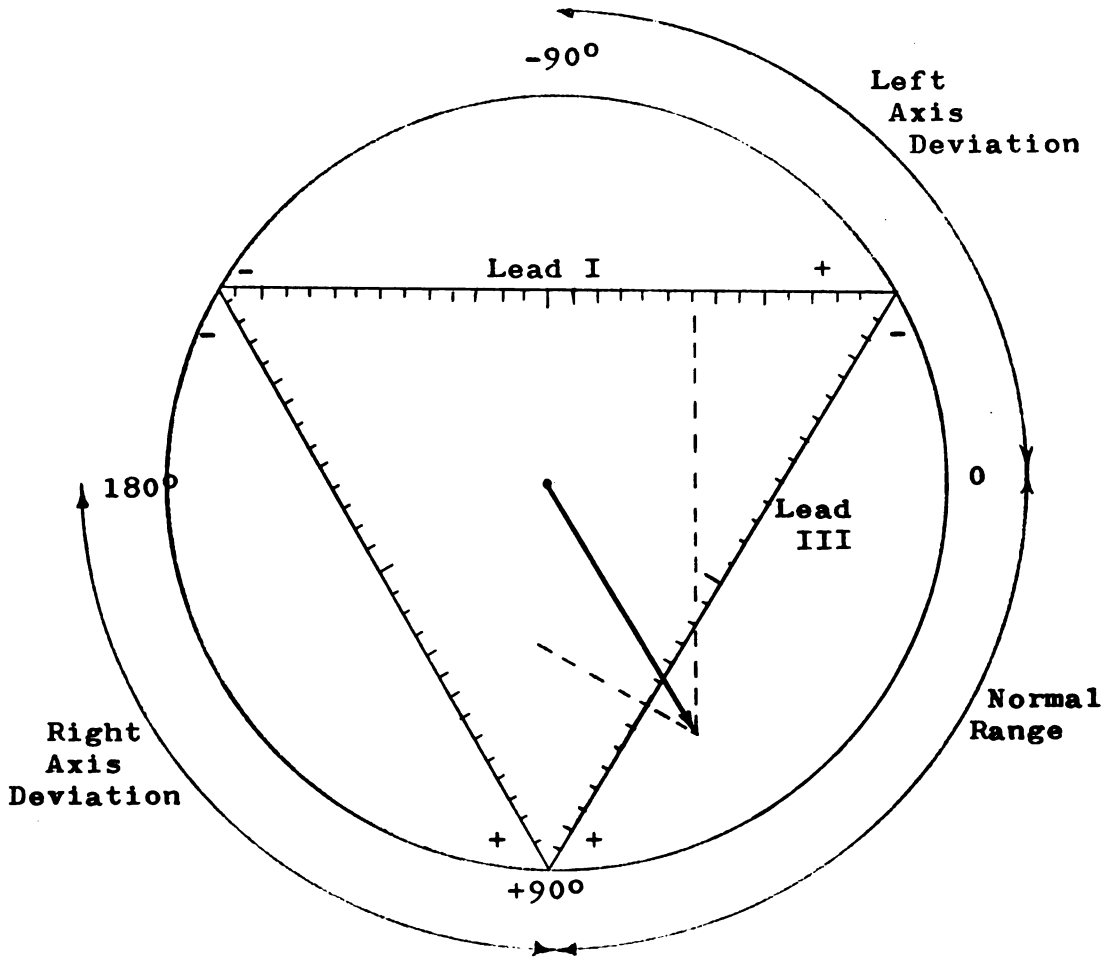


Figure 18 Mean Electrical Axis

Mean Electrical Axis

As shown in figure 18, the mean electrical axis (M.E.A.) was computed from leads I and III. The sum of the downward deflections of the QRS complex were subtracted from the sum of the upward deflections. The point of net amplitudes of the leads were found on the chart. From these points, perpendiculars from the respective sides of the triangle were erected to intersect each other. An arrow drawn from the center of the triangle to the intersection of these two perpendicular lines was the "mean electrical axis". (Rushmer, 1961).

Mean Electrical Axis of the Isolated Heart

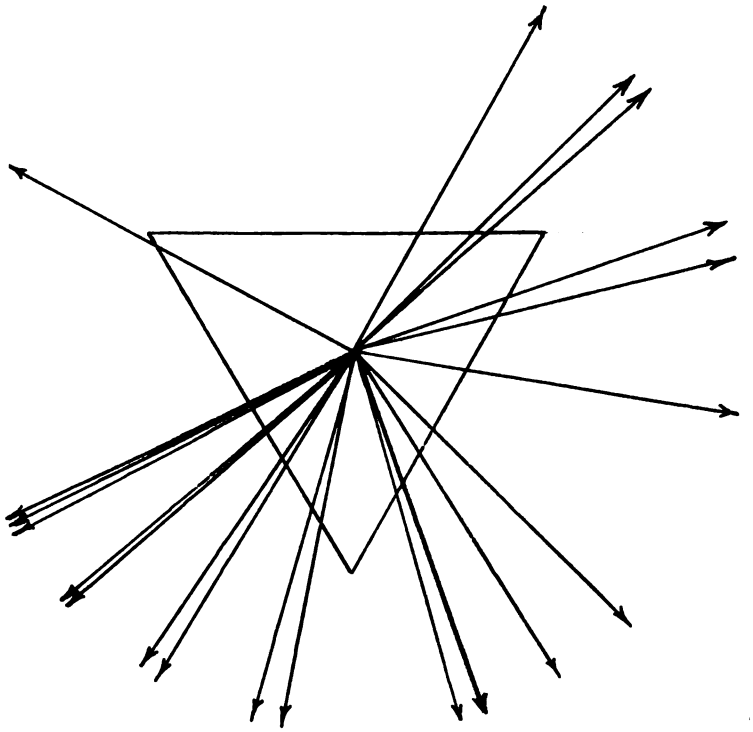


Figure 19 Intact Heart (1-20)

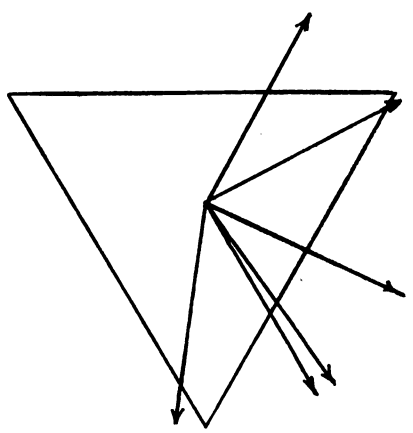


Figure 20 Without Right Atrium (1-5)

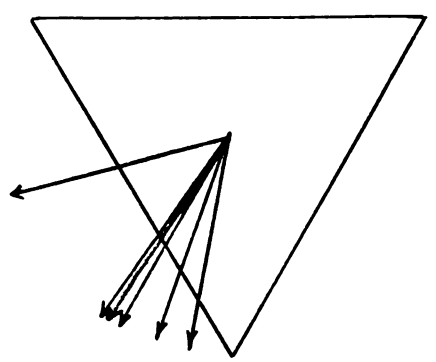


Figure 21 Without Left Atrium (6-10)

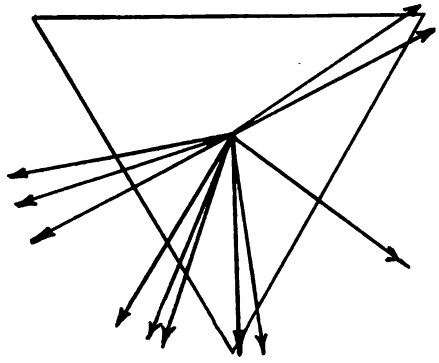


Figure 22 Ventricles Only (1-10)

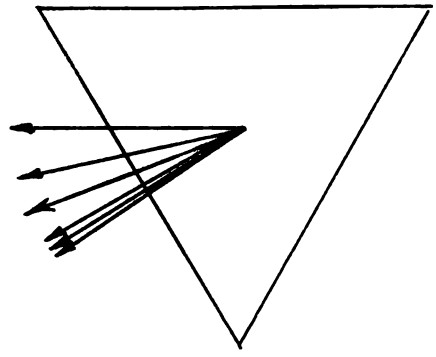


Figure 23 Left Ventricle Only (1-5)

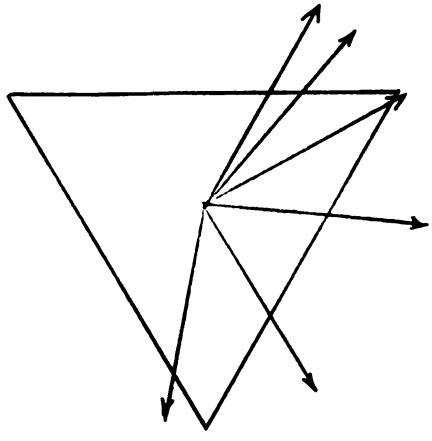


Figure 24 Right Ventricle Only (6-10)

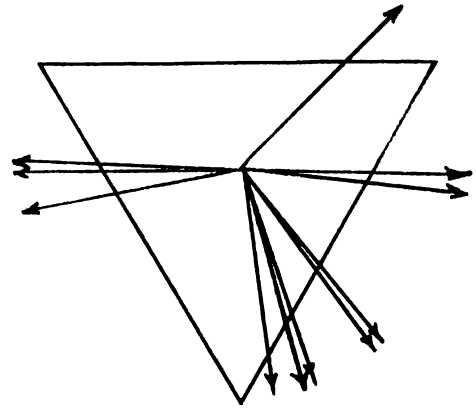


Figure 25 Septum Only (1-10)

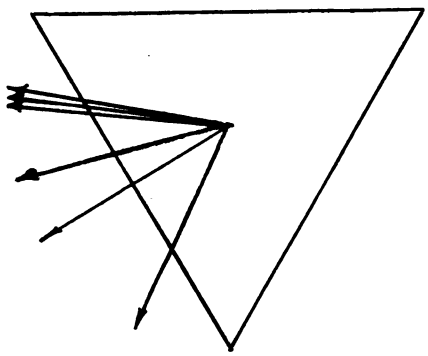


Figure 26 Right Coronary Ligation (11-15)

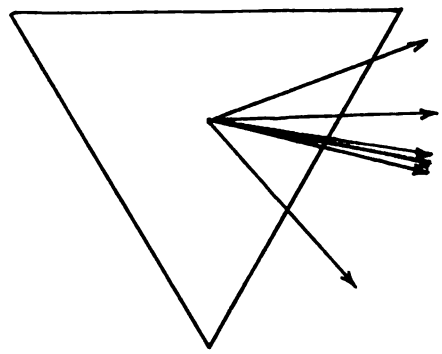


Figure 27 Left Coronary Ligation (15-20)

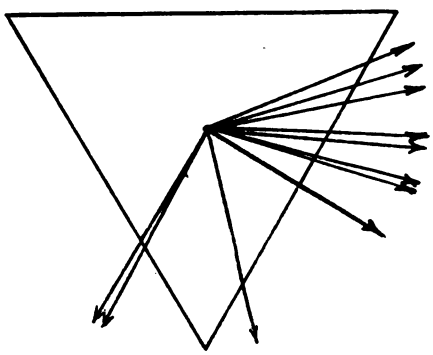


Figure 28 After 5 Minutes with Both Coronaries Ligated (11-20)

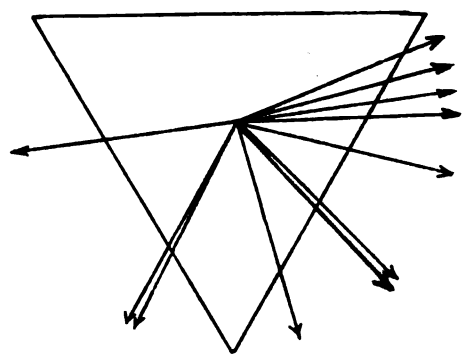


Figure 29 After 10 Minutes with Both Coronaries Ligated (11-20)

DISCUSSION AND CONCLUSIONS

The P-Q-R-S-T time intervals in the intact, isolated, perfused heart, as shown in table 2 and figure 8, agreed closely with those found in the intact animal by previous investigators, although the average rate in the perfused heart was about 80 beats slower. The P wave, when present, was upright in leads I, II, III, AvL and AvF. Occasionally, the P wave was inverted in AvR and tended to be absent in leads II and III. The tendency of leads I and III was positive, while lead II was generally negative. AvR and AvL were usually negative, while AvF was generally positive. In the majority of cases the sum of leads I and III equaled lead II. The mean electrical axis (M.E.A.) was 68.5° with a range from -62° to 207° (figure 19). Graybiel et al. (1944) analyzed electrocardiograms of 1000 young, healthy aviators and obtained a M.E.A. of 64.2° with a range from -36° to 120°. Although Lepeschkin (1944) refers to a rotating vector in the isolated heart, this is apparently the only work which refers to an electrical axis in the isolated heart.

The average ventricular tension of the isolated heart at the height of mechanical systole was 16.2 grams. There was an average latent period of .05 sec. from complete depolarization (ECG) to onset of contraction (force gauge).

As shown, for example, in figure 8, there was in 60% of the hearts a rhythmic change of contraction tension which occurred in groups of two, three, four, or five beats. In each group there was a regular decrease in tension which recurred rhythmically. These changes were accompanied by slight proportional changes in the QRS complex with no observable change in the P wave.

There seemed to be no correlation between heart weight, rate, and contraction tension. Summation and incomplete tetanus were not observed.

Removal of the right atrio-superior vena caval junction constitutes the removal of the sinoatrial (SA) node--the "pacemaker" of the heart. The heart initially stopped for a few seconds until a lower center, presumably the atrio-ventricular (AV) node, began to initiate a slower, weaker stimulus with the heart responding accordingly (compare figures 8 and 9). The new rate was significantly* less than the original. Assuming the greater cardiac reserve is in the left ventricle, the weaker stimulus from the AV node may be below threshold for motor units which were previously excited by SA node impulses. This is also evident in the attenuation of contraction tension which was 75% of the original. All Q-R-S-T intervals remained virtually the same (table 2). The

*Unless stated otherwise, significance in this discussion is at the 10% level as determined by the t distribution.

AvL deflections were positive. There was no significant difference in duration of mechanical systole and diastole between control hearts and those without right atria. As shown in figure 9, the rhythmical changes of contraction disappeared. There was a slight, insignificant M.E.A. deviation to the left (figure 20).

With removal of the left atrium from the intact heart, the P wave remained and there was a small, but insignificant, M.E.A. deviation on to the right. Heart rate and average contraction tension showed no significant difference from the controls. The dynamic rhythmic change of contraction tension was still present.

The general picture of the two isolated ventricles (figures 10, 11, and 12, and tables 5 and 13) showed a deviation from the intact heart in the slower rate, which is significantly less at the 0.5% level, absence of P wave, and a 25% attenuation in contraction tension. The rates, contraction tensions, and mean electrical axes of the ventricles with the left atrium and the ventricles alone showed no significant difference. However, the rates of the ventricles with the right atrium and the ventricles alone are significantly different, although the mean electrical axes and contraction tensions are not.

The most noticeable effect of removal of the right

ventricular wall from a heart without atria was the marked M.E.A. deviation to the right (figure 23) and the slight attenuation of contraction tension (tables 6 and 13). The septum is the most highly innervated portion of the heart and holds little or no reason for reserve. It is as thick as the remaining wall of the left ventricle and probably contributes to the marked M.E.A. deviation because its motor units have low threshold, whereas those of the ventricle wall have higher threshold.

With removal of the left ventricular wall from a heart without atria, there was a significant M.E.A. deviation to the left, again, in favor of the septum (figure 24). The contraction tension is reduced to half that of the preceding example (tables 7 and 13). This may be partially dependent upon the thinner wall of the right ventricle compared to the left.

The interventricular septum alone (figure 25) shows a significant difference from the intact heart in diminution of contraction tension and rate (tables 8 and 13). The average M.E.A. is not significantly different from the intact heart or ventricular average axes.

Ligation of the right coronary artery immediately eliminated the rhythmical cycles of decreasing contraction tension. The same effect was produced by removal of the right

atrium. After five minutes there was a noticeable shift of the M.E.A. to the right (figure 26), which is significant at the 1% level, with a slight, questionable decrease in contraction tension. As shown in table 9, the AvR tends to be more positive and the AvL more negative than controls. In early stages of anoxia or hypoxia, the general cardiac response is excitation. This was manifest in the well-maintained rate and the normal values of the P-Q-R-S-T intervals despite the possible lack of nutritive materials due to decreased coronary supply.

In a recent study by Kardesch et al. (1958) of intact rabbit and dog hearts perfused through the coronary arteries, it was found that cessation of perfusion, which resulted in anoxia, produced changes in transmembrane potentials similar in magnitude and time of appearance as those caused by anoxia without stopping perfusion.

After five minutes of ligation of the left coronary artery (figure 27), there was a noticeable, but insignificant, shift of the M.E.A. to the left with a large decrease in contraction tension (table 10), which is significantly less at the 1% level. The average AvR tended to be more negative whereas the average AvL was more positive than controls. Again, anoxia may have caused greater excitation and depolarization on the ligated side. The greater decrease in contraction

tension and rate after left coronary ligation, compared to effects of right vessel ligation, may be dependent upon the greater arterial network on the left. This is indicated by the plastic corrosion model(figure 3). The experimental effect is emphasized by the greater loss of circulation after ligation on the left side.

After five minutes of ligation of both coronary arteries (table 11), there was an increase in the average P-Q, QRS, and Q-T intervals. The contraction tension and rate were significantly diminished, but there was no significant difference in the M.E.A. from intact hearts. Average mechanical systole and diastole durations were increased. AvR showed a greater negativity and AvL a greater positivity than normal.

After ten minutes of right and left coronary artery ligation, the average P-Q, QRS, and Q-T intervals remained increased in duration. However, the average contraction tension and rate are diminished further. The M.E.A. was still not significantly different from controls. Mechanical systole and diastole are further lengthened in duration. The average AvR was positive.

The rhythmical changes in contraction tension, mentioned above, were seen in 60% of hearts when the SA node was present and coronaries open. The absence of the rhythmical changes in some hearts might have resulted from unavoidable variations of

procedure during the initial stages of perfusion. It is suggested that these changes were caused by a spontaneous dynamic vasomotion of the coronary arteries. There are few references in the literature to spontaneous vasomotion of the coronary bed or to the role of coronary distension in cardiac rhythmicity. Sollman (1905) perfused isolated hearts with cottonseed oil and maintained viability for over 1/2 hour. He concluded that the origin of the cardiac beat lay in the distension of the coronary artery. Magnus (1902) used oxygen or hydrogen gas and obtained similar results.

Bozler (1936) showed that smooth muscle may undergo enormous changes in length, and that if a constant load is placed on a strip of smooth muscle, it will, after an initial rapid elongation, stretch at a constant speed until there is a 50% change in length. Thereafter the speed slows, probably because the tension-induced depolarization initiates active contraction. In the perfused heart there is a constant load of 40 cm. of water upon the coronary vessels. If coronary vasomotion could affect the amplitude of the stimulus received by the Purkinje system from the SA node, this effect could be altered either by ligation of the coronary artery or removal of the SA node. In both cases there was an immediate attenuation of contraction tension and a cessation

of the rhythmic changes in contraction tension. This result was presumably due to a weaker, constant amplitude stimulus to the Purkinje fibers, thereby stimulating fewer motor units and eliminating the response of those motor units of higher threshold.

Upon commencing perfusion, the perfusate volume, returning to the ventricles from the myocardial vascular bed by way of the thebesian veins, gradually increased in the ventricles causing a gradual increase in contractions. Eventually the diastolic filling was great enough to induce the ventricles to spill a major portion of their contents. Ventricular filling then occurred to repeat the cycle. Removal of the SA node would be expected to lengthen the cycle and allow greater diastolic filling per beat to account for more rhythmic, even contractions, and the average contraction tension would increase. Since, upon removal of the SA node in the present work, the contraction tension was attenuated 25% and the serial changes in contraction tension were decreasing instead of increasing, the preceding explanation is not feasible.

Summation and incomplete tetanus were not obtained with a physiological perfusion. Wiggers (1925) showed ventricular tension generated by a premature beat was less than that developed by a normal beat. As shown in figure 30,

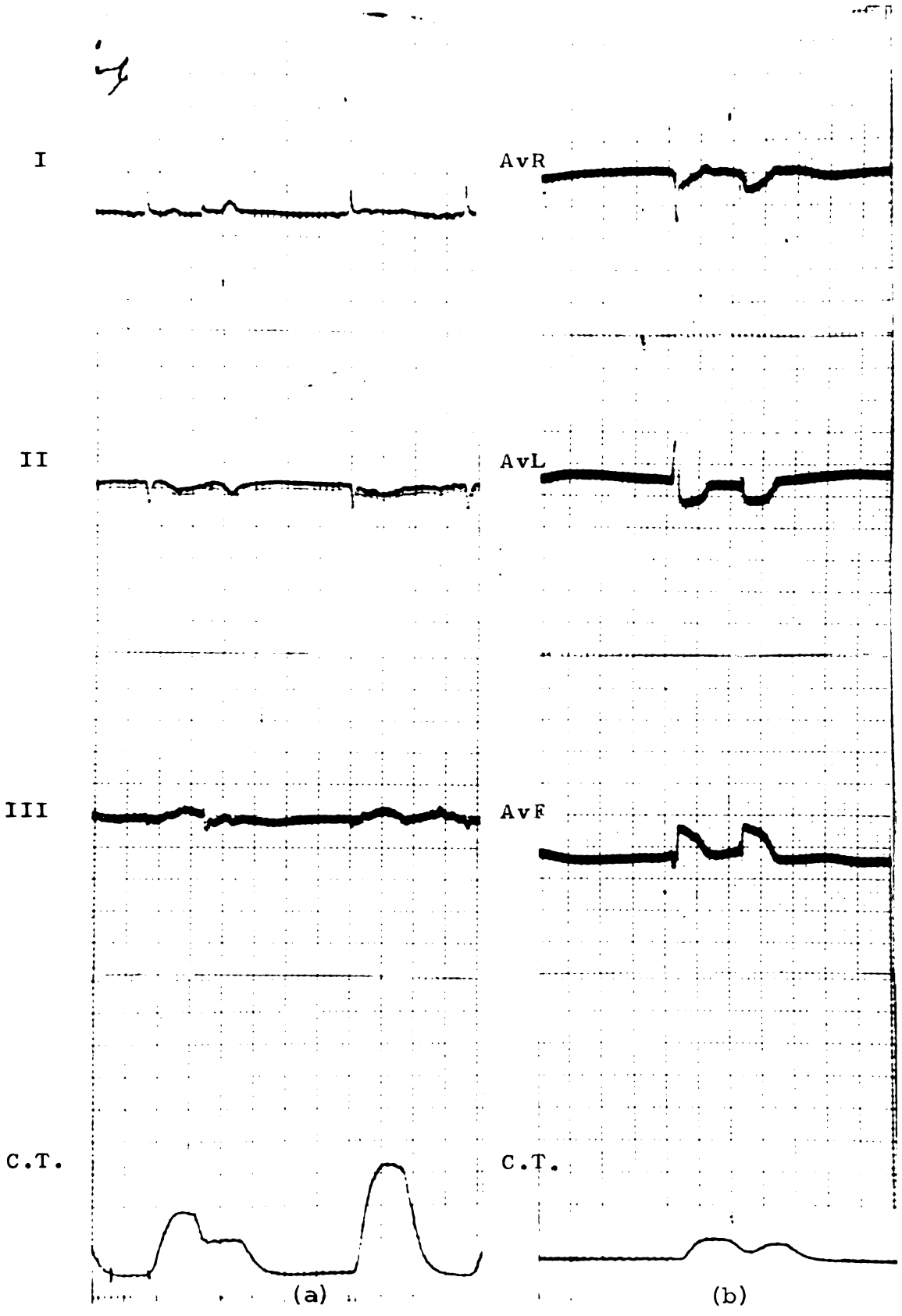


Figure 30 Extrasystoles

extrasystoles, as a result of a stimulus of ectopic nature, develop less tension than those developed by a normal stimulus. In "a" the first contraction is preceded by a P wave, but the extrasystole is not preceded by a P wave. The extrasystole is presumably a result of an ectopic stimulus in the Purkinje system and shows a diminished contraction over the first beat. It may be speculated that summation could occur if the first stimulus was from the AV node or lower in the conduction system, and the second, or summated stimulus, occurring immediately at the termination of the absolute refractory period, was from the SA node. This might occur under nonphysiological conditions, as mentioned earlier. In "b" of figure 30, the second impulse, as shown by the greater potential in AvL, originates low in the conduction system. A weaker contraction is the result.

It is interesting to note that many of the QRST action potentials (ECG) had the characteristic pattern of the potentials of single cardiac cells (figures 9, 12, 13, and 14) as described by Cranefield and Hoffman (1958). As shown in figure 31, the action potential of the single cardiac cell, which typifies many of the action potentials of the ventricles of the isolated heart, is shown initially in the resting state (4). There is a rapid depolarization (0), followed by a short

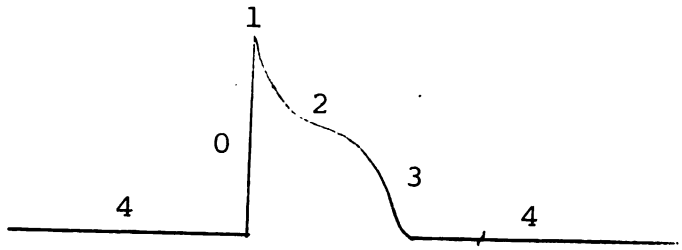


Figure 31 Action Potential of a Single Cardiac Cell

latent period (1); a period of slow repolarization (2); and a period of rapid repolarization (3) to the resting potential (4). In the electrocardiogram of the isolated heart, as in the single cardiac cell, the T wave is not a separate part of the action potential but included in the initial deflection.

In conclusion, the investigation of progressive regional ablation on the isolated, perfused rabbit heart is apparently unique, and offers to the experimenter a method for studies on living isolated regions of the beating heart. However, coronary insufficiency in isolated perfused hearts has been studied previously with regard to transmembrane potentials. The incorporation of the direct three lead electrocardiogram (ECG) and force gauge makes it possible to record simultaneous electrical and mechanical events in the perfused heart. It is possible, using leads I and III, to apply Einthoven's law to the isolated perfused heart. With the three unipolar leads, AvR, AvL, and AvF, the regional location of the initiating stimulus in the isolated heart

is roughly indicated, just as in the intact animal.

The occurrence of the serially, decreasing rhythmic changes of contraction tension was thought to be associated with a spontaneous vasomotion of the coronary arteries. The rhythmic change of contraction tension stopped with excision of the sino-auricular (SA) node or ligation of the coronary artery. Only if the SA node is functionally present and the coronaries are open will the rhythmic changes occur. In addition, since isolated hearts function also when perfused with oils or gases, it might be speculated that there is a functional relationship between the SA node impulse to the Purkinje system and the relative distension of the coronary artery.

The removal of the SA node and the subsequent relocation of the cardiac stimulus produces a slight diminution in the ECG potential, absence of P wave, and a 25% attenuation of contraction tension. If the myocardium were a syncytium, then, on the basis of the all-or-none law, no change in the ECG or contraction tension would be expected from the relocation of the stimulus to the AV node from the SA node. Whether the stimulus arises from the SA node or the AV node, the expected pathway of excitation in the Purkinje system would be the same. The weaker AV impulse, in comparison to the SA impulse, fails to induce the response of a number of

previously active motor units of high threshold.

Under normal perfusion conditions the P-Q-R-S-T time intervals in the isolated rabbit heart agree closely with those obtained on intact rabbits by earlier investigators, however, the rate of the perfused heart is somewhat slower.

Removal of either ventricle in the isolated heart produces a marked M.E.A. deviation toward the septum. Apparently the motor units of the septum have low threshold and are all utilized at each beat.

Ligation of either the right or left coronary artery produces a marked axis change toward the ligated side. Here, hypoxia causes an excitation and greater depolarization on the ligated side.

After ligation of the second coronary artery, for five minutes, on a heart, which initially had one coronary tied, the M.E.A. swung back to the normal range. There was an increase in the P-Q-R-S-T time intervals and action potential (ECG), although there was a large diminution in contraction tension. In this circumstance, the action potential is not proportional to the contraction force.

Prolongation of bilateral coronary ligation to ten minutes shows a further increase in P-Q-R-S-T intervals and a decrease in action potential from the earlier bilateral ligation. Contraction tension is further diminished.

The later response of the myocardium to anoxia is depression.

Summation and incomplete tetanus were not observed, but it was thought that under the proper set of conditions it could occur in the mammalian heart.

The action potential of the ventricles (QRS-T) in the isolated perfused rabbit heart simulates the action potential of a single cardiac cell, which was determined by earlier investigators.

SUMMARY

1. Isolated, perfused rabbit hearts were used for studies of progressive regional ablation and coronary insufficiency. A direct three-lead electrocardiogram, simulating the standard limb placement of electrodes on the intact animal, was used in conjunction with a force gauge. The latter recorded contraction tension. This provided a method of recording simultaneous electrical and mechanical events in an isolated heart.

2. Using leads I and III, Einthoven's law was utilized to determine the mean electrical axis of the heart. In the majority of cases, the sum of leads I and III equaled lead II. Unipolar Av leads were also recorded to determine the regional location of the cardiac stimulus.

3. Rhythmic, decreasing, serial cardiac tension changes were observed in 60% of the hearts. These were thought to be associated with a possible spontaneous vasomotion of the coronary arteries. Since the cyclic changes disappear with the ablation of the sinoatrial node or ligation of the coronary arteries, it follows that vigorous coronary vasomotion may affect the amplitude of the cardiac impulse en route to the ventricular myocardium.

4. The contemporary motor unit theory of the heart was utilized to explain the decreased contraction tension of the

heart with the sinoatrial node removed. The motor unit theory also may explain the marked shift of the mean electrical axis toward the septum with ablation of either ventricular wall.

5. The P, QRS, and T segments of the tri-lead electrocardiogram of the isolated rabbit heart were compared to the standard electrocardiogram of the intact rabbit, as recorded by previous investigators. Moreover, the electrocardiogram of the isolated heart simulated in configuration the action potential of a single cardiac cell as described by earlier investigators.

6. Unilateral ligation (5 min.) of the coronary arterial network produces a marked mean electrical axis shift toward the ligated side. With bilateral coronary ligation (5 min.), the electrocardiogram action potential is initially increased, whereas the contraction tension is decreased. Under these conditions the contraction tension and electrocardiogram action potential are not proportional. Ligation for ten minutes produced a decrease in both the electrocardiogram action potential and contraction tension. These effects are likely manifestations of myocardial hypoxia.

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