*From the Third Medical Clinic, Faculty of Medicine, Kyoto University
(Director: Professor Magojiro Maekawa, M. D.)*

The Electrocardiogram in Experimental Coronary Insufficiency; with Special Reference to Hemodynamics and Myocardial Oxygen Metabolism (II)*

By

CHUICHI KAWAI

(Received for Publication. Aug. 14, 1959)

SECTION 1: HEMODYNAMIC AND ELECTROCARDIOGRAPHIC CHANGES IN THE DOG WITH AN INCREASED LOAD ON THE HEART

INTRODUCTION

Electrocardiographic changes during exercise in patients with coronary insufficiency are rather common in the clinic, but as far as the author knows, there are only two reports on hemodynamic as well as coronary circulatory changes during exercise in patients with coronary insufficiency: Lombardo et al.¹⁾ in America and Hara²⁾ in Japan. (Hara's case, in which hypoxia—inhale of 10% oxygen—was induced for 20 minutes in a patient with a history of angina pectoris, can be considered in the wider sense to be a case of increased load in a patient with coronary insufficiency.) It is quite natural that the number of cases is limited in men because of the expected risks. Thus, further study of the problem necessarily depends upon animal experiments.

In Part I of this paper³⁾ the author described his method of preparing experimental dogs with coronary insufficiency through coronary arterial catheterization and explained that the electrocardiographic change of S-T depression in the leads which face the epicardial surface was obtained in the closed-chest dog under more physiological conditions than had ever been done. The author also emphasized that in studying electrocardiograms of coronary insufficiency the consideration of coronary blood flow only, as in the past, was insufficient, and that it is always necessary to consider both the oxygen demand and the oxygen supply in the myocardium, that is, the relative changes in myocardial oxygen consumption and work of the heart. With this purpose in mind myocardial oxygen con-

sumption was measured by the author's coronary artery catheterization³⁾ and by Goodale et al.'s⁴⁾, coronary sinus catheterization, cardiac output by Fick's method, and furthermore, left ventricular work by the product of cardiac output and mean aortic pressure. Part I of this paper described these experiments.

Part II, to make a further step, describes the author's attempts to examine changes in the electrocardiogram, especially in the S-T segment, corresponding to changes occurring in the myocardial oxygen demand and supply when mechanical as well as pharmacological loads were imposed on hearts with coronary insufficiency. The meaning of the S-T segment depression, which had been considered one of the characteristic findings in electrocardiograms of coronary insufficiency in the past, was thus further clarified. At first the relationship between electrocardiograms and hemodynamic changes under increased load on the dog's heart without coronary insufficiency was investigated.

The fact that electrocardiographic changes, called the "strain pattern", are produced by increasing the load on the ventricle has often been discussed since Barnes and Whitten⁵⁾ first wrote about it in 1929. However, the relationship between electrocardiograms of ventricular strain and of coronary insufficiency still remains obscure. Therefore, the following experiments were first carried out to see whether ventricular loading could bring about the electrocardiographic changes of coronary insufficiency or of strain pattern in dogs without coronary insufficiency.

* The outlines of this paper were read by Prof. M. Maekawa at the symposium on angina pectoris before Joint Meeting of the 53rd. Annual Meeting of the Japanese Society of Internal Medicine and the 20th Annual Meeting of the Japanese Circulation Society (Fukuoka, April 1-3, 1956), and also by the author at the 22nd Annual Meeting of the Japanese Circulation Society (Sendai, April 29-May 1, 1958).

METHOD

Eleven adult dogs, unselected as to breed and sex and weighing 9 to 19kg., were anesthetized with isomylal (50mgm. to 75mgm. per kilo intraperitoneally.) Anesthesia was kept light and the dogs were placed on their backs. 400 units per kilo of heparin following 20 to 30 mgm. oral administration of sintrom were given intravenously. The dose of heparin was repeated if necessary. Under fluoroscopic control a catheter with a deflated balloon on the tip (Fig. 1)

Fig. 1. Photo shows catheters with an inflated (left) and deflated (right) balloon.

was introduced into the pulmonary artery through the jugular vein or into the aorta through the common carotid artery for the experiment of right or left ventricular loading, respectively. In order to increase the load on the ventricle, intraventricular pressure was raised by inflating the balloon with urographin. In this series the chest and abdomen were not opened throughout the whole procedure. A #7F or 8F catheter placed in the right ventricle from the jugular vein or in the left ventricle from the femoral artery was connected with a manometer and pressure recorder to measure the elevation of intraventricular pressure. The zero point was set in the same way as described in Part I. Pulmonary artery wedge pressures were also measured in the experiments of left ventricular loading. Fig. 2 presents a roentgenogram of #345 dog showing the balloon inflated in the ascending aorta. Thus, this series includes 4 cases of right ventricular loading, 6 cases of left ventricular loading and 1 case with an inflated balloon in the left atrium. Of 6 cases of left ventricular loading, the inflated balloon was placed in the descending aorta in 2, the aortic arch in 1, the ascending aorta in 2, and just above the aortic valve in 1. Pressures were recorded by

Fig. 2. Roentgenogram showing the balloon inflated in the ascending aorta (# 345). Tips of the catheters are in the pulmonary capillary (PC) and the left ventricle (LV) in the dog.

means of the Hamilton manometer^{17a) b)} on the optical system, two manometers being used, if necessary, for the purpose of simultaneous recording of pressures at two sites such as the left and right ventricle. Mean pressures were measured by Takezawa's method⁶⁾ of clamping the perfusion rubber tube used as the side branch in the pressure recording system. For measuring pressures the values during a respiratory cycle were averaged since respiratory movements were apt to affect the pressure curve. Cardiac output was estimated by an adaptation of the Fick principle before and 30 to 60 minutes after inflation of the balloon in the experiments of left ventricular loading. In addition, right and left ventricular work was calculated to determine the hemodynamic changes during an increased load on the left ventricle. Cardiac output was measured 30 to 60 minutes after inflation of the balloon, because by that time the transient changes in pressure occurring immediately after inflation of the balloon had subsided and a stable status had usually been attained. Electrocardiograms were recorded in combinations of leads I and II, leads I and III, and right ($C\phi_D$) and left precordial leads ($C\phi_S$) on a 2-channel photographic recorder. With lead $C\phi_D$ or S , the central terminal of Maekawa^{7a) b)}, midway between the right arm and left foot with high ohm resistors between them was used as an indifferent electrode, while the different electrodes were placed on the right and left sides of the chest wall. Hemodynamic values were calculated from the following formulae:

$$\text{Cardiac output (cc./min.)} = \frac{\text{O}_2 \text{ consumption (cc./min.)}}{\text{Arterio-mixed venous O}_2 \text{ difference (vol. \%)}}$$

$$\text{Pulmonary arteriolar resistance (PAR) (dynes}\cdot\text{sec/cm}^5) = \frac{\text{PAm} - \text{PCm (mm.Hg)}}{\text{Cardiac output (cc./sec.)}} \times 1332$$

$$\text{Total peripheral resistance (TPR) (dynes}\cdot\text{sec/cm}^5) = \frac{\text{Mean aortic pressure (mm.Hg)}}{\text{Cardiac output (cc./sec.)}} \times 1332$$

$$\text{Left ventricular work (kg}\cdot\text{M/min.)} = \text{Cardiac output (cc./min.)} \times \text{Mean aortic pressure (cm.Hg)} \times 13.6 \times 10^{-5}$$

$$\text{Right ventricular work (kg}\cdot\text{M/min.)} = \text{Cardiac output (cc./min.)} \times \text{Mean pulmonary arterial pressure (cm.Hg)} \times 13.6 \times 10^{-5}$$

TABLE I ECG AND HEMODYNAMICS IN RIGHT VENTRICULAR STRAIN

Dog No.	Weight and Sex of dog	Site of balloon	Right ventricular pressures systolic/diastolic (mean) mm.Hg	ECG
#317	14Kg ♂	Pulmonary artery	12/5 (10)	control period
			25/0 (10)	2hr. & 10 min. after inflating balloon
				3 hr. & 50 min. after inflating balloon
#337	10Kg ♂	Pulmonary artery	45/8	control period
			48/0	20 min. after inflating balloon
			39/-2	2 hr. & 15 min. after inflating balloon
#338	11Kg ♂	Pulmonary artery	52/22	3 hr. after inflating balloon
			died	5 hr.
			29/-1	control period
#353	14.5Kg ♂	Pulmonary artery	80/-11	5 min. after inflating balloon
			45/-1	1 hr. and half after inflating balloon
			51/-3	2 hr. after inflating balloon
#353	14.5Kg ♂	Pulmonary artery	died	2 hr. 20 min.
			16/0	control period
			28/6	20 min. after inflating balloon
#353	14.5Kg ♂	Pulmonary artery	28/2	1 hr. & a half after inflating balloon
			46/1	3 hr. after inflating balloon
			died	4 hr.

RESULTS

(1) Right ventricular loading

Table 1 shows the hemodynamic values in 4 cases of right ventricular loading and Fig. 3 is a presentation of relations between changes in the pressure curve tracing and electrocardiogram obtained in #317. Following are descriptions of each experiment.

Dog #317: Inflation of the balloon caused a mean elevation of right ventricular pressure of 10 mm.Hg at $2\frac{1}{6}$ hours and further inflation increased the systolic pressure by 13 mm.Hg at $3\frac{5}{6}$ hours. The electrocardiogram showed a tendency towards T wave flattening in the right and left precordial leads after inflation of the balloon. These changes were not those of a typical strain pattern.

Dog #337: There were no particular changes in right ventricular pressure or electrocardiogram.

Dog #338: Right ventricular pressure was markedly elevated by 51 mm.Hg in systole at 5

minutes, 16 mm.Hg at $1\frac{1}{2}$ hours and 22 mm.Hg at 2 hours after inflation of the balloon. The T wave was inverted in leads II and III and the left precordial lead ($C\phi_s$) immediately after inflation of the balloon. The T wave had returned to normal at $1\frac{1}{2}$ hours and no electrocardiographic change was seen at 2 hours. Then the dog stopped breathing and died at $2\frac{1}{3}$ hours.

Dog #353: Right ventricular pressure was elevated by 12 mm.Hg in systole at 20 minutes and 1 hour, and by 30 mm.Hg in systole at 3 hours after inflation of the balloon. The S-T segment was slightly depressed in both precordial leads ($C\phi_D$ and $C\phi_s$) immediately after inflation of the balloon, but returned to normal at 3 hours.

(2) Left ventricular loading

Table 2 shows hemodynamic values and electrocardiographic changes in 6 cases of left ventricular loading. Fig. 4 and Fig. 5 present of relations between changes in the pressure curve tracing and electrocardiogram obtained in #343 and #345, re-

Fig. 3. Pressure curve tracings (A) in the right ventricle and electrocardiogram (B) (C) before and after inflation of the balloon in the pulmonary artery. # 317.

spectively. Fig. 6 a), b), c) and d) presents the course of the pressure changes in experiments #343, #345, #352 and #356, in which pulmonary artery wedge pressures could be measured. Following are descriptions of each experiment.

Dog # 319: Both systolic and mean left ventricular pressure was elevated by 30 mm.Hg (systolic

from 110 mm.Hg to 140 mm.Hg) after inflation of the balloon in the ascending aorta. That pressure level lasted for 3 hours. There was no marked change in the electrocardiogram.

Dog # 343 (Fig. 4 and Fig. 6 a)): After inflation of the balloon in the descending aorta, the left ventricular systolic pressure was elevated so

TABLE II ECG AND HEMODYNAMICS IN LEFT VENTRICULAR STRAIN

Dog No.	Site of balloon	Left ventricular pressures systolic/diastolic (mean) mm.Hg	E C G	Respiration rate per min	V.R. per min	Mean wedge pressure mmHg	O ₂ consumption cc/min	A-V difference for putative resistance cc/min	Cardiac output l/min	Pulmonary artery resistance dynes/cm ⁵	Total peripheral resistance dynes/cm ⁵	Mean pulmonary pressure mmHg	Right ventricular pressure mmHg	Percentage increase of right vent work %	Mean Left ventricular pressure mmHg	Percentage increase of left vent work %
#319	8kg ♀ Ascending aorta	110/5(10) 140/5(70) 140/5(60) 0	Control period T inverted in all leads 30min after inflating balloon ess. no change except for bradycardia 1 hr. " 3 hr. " 4 hr. 30min. "	150 150 134 120												
#343	19kg ♂ Descending aorta	102/6 164/8 164/107* 260/157* 13/7 *	control period normal pattern 40min. after inflating balloon increased amplitude in left precordial lead 3 hr. " 6 hr. " ST elevated in right and left precordial leads 9 hr. " standstill	18 18 10 0	140 128 90 75	4 17(4hr 30min.)	203 161	6.29 4.24	3227 3797	174 148	2330 2610	14 15	0.62 0.77	24	94 124	4.15 6.4 54
#345	9.4kg ♂ Ascending aorta	134-1(55) 158-10(55) 160/0 146/9 0	control period normal pattern 35 min. after inflating balloon ess. no change 1 hr. " 3 hr. " 14hr. " ST elevated in left precordial standstill	40 40 38 30 0	100 100 110 100 39	0.5 1.0 3.0	64.5 83	7.88 4.50	818 1850	1070 515	9300 5050	12 13	0.133 0.328	146	95 117	1.06 2.55 178
#350	11kg ♀ just above the Aortic valve		died 5 min. after inflating balloon													
#352	16kg ♂ Aortic arch	93/4 177/-6 145/0 106/8 (7)	control period normal pattern 30min. after inflating balloon no change 1 hr. " 3 hr. " 5 hr. " ST depressed in left precordial lead, ventricular fibrillation	20 20 20 16 0	133 133 125 96 200	4 5 9	96.965.26 08.9	1840 5.52	1650	305 365	3170 6450	11 12	0.275 0.270	-1.8	73 133	1.82 2.93 64
#367	18kg ♂ Descending aorta	93/90(91) 161/140(145) 161/140(145) 161/140(145)	control period normal pattern 8min. after inflating balloon large T in all leads 40min. after inflating balloon no change 4 hr. " gradual decrease of ventricular rate 8 hr. " standstill	136 133 44 40 26 0	116 60 134 134 86 20	5.5 -2 -2 17	94 63	7.33 4.63	1280 1360	720 765	5480 2940	6 11	0.105 0.205	95	88 50	1.53 0.92 -40

* aortic pressure † brachial pressure

Fig. 4. Pressure curve tracings and electrocardiograms before and after inflation of the balloon in the descending aorta. # 343, 19kg ♂ PC: Pulmonary capillary pressure (wedge pressure) LV: Left ventricular pressure PA: Pulmonary arterial pressure Asc. aort.: Pressure in the ascending aorta

markedly (from 102 to 164 mm.Hg) that a catheter in the left ventricle was forced out into the aorta. The aortic systolic pressure remained at 160 mm.Hg for 5 hours, then suddenly rose to 260 mm.Hg at 5½ hours, and thereafter gradually fell, the dog dying at 9 hours. The electrocardiogram revealed high voltage in the left precordial lead ($C\phi_s$) at 40 minutes after inflation of the balloon and a tendency towards elevation of the S-T segment in both precordial leads at 6 hours. These changes were different from those of the so-called "strain pattern." Cardiac output, total peripheral resistance, and right and left ventricular work increased, while pulmonary arteriolar resistance decreased 40 minutes after inflation of the balloon. Pulmonary artery wedge pressure gradually rose, until it reached its maximum, 17 mm.Hg, at 4½ hours. Pulmonary arterial pressure was scarcely elevated at 40 minutes. This experiment was successful in both the degree and the duration of left ventricular pressure elevation.

Dog # 345 (Fig. 5 and Fig. 6 b)): After inflation of the balloon in the ascending aorta, left

ventricular pressure was elevated from 134 to 160 mm.Hg. The pressure stayed at 160 mm.Hg for one hour, 150 mm.Hg until 7 hours after inflation of the balloon, then gradually decreased. The dog died at 14 hours. The electrocardiogram showed little change except for S-T segment elevation in the left precordial lead ($C\phi_s$) just prior to death. The mean pulmonary artery wedge pressure was not elevated at all in this case. Cardiac output, pulmonary arteriolar resistance, and right and left ventricular work increased, while total peripheral resistance decreased. There was no change in the pulmonary arterial pressure.

Dog # 350: The dog died following ventricular fibrillation 5 minutes after inflation of the balloon. It was assumed that the balloon inflated just above the aortic valve might have occluded the coronary orifice. It was interesting that left bundle branch block, soon followed by ventricular fibrillation, occurred after inflation of the balloon.

Dog # 352 (Fig. 6 c)): After inflation of the balloon in the aortic arch, left ventricular pressure was elevated from 93 to 177 mm.Hg at 30 minutes.

Fig. 5. Pressure curve tracings and electrocardiograms before and after inflation of the balloon in the ascending aorta. # 345, 9.4 kg ♂ FA: Femoral artery pressure LV: Left ventricular pressure PA: Pulmonary artery pressure PC: Pulmonary capillary pressure (wedge pressure)

Fig. 6. (a), (b), (c), (d). Complete follow-up of respiration, heart beat and pressure changes in each experiment of left ventricular strain. ○ PCm: Mean wedge pressure × LVs (d): Systolic (diastolic) left ventricular pressure ● PAs (d): Systolic (diastolic) pulmonary arterial pressure □ RAM: Mean right atrial pressure △ Respiration rate VR: Ventricular rate

(c)

(d)

That level of pressure did not last but fell to 145 mm.Hg at 1 hour, 106 mm.Hg at 3 hours, and the dog died at 5 hours. The electrocardiogram showed little change except for S-T segment depression, followed by ventricular fibrillation, in the left precordial lead ($C\phi_s$) just prior to death. Cardiac output decreased, after inflation of the balloon, while pulmonary arteriolar resistance, total peripheral resistance and left ventricular work increased. Right ventricular work remained unchanged. Mean pulmonary artery wedge pressure as well as right atrial pressure was slightly elevated just prior to death. There was no change in pulmonary arterial pressure.

Dog # 367: Hemodynamic values were measured 8 minutes after inflation of the balloon in the descending aorta in order to determine the hemodynamics immediately after inflation of the balloon. Brachial arterial pressure was elevated from 93/90 (mean: 91) to 161/140 (mean: 145) mm.Hg. The electrocardiogram showed high voltage of the T wave in all leads. Cardiac output decreased, while total peripheral resistance and left ventricular work increased.

Addendum

Dog # 356 (Fig. 6 d): In the series of experiments of left ventricular strain described above, mean pulmonary artery wedge pressure was not so easily elevated as expected. It was only elevated at $4\frac{1}{2}$ hours in some cases and not elevated at all in others. In order to examine the hemodynamic changes with a balloon inflated in the left atrium, the pressure of which is considered mostly to affect pulmonary arterial wedge pressure, a catheter with a deflated balloon at the tip was introduced into the left atrium through the common carotid artery and the left ventricle. Then the balloon was inflated in the left atrium. The site of the inflated balloon was ascertained by autopsy.

The left ventricular pressure naturally decreased as expected after inflation of the balloon in the left atrium. The electrocardiogram remained almost unchanged until standstill of the heart at 8 hours, although the S-T segment in leads II and III and in the left precordial lead was already depressed in the control period. Ventricular rate decreased in parallel with respiratory rate. Mean pulmonary artery wedge pressure began to rise only 5 minutes prior to standstill of the heart. Pulmonary artery pressure tended to rise 5 hours after

inflation of the balloon and reached its maximum 5 minutes prior to standstill of the heart. This case could be considered to be an experiment of right ventricular strain, because total peripheral resistance and left ventricular work decreased, while pulmonary arteriolar resistance right ventricular work increased 40 minutes after inflation of the balloon.

DISCUSSION

(1) *The experimental method*

Generally speaking, an increase in work can be produced either by increasing the cardiac output or by raising the blood pressure. An increase in the cardiac output has been accomplished by rapid infusions of a large amount of physiologic saline or glucose solution (Wiggers et al.⁸), Warthen⁹ and Yeomen et al.¹⁰), by infusions of gum acacia (Harrison¹¹) and Gowday et al.¹²) or of a large amount of albumin, heparinized horse or dog blood (Huckabee et al.¹³) and Gregg et al.¹⁴). An elevation of the arterial blood pressure can be achieved by ligating or by clamping the aorta or the pulmonary artery as Wiggers^{15a)b}) and many other investigators have done. Many investigators like Harrison¹¹) and others also used epinephrine injections to increase the work of the heart. Examining the methods previously used to increase the work, the author came to the conclusion that procedures increasing the cardiac output are not adequate in experiments attempting increase the work of the left and right ventricles separately, but a procedure raising the arterial blood pressure by mechanical narrowing of the artery should be used in a "pure" experiment to increase the work of the ventricle. By using this method, the author intended to see the "pure" effect of ventricular loading on the hemodynamic and electrocardiographic changes, and to prevent the influence of metabolic changes, such as might occur with the use of epinephrine. In this respect, nor-epinephrine having less effect on the metabolism seemed to be more suitable than epinephrine for increasing the work, if chemical agents are to be used.

In order to raise the arterial blood pressure as high and for as long as possible, the author avoided the fall in blood pressure caused by such experimental procedures as open the chest or abdomen to expose the artery. The intraventricular pressure was elevated by the author's original

method in which a catheter with deflated balloon was introduced into the pulmonary artery through the jugular vein or into the aorta through the common carotid artery under fluoroscopic control, then the balloon was inflated with urographin at any site desired. With this method, the blood pressure before inflating the balloon was kept over 100 mm.Hg in almost all cases.

The degree and the duration of elevation of right ventricular pressure were the indices of increased right ventricular work, because hemodynamic values were not measured in the experiments of right ventricular loading. As shown in Table 1, in 3 of 4 cases 10 to 50 mm.Hg elevation in the right ventricular systolic pressure lasted for 2 to 4 hours (up to 10 hours in # 317). The figures seemed to be sufficient for loading of the right ventricle.

In 4 of 5 cases in the experiments of left ventricular loading, hemodynamic values including work of the heart were measured to determine the degree of increase in loading. As shown in Table 2, the elevation of the left ventricular systolic pressure by 25 to 80 mm.Hg lasted for 2½ to 8 hours, and the left ventricular work also showed an increase of 31% to 178%. These figures, too, seemed sufficient for loading of the left ventricle. As for the site of inflating the balloon, the descending aorta seemed the best portion of the aorta for degree and duration of elevation of left ventricular pressure. This is because the cerebral circulation could be maintained in good condition with the balloon inflated in the descending aorta.

(2) *Electrocardiographic changes*

Among four cases with right ventricular loading, there was flattening of the T wave in both precordial leads in one, a slight depression of the S-T segment in one, an inversion of the T wave in leads II and III and the left precordial lead in one, and a large T wave in both precordial leads in one. Some change in the S-T segment or T wave, partly like the "strain pattern", was seen in all cases with right ventricular loading. On the other hand, it should be noted that no case had changes like the "strain pattern" in the experiments of left ventricular loading. Among 6 cases of left ventricular loading, there was an elevation of the S-T segment in both precordial leads long after inflation of the balloon in one and just prior to death in the other, a depression in the S-T seg-

ment just prior to death in two, a tall T wave in one and no change except bradycardia in one. It is assumed that the balloon inflated in the pulmonary artery to load the right ventricle induced hypoxemia which caused a tendency to coronary insufficiency or "strain pattern" in the electrocardiogram, while the balloon in the aorta, as long as it was placed distal to the coronary orifices so as to avoid reduction of the coronary blood flow, did not. The results of the present experiment were in accord with Maekawa's opinion¹⁸⁾ that electrocardiographic changes of coronary insufficiency rarely occur in the normal heart with increased load, and that the presence of the coronary insufficiency pattern with an increased load means the presence of some latent disease such as hypoxemia or latent coronary insufficiency.

The fact that T wave inversion occurred in the left precordial lead in spite of an increased load on the right ventricle in # 338 may be explained as follows: (1) the balloon inflated in the pulmonary artery put pressure upon the main branch of the left coronary artery which runs under the root of the pulmonary artery, and/or (2) an elevation of the right ventricular pressure caused a rise in right atrial pressure, then in coronary sinus pressure, so that the coronary blood flow was reduced to bring about coronary insufficiency in the left ventricular site, because Thebesian veins are more numerous in the right ventricle and atrium than in the left¹⁶⁾, and/or (3) reflex of coronary vessel spasm occurred selectively in the left coronary artery. But these are nothing but assumptions.

(3) *Hemodynamic changes* (see Table 2)

i) *Respiration and cardiac rate*

Generally speaking, both were reduced in parallel after inflation of the balloon. However, reduction of respiratory rate was marked in # 319, # 345, # 350 (died immediately) and # 356, in which the cerebral circulation was more or less likely to be disturbed because the balloon was inflated in or proximal to the ascending aorta. Ventricular fibrillation followed death appeared only in # 352 with the balloon inflated in the aortic arch, among # 343, # 345, # 352 and # 356 which lived longer than 5 hours with the balloon inflated.

ii) *Mean pulmonary artery wedge pressure (WPM)*

As previously described, WPM was hardly elevated in the experiment of left ventricular load-

ing. In #352 and #356 which had an elevated Wpm just prior to death, an elevation of left ventricular diastolic pressure was seen in advance of or in parallel with that of Wpm. There was no elevation of the left ventricular diastolic pressure in #345 which showed no elevation of Wpm. Thus Wpm seemed to be elevated as left ventricular diastolic pressure rose in the experiment of left ventricular loading. It could be said that Wpm was elevated backward when the left ventricle failed because of increased loading.

#356, in which a rise of the left atrial pressure was intended, showed no immediate elevation of Wpm after inflation of the balloon, although the right ventricular systolic pressure was slightly elevated. Wpm started to rise about $7\frac{1}{3}$ hours after inflation of the balloon, when the left ventricular diastolic pressure also started to rise. It is assumed that because of an insufficient rise of left atrial pressure with the inflated balloon, Wpm at last started to rise backward when left ventricular failure developed.

iii) Systemic arterial pressure and pulmonary arterial pressure in left ventricular loading

As shown in Fig. 6 a), b), c) and d), an elevation of the left ventricular pressure with the inflated balloon caused scarcely any rise in the pulmonary arterial pressure. The author had studied a clinical case with probable pheochromocytoma, in whom an attack of hypertension was brought on during cardiac catheterization. In this case a rise in the systemic arterial pressure did not affect the pulmonary arterial pressure. Table 3 presents the cardiac catheterization findings.

TABLE III CARDIAC CATHETERIZATION FINDINGS

K.N. 53 ♀		Ht: 148.5cm	Wt: 47kg	Body surface: 2.28m ²
		Date: Nov. 17, 1958	Usual blood pressure: 130/80-80	
		Before attack(1.50p.m.)	During attack(3.50p.m.)	After attack(4.00p.m.)
Brachial artery	P1	182 mm.Hg	220	150
	P4	100	140	120
	P5	96	140	120
PC (Wedge pressure)	mean	3	3	1
PA	Syst.	18	17	16
	diast.	6	4	4
	mean	8.5	7.5	6
RV (Outflow)	Syst.	17		22
	diast.	-3		-3
	end-diast.	-1.5		1
	mean	5		
RA	mean	-2		
SVC	mean	-1		
IVC	mean	1.5		
Cub. V	mean	0		
Arterio-venous O ₂ difference		9.80 vol%		
O ₂ consumption		196 cc/min.		
Cardiac output		2000cc/min.		
Cardiac Index		0.9 l/min./m ²		
eff. MVA		1.57 cm ²		
PAR		220 dynes.sec.cm ⁻⁵		

The patient, a 55-year-old Japanese female, was hospitalized at Kyoto University Hospital with a diagnosis of probable pheochromocytoma. Cardiac catheterization was performed to measure catecholamine in the renal veins on November 17, 1958. Systemic blood pressure, usually 130/80-80 mm.Hg, was elevated to 182/100-96 probably because of psychic tension on the day of the catheterization. While the right atrial pressure was measured, the patient suddenly had an attack of shivering starting in both hands, then the lips, and the blood pressure rose to 220/140-140. The catheter was then promptly advanced into the pulmonary artery. The pulmonary arterial pressure during the attack was quite as normal as before the attack. About 10 minutes later the attack spontaneously subsided and the blood pressure went down to 150/120-120. The pulmonary arterial pressure as well as the Wpm showed little change before, during and after the attack. These clinical findings were in accord with the results of the experiments in dogs.

iv) Cardiac output, pulmonary arteriolar resistance, total peripheral resistance, and right and left ventricular work

Harrison et al.¹¹⁾ and Huckabee et al.¹³⁾ reported an increase in cardiac output, an elevation of mean arterial pressure, thus an increase in work, following injections of epinephrine, or of a large amount of saline, or clamping of the carotid artery in dogs. Lombardo et al.¹⁾ observed an increase in cardiac output, an unchanged or a slightly elevated mean arterial pressure, thus an increase in work in man during exercise. In the author's experiments the cardiac output was increased in 2 and decreased in 2 of 4 cases with increased loading of the left ventricle by inflating a balloon in the aorta. In the cases with decreased output, #352 and #367, the balloon seemed to be inflated tightly enough in the aorta so to nearly obstruct the blood flow. Naturally, the mean arterial pressure as well as the total peripheral resistance was markedly elevated in these two cases, so that the left ventricular work was increased in all 4 cases with left ventricular loading. Changes in the right ventricular work in cases with left ventricular loading depended upon those in cardiac output, because the mean pulmonary arterial pressure remained almost unchanged during elevation of the systemic arterial pressure. There was no relation between

right and left ventricular work.

356 with the balloon inflated in the left atrium showed increased right ventricular work and decreased left ventricular work. The results indicated that # 356 was an experiment of right ventricular loading instead of left. An increase in the pulmonary arteriolar resistance in # 356 also supported this opinion.

SUMMARY

1) Electrocardiographic as well as hemodynamic changes were studied in cases of acutely increased loading of the right or left ventricle with the balloon inflated in the pulmonary artery or the aorta in dogs. The experimental methods were also examined.

2) A slight tendency in the electrocardiogram to a coronary insufficiency pattern or a "strain pattern" was seen in the cases of right ventricular loading, because the balloon inflated in the pulmonary artery may have caused hypoxemia. This was not found in the cases of left ventricular loading, as long as the balloon was inflated in the aorta distal to the coronary orifices so as to avoid reduction of the coronary blood flow.

3) Therefore, it is assumed that the development of the coronary insufficiency or the "strain pattern" in the electrocardiogram by an increased load means the presence of some latent disease like hypoxemia or latent coronary insufficiency.

4) The mean pulmonary artery wedge pressure was scarcely elevated in the cases of left ventricular loading due to elevation of the systemic arterial pressure. The elevation of the mean pulmonary artery wedge pressure started as left ventricular failure developed.

5) As long as left ventricular failure does not develop, an elevation of the systemic arterial pressure does not have any influence on the pulmonary arterial pressure. This fact could be ascertained not only in dogs, but also in a patient with probable pheochromocytoma through cardiac catheterization.

6) In this series of experiments with left ventricular loading, the cardiac output was increased in two, and decreased in two of four cases, while the left ventricular work was increased in all four cases. The cardiac output was decreased in two cases with a marked increase in total peripheral resistance.

SECTION 2: CHANGES IN HEMODYNAMICS, CORONARY CIRCULATION AND MYOCARDIAL OXYGEN METABOLISM, AND RELATIONS OF THOSE TO ELECTROCARDIOGRAM DURING INCREASED LOAD IN THE CLOSED-CHEST DOG WITH INDUCED CORONARY INSUFFICIENCY

INTRODUCTION

It was repeatedly emphasized in Part I³⁾ that in studies of the electrocardiogram in coronary insufficiency both the work of the heart and the myocardial oxygen consumption must be taken into consideration, since coronary insufficiency is induced by imbalance in the demand and supply of myocardial oxygen. This was confirmed from the results reported in Section 1. Electrocardiographic changes of the coronary insufficiency or the "strain pattern" type were not present in the cases with

31 to 178% increased loading of the left ventricle in dogs under almost physiological conditions, and thus it was assumed that the myocardial oxygen supply also increased in these cases as the work of the heart, that is, myocardial oxygen demand increased. The purpose of this section is to investigate the relationship between changes in the electrocardiogram and changes in hemodynamics and myocardial oxygen metabolism during an increased load on the dog's heart with coronary insufficiency induced by the method described in the previous paper³⁾. Another purpose is to compare

changes in hemodynamics during an increased load on the dog's heart with induced coronary insufficiency with those during an increased load on the dog's heart under nearly physiological conditions as attained in Section 1 of this report.

METHOD

Eight of the twenty one dogs used in the experiments reported in Part I³⁾ survived until the period—about 10 minutes after insertion of the catheter into the coronary artery—when transient changes in the electrocardiogram as well as in hemodynamics subsided after starting coronary perfusion with the dog's

by the methods described in Part I³⁾ and in Section 1 of Part II. As also described in the previous paper, left coronary blood flow was determined before insertion of the catheter into the left coronary artery, if necessary, based on the values of Gregg et al.¹⁹⁾ and of Eckenhoff et al.²⁰⁾, both coincidentally 74 cc/min./100 gm. left vent., in the anesthetized dog. The assumption that the left ventricle accounts for about 52 per centage²¹⁾ of the weight of the entire heart was also used in the calculation. Myocardial oxygen consumption of the left ventricle (or left ventricular oxygen consumption) and left ventricular work equivalent of oxygen were measured from the following formulae:

$$\text{Myocardial oxygen consumption of the left ventricle (cc./min.)} = \frac{\text{Left coronary blood flow (cc./min.)} \times \text{Coronary arteriovenous oxygen difference (vol. \%)}{100}$$

$$\text{Left ventricular work equivalent of oxygen (cc./kg.-M.)} = \frac{\text{Myocardial oxygen consumption of the left ventricle (cc./min.)}}{\text{Left ventricular work (kg-M/min.)}}$$

own arterial blood through the catheter inserted into the left coronary artery. As described in Part I, three other catheters were placed in the coronary sinus, pulmonary artery and branchial artery. In the present experiment I investigated the relationship between changes in the electrocardiogram and changes in cardiac output, left ventricular work, total peripheral resistance, coronary arteriovenous oxygen difference, myocardial oxygen extraction coefficient, left coronary blood flow, myocardial oxygen consumption in the left ventricle and the left ventricular work equivalent of oxygen in eight dogs with increased load produced by inflating a balloon in the abdominal aorta or by intravenous injection of nor-epinephrine. During this experiment, there were some accidents: a catheter in the coronary sinus slipped off while being moved a little because of the difficulty of obtaining a sample of blood from the coronary sinus: the ventricular loading failed because of rupture of the inflated balloon: ventricular fibrillation occurred immediately after administration of nor-epinephrine. In all the experiment was successfully performed seven times in four of the eight dogs. The balloon was inflated in the abdominal aorta under fluoroscopic control, because the results of the experiment reported in Section 1 indicated that for successful loading of the left ventricle the balloon should be inflated in the abdominal aorta so as to maintain cerebral blood flow. In addition, 4 cm. below the diaphragm in the abdominal aorta was selected as the best site for inflating the balloon in order to maintain renal blood flow, too. In using nor-epinephrine, 10 to 20 γ per kilo in 50 cc. of physiologic saline was infused into the femoral vein. Cardiac output, left ventricular work, total peripheral resistance, myocardial oxygen extraction coefficient and left coronary blood flow were measured

Electrocardiograms were taken simultaneously in lead III, and left and right precordial leads (Vs and Vd); leads CRs and CRd were used only in #361 as precordial leads.

RESULTS

Table 1 (a) (b) (c) and (d) shows the detailed values of hemodynamics, coronary circulation and electrocardiograms in each experiment, while changes in hemodynamics and coronary circulation are summarized in Fig. 1. The figures on the abscissa in Fig. 1 represent time after the start of the experiment. These figures are common to Table 1 (a) (b) (c) and (d).

1) Hemodynamic changes (Fig. 1)

i) Respiratory oxygen consumption

Oxygen consumption was reduced in all cases about 10 minutes after the start of coronary artery perfusion with dog's own arterial blood through the catheter inserted into the left coronary artery. It was somewhat increased in #375 as time passed, but was much diminished after inflation of the balloon. Infusion of nor-epinephrine slightly increased the oxygen consumption, again.

ii) Cardiac output (CO)

Cardiac output was reduced in all cases about 10 minutes after the start of coronary artery perfusion with the dog's own arterial blood through a catheter inserted into the left coronary artery. It was much reduced in 3 of 4 cases after inflation of the balloon; it was slightly increased in one, but did not return to the control value. Infusion of nor-epinephrine increased it over the control value.

Fig. 1. Effects of balloon inflation in the aorta and nor-adrenalin infusion on the heart and coronary circulation in the anesthetized, closed-chest dogs with coronary insufficiency. ○ #361, × #368, △ #375, □ #386. LVW: Left ventricular work, MQC: Myocardial Oxygen consumption, LVWEqO₂: Left ventricular work equivalent of oxygen

iii) Myocardial oxygen extraction coefficient ($\Delta\phi_2$)

The myocardial oxygen extraction coefficient was decreased in 3 and increased in 1 of 4 cases in this experiment about 10 minutes after the start of coronary artery perfusion with the dog's own arterial blood through a catheter inserted into the left coronary artery. However, as described in the previous paper³⁾, 4 of 7 cases showed a decrease in it at this period. The cases once decreased at this time (#361, #368) showed an increase after

inflation of the balloon, while one case once increased (#386) showed a decrease. But the values in both, after inflation of the balloon, were higher than in the controls. Infusion of nor-epinephrine increased $\Delta\phi_2$.

iv) Mean arterial blood pressure

As described in the previous paper³⁾, blood pressure fell in all cases, in half more than 30%, about 10 minutes after the start of coronary artery perfusion with the dog's own arterial blood through the catheter inserted into the left coronary artery.

TABLE I COMPLETE DATA FOR EACH EXPERIMENT ON CORONARY CIRCULATION, MYOCARDIAL OXYGEN METABOLISM, HEART WORK AND ECG.

* values/100gm left ventricle/min.

(a) #361 18kg Heart weight 130gm.

		① Control		② 13 to 21 min. after start of coronary perfusion		③ 5 to 11 min. after inflating balloon	
O ₂ and CO ₂ content vol%	EA	32.10	16.23 (sat. 16.48)	30.50	13.03	31.30	10.82
	RV	40.53	8.61	36.11	6.15	36.38 (PA)	3.44 (PA)
	Sinus	45.21	2.71	41.20	2.46	39.12	1.23
Sys. Δ O ₂ vol%			7.62		6.88		7.38
Cor. Δ O ₂ vol%			13.52		10.57		9.59
O ₂ consumpt. cc/min.		130		88		41	
CO cc/min.		1700		1280		555	
Myocard O ₂ extract. coeff. ($\Delta\phi_2$)		83		82		89	
BAm mm.Hg		112		96		119	
LVW Kg-M/min.		2.58		1.69 (-34.5%)		0.90 (-65%)	
CBF (Left vent.) cc/min.		52 (Gregg) 75 *		5.0 7.25 *		4.4 6.4 *	
MO ₂ C (Left vent.) cc/min.		7 10.2 *		0.53 (-92%) 0.77 *		0.42 (-94%) 0.61 *	
TPR dynes sec/cm ⁵		5250		5950		20500	
LVWEqO ₂ cc/kg-M		2.7		0.315 (-88%)		0.47 (-81.5%)	
ECG findings	QRS (III) sec.	0.05		0.05		0.05	
	PR sec.	0.35		0.38		0.40	
	QT sec.	0.2		0.2		0.225	
	QT calculated sec.	0.191 - 0.271		0.20 - 0.28		0.206 - 0.286	
	mV III	0		-0.12		-0.1	
	ST displacement	0		-0.12		-0.04	
	CRd	0		-0.4		-0.34	

(b) #368 15kg Heart weight 115gm.

		① Control	② 10 to 14 min after start of coronary artery perfusion	③ 6 to 10 min after inflating the balloon
vol% content	BA	15.78	14.65	13.89
	PA	9.60	9.09	6.82
	Sinus	3.28	3.66	2.52
Sys. Δ O ₂ vol%		6.18	5.56	7.07
Cor. Δ O ₂ vol%		12.50	10.99	11.37
O ₂ Consumpt. cc/min.		132	83	52
CO cc/min.		2150	1500	740
Myocard. O ₂ extract. coeff. ($\Delta\phi_2$)		79	75	82
BAm mm.Hg		91	70	120
LVW Kg-M/min		2.65	1.43 (-46%)	1.21 (-54.5%)
CBF (Left vent.) cc/min.		455 (Gregg) 75 *	3.45 5.67 *	4.2 6.9 *
MO ₂ C (Left vent.) cc/min.		5.7 9.4 *	0.375 (-93.5%) 0.62 *	0.475 (-91.5%) 0.78 *
TPR dynes sec/cm ⁵		3400	3750	13000
LVWEqO ₂ cc/kg-M		2.15	0.26 (-88%)	0.39 (-82%)
ECG findings	QRS (III) sec.	0.035	0.035	0.035
	RR sec.	0.51	0.47	0.47
	QT sec.	0.24	0.23	0.23
	QT calculated sec.	0.238 - 0.318	0.227 - 0.307	0.227 - 0.307
	mV III	0	0.22	0
	ST displacement	0	-0.09	0
	Va	0	-0.08	0

BA: Brachial artery RV: Right ventricle Sinus: Coronary sinus
 Sys Δ O₂: Systemic arterio-venous oxygen difference
 Cor. Δ O₂: Coronary arterio-venous oxygen difference
 O₂ consumption: Oxygen consumption CO: Cardiac output
 Myocard. O₂ extract. coeff: Myocardial oxygen extraction coefficient ($\Delta\phi_2$)
 BAm: Mean brachial arterial pressure LVW: Left ventricular work
 CBF: Coronary blood flow MO₂C: Myocardial oxygen consumption
 TPR: Total peripheral resistance
 LVWEqO₂: Left ventricular work equivalent of oxygen

(c) #375 11kg Heart weight 80gm.

		① Control	② 11 to 15 min. after start of coronary artery perfusion	③ 80 min. after start of coronary artery perfusion	④ before inflating balloon (6 hr. after start of coronary artery perfusion)	⑤ 10 min. after inflating balloon
vol % content	BA	14.26	13.76	14.96	12.96	8.97
	PA	7.38	7.50	10.22	6.98	2.99
O ₂ Sinus		2.00	4.00	1.75	-	-
Sys. Δ O ₂ vol%		6.88	6.26	4.74	5.98	5.98
Cor. Δ O ₂ vol%		12.26	9.76	13.21	(10.00) [†]	-
O ₂ consumpt. cc/min.		144	55	63	69	35
CO, cc/min.		2100	880	1330	1160	585
Myocard O ₂ % extract coeff. (Δ P ₂)		86	71	87	> 46	> 67
RAM mm. Hg		118	108(-8.5%)	76	60	46
LVW Kg-M/min.		3.38	1.29(-62%)	1.37(-60%)	0.95(-72%)	0.365(-89%)
CHF (cc/min. Left vent.)		32 (Gregg) 75*	6 14.2 *	3.6 8.5 *	3.8 9.0 *	2.8
MO ₂ (cc/min. Left vent.)		3.9% 9.3 *	0 585(-85%) 1.38 *	0.475(-88%) 1.12 *	(0.38/-90%) 0.9 *	0.9 *
TPR dynes.sec/cm ⁵		4500	9800	4550	4130	6300
LVWEq O ₂		1.17	0.455(-61%)	0.348(-70%)	(0.40(-66%)) [†]	-
ECG findings	sec. QRS (III)	0.035	0.035	0.035	0.035	
	RR sec.	0.34	0.40	0.35	0.45	
	QT sec.	0.19	0.225	0.235	0.24	
	QT calcu- lated	0.187 - 0.267	0.206 - 0.286	0.191 - 0.271	0.221 - 0.301	
	ST dis- place- ment					
mv III		0	-0.23	-0.41	-0.22	
Vp		0	0	-0.23	-0.07	
Vs		0	0.13	-0.41	-0.36	

(d) #386 11kg Heart weight 9.0gm.

		① Control	② 4 to 9 min. after start of coronary artery perfusion	③ 2 to 6 min. after inflating balloon	④ 2 to 6 min after infusion of nor-adrenalin	④ 38 to 42 min. after infusion of nor-adrenalin	⑤ 15 min after occlusion of coronary artery	⑤ 25 min. after occlusion of coronary artery
vol % content	BA	10.44	10.19	8.48	6.98	6.23		
	PA	4.22	2.49	3.48	2.74	1.99		
O ₂ Sinus		3.73	1.99	1.99	1.00	1.75		
Sys. Δ O ₂ vol%		6.22	7.70	5.00	4.24	4.24		
Cor. Δ O ₂ vol%		6.71	8.20	6.49	5.98	4.48		
O ₂ consumpt. cc/min.		60	54	40	52	48		
CO cc/min.		965	700	800	1230	1130		
Myocard O ₂ % extract coeff. (Δ P ₂)		64%	80%	76%	86%	72%		
RAM mm Hg.		47	25	80	98	40	16/0	0
LVW Kg-M/min.		0.62	0.24(-61%)	0.87(40.3%)	1.64 (165%)	0.62(0%)		
CHF (Left vent) cc/min.		35.5 (Gregg) 75 *	0.88 1.85 *	5.4 11.3 *	9.4 19.7 *	3.75 7.9 *		
MO ₂ (Left vent) cc/min		12.38 4.95 *	0.072(-97%) 0.15 *	0.35(-85%) 0.73 *	0.56(-77%) 1.18 *	0.17(-93%) 0.36 *		
TPR dynes sec/cm ⁵		3900	2850	8000	6300	2830		
LVWEq O ₂ cc/kg-M		3.85	0.3 (-92%)	0.4 (-90%)	0.34 (-91%)	0.27 (-93%)		
ECG findings	sec. QRS (III)	0.05	0.05	0.05	0.05	0.05	0.05	0.05
	RR sec.	0.37	0.39	0.395	0.38	0.40	0.38	0.75
	QT sec.	0.23	0.23	0.235	0.24	0.21	0.235	0.29
	QT calcu- lated	0.167-0.247	0.204-0.284	0.205-0.285	0.20-0.28	0.205-0.285	0.214-0.294	0.20-0.28 0.298-0.378
	ST dis- place- ment							
mv III		-0.08	-0.1	-0.1	0	-0.06	-0.06	0
Vp		-0.06	-0.06	-0.06	-0.04	-0.06	-0.04	0
Vs		-0.18	0	0.36	0.44	-0.1	0.1	0.74

Inflation of the balloon caused a rise in blood pressure above that of the control in 3 of 4 cases, but even caused a fall in one dog (#375), whose heart seemed to have been extremely weakened, since 6 hours had elapsed before inflation of the balloon.

v) Total peripheral resistance (TPR)

Total peripheral resistance was increased in 3 of 4 cases, while it was diminished in one case about 10 minutes after the start of coronary artery perfusion. Inflation of the balloon increased TPR above that of the control in all cases.

vi) Left ventricular work (LVW)

Left ventricular work was diminished in all cases about 10 minutes after the start of coronary artery perfusion. Further diminution in left ventricular work followed inflation of the balloon in 3 of 4 cases, while in one case (#375) inflation of the balloon increased TPR, which was further increased by nor-epinephrine injection, above that of the control.

vii) Myocardial oxygen consumption
(in the left ventricle) (MO_2C)

The values corresponding to phases ① and ② in Fig. 1 are connected with dotted lines, because determination of the controls was based on Gregg's value, and so they were not used as controls in the true sense. A slight decrease or no change was seen in two, and an increase in one after inflation of the balloon.

viii) Left ventricular work equivalent of oxygen (LVWEqO_2)

The values corresponding to phases ① and ② in Fig. 1 are connected with dotted lines for the same reason. LVWEqO_2 as well as MO_2C was markedly diminished in all cases at the period of ②, i. e. about 10 minutes after the start of coronary artery perfusion. A slight increase in LVWEqO_2 occurred following inflation of the balloon in all three cases, while nor-epinephrine injection decreased LVWEqO_2 through an increase in LVW dominant over that in MO_2C .

2) Electrocardiographic changes

Transient changes in the electrocardiogram immediately after the start of coronary artery perfusion through a catheter inserted into the left coronary artery have already been described in the previous paper³⁾. In the present experiment electrocardiographic changes occurring after the transient changes had subsided were studied in relation

to hemodynamics, especially to LVWEqO_2 , without applying any procedure but in some cases inflating the balloon to alter the hemodynamic status. The results of each experiment are shown Table 1 (a) (b) (c) and (d). Deviation of the S-T segment was measured according to Goldberger's criteria³⁹⁾; and Hegglin and Holzman's formula⁴⁰⁾ was used in calculating the standard Q-T interval. Following are the details of each experiment.

Dog #361 (Table 1 (a)): Depression of the S-T segment was seen in lead III and both precordial leads (CR_D and CR_S), especially in the left precordial lead (-0.4 mV.) 13 to 21 minutes after the start of coronary artery perfusion. The S-T segment depression in lead III was further slightly increased at 40 minutes. Then the balloon was inflated, and a diminution in the amount of S-T segment depression occurred 5 to 10 minutes after inflation in all leads, especially in leads CR_D and CR_S . There were no significant changes in the QRS complex or the Q-T interval.

Dog #368 (Table 1 (b)): 10 to 14 minutes after the start of coronary artery perfusion, the S-T segment was slightly elevated in lead III ($+0.22\text{ mV.}$) and depressed in lead V_S (-0.08 mV.) and in lead V_D (-0.09 mV.), while peaked T waves occurred in all leads. The balloon was inflated 14 minutes after the start of coronary artery perfusion. 6 to 10 minutes after inflation of the balloon the S-T segment returned to the isoelectric line in all leads, and the peaked T waves also diminished. There were no marked changes in the QRS complex and the Q-T interval.

Dog #375 (Table 1 (c)): 11 to 15 minutes after the start of coronary artery perfusion the S-T segment was depressed in lead III (-0.23 mV.) and in the isoelectric line in both precordial leads (V_S and V_D). In experiment #375, electrocardiographic changes were traced as time passed without inflating balloon for up to 6 hours. The S-T segment was markedly depressed in all leads (-0.41 mV. in lead III, -0.23 mV. in lead V_D and -0.41 mV. in lead V_S) at 80 minutes; the degree of depression of the S-T segment again decreased in all leads (-0.22 mV. in lead III, -0.07 mV. in lead V_D and -0.36 mV. in lead V_S) at 6 hours. The balloon was then inflated but no marked changes were seen except for the gradual development of bradycardia. The QRS complex and the Q-T interval showed no essential changes.

Dog #386 (Table 1 (d)): The S-T segment in all leads was already slightly depressed in the control period. 5 to 9 minutes after the start of coronary artery perfusion the electrocardiograms were still unstable; at 8 minutes the S-T segment was slightly depressed in lead III and nearer to the isoelectric line in lead Vs as compared with the control, while at 9 minutes, only 1 minutes later, the S-T segment in lead Vs showed an elevation (+0.36 mV.). The balloon was inflated at 21 minutes; the more elevated S-T segment (+0.44 mV.) was recorded in lead Vs 2 to 6 minutes after inflation of the balloon. The S-T segment deflection disappeared and the T wave was inverted 20 minutes after inflation of the balloon. Infusion of nor-epinephrine was then started with the balloon still inflated. The S-T segment was depressed (-0.1 mV.) at 2 minutes after the infusion, returned to the isoelectric line at 4 minutes and again showed a marked elevation (+0.74 mV.) at 6 minutes in lead Vs. Mean arterial blood pressure and left coronary blood flow were lower, 59 mm. Hg and 6.8 cc./min. respectively, at 6 minutes than at 4 minutes after the infusion. The elevation of the S-T segment decreased (+0.54 mV.), with the mean arterial blood pressure of 40 mm. Hg and the left coronary blood flow of 3.75 cc./min., at 38 to 42 minutes after the infusion, when the effect of nor-epinephrine seemed to have completely disappeared. The coronary artery perfusion was then stopped; a marked elevation of the S-T segment (+0.74 mV.) appeared again in lead Vs 15 minutes later. The mean arterial blood pressure was 16/0 mm. Hg at that time, then dropped to 0 mm. Hg 25 minutes after stopping the infusion when the elevated S-T segment in lead Vs nearly returned to the base line (+0.1 mV.) and the T wave was inverted for the first time in lead Vd. In this case from beginning to end electrocardiographic changes were found only in the S-T segment and T wave in the left precordial lead, Vs, while there were scarcely any in lead III and the right precordial lead, Vd. There were no marked changes in the QRS complex or the Q-T interval in this case, either.

In all the cases mentioned above, electrocardiographic changes were seen only in the S-T segment and the T wave, and none had any changes in the QRS complex. It was interesting that the cases with S-T segment depression in the left precordial lead (Vs) such as #361, #368 and #375 also showed

some deflection of the S-T segment in lead III and the right precordial lead (Vd)—usually S-T segment depression in Vd—, while in #386 which had S-T segment elevation in the left precordial lead (Vs) the change was present only in the left precordial lead (Vs).

DISCUSSION

1) The experimental method

The present experiment is a combination of the experiment of preparing closed-chest dogs with coronary insufficiency as described in Part I and that of causing an increased load on the dog's heart by inflating a balloon as described in Section 1 of Part II. Both experiments have already been discussed. It is assumed that even with the disadvantage of being unable to measure coronary blood flow before insertion of a catheter into the left coronary artery, the author's experiment with less operative invasions can serve the purpose of investigating changes in hemodynamics, coronary circulation and myocardial oxygen metabolism, and the relation between these and the electrocardiogram during a period of increased load on the left ventricle of the dog with coronary insufficiency.

2) Changes in hemodynamics, coronary circulation and myocardial oxygen metabolism during a period of increased load on the left ventricle of the dog with coronary insufficiency

i) Changes in hemodynamics

Changes in hemodynamics with an increased load on the left ventricle of dogs with induced coronary insufficiency were compared with those in dogs without coronary insufficiency. The latter changes were described in Section 1 of the present report.

Fig. 2. Relation between mean arterial pressure and cardiac output in dogs with and without coronary insufficiency.

As shown in Fig. 2, an elevation of mean arterial blood pressure following inflation of the balloon increased cardiac output in 2 and decreased it in 2 of 4 cases without coronary insufficiency, while it decreased cardiac output in all 4 cases with coronary insufficiency. In one of the latter 4 cases the mean arterial blood pressure did not rise even

Fig. 3. Relation between total peripheral resistance and cardiac output in dogs with and without coronary insufficiency.

Fig. 4. Relation between total peripheral resistance and left ventricular work in dogs with and without coronary insufficiency.

with an inflated balloon in the aorta.

As shown in Fig. 3 and Fig. 4, an increase in total peripheral resistance caused less decrease or even an increase in cardiac output in some, and increased left ventricular work in all dogs without coronary insufficiency, while it decreased cardiac output in all, and also decreased left ventricle work in almost all dogs with coronary insufficiency. Eckenhoff et al.²²⁾²³⁾ reported that a primary increase in mean arterial blood pressure (i. e. an increase in resistance) by constriction of the high abdominal aorta increased coronary flow and myocardial oxygen consumption, while it decreased cardiac output, cardiac work and cardiac efficiency. Their results were obtained in anesthetized, open-chest and open-abdomen dogs and coronary blood flow (left coronary inflow) was determined by the bubble flow meter while the author worked with anesthetized, closed-chest and closed-abdomen dogs and measured coronary blood flow (left coronary inflow) by the drip counter. In the experiment of Eckenhoff et al., cardiac work was decreased as the result of a decrease in cardiac output dominant over an increase in mean arterial blood pressure. The results of Eckenhoff et al. are in accord with those in the dogs with coronary insufficiency in the author's experiment. Meanwhile, Gregg and Shipley²⁵⁾ have reported that an increased load on the left or right ventricle caused by ligating the aorta or pulmonary artery much increased cardiac work as the net result of a marked elevation in mean arterial blood pressure dominant over a decrease in cardiac output. The results in the experiment of Gregg and Shipley are in accord with those in dogs without coronary insufficiency in the author's experiment. In the experiment of Eckenhoff et al. coronary blood flow was 65 cc./100 gm. of left vent./min., which increased to 110 cc./100 gm. of left vent./min. when mean arterial blood pressure was elevated. The latter value seems high enough to prevent the dog from developing coronary insufficiency during a rise in blood pressure, but it still seems to be lower than that during a rise in blood pressure under physiological conditions, since high resistances such as the bubble flow meter and the cannula were placed between the common carotid artery and the left coronary artery, and since they performed a large operation in opening the chest and abdomen. It can be said, therefore, that the results obtained by Eckenhoff et al. are

those of coronary insufficiency. In cases without coronary insufficiency, that is, under nearly physiological conditions as in the experiments of Gregg and Shipley, and of the author, cardiac work is augmented during an increased load as a result of a marked elevation in mean arterial blood pressure dominant over a less decreased cardiac output (cardiac output is even increased in some cases).

It can also be said that the heart appears to be safeguarded against dangerous anoxia induced by an increased peripheral resistance during coronary insufficiency by reducing cardiac output and work. Eckenhoff et al. mentioned a decrease in cardiac work as one of the mechanisms whereby the heart can be safeguarded against dangerous anoxia. The author wants to add that the opinion of Eckenhoff et al. may be true in cases with coronary insufficiency, in other words, in the heart with reduced cardiac reserve. The author believes that the effect of the vagus, as Kimura et al.²⁷⁾ pointed out in the control of coronary blood flow, should also be considered as one of the safeguarding mechanisms of the heart during coronary insufficiency.

ii) Changes in coronary circulation and myocardial oxygen metabolism

An increase in coronary blood flow during increased loading was noted in the dog by Gregg and Shipley²⁵⁾ and Eckenhoff et al.²³⁾ The former also reported that in the presence of a constant cardiac work, coronary arteriovenous oxygen difference

(ΔO_2) was diminished by half when coronary blood flow was increased three times, while in the presence of an increase in cardiac work coronary arteriovenous oxygen difference (ΔO_2) was increased at the same time as coronary blood flow was increased, so that the myocardium might take as much oxygen as possible. According to Eckenhoff et al.²⁴⁾, myocardial oxygen consumption decreases proportionately with coronary blood flow in hypotension induced by tetraethyl ammonium chloride or procaine hydrochloride. It is said that with a decrease in coronary blood flow myocardial oxygen consumption is decreased after all as the result of a decrease in coronary blood flow despite an increase in ΔO_2 because of little room for removing appreciably larger amounts of oxygen from the normally low oxygen content of coronary sinus blood in response to an increased demand. Hence, Eckenhoff et al.²²⁾ have shown a close correlation ($r=0.85$, $p<0.001$) between myocardial oxygen consumption and coronary blood flow. The author also found a close correlation ($r=0.78$, $PEr<0.23$) (Fig. 5) between them, although the number of cases is small.

Kobayashi et al.²⁶⁾ found that ΔO_2 increased proportionately with arterial oxygen content. Therefore, it is believed that the myocardial oxygen extraction coefficient ($\Delta\phi_2$) is a better index of the oxygen uptake ability of the myocardium. Here, the author investigated alterations in $\Delta\phi_2$, coronary

Fig. 5. Relation between myocardial oxygen consumption and coronary blood flow. ○ #361, #368, #375, ● #386. #386 shows a low myocardial oxygen consumption in a given coronary blood flow, as compared with the other three cases. It is because the arterial oxygen content was extremely low in the control and consequently, the myocardial oxygen extraction could not rise as high as the others. S-T segment in #386 was elevated, while in the other three it was depressed.

blood flow and myocardial oxygen consumption during an increased load in the dog with induced coronary insufficiency.

As shown in Fig. 1 and Table 1 (a) (b) (c) and (d), left ventricular work, coronary blood flow and $\Delta\phi_2$ are all decreased with the exception of increased $\Delta\phi_2$ in #386 about ten minutes after the start of coronary artery perfusion by the dog's own arterial blood. When a load is placed on the left ventricle in a dog with coronary insufficiency, the alterations show various combinations such as a decrease in left ventricular work and coronary blood flow, and an increase in $\Delta\phi_2$ (#361); a decrease in left ventricular work, and an increase in coronary blood flow and $\Delta\phi_2$ (#368); a decrease in $\Delta\phi_2$, and an increase in left ventricular work and coronary blood flow (#386). From the standpoint of oxygen economy in the myocardium, experiment #368, in which after inflation of the balloon left ventricular work was decreased, while coronary blood flow and $\Delta\phi_2$ were increased, is the best among these combinations. Thus the electrocardiogram in #368 would be expected to improve after inflation of the balloon corresponding to the improvement in oxygen economy. The facts as shown in Table 1 (b) and Fig. 6 (b) (ECG at phase ② and ③) support this assumption. Details of other combinations will be discussed later in the reports on each experiment.

In this series coronary blood flow was increased in two cases (#386 ②→③, #386 ③→④) and decreased in one case (#375 ②→②') when cardiac work was increased during an increased load in dogs with coronary insufficiency. Anrep et al.⁴⁴⁾, Katz et al.⁴⁵⁾ and Eckenhoff et al.²³⁾ reported that the coronary blood flow increased with augmented cardiac output. Although the author's experimental conditions were quite different from theirs, it was interesting that in #375 the coronary blood flow decreased with augmented cardiac work as the result of an increased mean arterial blood pressure; this condition of an increased cardiac output with a decreased mean arterial blood pressure was unexpectedly brought about 80 minutes after the start of coronary artery perfusion in #375.

In none of the experiments was there the worst combination for myocardial oxygen economy such as an augmented cardiac work with a decreased coronary blood flow and myocardial oxygen extraction coefficient. Along with the fact, as des-

cribed previously, that the heart in coronary insufficiency responds to an augmented resistance load with decreased cardiac output and work, this also arouses keen interest as one of the safeguarding mechanisms of the heart.

3) *Changes in left ventricular work equivalent of oxygen (LVWEqO₂) and electrocardiogram*

Wégria²⁸⁾ reported that in anesthetized, open-chest dogs with a constant blood pressure a slight change in the S-T segment and T wave—S-T segment elevation in his experiment—was usually found with a decrease of 35 to 70 per cent in coronary blood flow, while a marked change occurred with a decrease of 70 to 100 per cent. Kimura et al.²⁹⁾³⁰⁾ have concluded that S-T segment depression appears when coronary blood flow is reduced to 50 to 60 cc./100 gm. of left vent./min., that is, one third to two fifths normal flow. Meanwhile, Dietrich et al.^{31)–33)}, Hara²⁾ and Hayase³⁴⁾ pointed out that electrocardiographic changes in coronary insufficiency could not be explained solely by reduction in coronary blood flow. Kimura et al. also observed that coronary blood flow producing electrocardiographic change was lower with a concurrent fall in systemic blood pressure and coronary blood flow produced by depressor agents than with reduction of the coronary blood flow alone and no change in the systemic blood pressure. This is due to nothing more than that a decrease in cardiac work caused by a fall in systemic blood pressure lowered the oxygen demand of the myocardium. Therefore, as repeatedly emphasized in Part I, studies on the electrocardiogram of coronary insufficiency should always take into consideration both the work of the heart and the myocardial oxygen consumption, since coronary insufficiency is induced by a relative shortage of oxygen supply to oxygen demand in the myocardium. This is the reason why the author attempted to study the electrocardiographic changes of coronary insufficiency in comparison with changes in the left ventricular work equivalent of oxygen, that is, the ratio of myocardial oxygen consumption in the left ventricle to left ventricular work, which appears to represent most faithfully the relationship between oxygen supply and oxygen demand in the myocardium.

Hara²⁾ reported two patients with circulatory disturbances and one with coronary disturbance, who showed no electrocardiographic changes during

the hypoxia test because of an increased left ventricular work equivalent of oxygen as the result of a more marked decrease in left ventricular work in spite of the presence of a marked decrease in myocardial oxygen consumption. In the author's experiment the same result was obtained in two cases, #361, #375. In these two the S-T segment depression was improved corresponding to an increase in the left ventricular work equivalent of oxygen through a marked decrease in left ventricular work dominant over a marked decrease in myocardial oxygen consumption (see Table 1 (a), Fig. 6 (a), ②→③; Table 1 (c), Fig. 6 (c), ②'→②''). Fig. 6 (a) (b) (c) and (d) indicate the relationship between electrocardiographic changes and coronary blood flow, myocardial oxygen consumption of the left ventricle, left ventricular work and left ventricular work equivalent of oxygen in each experiment.

The degree of S-T segment depression in #361 (Fig. 6 (a) phase ②→③) decreased in all leads as the left ventricular work equivalent of oxygen increased after balloon inflation due to a marked decrease in left ventricular work dominant over a decrease in coronary blood flow and myocardial oxygen consumption.

In #368 (Fig. 6 (b), phase ②→③) the depressed S-T segment in lead V_b and V_s and the elevated S-T segment in lead III all returned to the base line after balloon inflation as the left ventricular work equivalent of oxygen increased due to an increase in coronary blood flow and myocardial oxygen consumption in the presence of a decrease in left ventricular work.

In #375 (Fig. 6 (c)) at 80 minutes after the start of coronary artery perfusion (phase ②') the left ventricular work equivalent of oxygen decreased as the result of an increase in left ventricular work in the presence of a decrease in myocardial oxygen consumption; the latter was caused by a decrease in coronary blood flow in spite of an increase in the myocardial oxygen extraction coefficient ($\Delta\phi_2$). Obviously there was little room for removing larger amounts of oxygen from the coronary sinus blood in response to an increased demand even in the presence of an increased $\Delta\phi_2$. Thus, the S-T segment was much more depressed in all leads at phase ②' than at phase ②. In this experiment the course was followed without applying any more procedures until 6 hours after the start of coronary

artery perfusion. The ventricular work equivalent of oxygen increased at 6 hours as the result of a decrease in left ventricular work dominant over a decrease in myocardial oxygen consumption. (As it became impossible to take blood sample from the coronary sinus at 6 hours, the presumptive value of coronary arteriovenous oxygen difference had to be used for calculation.) Thus, the relationship between myocardial oxygen demand and supply were improved at 6 hours (phase ②'') rather than at 80 minutes (phase ②') after the start of coronary artery perfusion. The electrocardiogram showed a decrease in the S-T segment depression in all leads at phase ②'' as compared with phase ②'.

In #386 (Fig. 6 (d)) the S-T segment was elevated in lead V_s instead of depressed as seen in the other three. The author described in Part I the S-T segment elevation with a marked diminution in coronary blood flow. Moreover, in #386 attention should be paid to the low oxygen content of arterial blood in the control period which caused a poor coronary arteriovenous oxygen difference, and thus a poor oxygen uptake in the myocardium (see Table 1 (d)). This fact is also obvious in Fig. 5. In #386 (black dots) the myocardial oxygen consumption is lower at a given coronary blood flow than in the others (white dots). It is to be expected that S-T segment elevation, as well as depression, increases in parallel with a decrease in the left ventricular work equivalent of oxygen, since S-T segment elevation represents severe myocardial anoxia. As shown in Fig. 6 (d), the electrocardiograms of #386 are so changeable at 5 to 9 minutes after the start of coronary artery perfusion (phase ②) and at 2 to 6 minutes after infusion of nor-epinephrine (phase ④) that they cannot be correlated with hemodynamic values, including cardiac output as determined by Fick's method. Therefore, correlation should be done at 2 to 6 minutes after inflation of the balloon (phase ③) and at 38 to 42 minutes after infusion of nor-epinephrine (phase ④'), when the electrocardiogram has become quite stable. The left ventricular work equivalent of oxygen was decreased more at phase ④' than at phase ③ as the result of a decrease in myocardial oxygen consumption dominant over a decrease in left ventricular work. The elevation of the S-T segment in lead V_s at phase ③ (+0.44 mV.) was further increased at phase ④' (+0.54 mV.).

Throughout the experiments there were no

Fig. 6. (a), (b), (c) and (d). Relationship of electrocardiogram to coronary blood flow (CBF), myocardial oxygen consumption (MO_2C), left ventricular work (LVW) and left ventricular work equivalent of oxygen ($LVWEqO_2$) in each experiment.

changes in the QRS complex, which differentiated the author's experiment from myocardial infarction. At autopsy no distinct infarction was noted in any case.

In regard to the S-T segment deviation, it has been shown by experiments in the dog by Wol-

jury to the heart.

4) *Left ventricular work equivalent of oxygen and mechanical efficiency of the heart (cardiac efficiency)*

The mechanical efficiency of the heart is determined by the following formula:

$$E = \frac{\text{Left ventricular work (kg-M/min.)}}{\text{Left ventricular energy consumption (kg-M/min.)}} \\ = \frac{\text{CO (cc./min.)} \times \text{mean arterial blood pressure (cm. Hg)} \times 13.6}{\text{MO}_2\text{C (cc./min.)} \times 2.057}$$

ferth et al.³⁵⁾, in the turtle by Pruitt and Valencia³⁶⁾ and by other investigators³⁷⁾³⁸⁾ that myocardial anoxia or acute coronary insufficiency produces a depressed S-T segment in leads that face the injured epicardial surface of the heart because of injury of the endocardial surface of the ventricles, while myocardial infarction produces an elevated S-T segment in the same lead because of injury of the epicardial surface or transmural region of the ventricles. In opposition to the conventional theory Kimura et al.³⁰⁾ stated that even myocardial anoxia or acute coronary insufficiency produces injury in the transmural region of the ventricle just as coronary occlusion does, and concluded that a diminution in coronary blood flow in one branch of the coronary artery produces S-T segment elevation in a lead placed on the injured epicardial surface of the heart, while a diminution in flow through the entire coronary artery produces S-T segment depression in the same lead. Recently, Zao et al.⁴¹⁾ reported that in acute coronary occlusion in the dog produced by ligating the two coronary artery branches which supply the apex S-T segment elevation in a bipolar lead between the apex and the base parallels the myocardial oxygen gradient between the apex and the base.

In the author's experiment, the S-T segment in lead Vs appears to be elevated in the cases with low oxygen content in the arterial blood in the control period, and with markedly reduced coronary blood flow at the start of coronary artery perfusion. Moreover, in #386 the S-T segment elevation is reversible; there are no changes in the QRS complex and autopsy reveals no myocardial necrosis. Therefore, it is concluded that myocardial anoxia or acute coronary insufficiency, when it is severe, produces a reversible S-T segment elevation in the lead facing the injured epicardial surface of the ventricle as the result of transient transmural in-

jury to the heart. From the above formula it is obvious that cardiac efficiency is in inverse relation to the left ventricular work equivalent of oxygen.

Lombardo et al.¹⁾ reported that in patients with myocardial failure cardiac efficiency decreased when the load of the heart was increased, while in normal subjects it increased. Eckenhoff et al.²²⁾ also noted a decrease in cardiac efficiency with an increased resistance load caused by ligating the abdominal aorta in the dog. In the author's experiment, too, an increase in the left ventricular work equivalent of oxygen was noted during an increased load on the left ventricle caused by inflating a balloon in the abdominal aorta of the dog with induced coronary insufficiency (see LVWEqO₂ at phase ② and ③ in Fig. 1 and Fig. 6 (a) (b) and (d)). Thus, since an increase in the left ventricular work equivalent of oxygen means a decrease in cardiac efficiency, the result of the author's experiment is in accord with that of Lombardo et al. and Eckenhoff et al. in regard to a decrease in cardiac efficiency during an increased load on the heart with coronary insufficiency. The author, however, agrees with the opinion of Eckenhoff et al.²⁴⁾ that a decrease in cardiac efficiency does not necessarily mean a decrease in cardiac function. Because in the author's experiment, electrocardiographic changes, especially changes in the S-T segment are indeed improved with an increase in the left ventricular work equivalent of oxygen, that is, a decrease in cardiac efficiency. Eckenhoff et al.²⁴⁾ pointed out the presence of myocardial oxygen utilization without performance of cardiac work such as resting or maintenance energy utilization during the isometric contraction phase of the ventricles. Recently, Gregg et al.⁴²⁾ and Bing et al.⁴³⁾

also have mentioned the necessity of reevaluating the calculation of cardiac efficiency used so far. Moreover, in the author's opinion, it is assumed that in coronary insufficiency cardiac efficiency calculated from the above formula more or less loses its original meaning, because left ventricular energy consumption does not seem to be equal to the product of myocardial oxygen consumption by 2.057 as the result of presumably increased anaerobic energy production to supplement the oxygen supply to the myocardium in coronary insufficiency.

SUMMARY

1) A #7F or #8F cardiac catheter was introduced into the left coronary artery or its branch through the common carotid artery in anesthetized, closed-chest dogs under fluoroscopic control.

By adjusting coronary blood inflow perfused from the dog's own femoral or brachial artery through the catheter, the author succeeded in preparing dogs with coronary insufficiency in which a lead facing the epicardial surface of the heart showed a depressed S-T. Changes in hemodynamics and myocardial oxygen metabolism, and the relationship between those changes and the electrocardiogram were observed during an increased load on the left ventricle caused by inflating a balloon in the aorta or by nor-epinephrine injection in dogs with induced coronary insufficiency. In addition, the hemodynamic changes were compared with those during an increased load in dogs without coronary insufficiency.

2) Cardiac output was decreased in all four cases, and left ventricular work in three of four cases during an increased load on the left ventricle in dogs with induced coronary insufficiency, while the former was decreased in two of four cases, and the latter was increased in all four cases during an increased load in dogs without coronary insufficiency. The experimental results of Eckenhoff et al. that cardiac output as well as left ventricular work decreased in dogs with an increased resistance load on the left ventricle caused by ligating the abdominal aorta were in accord with the author's experiment in dogs with coronary insufficiency; while those of Gregg et al. that cardiac work increased markedly in dogs with an increased load on the left or right ventricle caused by ligating the aorta or pulmonary artery were in accord with

the author's experiment in dogs without coronary insufficiency.

3) The heart in coronary insufficiency appears to be safeguarded against dangerous myocardial anoxia in oxygen demand by reducing cardiac output and cardiac work.

4) Coronary blood flow in the dog with coronary insufficiency depends largely upon mean arterial blood pressure during an increased load. None of the cases in this series showed a decrease in both coronary blood flow and myocardial oxygen extraction coefficient. Thus, the safeguarding mechanism in dogs with coronary insufficiency is noted not only in oxygen demand but also in oxygen supply to the myocardium.

5) The electrocardiogram in coronary insufficiency should always be studied with consideration to both cardiac work and myocardial oxygen consumption, since coronary insufficiency can be induced by a relative shortage of oxygen supply to oxygen demand in the myocardium. The author attempted to study the electrocardiographic changes—especially, S-T segment deviation—in correlation with changes in the left ventricular work equivalent of oxygen, that is, the ratio of left ventricular oxygen consumption to left ventricular work. From the results obtained in the experiment, it is concluded that the degree of S-T segment deviation increases as the left ventricular work equivalent of oxygen diminishes.

6) In regard to S-T segment deviation it has been said so far that myocardial anoxia or acute coronary insufficiency produces a depressed S-T segment in a lead that faces the epicardial surface of the heart because of injury on the endocardial side of the ventricles, while myocardial infarction causes an elevated S-T segment in the same lead because of injury on the epicardial side or in the transmural region of the ventricles. The author pointed out that myocardial anoxia or acute coronary insufficiency, when it is severe, can produce a reversible S-T segment elevation without any change in the QRS complex in a lead that faces the injured epicardial surface of the heart presumably because of transient transmural injury of the ventricles.

7) Mechanical efficiency of the heart calculated from the formula,

$$\frac{\text{Cardiac output (cc./min.)} \times \text{mean arterial blood pressure (cm. Hg)} \times 13.6}{\text{Left ventricular oxygen consumption (cc./min.)} \times 2.057},$$

cannot represent the state of cardiac function especially in the heart with coronary insufficiency.

Acknowledgements

The author wishes to express his sincere gratitude to Prof. M. Maekawa for his guidance and encouragement. The author also wishes to acknowledge the collaboration of Dr. Y. Ogata (Instructor) and the members of the cardiac catheterization team of Prof. Maekawa's Clinic.

REFERENCES

- 1) Lombardo, T. A., Rose, L., Taeschler, M., Tuluy, S. and Bing, R. J.: The effect of exercise on coronary blood flow, myocardial oxygen consumption and cardiac efficiency in man. *Circulation* **7**: 71, 1953.
- 2) Hara, K.: Clinical investigation of the behavior of the coronary circulation and myocardial metabolism and their correlation with the electrocardiographic changes in induced hypoxemia. *Jap. Circulation J.* **20**: 371, 1956.
- 3) Kawai, C.: The electrocardiogram in experimental coronary insufficiency; with special reference to hemodynamics and myocardial oxygen metabolism. Part I. *Jap. Circulation J.* To be published.
- 4) Goodale, W. T., Lubin, M., Eckenhoff, J. E., Hafkenschiel, J. H. and Banfield, W. G.: Coronary sinus catheterization for studying coronary blood flow and myocardial metabolism. *Amer. J. Physiol.* **152**: 340, 1948.
- 5) Barnes, A. R. and Whitten, M. B.: Study of T wave negativity in predominant ventricular strain. *Am. Heart. J.* **5**: 14, 1929.
- 6) Takezawa, H.: Studies of pulmonary circulation (1). *Jap. Circulation J.* **20**: 546, 1956.
- 7) a) Maekawa, M.: Denshinzu yori mitaru seibutsudenki no ichi shin riron (sotaidensetsu). *Nippon Junkan-ki Byo-gaku* **10**: 44, 1944 (Japanese).
b) Maekawa M.: Hyojun shishi yudo-ho ni wa Einthoven no seisankaku mokei yori wa mushiro chokkaku nitohen sankaku zahyo o teki ou subeki de aru. *Nippon Junkan-ki Byo-gaku* **10**: 51, 1944 (Japanese).
- 8) Wiggers, C. J. and Katz, L. N.: The contour of the ventricular volume curves under different conditions. *Am. J. Physiol.* **58**: 439, 1922.
- 9) Warthen, H. J.: Massive intravenous injections. *Arch. Surg.* **30**: 199, 1935.
- 10) Yeomans, A., Porter, R. R. and Swank, R. L.: Observations on certain manifestations of circulatory congestion produced in dogs by rapid infusion. *J. Clin. Invest.* **22**: 33, 1943.
- 11) Harrison, T. R., Friedman, B. and Rensnik, H. Jr.: Mechanism of acute experimental heart failure. *Arch. Int. Med.* **57**: 927, 1936.
- 12) Gowday, C. W. and Loynes, J. S.: Acute experimental heart failure, produced by intravenous gum acacia infusion. *Canadian J. Med. Sc.* **30**: 314, 1952.
- 13) Huckabee, W., Casten, G. and Harrison, T. R.: Experimental hypervolemic heart failure: its bearing on certain general principles of heart failure. *Circulation* **1**: 343, 1950.
- 14) Gregg, D. E. and Wiggers, C. J.: The circulatory effects of acute experimental hypervolemia. *Am. J. Physiol.* **104**: 423, 1933.
- 15) a) Wiggers, C. J.: Pressure pulses in the cardiovascular system. New York and London, Longmans, Green, 1928.
b) Wiggers, C. J.: Studies on the consecutive cases of the cardiac cycle. II The laws governing the relative durations of ventricular systole and diastole. *Am. J. Physiol.* **56**: 439, 1921.
- 16) Mori, M.: Kanjunksu no kaibo-gaku teki kosatsu (Anatomical view of coronary circulation). *Clinic All-Round (Sogo-Rinsho)* **5**: 37, 1956 (Japanese).
- 17) a) Hamilton, W. F., Brewer, G. and Brotman, I.: Some simplifications and improvements in the technique of optical recording. *Am. J. Physiol.* **105**: 44, 1933.
b) Hamilton, W. F., Brewer, G. and Brotman, I.: Pressure pulse contours in the intact animal. *Am. J. Physiol.* **107**: 427, 1934.
- 18) Maekawa, M.: Angina pectoris, its diagnostic aspect. *Jap. Circulation J.* **20**: 457, 1956.
- 19) Gregg, D. E.: Coronary Circulation in Health and Disease. Philadelphia, Lea & Febiger, 1950.
- 20) Eckenhoff, J. E., Hafkenschiel, J. H., and Landmesser, C. M.: Measurement of coronary blood flow by nitrous oxide method. *Am. J. Physiol.* **152**: 356, 1948.
- 21) Bing, R. J., Hammond, M. M., Handelsman, J. C., Powers, S. R., Spencer, F. C., Eckenhoff, J. E., Goodale, W. T., Hafkenschiel, J. H. and Kety, S. S.: The measurement of coronary blood flow, oxygen consumption and efficiency of the left ventricle in man. *Am. Heart J.* **38**: 1, 1949.
- 22) Eckenhoff, J. E., Hafkenschiel, J. H. and Landmesser, C. M.: Coronary circulation in the dog. *Am. J. Physiol.* **148**: 582, 1947.
- 23) Eckenhoff, J. E., Hafkenschiel, J. H., Landmesser, C. M. and Harmel, M.: Cardiac oxygen metabolism and control of the coronary circulation. *Am. J. Physiol.* **149**: 634, 1947.
- 24) Eckenhoff, J. E., Hafkenschiel, J. H., Foltz, E. L. and Driver, R. L.: Influence of hypotension on coronary blood flow, cardiac work and cardiac efficiency. *Am. J. Physiol.* **152**: 545, 1948.
- 25) Gregg, D. E., and Shipley, R. E.: Augmentation of left coronary inflow with elevation of left ventricular pressure and observations on the mechanism for increased coronary flow with increased cardiac load. *Am. J. Physiol.* **142**: 44,

- 1944.
- 26) Kobayashi, T., Ito, Y. and Nakanishi, A.: Myocardial metabolism in health and disease, studies by coronary sinus catheterization. *Jap. Circulation J.* **20**: 387, 1956.
- 27) Kimura, E. and Suzuki, N.: Kanketsuryuryo no zogen to sore ni ei-kyo suru syoinshi. *Clinic All-Round (Sogo-Rinsho)* **7**: 375, 1958 (Japanese).
- 28) Wégria, R., Segers, M., Keating, R. P. and Ward, H. P.: Relation between the reduction in coronary flow and appearance of electrocardiographic changes. *Am. Heart J.* **38**: 90, 1949.
- 29) Kimura, E. et al.: Kanfuzen shinden zu (Electrocardiogram in coronary insufficiency). *Shinryo* **9**: 35, 1956 (Japanese).
- 30) Kimura, E., Kanazawa, T., Suzuki, N., Ohara, F., Yamamoto, T., Suzuki, U., Takahashi, A. and Takahashi, N.: Kanfuzen-shinden zu, Kanheisoku-shinden zu, Kanbunshifuzen-shinden zu. *Naika (Internal Medicine)* **1**: 45, 1958 (Japanese).
- 31) Dietrich, S.: Electrocardiogram und Coronardurchblutung. *Verh. Dtsch. Ges. inn. Med.* **44**: 525, 1932.
- 32) Dietrich, S. und Schwiegk, H.: Das Schmerzproblem der Angina pectoris. *Klin. Wschr.* **12**: 135, 1933.
- 33) Dietrich, S. und Schwiegk, H.: Angina pectoris und anoxie des Herzmuskels. *Z. Klin. Med.* **125**: 195, 1933.
- 34) Hayse, S.: Coronary circulation, its physiological aspect. *Jap. Circulation J.* **21**: 227, 1957.
- 35) Wolferth, C. C., Bellet, S., Livezey, M. M. and Murphy, F. D.: Negative displacement on the RS-T segment in the electrocardiogram and its relationships to positive displacement; An experimental study. *Am. Heart J.* **29**: 220, 1945.
- 36) Pruitt, R. D. and Valencia, F.: The immediate electrocardiographic effects of circumscribed myocardial injuries: an experimental study. *Am. Heart J.* **35**: 161, 1948.
- 37) Hellerstein, H. K. and Katz, L. N.: The electrical effects of injury at various myocardial locations. *Am. Heart J.* **36**: 184, 1948.
- 38) Kish, B., Nuhum, L. H. and Hoff, H. Z.: The predominance of surface over deep cardiac injury in producing changes in the electrocardiogram. *Am. Heart J.* **20**: 174, 1940.
- 39) Goldberger, E.: Unipolar Lead Electrocardiography and Vectorcardiography, 3rd. ed.; Philadelphia: Lea and Febiger, 1954.
- 40) Hegglin, M. and Holzmänn, R.: Die klinische Bedeutung der verlängerten QT-Distanz (Systolendauer) im Elektrokardiogramm. *Z. Klin. Med.* **132**: 1, 1937.
- 41) Zao, Z., Yen, M. and Herrmann, G.: Relation between S-T segment elevation and experimental myocardial oxygen gradient. *Am. J. Physiol.* **196**: 207, 1959.
- 42) Gregg, D. E. and Sabiston, D. C., Jr.: Current research and problems of the coronary circulation. *Circulation* **13**: 6, 1956.
- 43) Beuren, A., Sparks, C. and Bing, R. J.: Metabolic studies on the arrested and fibrillating perfused heart. *Am. J. Cardiol.* **1**: 103, 1958.
- 44) Anrep, G. V. and Segall, H. N.: Regulation of the coronary circulation. *Heart* **13**: 239, 1926.
- 45) Katz, L. N., Wise, W. and Jochim, K.: The control of the coronary flow in the denervated isolated heart and heart-lung preparation of the dog. *Am. J. Physiol.* **143**: 479, 1945.