Pathophysiological Studies on Postalimentary Lipemia in Coronary Sclerosis by Means of Electrocardiogram

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Ischemic change on E.C.G. was found in postalimentary lipemia in coronary sclerotic patients. It is interesting to note the ischemic change was readily reversible with heparin administration. So it would be reasonable to consider that oxygen supply to heart muscle is affected by change of plasma lipid level. In order to clarify the mechanism of appearance of the ischemic change on E.C.G. during postalimentary lipemia, 100 gm of raw-cream was given to patients with coronary sclerosis and PaO_2 was measured before and after fat intake. PaO_2 was found to be decreased during the period of 4 hours after fat intake and then restored to the fasting level in 30 minutes after heparin injection. From these results, it has been suggested that oxygen diffusion in the lung and oxygen transport to the heart muscle were impaired by fat loading.

RECENTLY, it has been noticed that lipid metabolism plays an important role in the pathogenesis and development of atherosclerosis. One abnormal aspect of lipid metabolism in atherosclerosis, it has been stated, is a lack of enzymatic removal of alimentary lipids^{1,2} from the blood stream, due to an insufficiency of "clearing factor".

Concerning oral fat loading, there are many reports^{3,4} of increased periods, i.e. in comparison with normal, during which chylomicrons remain in the blood stream of patients with coronary sclerosis. This, it is suggested, results from "clearing factor" insufficiency.

Concerning pathophysiologic changes induced by prolonged lipemia, there have been many observations: for instance, hypercoagulability of the blood⁵; increase in platelet adhesiveness⁶; increase in blood viscosity⁷ and inhibition of fibrinolysis⁸, which occur during alimentary lipemia. Such pathophysiologic changes are especially harmful in coronary sclerosis, since it has been shown that coronary blood flow is diminished when there is inadequate supply of oxygen to the muscle of the heart. WILLIAMS⁹ studied

the effect of postprandial fat ingestion in patients with coronary insufficiency, and found that blood cell agglutination occurred as a result of the presence of chylomicrons in the blood stream, and suggested that this phenomenon caused the coronary blood flow to drop.

Since arterial oxygen saturation decreased when fat emulsion has been injected into coronary sclerotic patients, KUO¹⁰ suggested that alimentary lipemia is frequently a cause of arterial oxygen saturation decrease in coronary sclerosis. Furthermore, in patients with angina pectoris, who were given oral fat loading, he observed the appearance of anginal pain five hours after such loading. This pain was relieved by the injection of heparin.¹¹

As mentioned above, various harmful pathophysiologic changes are induced by oral fat loading in coronary sclerotic patients: and it is well known that, as a result, the disease becomes worse. Nevertheless, there are many aspects of the mechanism of appearance of such changes which still remain unknown. The author has taken as his object of study the electrocardiographic changes which result from the influence

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TABLE I CHANGE OF ST SEGMENT AND T WAVE ON E.C.G. FOLLOWING FAT LOADING

Change on electro-cardiographic pattern	More than 1 mm of ST segment	More than -1 mm of ST segment	More than 2 mm of T wave	More than -2 mm of T wave
Young control (17)	5	2	6	6
The aged control (16)	2	5	4	6
Myocardial infarction (7)	1	2	0	3
Angina pectoris (18)	4	11	3	10
Probable cases (25)	5	9	8	12

Fig.1. The ischemic change on E.C.G. after fat loading in 65 years old coronary sclerotic patient. (A: Fasting state before fat loading. B: 2 hours after fat loading. C: 4 hours after fat loading. D: 6 hours after fat loading.)

of postprandial lipemia on coronary sclerosis. In addition, the mechanism of appearance of these changes was investigated through measurements of arterial and venous oxygen tension.

1. CHANGES ON E.C.G. CAUSED BY POSTPRANDIAL LIPEMIA AND THE EFFECT OF HEPARIN MATERIALS AND METHODS

Fifty coronary sclerotic patients and a control group of thirty-three non-sclerotic patients were chosen on the basis of the clinical diagnosis criteria given by the arteriosclerosis research group of the Ministry of Education.¹² The coro-

nary sclerotic patients included seven individuals with myocardial infarction (one female): eighteen with angina pectoris (seven female): and twenty-five probable cases of sclerosis (six female). The non-sclerotic control group included old-aged, healthy subjects, over forty (five female): and seventeen young, healthy subjects (five female). The fat loading methods used consisted of oral administration of 100 grams of raw cream (25% fat), given in the early morning when the subjects were at rest, after a 24 hour fast. E.C.G. records were made before, and at 2, 4 and 6 hours after fat loading; the leads chosen being the standard leads and V₄, V₅, and V₆ of the

precordial leads. The positions of the latter were marked to ensure consistency in the point of application. All test subjects were kept in a recumbent position and not allowed to smoke until all E.C.G. recordings had been completed. A part of the fat-loading subjects underwent MASTER's two-step exercise test on the following day. The amount of exercise was 'double' for such individuals, and they were judged by MASTER's new criteria.¹³

RESULTS

1) Deviation of the ST segment and the T wave

The Q-Q line¹⁴ was taken as the base-line for measurements made on the E.C.G.. The portion of each E.C.G. which showed the greatest ST and T deviation after fat loading was selected for measurement. Table I shows the values of the deviation of the ST and T waves in comparison with those seen in the fasting E.C.G..

There was no difference in the incidence of ST segment elevation of more than 1 mm, after fat loading; i.e. between the coronary sclerosis and control groups. Among the seventeen young, healthy individuals, five showed some elevation of the ST segment, but this was no more than a slight shift from the base-line. In general, an increase or decrease in the T wave was produced along with some physiological change. (In passing it might be said that many theories have been put forward concerning such mechanisms¹⁵). There were many control subjects whose T wave was raised by more than 2 mm. Among the coronary sclerosis group, many individuals showed a decrease of more than 2 mm in the height of the T wave, after fat loading. That is to say, originally flat T waves became negative and originally negative T wave became more so.

Twenty-two out of the fifty coronary sclerotic patients showed an ST depression exceeding 1 mm after fat loading. On the other hand, only seven such individuals were found among the control group of thirty three. Thus, cases where ST changes induced by postprandial lipemia appeared were more frequent among coronary sclerotic patients.

In angina pectoris, ST depression appeared in a high percentage (eight cases among eighteen), and the degree of depression was greatly increased among those subjects whose E.C.G. had shown ischemic ST depression at rest.

Among the twenty-five possible coronary sclerotic patients, nine showed ST depression after fat loading. However, there were no great difference among the sixteen old aged control

group members, who showed five cases of ST depression.

Observations of ST depression, in each lead, for coronary sclerotic patients after fat loading, revealed the greatest frequency at chest lead V₄. Next, in order, were V₅, V₆ and standard leads III, I and II; i.e. the higher frequencies were mostly on the left side of the chest. Observations on the appearance time of ST depression in each lead showed the following: sixteen leads at two hours after fat loading; twenty-six leads after four hours; and twenty-five leads after six hours. Such data indicated that ST depression commenced two hours after fat loading, that it was at a peak two hours later, and that it lasted for six hours.

In the control group there were no differences in the appearance times of ST depression. Further, there was no tendency for the appearance time of T wave changes of over 2 mm to differ between the coronary sclerotic subjects and the control group.

One case showing changes of the ST segment and T wave is given in Fig. 1. After fat loading had been carried out on a sixty-five year old male patient, who had been troubled with essential hypertension and angina pectoris for a few years, it was observed that ST depression and negative T wave appeared at standard leads I and II six hours after fat loading. Further, at the chest leads V₄, V₅, and V₆, there was also depression of the ST and negative T wave, four and six hours after fat loading.

2) The relationship between changes of E.C.G. induced by fat loading and by exercise test

Among the eighty-three subjects who had fat loading, forty-one subjects (twenty-seven from the coronary sclerosis group and fourteen from the control group) were selected for MASTER's two-step exercise test. Of the twenty-seven coronary sclerotic subjects, twenty were positive on the exercise test; and there were fourteen who showed an ST depression of more than 1 mm due to the fat loading. Among the twenty subjects having positive exercise tests, thirteen showed ST depression after fat loading. In the angina pectoris group, eight subjects were positive on the exercise test, and seven showed more than a 1 mm depression following fat loading. Among the fourteen subjects who showed ST depression by fat loading, there was only one with a negative exercise test.

All the fourteen control subjects had negative exercise tests, and showed no ST depression after

TABLE II CHANGE OF OXYGEN TENSION IN THE BLOOD FOLLOWING HEPARIN INJECTION (AVERAGE VALUE AND STANDARD DEVIATION)

		Before heparin	5'	15'	30'	45'	60'
Arterial blood	During fat loading (15 cases)	77.2 ±5.2	81.8 ±5.5	84.3 * ±5.1	81.2 * ±5.8	82.1 * ±4.8	79.0 ±6.6
	During fasting state (10 cases)	81.5 ±11.0	77.2 ±8.2	77.8 ±12.6	79.7 ±13.3	82.5 ±11.4	81.5 ±10.1
Venous blood	During fat loading	52.7 ±13.1	56.7 ±11.4	57.6 ±12.9	55.2 ±13.3	60.3 ±14.9	54.0 ±13.2
	During fasting state	48.9 ±12.8	53.3 ±13.3	52.4 ±10.9	56.3 ±12.1	55.2 ±15.6	55.7 ±11.0

* $p < 0.05$

fat loading.

When fat loading and the exercise test were given to coronary sclerotic subjects, the changes on E.C.G. showed themselves in ischemic depression of the ST segment. It is thought that the fat loading as well as the exercise test could have produced the myocardial ischemia, and that it was such ischemic change which had appeared on the E.C.G..

3) The effect of heparin on E.C.G. changes induced by fat loading

It is well known that heparin has both an anticoagulative and an antilipemic action, and also that the chylomicron level reaches a maximum four hours after a fatty meal^{2,16}.

As has been mentioned, E.C.G. change induced by lipemia appears frequently at four to six hours after oral fat intake. The author tried to see whether this E.C.G. change could be corrected by the antilipemic action of heparin, in order to verify that the E.C.G. change was the result of a high level of chylomicron in the blood stream.

Twenty-three coronary sclerotic subjects (four cases of myocardial infarction, seven of angina pectoris, and twelve of coronary sclerosis were given fat loading and the E.C.G. recorded four hours later. Forty units/Kg of heparin were then injected intravenously. (This amount of heparin was used in all following experiments.) Thirty minutes after heparin injection, E.C.G.s were again made and the deviation of the ST segment was measured.

Among the twenty-three coronary sclerotic subjects, seventeen showed a difference in the depression of the ST segment of more than 0.5 mm four hours after fat loading; i.e. when compared with the fasting state. On these seventeen

subjects, twelve showed a recovery in the ST depression exceeding 0.1 mm, as a result of the heparin injection.

COMMENT

In coronary sclerotic patients, ischemic changes appeared in the left side of chest lead on the E.C.G. between four and six hours after fat loading; that is presumably at the time of the highest level of chylomicronemia. That the level of chylomicron had been decreased by the injection of heparin was shown, it is thought, in the disappearance of ischemic changes from the E.C.G..

The author concluded that the level of chylomicron in the blood stream after fat loading was very closely related to the appearance of ischemic changes on the E.C.G.. The pattern of ST depression after fat loading could be said to be of an ischemic type,¹⁷ owing to the fact that those subjects who had a positive exercise test had tended to show ST depression after fat loading.

2. CHANGES OF BLOOD OXYGEN TENSION BEFORE AND AFTER HEPARIN INJECTION DURING POSTPRANDIAL LIPEMIA

Following observations were done to clarify the mechanism of appearance of changes on E.C.G. induced by postprandial lipemia. Fifteen coronary sclerotic subjects (four cases of myocardial infarction, five of angina pectoris and six probable cases of coronary sclerosis) were given the fat loading mentioned previously. Four hours after fat loading, forty units/Kg of heparin which was seemed to clear away postprandial lipemia was injected intravenously in order to study the relationship between chylomicron level in the

TABLE III CHANGE OF $P(a-v)_2$ AFTER HEPARIN INJECTION (AVERAGE VALUE OF THE DIFFERENCE BEFORE AND AFTER HEPARIN INJECTION) (mmHg)

	Before heparin	5'	15'	30'	45'	60'
Fat loading	23.6 ± 3.2	-3.5 ± 3.9	$+0.7 \pm 3.6$	$+2.6 \pm 3.3$	-2.5 ± 2.4	$+0.5 \pm 3.1$
Fasting state	29.9 ± 2.2	-7.8 ± 2.1	-2.4 ± 2.2	-6.9 ± 2.6	-8.3 ± 3.6	-3.3 ± 3.4

blood and blood oxygen tension.

Arterial blood was taken from the brachial artery and venous blood from the deep median vein by Cournand needles which had been inserted beforehand. A blood sampling was slowly done so that the respiratory variations of blood oxygen tension could be avoided. The blood sample was taken at 5, 10, 15, 30, 45 and 60 minutes after heparin administration.

The blood oxygen tension was measured by the I.L. meter to which the principle of the polarography was applied. This I.L. meter has an electrode from a combination of silver-silver-chloride electrode and platinum electrode, and the surface of the electrode is covered with polyethylene membrane. Oxygen in blood samples diffuses through polyethylene membrane and deoxidizes the platinum electrode. An electric current on this deoxidization is directly proportional to the blood oxygen tension. The error of the measurement by this electrode shows within ± 1 mmHg.

So as to observe the peripheral circulation which might be influenced by heparin administration, the photoelectro-plethysmogram was put on the index finger of the opposite hand from the sample-taking arm and the volume pulse wave was recorded during the above experiment.

As an indicator of the level of chylomicron in the blood, the optical density of plasma (O.D.) was applied and the electrical spectrophotometer was set up at 650 m μ of wave length to measure it.

As for a control group experiment, sixteen cases of coronary sclerosis were administered heparin at fasting state without fat loading and blood oxygen tension, O.D. and volume pulse wave with above methods.

RESULTS

1) Changes of blood oxygen tension caused by heparin administration

It is well known that arterial oxygen tension (P_{ao_2}) reflects sharply arterial oxygen saturation rate even when it is within a normal range. It is technically difficult to analyze very small

changes in oxygen saturation rate that are within normal limits, by using the old VAN SLYKE gas analyser. However, very small changes in oxygen saturation rate within normal limits can be seen as clear changes of P_{ao_2} , according to oxygen dissociation curves.

The author found that the average P_{ao_2} among the coronary sclerotic group in a fasting state, was 81.5 mmHg, at an average of 57.2 years. This value is within normal limits, when compared with healthy subjects of similar age,¹⁸ and so is the arterial oxygen saturation rate.

P_{ao_2} at four hours after fat loading was 77.2 mmHg on average; that is significantly lower than in the fasting state. Concerning changes following heparin administration (see data in Table II) at four hours after fat loading, the P_{ao_2} was found to be increasing all the time. The increases in P_{ao_2} at 15, 30 and 45 minutes after heparin administration were statistically significant from the P_{ao_2} before heparin administration ($p < 0.05$). Thus heparin administration four hours after fat loading is concluded to cause significant increases in P_{ao_2} . However, in control subjects with heparin administration during a fasting state, the P_{ao_2} did not show any statistically significant changes ($p > 0.05$). These results suggest that P_{ao_2} which was decreased by fat loading, was recovering to a fasting state level by the lipemia-clearing effect of heparin.

As for venous oxygen tension (P_{vo_2}), it shows great physiological fluctuation and also it is apt to change easily by the dilatation or contraction of peripheral blood vessels. Thus, changes in venous oxygen tension do not always reflect the oxygen uptake state in peripheral tissues.¹⁹ Venous blood sampling was from the deep median vein, because that from the cubital vein contained venous return from the skin surface where the blood volume was much changed by environmental factors. As shows above, P_{vo_2} increased on heparin administration in the fasting state. This increase suggested that heparin had a vasodilatic action; however, the increase in P_{vo_2} on heparin administration was not statistically significant

Fig. 2. Relationship between the decrease of optical density (O.D.) and the increase of P_{aO_2} at 15 minutes after heparin injection during fat loading.

($p > 0.05$). Furthermore, change of the volume pulse wave of the finger tip, as mentioned later, was minimal.

P_{vO_2} after heparin administration following fat loading was increasing, as in the fasting state, but this increase also was not statistically significant. When the degree of increase in both was compared, the increase of P_{vO_2} at fat loading was less than that of P_{vO_2} at fasting state.

Arterial/venous oxygen pressure difference in the forearm was calculated according to the formula $P(a-v)O_2$. The increase of $P(a-v)O_2$ by heparin administration was found six cases out of fifteen at fifteen minutes, six cases at thirty minutes, and five cases at forty-five minutes after heparin administration during fat loading, but only two cases out of ten were observed at sixty minutes after heparin injection at fasting state. Table III shows values of $P(a-v)O_2$ between before and after heparin administration. According to this table, change of $P(a-v)O_2$ following heparin injection at fasting state showed the decrease each time. When heparin administration was done during fat loading, $P(a-v)O_2$ increased fifteen minutes and thirty minutes after heparin injection. The average of increase of $P(a-v)O_2$ thirty minutes after heparin injection was 2.6 mmHg. In case of fasting state, the average $P(a-v)O_2$ thirty minutes after heparin administration decreased to 6.9 mmHg. It can be clarified that $P(a-v)O_2$ increased following heparin administration during fat loading, in comparison with

TABLE IV THE BLOOD GAS ANALYSIS FOLLOWING HEPARIN INJECTION IN 62 YEARS OLD MALE WITH ANGINA PECTORIS ON FAT LOADING (mmHg)

	Before	5'	15'	30'	45'	60'
P_{aO_2}	70.0	71.0	81.0	84.0	76.0	75.0
P_{aCO_2}	33.0	33.0	34.0	33.5	32.7	32.0
$P(a-v)O_2$	13.0	19.5	25.0	29.5	18.5	19.5
PHa	7.400	7.370	7.370	7.405	7.405	7.405
O.D.	.062	.019	.012	.015	.017	.022

the decrease of $P(a-v)O_2$ during fasting state.

Generally speaking, the increase of $P(a-v)O_2$ in the peripheral blood means the increase of oxygen uptake at the peripheral tissue if there is no change of hemodynamics. It could be understood that the increase of $P(a-v)O_2$ after heparin administration during fat loading meant the increase of oxygen uptake at the peripheral tissue. If postprandial lipemia is thought to decrease oxygen uptake at the peripheral tissue, the increase of $P(a-v)O_2$ after heparin administration during fat loading means that the oxygen uptake at the peripheral tissue was corrected by "lipemia clearing" activity of heparin.

Heparin administration during fat loading decreased serum O.D. and increased P_{aO_2} at the same time. The relationship between the increase of P_{aO_2} and decrease of O.D. revealed a direct proportion as Fig. 2. This suggests that P_{aO_2} increases as heparin cleans serum lipids.

When fat loading was administered to 62 year-old male with angina pectoris, ischemic changes of E.C.G. was exacerbated, and it was corrected by heparin administration. As in E.C.G. (Fig. 3), terminal dipping of ST disappeared and T wave heightened at V_5 thirty minutes after heparin administration. In E.C.G. at sixty minutes, ST depression disappeared at V_5 and became mild at V_6 . As for blood gas analysis in this case, as in Table IV, P_{aO_2} increased after heparin administration as serum O.D. decreased. Maximum increase of $P(a-v)O_2$ was 16.5 mmHg. As above, E.C.G. changes after fat loading have a close relation to blood oxygen tension which is effected by the level of blood chylomicron.

2) Changes of the volume pulse wave by heparin

It comes into question that the increase of $P(a-v)O_2$ after heparin administration during fat loading means directly the rise of oxygen uptake

Fig.3. The ischemic change on E.C.G. following fat loading in 62 years old male with angina pectoris was corrected by heparin injection. (A: 4 hours after fat loading. B: 30 minutes after heparin administration. C: 60 minutes after heparin administration.)

at the peripheral tissue, because $P(a-v)O_2$ at the elbow is changed by the circulation flow from the forearm and finger.¹⁹ Changes of the volume pulse wave before and after heparin administration did not have any tendency to decrease or increase, and they were very small. That is to say, heparin administration did not cause any significant change to peripheral hemodynamic state.

COMMENT

Pao_2 increased after heparin administration, when it was given coronary sclerotic subjects four hours after fat loading. The difference of oxygen tension between the brachial artery and the deep median vein increased by heparin administration, too. The author analyzed that these increases occurred as result of "clearing activity" of heparin to postprandial lipemia. Therefore, it can presume that Pao_2 decreases on postprandial lipemia.

3. THE CHANGE OF Pao_2 AT FAT LOADING AND THE EFFECT OF HEPARIN

Ten coronary sclerotic subjects (myocardial infarction four, and angina pectoris six) were given fat loading with the method mentioned previously. Blood sampling from the brachial artery was taken before, and 2 and 4 hours after

fat loading, and then heparin was injected (the same dosis mentioned previously). Last sampling was taken at thirty minutes after heparin administration, that is, 4 hours and 30 minutes after fat loading.

Pao_2 after fat loading decreased at 2 and 4 hours (Fig.4.). Particularly, the decrease at 4 hours after fat loading was statistically significant ($p < 0.01$). Concerning the effect of heparin administration, Pao_2 which was decreased by fat loading, increased significantly at 30 minutes after heparin administration ($p < 0.01$). The change of O.D. showed an inverse proportion to that of Pao_2 , that is increased after fat loading and decreased by heparin administration. The author mentioned already that Pao_2 decreased as O.D. increased during fat loading. This means heparin administration acted to increase Pao_2 which was decreased by postprandial lipemia.

4. THE CHANGE OF OXYGEN CONSUMPTION VOLUME IN THE WHOLE BODY AFTER FAT LOADING AND THE EFFECT OF HEPARIN

The author mentioned already the possibility of decrease of oxygen uptake at the peripheral tissue during fat loading to coronary subjects. In order to verify it, 22 coronary sclerotic subjects (6 cases of myocardial infarction, 10 of

TABLE V CHANGE OF OXYGEN CONSUMPTION VOLUME BEFORE AND AFTER FAT LOADING AND THE EFFECT OF HEPARIN ADMINISTRATION (AVERAGE VALUE AND STANDARD DEVIATION)

Oxygen consumption volume (22 cases)	Before fat loading	2 hours after fat loading	4 hours after fat loading	30 minutes after heparin
	184.5 ± 25.5	208.5 ± 30.3	212.0 ± 33.9 *	232.0 ± 35.6 *

* $p < 0.01$

Fig. 4. The decrease of P_{aO_2} after fat loading and the increase at 30 minutes after heparin administration in patients with coronary sclerosis.

angina pectoris and 6 probable cases of coronary sclerosis) were given fat loading and oxygen consumption volume in the whole body was measured before and after fat loading with using Sanborn type metabolator. This method was done in the same way as at the basal metabolism rate.

As seen in Table V, the oxygen consumption volume increased 2 and 4 hours after fat loading due to non-specific dynamic action of fat. It increased more at 30 minutes after heparin injection, that is, 4 hours and 30 minutes after fat loading. This increase after heparin administration was statistically significant ($p < 0.01$). However, the increase between 2 hours and 4 hours after fat loading was not significant ($p > 0.05$).

This results mean that significant increase of oxygen consumption volume at 30 minutes after heparin injection is due to non-specific dynamic action of fat which is added by the effect of heparin. Concerning this increase of oxygen consumption volume and the increase of $P(a-v)O_2$ by heparin which was mentioned previously, the author concluded that low oxygen uptake at the peripheral tissue during postprandial lipemia was corrected by "lipemia clearing activity" of heparin.

DISCUSSION

The author noticed that ischemic change on E.C.G. appeared in many cases of coronary sclerotic subjects following fat loading. It has been noticed that E.C.G. changed after a meal, and SIMONSON²⁰ observed the change of E.C.G. before and after an ordinary diet to 99 cases of coronary insufficiency. Those changes of E.C.G. appeared mainly in T wave 30 to 60 minutes after a meal.

Concerning the change of E.C.G. after fat loading, KUO²¹ reported that the anginal attack was induced 3 to 5 hours after fat loading in 6 cases out of 14 angina pectoris. On E.C.G. during anginal attack, 4 cases had the depression of ST segment, and the decrease of T wave. He mentioned that the anginal attack and the E.C.G. change did not occur just after a meal, but at all times when the lipid level in the blood was high and he stressed those changes were due to postprandial lipemia.

The author gave fat loading to coronary sclerotic subjects and noticed that the change on E.C.G. appeared much frequently 4 to 6 hours after fat loading, and it was the time postprandial lipemia was most obvious. This change appeared in positive cases of MASTER's exercise test. The author presumed that ischemic changes on E.C.G. appeared due to myocardial ischemia induced by postprandial lipemia.

DR. KAGESHITA² in the author's department examined the lipid level in the blood throughout

fat loading and reported that in coronary sclerotic subjects it was late to be maximum and it took too much time to recover in comparison with normal persons. This long continuance of the hyper-chylomicronemia in coronary sclerotic subjects could induce the myocardial ischemia. "Lipemia clearing activity" of heparin corrected the change of E.C.G. after fat loading. This could be understood that the change on E.C.G. appeared as the lipid level in the blood changed.

The author observed the relationship between the blood oxygen tension and the lipid level in the blood, in order to verify the mechanism of appearance of ischemic changes on E.C.G. after fat loading. When the coronary sclerotic subjects were given fat loading, Pao_2 decreased as the chylomicron in the blood increased, and it was corrected following heparin administration which decreased the chylomicron level. As above, postprandial lipemia in the coronary sclerotic subjects decreased Pao_2 .

Generally speaking, there are many causes as a cause of the decrease of Pao_2 , such as the hypoventilation, abnormal relationship between the ventilation and the perfusion, disturbance of the diffusion, and the shunt in the heart and the lung. The author recorded breath rates and tidal volume during the measurement of the oxygen consumption volume, in order to verify that the change of Pao_2 was not due to the change of the ventilation. This result was not significant following fat loading and also heparin administration.

The author and et al²² examined the relationship between arterial carbon dioxide and pH. This experiments showed that heparin injection 4 hours after fat loading increased carbon dioxide tension and decreased pH at 15 minutes later. Therefore, the increase of Pao_2 by heparin administration after fat loading was not due to the hyperventilation.

BARBORIAK²³ administered heparin to lipemia state and examined carbon dioxide tension in alveoli. He mentioned that heparin did not effect the pulmonary ventilation and pulmonary blood flow.

It is impossible to think abnormal relationship between the ventilation and the perfusion as a cause of the decrease of Pao_2 by postprandial lipemia. Although the blood flow is changed in all capillaries by the change of physical nature of the blood such as aggregation and adhesiveness among red cells during postprandial lipemia²⁴ it is not possible to presume that the change of

blood flow occurred in limited area and induced abnormal relationship between the ventilation and the perfusion.

Pao_2 at fasting state in coronary sclerotic patients was within normal limits, and this means there is no shunt in the heart and the lung. Finally, as a cause of the decrease of Pao_2 by postprandial lipemia, disturbance of the diffusion has much possibility. Namely, any process of oxygen transport, through which oxygen is passed alveolar membrane, capillary endothelial membrane and red cell's membrane and combines with hemoglobine, might be disturbed by postprandial lipemia, and Pao_2 decreased.

ENGELBERG^{25,26} measured $P(a-v)o_2$ of coronary sclerotic subjects before and after heparin administration and thought that heparin had an action to increase the oxygen uptake at the peripheral tissue. He also measured oxygen consumption volumes in the whole body and reported that approximately 50% of coronary sclerotic subjects showed the decrease of oxygen consumption volume at rest, and heparin injection increased average 32% of oxygen consumption volumes in 20 cases of 46. In coronary sclerotic subjects, the increase of low density lipoprotein and β -lipoprotein fraction were found at rest, and he mentioned that the oxygen consumption volume increased in a direct proportion to the disappearance of large low-density lipoprotein from the blood induced by heparin administration.

In the author's results, $P(a-v)o_2$ in coronary sclerotic subjects did not increase following heparin administration at rest, but increased during postprandial lipemia. This increase was accompanied by the decrease of the lipid level in the blood. The author concluded that it occurred as a result that the oxygen uptake at the peripheral tissue which was disturbed by postprandial lipemia, was corrected by heparin.

ENGELBERG mentioned that $P(a-v)o_2$ at the forearm increased after heparin injection (100–200 mg) at fasting state. However, the author did not notice any increase of $P(a-v)o_2$ after heparin injection (20–30 mg) at fasting state, but $P(a-v)o_2$ increased after heparin injection during postprandial lipemia. As for this differences the author understood that dosis of heparin were different. Further, American have been taking much more fat than Japanese, and they always are put to great postprandial lipemia. This great postprandial lipemia may induce easily high lipid level in the blood at fasting state.

JOYNER JR²⁷ measured the oxygen tension at

the intradermal tissue of the toe before and after heparin administration during postprandial lipemia, and noticed that oxygen tension at the intradermal tissue increased average 21.7% as heparin cleared lipemia.

The author resulted in the significant increase of the oxygen consumption volume following heparin administration during postprandial lipemia. This result and the increase of Pao_2 and $P(a-v)O_2$ by "lipemia clearing activity" of heparin brought the author to following understanding; heparin corrected the oxygen uptake at the peripheral tissue which was disturbed by postprandial lipemia.

The author pointed out that in postprandial lipemia Pao_2 decreased due to abnormal diffusion at lungs and the oxygen uptake at the peripheral tissue was disturbed by lipemia. Furthermore, in coronary sclerosis the muscle of heart fell in ischemic state. Therefore, even mild disturbance of the oxygen uptake made the muscle of heart deficient in the oxygen.

DEININGER²⁸ injected fat emulsion to coronary artery of an isolated heart of a cat which was under artificial circulation, and noticed the decrease of coronary blood flow, the decline of contraction of heart muscle, and the decrease of the oxygen consumption volume in the muscle of heart. Phase contrast microscopical examination of this heart muscle revealed the occlusion of arterioles and capillaries with the fat particle and the aggregation of platelets. He stated that the coronary blood flow decreased due to embolism from fat emulsion at arterioles.

It has much possibility that the disturbance of coronary blood flow was induced by the same change at branches of the coronary artery during postprandial lipemia. It will be emphasized that postprandial lipemia is one of the cause which exacerbated the symptom of coronary sclerosis.

As for the mechanism of disturbance of the diffusion of oxygen at lungs by postprandial lipemia, ENGELBERG²⁹ presumed that lipid film existed over the endothel of capillary and the surface of red blood cell, and this lipid film disturbed the oxygen diffusion. MOSKOWITZ's³⁰ histochemical observation revealed that fat in the blood was absorbed to the endothel of capillary, and hydrolyzed there. The author cannot deny always lipid film formation theory of ENGELBERG, because there is strong affinity between the endothel of capillary and the fat particle as above.

Therefore, the author concluded that the

decrease of Pao_2 during postprandial lipemia was due to the diffusion disturbance at the endothel of pulmonary capillary by lipid film, and the ischemic change on E.C.G. was due to the disturbance of oxygen transport from red blood cells to the muscle of heart by lipid film.

SUMMARY

1. In coronary sclerotic subjects, postprandial lipemia by oral administration of raw-cream induced ischemic change on E.C.G.. This ischemic change was corrected by intravenous injection of heparin.

2. During postprandial lipemia, Pao_2 decreased as the chylomicron in the blood increased, and showed a significant rise following heparin injection. Heparin injection also caused increase in $P(a-v)O_2$.

3. Concerning the mechanism of appearance of ischemic change on E.C.G. during postprandial lipemia, the author concluded that the muscle of the heart was reduced to a low oxygen state owing to disturbance of oxygen diffusion in the lung, and also disturbance of oxygen transport to the heart muscle itself.

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