Studies on the Mechanism of Postalimentary Lipemia in Atherosclerosis

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Present studies have been undertaken to make observations on the possible correlation between heparin and LPL activity from the viewpoint of the mechanism for disposing ability of alimentary lipemia. In vitro study has revealed the fact that releasing of LPL from the rat's tissue was responsible to the biochemical action of heparin. Following the intraarterial or intravenous infusion of heparin, LPL seemed to be released rapidly, suggesting that LPL may be mobilized from the vascular wall or adjacent tissues. No difference of plasma LPL activity after heparin injection in the fasting state between young healthy persons and patients with atherosclerosis was found. Moreover, no difference could be observed between the effect of heparin injection on the changes of plasma OD and LPL activities following fat intake in the controls and patients. An assumption was made that deficiency of apoenzyme could not be considered for the interpretation of disturbance in disposing ability of absorbed fat. Heparin-like substance in plasma was measured in the groups on fasting and postalimentary state. Plasma contents of heparin-like substance on fasting are found to be lower on the patients than the controls. One hour increase after fat intake failed to occur in the former, contrary to the latter, thus it is assumed that with the atherosclerotic patients the deficiency of heparin with disturbed releasing biochemical process are the responsible factor concerned. Further, the disturbed disposing ability of NEFA from blood stream is another factor to be considered in the abnormal metabolic process following fat absorption.

Many theories have been advanced on the etiology of atherosclerosis and the disturbance of lipid metabolism has been assumed as one of the most important factors. It is quite evident that in the atherosclerotic patients the lipid substance is deposited in the arterial wall, and it has been proved that atherosclerotic changes similar to human type could be produced in the rat fed with fat diet. In atherosclerotic patients, the serum lipid level is definitely higher than in young healthy adults, while, similar vascular lesion could readily be observed in the diseases associated with hyperlipemia such as diabetes mellitus and myxedema, moreover, statistical survey has revealed that the habit of overeating the food containing the saturated fat seemed to be related with the incidence of atherosclerosis. Among a number of problems related to lipid metabolism in such patients, the ability of disposing the ingested fat is considered to be an important factor by several investigators; Levine et al. reported that plasma optical density following oral fat intake showed the maximum value invariably and its recovery seemed to be retarded in the patients with atherosclerosis compared with the healthy subjects.

As one of the factors which brought forth prolongation of the postalimentary lipemia, Kageshita pointed out reduction of the endogenous lipolytic activity induced by oral fat loading. In 1943, Hahn reported that the postalimentary lipemia in dog could be cleared by the injection of heparin and in 1955, Korn interpreted this phenomenon to be a hydrolytic reaction by lipoprotein lipase (LPL) in

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reference to accumulative findings\textsuperscript{6-9}. Yet, in lipemic plasma, the fact that the condition could hardly be cleared in vitro by adding heparin seemed to suggest possible participation of tissue factor in the activation of LPL. Releasing mechanism of blood LPL following oral fat intake and the cause of lowered LPL activation on the patients with atherosclerosis have yet hardly been clarified. The author has attempted to pursue further on the cause of reduced activity from the biochemical aspect. Following experiments were carried out in the present studies.

**Experiment I** Relation between Heparin and LPL

Correlation between heparin and tissue factor was observed in vitro and subsequently the effect of heparin on the activation of LPL was observed in vivo.

Method and Subjects

A) Effect of heparin on the release of LPL from tissues.

The male rat (body weight 150–200 g), fasting for 6 hours at least, was killed by the blow on the head, the heart and epididymal fat were taken out immediately, washed with cold physiological saline for 3 times, minced with the scissors, wiped off remaining water with the filter paper and weighed and then treated with the following procedures.

Enzyme source: The tissues weighing 0.1 g were placed in 5 ml test tubes, each containing 1 ml of Krebs Ringer phosphate buffer (pH 7.4), 5 per cent bovine albumin and 30 mcg/ml of heparin, and incubated at 37°C for 40 minutes with gentle agitation. Physiological saline served as a control for the substitution.

Substrate: 0.2 ml of 10 per cent Fatgen (Artificial fat emulsion oil obtained from Dai Nippon Seiyaku Co.) and 0.3 ml of fresh human serum were mixed and incubated at 37°C for 30 minutes.

Assay system: An equal volume of the substrate and enzyme source was mixed and adjusted to pH 8.5 by titration with ammonium hydroxide and incubated at 37°C for 1 hour, then non-esterified fatty acid (NEFA) in the medium was measured before and after the incubation. LPL activity of the medium was assayed for its ability to produce NEFA from the substrate, Fatgen. LPL activity induced by heparin was determined as difference of NEFA production between the control and experiments. NEFA was determined by DOLE's method\textsuperscript{11}.

B) LPL activity in human plasma after injection of heparin.

Observation was made with the inpatients of our hospital, who were men of 20 to 40 years of age in recovering stage who had no metabolic disorders.

1) Heparin 40 U/kg was injected into the brachial artery in the early morning after overnight fasting, and the blood samples removed from the cubital vein by the syringe containing 1/10 volume of sodium citrate were taken immediately before, and 0.5, 1, 3, 5, 10, 15, 30 and 60 minutes after the injection of heparin and stored in the refrigerator. After the end of blood sampling, plasma was separated by centrifuging at 3000 r.p.m. for 15 minutes.

2) Heparin 40 U/kg was injected into the cubital vein and blood samples were removed from brachial artery in the above manner. Plasma was similarly obtained in the same procedure.

3) After injection of 40 U/kg of heparin into the cubital vein, blood samples were removed simultaneously from both the brachial artery and cubital vein. The plasma samples were obtained in the same procedure. The substrate was prepared with mixing 2.0 ml of 10 per cent Fatgen and 10 ml phosphate buffer containing 3 per cent bovine albumin, adjusted pH to 7.4.

Assay system: Plasma 1 ml of the enzyme source and 4 ml of substrate were mixed well and incubated at 37°C for 30 minutes. LPL activity was assayed for its ability to produce NEFA from the substrate.

Results:

a) By adding heparin to the medium containing the minced tissue of rat's heart or epididymal fat, it was found that activity of LPL was demonstrated to be definitely higher compared with the control medium added with physiological saline (Table I).

b) 1) LPL activity in the venous blood after intraarterial injection of heparin showed some
Table I  Effects of Heparin on LPL Release from the Heart and Adipose Tissue of Rats

<table>
<thead>
<tr>
<th>Case No</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
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</thead>
<tbody>
<tr>
<td>Tissue</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heart</td>
<td>77</td>
<td>155</td>
<td>150</td>
<td>80</td>
<td>102</td>
<td>70</td>
<td>80</td>
</tr>
<tr>
<td>Adipose</td>
<td>12</td>
<td>272</td>
<td>40</td>
<td>5</td>
<td>70</td>
<td>10</td>
<td>50</td>
</tr>
</tbody>
</table>

(unit: mcEq/L/0.1 g/hr.)

Fig. 1. Changes of lipolytic activity in venous blood after intraarterial injection of heparin.

elevation on 3 minutes, reaching to the maximum value in 5 minutes and thereafter showed gradual decrease (Fig. 1).  
2) LPL activity in arterial blood after intravenous injection of heparin showed some elevation after 3 minutes reaching the maximum value in 10 to 15 minutes and thereafter decreased gradually (Fig. 2).

3) Both of LPL activity in the arterial blood and in the venous blood after the intravenous injection of heparin were compared; The former was found to reach to its peak much earlier than the latter (Fig. 3).

It was revealed that LPL was released in the medium in vitro and in the blood stream in vivo with heparin.

Experiment II  On the Postheparin LPL Activity at Fasting and after Oral Fat Intake

Whether or not LPL activity between the patients with atherosclerosis and control subjects differed was studied. Comparative studies were made in LPL activity induced by heparin in fasting and after oral fat intake.

Method and Subjects:

A) The subjects were 14 young healthy adults (control group), 15 patients with arteriosclerosis (patients group) and nonsclerotic elderly adults. After 40 U/kg of heparin was injected into the cubital vein in the early morning.
after overnight fasting, venous blood samples were withdrawn before and 5, 10, 30 and 60 minutes respectively following the intravenous administration.

In this case, young healthy adults, less than 40 years of age were the members of our attending staffs and nurses of the hospital, including the patients who were in their convalescent stage, having verified none of suffering from the metabolic disease. The patients with arteriosclerosis were the subjects who came under A or B group of the standard classification of the cerebral or coronary arteriosclerosis based on the findings of the study group on the arteriosclerosis reported to the Ministry of Education. Nonsclerotic elderly subjects were the patients who were older than 40 years old who presented no signs of arteriosclerosis and metabolic disorders.

B) The subjects were 9 young healthy adults (control group) and 6 patients with arteriosclerosis (patients group). They were injected heparin 40 U/kg into the cubital vein and blood samples were obtained before and 5, 10, 15, 30 and 60 minutes respectively after the injection, subsequently an equal volume of heparin was reinjected into them. Blood samples were obtained in the same manner and their plasma LPL activities were measured.

C) The subjects were 8 young healthy adults (control group) and 10 patients with arteriosclerosis (patients group). They were injected with 40 U/kg of heparin in the cubital vein 4 hours after oral fat intake (200 g of cream), and blood samples were obtained before and 5, 10, 15, 30, 45 and 60 minutes after the administration and optical density (OD), NEFA and LPL activities were determined. OD was determined as follows; Plasma was diluted to 6 times with distilled water and its turbidity was measured by using electrospectrophotometer at 650 mμ and expressed by 1000 times value. Substrate and assay system in a) b) and c) were the same as those in experiment I.

Results:

a) There was no difference in the pattern of LPL activity between the control group and patients group observed after heparin injection on fasting. It was found that the activities in both groups were increased rapidly in 5 minutes reaching the peak in 10 to 30 minutes, but these decreased gradually until 60 minutes after the injection (Fig. 4, 5.). No difference could be found in LPL activity 10 minutes after administration of heparin between the nonsclerotic elderly group (B) and patients group (C). In the control group (A) it was shown that LPL activities were divided into the high and low level group. The influence of aging on LPL activity therefore was observed (Fig. 6). It was revealed that the low activities of LPL were found especially in 10 age, but no clear differ-

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**Figure 4.** Changes of postheparin lipolytic activity at fasting in the young healthy adults.

**Figure 5.** Changes of postheparin lipolytic activity at fasting in the arteriosclerotic group.

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ence could be found among the other age groups. The cases with myocardial infarction, indicated by black point in figure 6, revealed lower activities than those of arteriosclerotic patients.

b) LPL activity on fasting after double injections of heparin, indicated no difference in the pattern between the both groups and rose to the peak after 10 to 15 minutes in both occasions (Fig. 7, 8,). There was hardly any difference of the ratio of LPL activity after 10 minutes of the first administration of heparin to the second one between two groups (Fig. 9).

c) Plasma OD was found to decrease apparently in the respective group after 5 minutes of heparin administration following oral fat ingestion and reached the minimum value in 10 to 30 minutes and showed gradual increase thereafter though no difference in the pattern of OD could be seen in both groups.

LPL activity was increased considerably after 5 minutes of heparin injection, arrived at the maximum value within 15 minutes and turned to gradual decrease, though no difference could be observed between two groups. Plasma NEFA value was increased markedly after 5 minutes of heparin injection and reached the

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Fig. 6. Lipolytic activity 10 min. after heparin injection.

Fig. 7. Changes in plasma LPL activity induced by double injection of heparin.

Fig. 8. Changes in plasma LPL activity induced by double injection of heparin.

Fig. 9. Ratio of LPL activity induced by the repeated injection of heparin; LPL in second/LPL in first.

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maximum value in 30 minutes and maintained nearly the same value. As to the pattern there was no difference between the both groups (Fig. 10, 11.). Higher level of LPL activity was found on 7 patients who were administered of heparin after taking of fat orally, with the exception of one patient, as compared with the cases which were administered of heparin on fasting. (Fig. 12)

**Experiment III Study on the Heparin-like Substance in Blood**

Foregoing findings have proved to show no differences in the postheparin LPL activity of the groups on fasting or after fat intake. It is possible to enhance the LPL activity in the arteriosclerotic group by the injection of heparin after taking of fat and the ability to remove blood lipid from the circulatory blood seemed to be practically the same as in the control groups. It is reasonable to assume, therefore, that a decrease of Endogenous Lipoprotein Lipase Activity (ELA) in the patients after oral fat ingestion could be induced not by the deficiency of apoenzyme, but by the lack of the endogenous heparin which might be regarded as a LPL releaser. The author has measured the blood heparin levels on fasting as well as lipemic state, and comparative studies of two groups were made.

**Method and Subjects:**

a) Determination of heparin-like substance

Subjects were 13 controls and 16 patients and the blood samples were obtained with 1/10 volume of sodium citrate in fasting. In 6 controls and 8 patients blood samples were obtained and 1, 2 and 4 hours following ingestion of 200 g raw cream. Heparin-like substance were determined by the method of Gibbon (Table II). The recovery rate allowing errors in estimation are referred in the Table III.

b) Determination of recalcified clotting time

In addition to the determination of heparin-like substance, recalcified clotting time was measured for the same subjects.

**Procedures:** 2 ml of blood sample containing exactly 1/10 vol. of 3.8 per cent sodium citrate was obtained. After centrifugation at the speed of 1000 r. p.m. for 5 minutes, 0.2 ml of plasma was placed in test tube and warmed to 37°C in the water bath, then 0.2 ml of 1/10 M calcium dichloride was added to the test tube. Clotting
POSTALIMENTARY LIPEMIA IN ATHEROSCLEROSIS

TABLE II  THE METHOD FOR THE ASSAY OF PLASMA HEPARIN-LIKE SUBSTANCE

5 ml of oxalated plasma
- diluted with 5 ml of Phos. Buffer (Ph 6.1)
- added 2 ml of N-Octylamine Hydrochloride Sol. in 5 ml portion
- centrifuged for 15 min, at 3000 r. p. m.
- washed with 10 ml of water

- added 1 ml of N/5 NaOH
- mixed with 10 ml of saline
- heated at 60~70°C in a water bath for 15 min.
- added 1 ml of N/5 ZnSO₄ after cooling
- allowed to stand at room temp. for 30 min.

- extracted with 5 ml of water plus 5 ml of Phos. Buffer (Ph 7.8)
- heated at 65~70°C with stirring for 15 min.

- added 0.3 ml of Toluidin Blue Sol.
- allowed to stand at room temp. for 24 hr.

- washed with 10 ml of water
- added 1 ml of N/10 NaOH and 4 ml of alcohol

--- read at 540 mμ in a Coleman Jr. Spectrophotometer

TABLE III  RECOVERY AND TECHNICAL ERRORS FOR MEASURING HEPARIN-LIKE SUBSTANCE BASED ON THE GIBSON’S PROCEDURE

<table>
<thead>
<tr>
<th>Case</th>
<th>Initial Plasma Level (mcg/dl)</th>
<th>Added Heparin (mcg)</th>
<th>Total (mcg)</th>
<th>Recovery (%)</th>
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<tr>
<td>1</td>
<td>8</td>
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<td>4</td>
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<td>20</td>
<td>30</td>
<td>96.6</td>
</tr>
</tbody>
</table>

Fig. 13. Values of heparin-like substance in plasma at fasting.

time was measured with gentle agitation.

Results:
a) Plasma heparin like substance obtained on fasting showed much higher value in the control group than in the patients (Fig. 13). Heparin-like substance in the control group seemed to have increased after 1 hour of fat intake. After transient decrease, it was gradually elevated. However, with patients such elevation could hardly be observed after one hour, and its later rise was slightly observed (Fig. 14).
b) When fat was taken, recalcified clotting time of healthy subjects had delayed after one hour, showing lesser time. With the patients there occurred no prolongation, indicating that the time required was much less from the beginning.

These results have proved to show the difference of clotting time between the two groups one hour following fat intake, corresponding with variation of heparin-like substance (Fig. 15).
EXPERIMENT IV  STUDY ON THE CHANGES OF THE PLASMA NEFA VALUE FOLLOWING FAT INGESTION

For the disposal of postalimentary lipemia, the presence of LPL activity is imperative. NEFA, the product of lipolysis, should be removed quickly from the blood stream. This investigation involves the changes in plasma NEFA.

Method and Subjects:
The subjects consisted of 15 controls and 22 patients. To these 200g of raw cream was orally given in the early morning after overnight fasting. The blood samples were taken before and 4 hours after fat intake. NEFA content prior to and after the incubation of each plasma at 37°C for 60 minutes was determined.

Results:
The ELA 4 hours after fat intake showed marked lowering in the arteriosclerotic patients than in the control subjects, however, no difference in the elevation of plasma NEFA could be observed between the two groups (Fig. 16). While NEFA value before fat intake seemed to show inverse relation between the pre- and post value of 4 hour fat tolerance between the two groups. The curve of patients were less marked than the those of controls (Fig. 17).

DISCUSSION
Much has been reported in the pathogenesis of atherosclerosis. Some investigators have stressed that the ability of rapid removal of the absorbed fat from the blood stream is important.
act as the LPL releaser, hence, correlation between heparin and LPL is yet to be pursued. In the examination of LPL activity in the tissue induced by heparin in the rat's heart and adipose tissue, the results seemed to have agreed with the observation made by various reporters.

Heparin trial in human subjects and their LPL variation were observed next. LPL was estimated following the intravenous and intraarterial administration of heparin, through the cubital vein and brachial artery respectively and compared the results. It has been found that within 3 minutes plasma LPL could easily be detected either in arterial or venous blood. It is most likely that the vascular wall or peri-vascular tissue may be responsible for release of this particular enzyme, and that arterial blood has proved to show a higher value than the venous blood. Simultaneous estimation of both samples of blood has also substantiated a higher arterial value which undoubtedly suggest possible participation of the pulmonary biochemical process of disposal in the release of LPL supporting INDERBITZEN who proposed involvement of lung tissue in the correlation of alimentary lipemia. ROBINSON and JEFFRIES suggested the release of LPL from the vessel wall based on the rapidity of the appearance in blood in less than one minute. The difference in the time of LPL detection between these reports and the author's might be due to the variable animal species. Some investigators have reported that plasma LPL activity upon heparin administration on fasting was found to be reduced with development of atherosclerosis when compared with young healthy adults, while others have failed to observe, and no unanimity in their findings.

The results of present investigation revealed no difference in the pattern of LPL activity between the patients and controls, yet, it is our interest to know that LPL activity induced with heparin would be rather low 10 minutes after injection in the teen age and the patients who had myocardial infarction. When the LPL activity was measured in the atherosclerotic patients who were administered of heparin 4 hours after fat injection, its value remained practically the same as that of the control subjects. As

factor in consideration of the prevention and the development of atherosclerosis. The present studies attempt to elucidate the reason for prolonged mechanism of postalimentary lipemia in the patients with atherosclerosis.

Clearance of postalimentary lipemia by injection of heparin, as reported by HAHN and subsequent reports of the other investigators seemed to have substantiated on the action of heparin: nevertheless, no conclusive study from the enzymatic aspect, Lipoprotein Lipase, has yet been reported. On the mechanism involved in the clearing factor, KORN disclosed that a true lipolysis of the lipoprotein of low density mainly consisting of neutral fat does occur with the products of nonesterified fatty acid, glycerol and high density lipoprotein. Other investigators have cleared that this enzyme in heparinized plasma was unlike that of the pancreatic origin from their inhibitory studies and that it is identifiable with the endogenous lipoprotein lipase in plasma devoid of heparin.

Since the active LPL could hardly be observed in the plasma with an addition of heparin in vitro, it is most probable that participation of the tissue is involved when heparin is present. An assumption is that heparin would

Fig. 17. Correlation between serum level of NEFA in fasting state and increment of NEFA in 4 hours after oral fat intake.
to OD and NEFA the changes were the same whether the patients or control subjects, signifying that the postheparin LPL seemed to dispose alimentary lipemia to the same degree. However, on fasting, the value of LPL activity following treatment with heparin was found to be lesser than the value of the same patient measured at 10 minutes of heparin injection 4 hours after the fat loading. This apparently suggests that ELA mobilized upon fat ingestion has been added to the postheparin LPL activity or the response of LPL to heparin has been enhanced by fat ingestion. In other words in patients with atherosclerosis response to the exogenous heparin is demonstrable as much as in control subjects in spite of decreased ELA upon fat loading. Hence, it is apparent that decreased ELA could not be explainable on the basis of deficient apoenzyme, it is most probably attributed to the disturbed releasing process of heparin or to the chemical nature of heparin per se. Accordingly, heparin-like substance in plasma on fasting and after fat intake with arteriosclerotic patients and control subjects were studied and compared.

Up to the present, we know of no direct method for the assay of plasma heparin, however reported indirect method could be summarized as follows.

1) Photometric method for determination of heparin-like substance based on its property to conjugate with various basic dye\textsuperscript{14,30}.

2) Method of measuring thrombin time and prothrombin time based on the anticoagulant effect of heparin\textsuperscript{31}.

3) Combined chemical and anticoagulant method\textsuperscript{32}.

4) Method of measuring anticoagulant effect after trypsin digestion and dialyzing\textsuperscript{33}.

As the assay method of heparin-like substance by Gibson with the use of octylamine is relatively simple procedure with little technical error and has proved to be good, it has been used for detecting heparin like substance in plasma. Recalculated clotting time measurement is required in those cases when fresh cream is fed with a view to making sure of the value of heparin-like substance obtained by Gibson's method. Nikkilä\textsuperscript{34}, Murakami\textsuperscript{35} have found that these patients had lower heparin-like sub-

stance on fasting than the controls, though Takahashi\textsuperscript{36} stated hardly any difference to be seen between the two. In the present study, the value observed in the patients showed the lower figure than the controls. Although successive measurement of the level of heparin-like substance after intake of fat have been limited, Takahashi\textsuperscript{36} has found increased quantity in one hour which eventually reached to the maximum in 3 to 5 hours. It was shown that there was a rise after one hour in the controls which lowered temporarily for a while before the steady trend of rise. On the other hand with the patients, the initial elevation would not occur, it was a type of steady rise which was lower than the control group.

Much has been studied on the coagulability of blood following fat ingestion. Waldron\textsuperscript{37} and O'Brien\textsuperscript{38} reported on the hypercoagulability while Mandel\textsuperscript{39} stressed the degree of hypercoagulability which correlated with the optical density of plasma. According to Nitzberg\textsuperscript{40}, Sheehy\textsuperscript{41} blood coagulability had no way related to the postmeal state. It appears then, as far as correlation between the postmealary lipemia and blood coagulability is concerned, there has been little agreement. This is perhaps due to complexed mechanism of blood coagulation and difference in technique employed. Many investigators\textsuperscript{42-45} have agreed, however, that blood coagulability could be accelerated in postmealary state, after the technique of the Stypven time. Concerning the intravenous loading of fat no fewer reports have been agreeable in the influence of hypercoagulability. It is reasonably possible that the fat would accelerate the coagulability of blood in some way. The results have demonstrated that recalculated coagulation time after oral fat intake in young healthy group could be prolonged a little by one hour period, then shortened in time parallel with increase of plasma OD, but this is not the case with the patient group. This result seemed to invariably coincide with significant increase of the heparin-like substance with the control subjects by one hour following fat intake, contradictory to the reduced value of the patients group. Despite of increased plasma heparin like substance affecting lesser blood coagulation time as the result of adding
fatty substance, it has been suggested that heparin which combines with a number of substance may have reacted preferentially with LPL in the post吃饭的lipemia, and made little effect on the anticoagulant action, as Spitzer stated, and that the effect of lipemia itself on the blood coagulability surpassed the influence of the endogenous heparin on coagulability. Thus it is highly probable that the mechanism of poor disposal state of alimentary lipemia in the patients with atherosclerosis could be decreased LPL activity induced by heparin deficiency after fat intake. On the other hand, for the enzymatic reaction to be accomplished quickly from the circulation, ELA and increment of NEFA 4 hours after fatty meal need to be evaluated. Although the amount of NEFA produced should be theoretically lower in the patients than in the controls, actually the increment of NEFA was identical in degree between the two, which offers evidence for disturbed process of eliminating NEFA from the circulatory blood. Further, plasma NEFA level on fasting has demonstrated a negative correlation with a increment of NEFA 4 hours after fat intake, that is to say, the higher the plasma level of NEFA on fasting, the lesser the increment of the post吃饭的lipemia NEFA. It is assumed that this may be attributed to a possible plasma NEFA pool, depending on the produced NEFA by the process of lipolysis in blood and eliminating mechanism of NEFA from the blood stream. Presence of the positive correlation of NEFA content in plasma with turnover rate in young healthy adult has been reported by Armstrong, pointing out the normal disposal ability of NEFA.

As is shown in Fig. 17, the slower slope of correlation curve between the plasma NEFA content on fasting and its increment after fat intake in the patients could be interpreted as retarded turnover rate of NEFA, suggesting that disposing ability of NEFA has decreased in the patients with atherosclerosis on the post-alimentary state.

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