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# DISTURBANCES OF LIPID METABOLISM IN PANCREATIC DISORDERS WITH SPECIAL REFERENCE TO SERUM LIPOPROTEIN LIPASE ACTIVITY

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ABSTRACT

In order to clarify the mechanism of hyperlipemia during pancreatic disorders, investigations on changes of serum lipids, measurements of lipoprotein and number of chylomicra after oral administration of fat (safflower oil or olive oil) and studies on post-heparin lipoprotein lipase were done on patients with chronic pancreatitis and on dogs with experimental pancreatic disorders. The results obtained were as follows. (1) $\beta/\alpha$ Lipoprotein indices and $\beta$-lipoprotein levels were increased in pancreatitis. (2) There was an impaired removal of chylomicra from plasma in pancreatitis. (3) Post-heparin lipoprotein lipase activities in the dogs with pancreatic disorders were significantly lower than those in the normal controls. (4) No inhibitor on lipoprotein lipase activity was detected in plasma in the dogs with pancreatitis. The possible relationships of these phenomena to the mechanism of lipid metabolism in pancreatic disorders have been discussed. It was concluded that the decreased delivery of the lipoprotein lipase into the circulation was one of the possible causes of hyperlipemia in pancreatic disorders.

## INTRODUCTION

Transient hyperlipemia has been known to occur in association with acute attacks of pancreatitis. Since Speck[1] had described the first case in 1865, several other cases have been reported.

The hyperlipemia in pancreatitis is due primarily to a marked increase in plasma triglycerides[2)3)4)]. Binet and Brocq[5)] observed transient increases in serum lipids in dogs with acute hemorrhagic pancreatitis. Although hyperlipemia in acute pancreatitis is supposed to be an uncommon manifestation of this disorder[6)7)8)], the incidence of serum lipid aberrations during the course of acute pancreatitis was found to be 52 per cent[9)].

A considerable number of explanations have been offered on the mechanism of the hyperlipemia accompanying acute pancreatitis in man and experimental animals in recent years, but little is known about the relation between pancreatitis and hyperlipemia. The suppression of an antilipemic factor re-

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sulting from pancreatic injury was presumed[10]. Digestion of peritoneal fat by pancreatic enzymes and subsequent absorption into the portal circulation was considered[7]. A disturbance in intermediate stage of fat metabolism has also been suggested[2)11)12)13)]. Chronic alcoholism and fatty liver were believed to be important factors[14)15)16)]. Transient elevation of plasma cholesterol has been observed in experimental animals after the administration of cobaltous chloride[17], which damages or destroys the $\alpha$-cells of the islands of Langerhans. Klatskin and Gordon[18] considered possible mechanisms in the production of pancreatitis by lipemia : xanthomatous lesions in the pancreas, atherosclerotic vascular changes, and embolization of pancreatic vessels by fat emboli.

It has been reported in recent years, that the lipoprotein lipase (LPL) which has lipemia clearing activity, reduces the hyperlipemia[19]. This enzyme hydrolyzes the triglycerides in chylomicra and other low-density lipoproteins[20] and facilitates the removal of particulate triglycerides from the circulation.

In various disorders accompanied by hyperlipemia, deficiency of mobilization of post-heparin LPL and the presence of a circulating inhibitor of LPL have been demonstrated[21)22)23)]. Recently Kessler *et al.* have reported evidence for inhibition of LPL by the plasma of rabbits with experimental acute pancreatitis[24] and have presented evidence for the presence of a LPL inhibitor in the pancreas and its exocrine secretion[25].

The present paper was designed to study the disturbances of lipid metabolism in the pancreatitis with special reference to the lipoprotein and on the lipolytic activities in circulating blood.

## MATERIALS AND METHODS

Acute pancreatitis was produced in dogs approximately 10 kg in weight by intraductal injection of 10 per cent gall powder solution (0.5 ml/kg body weight).

The clinical diagnosis of chronic pancreatitis was established by the serum amylase levels, prostigmin test, roentgenologic findings, and clinical findings.

Each blood sample was drawn after an overnight fast and was analysed immediately.

In order to investigate the changes of the lipoprotein indices, the $\beta$-lipoprotein levels and the chylomicron counts after administration of fat, olive oil or safflower oil was administered orally after fasting for 12 hours in a dose of 0.5 g/kg body weight both in man and in dog.

Blood samples were taken just before, and 2, 4 and 6 hours after the administration.

Heparin was given intravenously in a dose of 0.4 mg per kg of body weight to a dog after the fasting of 12 hours. Blood was withdrawn in chilled syringes containing 1/10 volume of sodium citrate before the injection of heparin and at 10, 20 and 30 minutes after the injection, and the plasma was analysed for

lipoprotein lipase and esterase activities without delay after withdrawal of the samples.

Total fatty acids in serum were determined by the method of Smith-Kik, free fatty acids by the Dole's method, phospholipids by the method of Fiske-Subbarow, serum cholesterol by the method of Sperry-Webb and total lipids by the Bloor's method. Serum amylase was determined by the method of Somogyi.

Lipoprotein indices were determined by the pre-staining procedure[26] of the electrophoresis of lipoprotein. The electrophoretic separation was carried out on Toyo filter paper No. 51, with a veronal buffer of pH 8.6 and the potential gradient of 8 V/cm for 3 hours. The strips were cut out and the dye eluted for one hour. Serial readings of optical density were made in a spectrophotometer at 590 m$\mu$.

The $\beta$-lipoprotein was measured by use of "$\beta$-L Test", commercially available from Hyland Laboratories, Los Angeles, Calif., U.S.A.

Chylomicron counts were made on plasma in a standard field under dark ground illumination. The number of chylomicra in 5 fields of vision was counted from which values was calculated the mean value, and then the number of chylomicra per cubic millimeter was calculated.

LPL activity was represented as the amount of FFA released into the incubation medium by a modification of the method described by Duncombe[27].

Esterase activity was also determined by assaying FFA, which dissociated by the method of MacDonald and Le Fave[28].

For investigating the presence of inhibitor, post-heparin plasma obtained 10 minutes after intravenous injection of heparin in normal dogs was mixed with an equal amount of plasma obtained before and at various intervals following induction of pancreatitis. The control consisted of a normal post-heparin plasma mixed with an equal amount of normal pre-heparin plasma. And the final lipolytic activity was measured as described above. The lipolytic activities of both mixtures were compared.

## RESULT

*1. The changes of the serum lipids in pancreatitis*

The changes of the serum lipids in the dogs with pancreatitis are shown in Table 1. Total and free cholesterols increased progressively after acute pancreatitis was produced. On the other hand, phospholipids and total fatty acids gave minimal changes. Free fatty acids increased slightly. Comparisons of the serum lipids between the patients with chronic pancreatitis and the normal controls are given in Table 2. Free cholesterols and phospholipids gave minimal changes. Total cholesterols did not alter and total fatty acids and free fatty acids were elevated in the patients.

Lipoprotein indices in the control dogs were 0.43. Three days after acute

TABLE 1. Changes of the serum lipids in the dogs with pancreatitis

| | before | 1 day | 2 days | 3 days | 6 days |
|---|---|---|---|---|---|
| Total cholesterol (mg/dl) | 113± 22.1 (9) | 107± 32.0(3) | 133± 68.5(5) | 158± 36.4(7) | 201± 53.3(5) |
| Free cholesterol (mg/dl) | 28± 12.0 (9) | 29± 13.6(3) | 30± 21.4(5) | 54± 22.8(7) | 74± 40.0(5) |
| Phospholipid (mg/dl) | 307± 47.9 (9) | 403±102.0(3) | 335± 51.9(3) | 333± 58.3(7) | 349± 93.0(5) |
| Total fatty acid (mg/dl) | 315± 97.9(11) | 324± 78.7(5) | 334± 69.2(5) | 389±130.4(8) | 353±137.3(7) |
| Free fatty acid ($\mu$Eq/l) | 553±154.9(11) | 700±116.0(4) | 618±178.9(7) | 700±183.0(9) | 570±194.0(7) |

Numbers in parentheses indicate case numbers.

TABEE 2. Comparisons of the serum lipids between the patients with chronic pancreatitis and the normal controls

| | Total cholesterol (mg/dl) | Free cholesterol (mg/dl) | Phospholipid (mg/dl) | Total fatty acid (mg/dl) | Free fatty acid ($\mu$Eq/l) |
|---|---|---|---|---|---|
| Patients with chronic pancreatitis | 189.5±49.3 (62) | 55.3±22.3 (61) | 241.9±65.7 (57) | 416.7±136.4 (64) | 700.8±138.9 (58) |
| Normal controls | 188.9±32.5 (100) | 47.2±15.9 (100) | 217.7±40.8 (100) | 334.3± 82.8 (100) | 548.9±144.9 (26) |

Numbers in parentheses indicate case numbers.

TABLE 3. Changes of lipoprotein indices and $\beta$-lipoprotein levels in the dogs with pancreatitis

| | before | 3 days | 7 days | 14 days | 21 days |
|---|---|---|---|---|---|
| Lipoprotein indices | 0.43±0.11(24) | 0.67±0.13(8) | 0.54±0.13(19) | 0.52±0.07(4) | 0.48±0.12(5) |
| ß-lipoprotein levels (mm) | 0.36±0.08 (9) | 0.69±0.26(8) | 0.55±0.25(11) | 0.40±0.16(6) | 0.46±0.15(7) |

Numbers in parentheses indidate case numbers.

pancreatitis was induced, they were markedly elevated to 0.67 (Table 3). Subsequently they were gradually reduced, but were still rather higher after 21 days than the value in the control dogs (0.48).

$\beta$-lipoprotein levels showed also similar tendency to lipoprotein indices. Three days after the induction, they gave extremely high values (0.69), and decreased thereafter. However, the levels after 21 days were still higher than those in the control dogs (0.46).

As seen in Table 4, the patients with chronic pancreatitis showed significantly higher lipoprotein indices than the normal controls.

TABLE 4. Comparison of lipoprotein indices between the patients with chronic pancreatitis and the normal controls

| | Lipoprotein indices |
|---|---|
| Chronic pancreatitis | 3.40±1.11 (24) |
| Normal controls | 2.40±0.69 (13) |

Numbers in parentheses indicate case numbers.

*2. Oral administration of fat*

*A. Administration of safflowe· oil*

*a. Changes of lipoprotein indices in the dogs with pancreatitis*

The oral administration of safflower oil gave no marked influences on the lipoprotein indices in the dogs with pancreatitis.

*b. Changes of β-lipoprotein levels in the dogs with pancreatitis*

Although the β-lipoprotein levels increased slightly after 4 hours, the oral administration of safflower oil gave no marked influences on the β-lipoprotein levels on the whole. The results failed to show any differences in the levels obtained from the dogs with pancreatitis and from the normal controls.

*c. Changes of the numbers of chylomicra in the dogs with pancreatitis* (Fig. 1)

In the acute stage (3 days and 7 days after the induction) the numbers of chylomicra showed almost no increase after the administration, whereas in the chronic stage (14 days and 21 days) they resulted in marked increases. In the normal controls they showed a moderate increase. In the normal controls the maximum number was obtained 4 hours after the administration of safflower oil. In the 14 day group the maximum was obtained at one hour after the administration, and returned gradually to the original level. In the 21 day group the maximum was at 4 hours after the administration and the numbers of chylomicra were still elevated than the original levels at 6 hours.

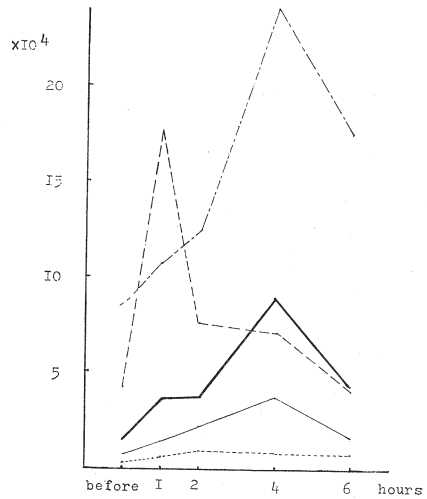


FIG. 1. Effect of oral administration of safflower oil on numbers of chylomicra in the dogs with pancreatitis.

Heavy solid, solid, dotted, dash and chain lines represent normal controls, 3, 7, 14 and 21 day group respectively.

Numbers of chylomicra per cubic millimeter are given.

*d. Changes of lipoprotein indices in the patients with chronic pancreatitis* (Table 5)

The oral administration of safflower oil gave no drastic influence on lipopro-

TABLE 5. Effect of oral administration of safflower oil on lipoprotein indices in the patients with chronic pancreatitis

| | before | 2 hours | 4 hours | 6 hours |
|---|---|---|---|---|
| Normal controls | 2.15±0.36(4) | 2.83±1.47(4) | 2.30±0.39(4) | 2.45±0.73(4) |
| Patients with chronic pancreatitis | 3.69±2.71(7) | 3.50±1.66(7) | 3.86±1.95(7) | 4.13±2.77(7) |

Numbers in parentheses indicate case numbers.

tein indices in the patients with chronic pancreatitis. The actual courses of the plottings were slightly different from those of lipoprotein indices in the dogs with pancreatitis. However, the overall patterns were the same.

*B. Administration of olive oil*

*a. Changes of lipoprotein indices in the dogs with pancreatitis*

The oral administration of olive oil caused no remarkable changes on the lipoprotein indices in the dogs with pancreatitis.

*b. Changes of β-lipoprotein levels in the dogs with pancreatitis*

There were no remarkable changes in the β-lipoprotein levels in the dogs with pancreatitis after the administration of olive oil.

*c. Changes of the numbers of chylomicra in the dogs with pancreatitis* (Fig. 2)

The changes were different from those after the administration of safflower oil. In the acute stage (3 days and 7 days) the chylomicra showed marked increases, and in the 14 day group of the chronic stage they gave the marked increase, whereas in the 21 day group of the chronic stage they showed as moderate an increase as those in the normal controls.

In the normal controls and in the 21 day group the maximal values were obtained 2 hours after the administration of olive oil, and the numbers returned to the original levels after 6 hours. In the 7 day and 14 day groups the maximal values were also 2 hours after the administration, but the numbers 6 hours after the administration were still elevated than the original levels.

In the 3 day group the maximum was one hour after the administration and the numbers of chylomicra returned to the original levels 6 hours after the administration.

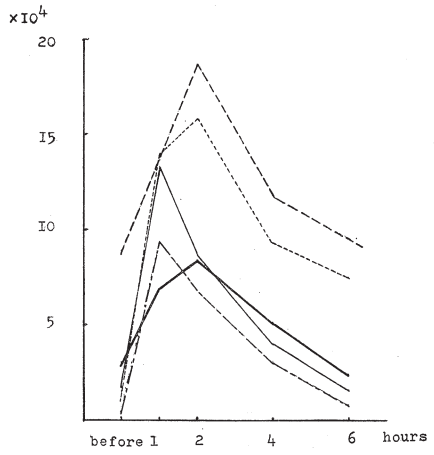


FIG. 2. Effect of oral administration of olive oil on the numbers of chylomicra in the dogs with pancreatitis.

Heavy solid, solid, dotted, dash and chain lines represent normal controls, 3, 7, 14 and 21 day group respectively.

Numbers of chylomicra per cubic millimeter are given.

*d. Changes of lipoprotein indices in the patients with chronic pancreatitis*

The oral administration of olive oil showed no drastic influence on lipoprotein indices in the patients with chronic pancreatitis.

*3. Studies on lipoprotein lipase (LPL)*

*A. LPL activity in the dogs with pancreatic impairments*

The changes of the LPL activity after the intravenous injection of heparin

to the normal dogs are illustrated in Fig. 3. The rapid rise of the LPL activity was observed immediately after the injection of heparin and the peak was reached within 20 minutes and showed a gradual fall thereafter.

The peak of post-heparin LPL activity was significantly reduced in the cases of acute pancreatitis (Fig. 4, 5, 6) than in the healthy control dogs (Fig. 3), while the changes of post-heparin LPL activity showed no significant differences between the controls (Fig. 3) and the dogs with chronic pancreatitis (Fig. 7).

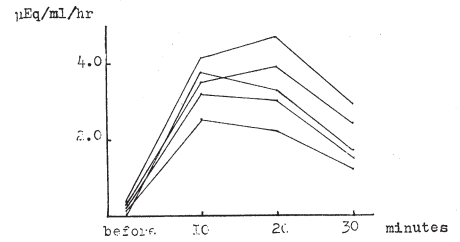


FIG. 3. Changes of post-heparin LPL activity in the normal dogs.

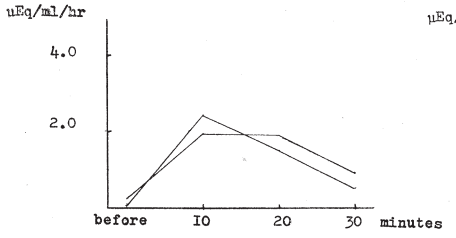


FIG. 4. 1 day group after operation.

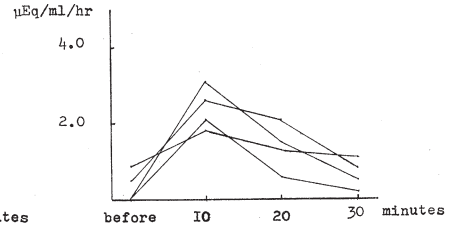


FIG. 5. 3 day group after operation.

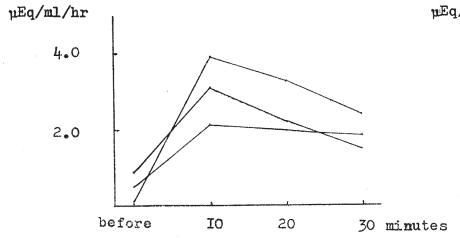


FIG. 6. 7 day group after operation.

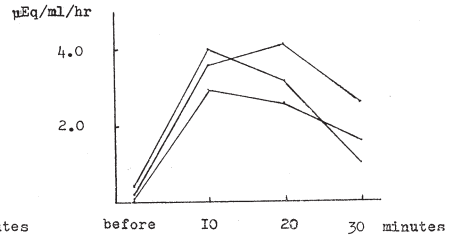


FIG. 7. 14 day group after operation.
Changes of post-heparin LPL activity in the dogs with pancreatitis.

As shown in Fig. 8, 3 days after operation, the peak of post-heparin LPL activity in the dogs with ligated pancreatic ducts was much lower than that of the controls. However, no significant differences were proved among the changes of LPL activity in the controls, in the 7 day group and in the 14 day group after operation (Fig. 9, 10).

The post-heparin LPL activity in the dogs with total pancreatectomy was markedly reduced and showed the slow elevation (Fig. 11), and the lipemia was the most prominent in these cases.

*B. Lipase activity in the dogs with pancreatic impairments*

As illustrated in Fig. 12, in the plasma of the dogs with acute pancreatitis,

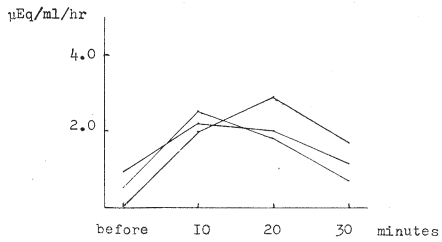


FIG. 8. 3 day group after operation.

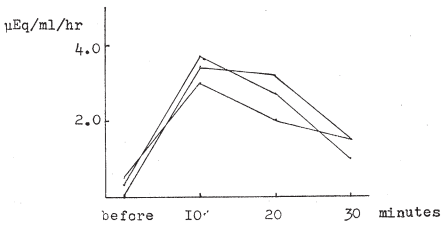


FIG. 9. 7 day group after operation.

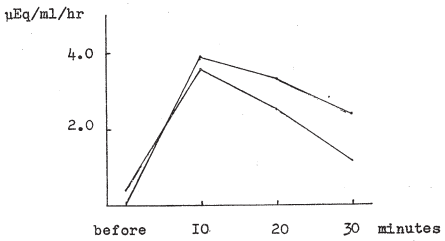


FIG. 10. 14 day group after operation.
Changes of post-heparin LPL activity in the dogs with ligated pancreatic ducts.

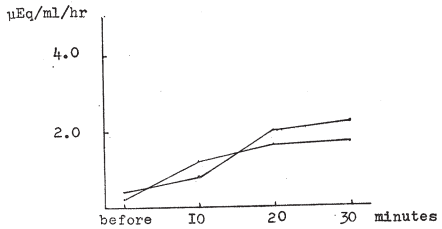


FIG. 11. Changes of post-heparin LPL activity in the dogs with total pancreatectomy.

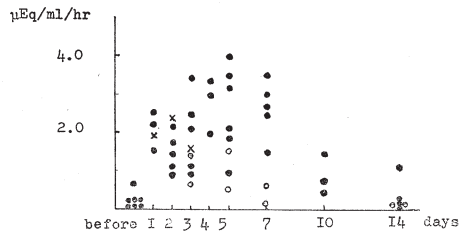


FIG. 12. Changes of lipase activity in the dogs with pancreatic impairments.

Solid circles, open circles and crosses represent the dogs with pancreatitis, ligated pancreatic ducts and total pancreatectomy respectively.

the lipase activity slightly increased 24 hours after operation, reached the highest peak after 5 to 7 days and returned gradually to the original level within two weeks.

The plasma of the dogs with ligated pancreatic ducts showed only a slight increase in the lipase activity. However, a considerable increase was found in the dogs with total pancreatectomy.

### *C. Relationship between lipoprotein lipaes and lipase in the dogs with pancreatic impairments*

The LPL activity in the normal controls was remarkably elevated after the injection of heparin, whereas there were minimal or no changes in the lipase activity (Fig. 13). Therefore it is apparent that the lipolytic activity released into the post-heparin plasma in the normal dogs depends for the most part upon the LPL activity.

As shown in Figs. 14, 15 and 16, there was an overlap between the lipase and the LPL activity in the plasma obtained from the dogs with pancreatitis. This fact may lead to a speculation that the true levels of LPL activity should be less than the observed levels in the dogs with pancreatitis. On the contrary, 14 days after operation, a similar tendency to the normal controls was observed

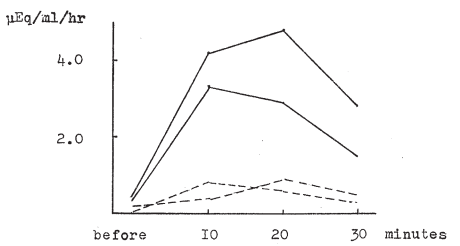


FIG. 13. Relationship between LPL and lipase activity in the normal dogs.
Solid and broken lines represent LPL and lipase activity respectively.

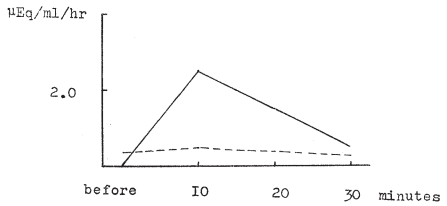


FIG. 14. 1 day group after operation.

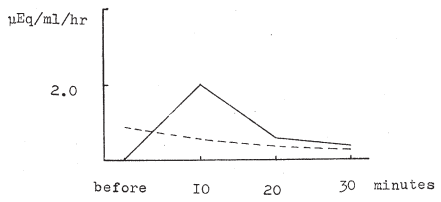


FIG. 15. 3 day group after operation.

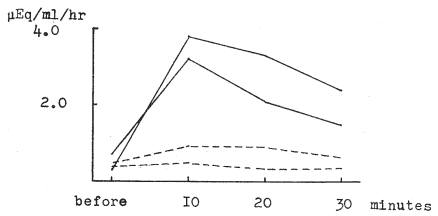


FIG. 16. 7 day group after operation.

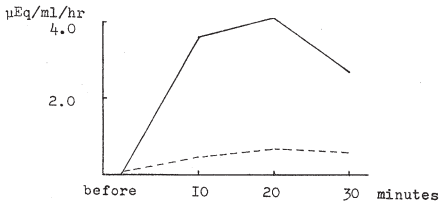


FIG. 17. 14 day group after operation.
Relationship between LPL and lipase activity in the dogs with pancreatitis.
Solid and broken lines represent LPL and lipase activity respectively.

(Fig. 17).

Similarly, the true LPL activity in the dogs with total pancreatectomy should be much lower than those in the dogs with pancreatitis, as clearly seen in Fig. 22.

In the dogs with ligated pancreatic ducts, similar tendency would be also suggested (Figs. 18–21).

*4. Study on the inhibitor of lipoprotein lipase*

No evidence was found for any inhibitory effect in the plasma of the dogs with pancreatitis on the normal post heparin LPL activity.

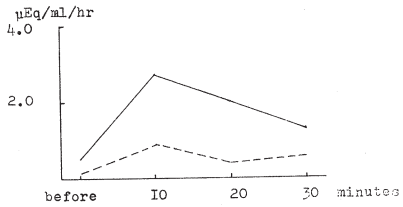


FIG. 18. 3 day group after operation.

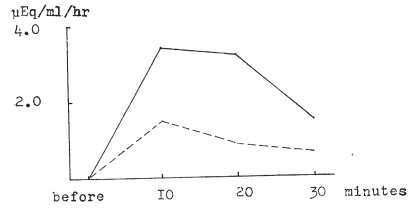


FIG. 19. 7 day group after operation.

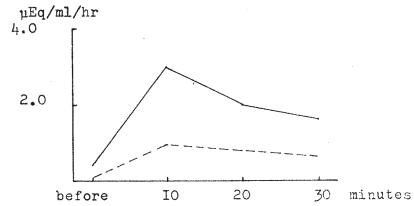


FIG. 20. 7 day group after operation.

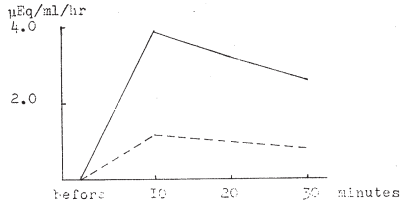


FIG. 21. 14 day group after operation.

Relationship between LPL and lipase activity in the dogs with ligated pancreatic ducts. Solid and broken lines represent LPL and lipase activity respectively.

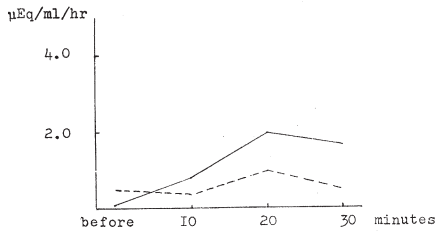


FIG. 22. Relationship between LPL and lipase activity in the dogs with total pancreatectomy.

Solid and broken lines represent LPL and lipase activity respectively.

## DISCUSSION AND CONCLUSION

Thannhauser[29] classified pancreatitis as one of the five causes of hyperlipemia. Although the relation between lipid alterations and lactescence of the serum in patients with acute pancreatitis and the episodes of acute pancreatitis in subjects with essential hyperlipemia has been discussed in detail[14)18)], this interrelation remains a very interesting and puzzling problem.

*Serum lipids:*

The elevation of serum lipid levels in experimental pancreatitis in the dog was reported in 1929[5]. It was also reported that acute pancreatitis produced experimentally in rabbits and dogs results in transient elevation of serum lipids for one to four days[30],

Although neutral fat levels were not determined in this study, the serum showed a very much thicker cream layer on standing, suggesting a marked increase in neutral fat. The determination of the blood lipids in this study confirms the reports that the lipemia associated with pancreatitis is due largely to an increase in neutral fat[2)3)4)] and that under some conditions the phospholipid and cholesterol fractions may also participate[2)3)4)12)31)].

*Lipoprotein:*

In this study, the remakable increases of $\beta/\alpha$ lipoprotein indices and of $\beta$-lipoprotein levels in both men and dogs with pancreatitis were observed. It may be probable that these elevations are closely connected with hyperlipemia in pancreatitis. Although only a few papers have been published on these subjects in pancreatitis, the increases should be quite reasonable, as the triglyceride level is elevated in pancreatitis. On the contrary, Kellen[32)] reported that significantly decreased $\beta$-lipoprotein levels had been observed in acute pancreatitis, but he confessed that the mechanism could not be explained.

Havel[33)] has reported on the idiopathic hyperlipemia that the concentration of very low density lipoproteins in the plasma markedly increased. The protein moiety of high density lipoproteins is known to be contained in chylomicra[34)], and during the disappearance of chylomicra with labeled proteins from the plasma, there is an immediate appearance of radioactivity in the high density lipoproteins[35)]. Therefore, the increases of $\beta/\alpha$ lipoprotein indices and of $\beta$-lipoprotein levels may be due to the metabolic defect in the removal of chylomicra from the blood probably resulted from rapid exhaustion of protein moieties in the high density lipoproteins.

Following a fat-containing meal, the blood is particularly rich in chylomicra which consist mainly of triglyceride. This substance functions as the major vehicle for the transport of the esterified fatty acids in plasma with the most rapid turnover rate[36)]. It has been asserted that the turbidity of lipemic serum is related to the number of visible particles demonstrated by dark-field illumination[37)], and that the chylomicron count parallels the neutral fat content of the serum[38)]. It is of interest that in the dogs under the same condition, the different kinds of fat (safflower oil and olive oil) seem to have a different effect on the chylomicron curve. In the normal dogs received safflower oil, the maximum number of chylomicra was obtained after 4 hours and the number of chylomicra returned gradually to the original level. In the normal dogs recieved olive oil, the peak was after 2 hours and the original value was attained after 6 hours. Gage and Fish[39)], and MacArthur[40)] came to nearly the same conclusion.

The time for the chylomicra to appear in the blood after oral administration of fatty food is from one half to one and one-half hours, and the time needed for disappearance from the blood varies from about six to ten hours[39)].

In the present experiments, there was marked increase of chylomicra in plasma after the oral administration of fat, except for the cases of safflower oil administration to the dogs with acute pancreatitis (3 and 7 days). Egawa[41] has reported that the dogs with acute pancreatitis and totally pancreatectomized dogs had both hypofunction of digestion and absorption, whereas the patients and dogs with chronic pancreatitis only of digestion. Muramatsu[42] has also reported similar result. Therefore, the marked increase in chylomicra for all the hypofunction of digestion and absorption indicates an impaired removal of chylomicra in pancreatitis.

*Lipoprotein lipase:*

Circulating triglycerides are carried predominantly as chylomicra and larger low-density lipoproteins. It is nowadays well recognized that normally the reticuloendothelial system does not play an important part in the removal of chylomicra from plasma. There are also evidences of various types that the liver does not play an essential role in the removal of alimentary triglyceride, and that extrahepatic hydrolysis in tissue with high activity of lipoprotein lipase precedes uptake of the liberated fatty acids. The view is widely held currently that the heparin-activated lipolytic enzyme, lipoprotein lipase, is the major pathway for the removal of alimentary and endogenous triglycerides from the blood.

An investigation on the lipoprotein lipase activity in pancreatitis, measuring the degree of decrease in optical density has been reported by Ito[43]. Since optical clearing had proved to be an inadequate measure of lipoprotein lipase activity in hyperlipemic plasma, further studies were carried out to determine the released free fatty acids as a measure of enzyme activity. In the present study, the post-heparin clearing activities in the dogs with pancreatic disorders were significantly reduced. The difference between Ito's observation and the present result might be due to the difference of method employed.

One factor contributing to the hyperlipemia is a decrease in rate of removal of chylomicron lipid from the circulation. In this study, a decrease in rate of removal of chylomicron lipid in pancreatitis was observed. Meng *et al.*[44] have reported that the clearing activity of post-heparin plasma of alloxan-diabetic and pancreatectomized rats was markedly reduced and that insulin treatment plus feeding of a diet containing either lyophilized beef pancreas or Lipormone, a purified lipocaic, was capable of restoring the post-heparin plasma clearing of alloxanized rats to the level of normal animals. They suggested therefore that a pancreatic factor might be necessary in the *in vivo* production of the heparin-induced clearing factor.

*Inhibitor of LPL:*

An inhibitor of lipoprotein lipase was demonstrated in the plasma of rabbits with experimental pancreatitis[24] and the possibility was thus raised

that the decreased rate of removal of chylomicra might be dependent on presence in plasma of an inhibitor to lipoprotein lipase. The results in this study, however, confirm the observation that no inhibitory effect was demonstrated in the plasma of dogs with experimental pancreatitis. These differences may be due to the severity of pancreatitis. Day *et al.*[23] concluded that an increase in inhibitor activity on clearing factor found in both the diabetic and nephrotic groups, may be attributed to the age factors of the subjects. It has been reported that in idiopathic hyperlipemia the defective removal of triglycerides from the plasma do not result from the presence of inhibitors in the plasma, but from a genetic deficiency of lipoprotein lipase[33]. This suggests therefore, that an inhibitor, if any, does not play a major role in chylomicron removal. There are evidences that chylomicra can be removed without prior hydrolysis by serum lipoprotein lipase[45].

Meng and Goldfarb[44] have shown that pancreatectomy reduced the lipemia-clearing property of the post-heparin plasma by more than 80%. And a significantly impaired post-heparin liberation of lipoprotein lipase was observed in patients with cystic fibrosis of the pancreas[46]. Le Veen *et al.*[47] concluded that one of the sources of lipoprotein lipase might be the pancreas itself. They have reported that isolation of the pancreas and injection of heparin into the pancreatic artery caused a significant rise in lipolytic activity of pancreatic venous blood.

The present paper demonstrated that the lipolytic activity released into the post-heparin plasma in the normal dogs depended for the most part upon the LPL activity. On the contrary, as demonstrated in this study acute pancreatic impairments are accompanied by a significant increase of pancreatic lipase in circulating blood, which was a part of emigration phenomenon of various pancreatic enzymes from the impaired pancreatic tissues into the blood. Pancreatic lipase can hydrolyze to a certain extent the triglycerides combined with lipoproteins as well as free triglycerides. And there was an overlap between the LPL and lipase activity in the plasma obtained from dogs with pancreatic impairments. These facts may lead to a speculation that lower LPL activities than the observed levels should be taken as the true levels in the dogs with pancreatic impairments. Since the experiments on inhibitor carried out at the same time failed to demonstrate the presence of inhibitors, it would be indicated that there was an actual deficiency of lipoprotein lipase activity in the pancreatitis.

It seems reasonable therefore to conclude that the decreased delivery of the lipoprotein lipase into circulation is one of the possible causes of the decreased rate of removal of chylomicra in pancreatic impairments.

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