Summary. Several synthetic 18-hydroxylated steroids lacking oxygen at carbon 11 were tested for mineralocorticoid properties in acute studies using adrenalectomized rats. A multiple dose assay with DCA described relative potencies of 4, 8 and 5% parenterally for 18-OH-DCA by the criteria of Na retention, K loss and reduction of the Na/K ratio in the urine. Approximately the same order of potency was found for the alcohol derivative, 18-OH-DOC. 18-OH-Progesterone was ineffective as a mineralocorticoid. No significant anti-mineralocorticoid activity was found with 18-OH-progesterone or 18-OH-DCA.

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Lipoprotein Lipase in Human Adipose Tissue.* (27399)

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Lipoprotein lipase(LL) catalyzes the hydrolysis of the triglyceride portion of plasma lipoproteins(1). Small amounts of this enzymatic activity are occasionally present in blood plasma in man(2-4) and in animals(1) but do not approach the high levels found after injection of heparin. However, LL activity is readily detected in several tissues of animals, heart and adipose tissue containing the largest amounts(1). There is considerable evidence that triglyceride hydrolysis catalyzed by LL occurs during removal of triglyceride fatty acids from the blood into extrahepatic tissues(5) and it has been shown that uptake of triglyceride fatty acids by adipose tissue *in vitro* is closely related to the local activity of lipoprotein lipase(6). On the other hand, the removal of chylomicrons from blood plasma does not depend to any significant extent on intravascular hydrolysis (7). It is therefore probable that LL is concerned more with the metabolism of triglyceride in tissues than with that in the circulating blood itself. The precise location of LL is uncertain but available evidence suggests that it is closely related to the capillary bed(8,9).

LL activity in human tissue has been difficult to demonstrate. Some lipase activity of a nonspecific nature has been identified in human adipose tissue by histochemical(10)

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TABLE I. Lipolytic Activity in Subcutaneous and Omental Adipose Tissue of 9 Subjects.

Diagnosis	Sex	Age	Lipolytic activity (units) Subcut.	Omental	Preparation of subject
Ureteric repair	♂	6	3.3	8.3	Fasted
Fibromyoma uteri	♀	52	2.8	8.3	"
Gastric ulcer	♀	50	5.5	7.7	"
Diverticulitis	♂	60	2.2	7.2	"
Herniated disc	♀	45	4.9	10.5	"
Fibromyoma uteri	♀	50	3.8	11.2	250 g glucose infusion
Cholecystectomy	♂	54	4.9	4.9	200 g " "
"	♀	35	3.9	7.2	200 g " "
Gastric ulcer	♂	55	2.2	6.6	300 g " "

and enzymatic methods(11). More recently, neither Angervaal(12) nor Engelberg(13) was able to find definite lipolytic activity in acetone powder extracts(1) of human adipose tissue obtained from subcutaneous depots, breast tissue and omentum.

Using a modification of the technic described by Cherkes and Gordon(14), as well as that of Korn(1), Havel, Felts and Bezman (15) found definite LL activity in omental adipose tissue of a patient with an insulin-secreting tumor of the pancreas. This paper presents further data on the presence of LL in adipose tissue in man.

Material and methods. LL activity was measured in samples of adipose tissue obtained from the abdominal subcutaneous tissue and omentum at the beginning of laparotomy in 9 subjects. The sex, age and disease of each subject are shown in Table I. No subject had lost any appreciable weight or had any general metabolic disturbance.

Five patients had fasted for approximately 12 hours before collection of the specimens. The other 4 had received infusions of 10% glucose in water during the preceding 8 to 16 hours. The 800 to 1,200 calories provided by the glucose resulted in slightly elevated blood glucose levels.

LL activity was measured in duplicate samples by the method of Cherkes and Gordon(14), except that tissue slices were used. Adipose tissue was cut into slices 0.5 mm thick with a McIlwaine slicer, and 200 mg of tissue was incubated in 2 ml medium which contained heparin in buffer to liberate the enzyme. Other slices were incubated with buffer alone. After one hour, aliquots of the medium were incubated for a further hour at a pH of 8.6 with an assay mixture containing albumin, fresh human serum and a coconut oil emulsion (Ediol®). Free fatty acids (FFA) were then extracted and measured according to Dole's method(16) and the results expressed in units (one unit = one micromole FFA produced per gram of tissue per hour). In 2 experiments aliquots of the medium were preincubated with protamine and sodium chloride, as described by Korn (17), to establish the specificity of the enzyme responsible for the lipolysis.

Results. The results are shown in Table I. Lipolytic activity was liberated by heparin from all samples of adipose tissue. The range of activity was remarkably small, although in nearly all subjects, activity in omental adipose tissue was 2 to 3 times as great as that found in subcutaneous tissue. The range was 2.2 to 5.5 units in subcutaneous tissue and 4.9 to 11.2 units in omental tissue. There was no difference in this respect between men and women, and the findings in the 6-year-old boy were similar. Prior infusion of glucose produced no detectable increase in lipolytic activity. Protamine sulphate (1×10^{-4} M) and a 0.5 M concentration of NaCl inhibited most of the enzyme activity (Table II). Moreover, no lipolytic activity was found in any of the samples which were incubated without heparin.

Discussion. These studies clearly demon-

TABLE II. Effect of Inhibitors of Lipoprotein Lipase on Lipolytic Activity of Extracts of Omental Adipose Tissue.

Subject	% inhibition Protamine sulphate 10^{-4} M	Sodium chloride .5 M
1	75	80
2	90	100

strate the presence of LL activity in human adipose tissue. The negative findings by Angervaal(12) and Engelberg(13) may have been due to their use of acetone powder extracts.‡ The inhibition by protamine and by 0.5 M NaCl is characteristic of LL(1).

The small range in activity was an interesting finding. The greater degree of activity in omental than in subcutaneous adipose tissue is consistent with the finding in dogs of greater uptake of triglyceride fatty acids of chylomicrons by omental, than by subcutaneous adipose tissue(5).

A prolonged infusion of glucose before collection of the samples did not increase the enzyme activity liberated by heparin in the 4 studies in which it was carried out. This is at variance with studies in rats(14) and rabbits(6), in which activity of LL in adipose tissue is greatly influenced by the nutritional state. The omental adipose tissue of the subject with an insulin-secreting tumor of the pancreas(15) was continuously exposed to large quantities of glucose and insulin, but the activity was 14 units, only slightly greater than that observed in the present study. It is possible that in man a more prolonged or intense change in nutrition is required to bring about measurable alterations in LL activity. The activities reported here, therefore, may be representative of usual physiologic conditions.

Our findings emphasize the probable importance in man of LL in removal of triglycerides from blood plasma. It remains to be determined whether a close correlation exists between uptake of triglyceride fatty acids and LL activity in human adipose, and possibly other, tissues.

‡ The lipolytic activity of acetone powder extracts from rabbit adipose tissue is variable, whereas the procedure used here gives reproducible results. (Unpublished observations).

Summary. Lipoprotein lipase activity was found in adipose tissue of all of 18 samples from 9 human subjects. Activity in omental tissue was 2 to 3 times greater than in subcutaneous tissue. It was similar in men and women. No increase in activity was produced by intravenous infusion of 200 to 300 g glucose during the 12 hours before the tissue was obtained.

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