Plasma Lipid Fatty Acids During Fasting

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THE FATTY acid composition of plasma lipids has been studied in five human subjects during six to fifteen day periods of starvation. Two of the subjects were women with simple exogenous obesity, one a diabetic man (noninsulin dependent) and two noninsulin dependent diabetic women with moderate obesity.

According to current concepts, the plasma free fatty acids, particularly during fasting, are derived almost entirely from adipose tissue. Only small amounts originate from other tissues. Most of the plasma triglycerides are derived from the liver. Free fatty acids from adipose tissue contribute to the liver pool of glycerides.[1]

Hirsch reported that the mobilization of fatty acids from adipose tissue occurred at random and that no change in the composition of depot fatty acids occurred in human subjects during twenty days of starvation or several months of low calorie, low fat intake.[2] He inferred that individual fatty acids are utilized at much the same rate, i.e., no one fatty acid is conserved. If this concept is correct, it might be expected that the fatty acid pattern of the plasma free fatty acids and glycerides, during fasting, would progressively approach that of the adipose tissue.

METHODS

Prior to admission to the metabolic ward, patients consumed more or less average mixed diets (excepting the diabetic subjects whose carbohydrate intake was slightly lower than average). The samples of depot fat were taken from the buttock by the aspiration method described by Hirsch.[2]

Blood for lipid analyses was obtained at least three times a week. Blood ketones were determined by the method of Michaels et al.,[3] plasma glycerides and free fatty acids by the method of Michaels,[4] cholesterol by a modification of the Schoenheimer-Sperry technic[5] and phospholipids by the method of Youngburg and Youngburg.[6]

Separation of the glycerides, free fatty acids, cholesterol esters and phospholipids was carried out by silicic acid or Florisil column chromatography.

Methylation of the fatty acids and analysis of the methyl esters was performed as described previously.[7]

RESULTS

Levels of plasma lipid and certain other constituents of the blood and urine in the four subjects who were fasted for twelve or more days are shown in Figure 1. Except for hyperketonemia, no consistent pattern was observed. Plasma free fatty acid and depot fat fatty acid levels in two of the patients whose fast extended for periods of twelve or more days are shown in Figures 2 and 3. It is apparent that the fatty acid composition at the termination of the fast varied from the depot fat composition to about the same degree as that observed at the beginning of the period of starvation. In the four patients whose fast extended for twelve or more days, the average values for oleic, palmitic and linoleic acids in the depot fat and plasma free fatty acids on days 0 and 12 through 15 of the fast, respectively, are shown in Table 1.

Representative patterns of fatty acid changes in the plasma glycerides during twelve to fourteen days of fasting are shown in Figures 4 and 5. In Table 1 are shown the average values for the three plasma glyceride fatty acids present in greatest amount at the beginning and at the end of starvation, in comparison with the levels of adipose tissue fatty acids and the free fatty acids in the four subjects fasted for twelve or more days. Changes in the

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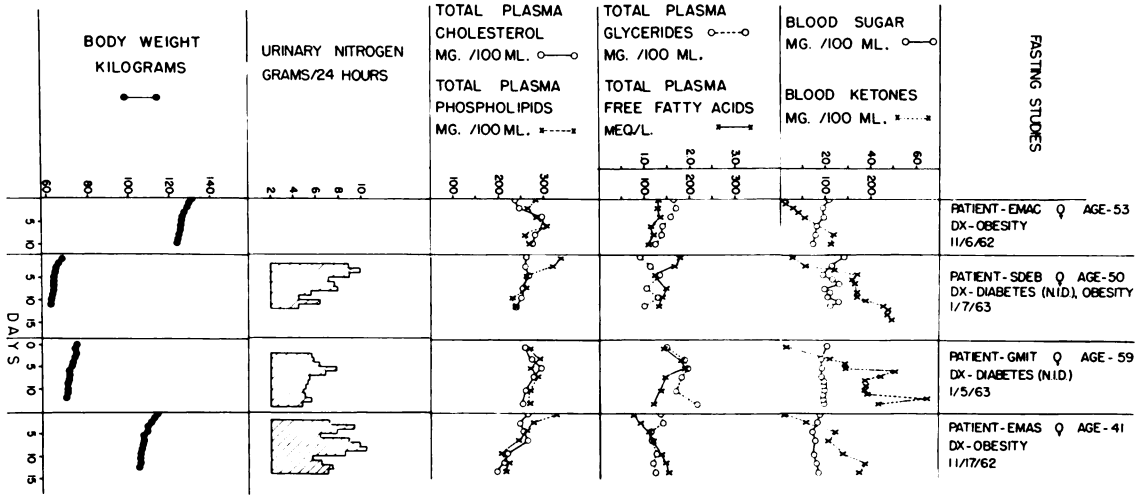

FIG. 1. Levels of plasma lipids and certain other constituents of the blood and urine in the four subjects who were fasted for twelve or more days.

direction of adipose tissue composition are not striking.

The values found in the diabetic man fasted for six days were as follows: depot fat oleate 47.8, plamitate 26.3 and linoleate 10.9 per cent; prefasting free fatty acid, oleic acid 32.4, palmitic acid 30.9 and linoleic acid 15.6 per cent; and on the sixth day of fasting, free fatty acid, oleic acid 40.0, palmitic acid 28.3 and linoleic acid 13.6 per cent. The glyceride oleate before fasting was 34.9 as compared to 37.1 per cent on day 6, palmitate 25.1 as compared to 25.4 per cent and linoleate 26.6 as compared to 24.0 per cent.

The plasma cholesterol ester fatty acid patterns during fasting in two of the subjects whose periods of starvation extended for twelve or more days are shown in Figures 6 and 7.

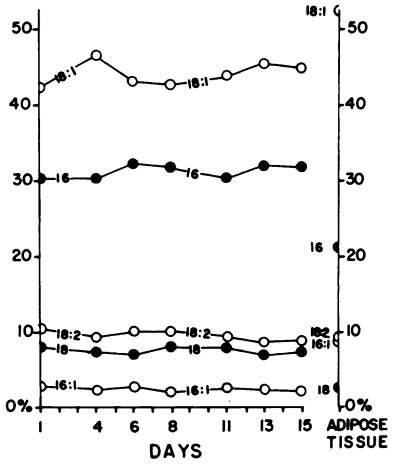

FIG. 2. Plasma free fatty acid composition during twelve days of total starvation in an obese, diabetic, fifty-nine year old woman (GMIT).

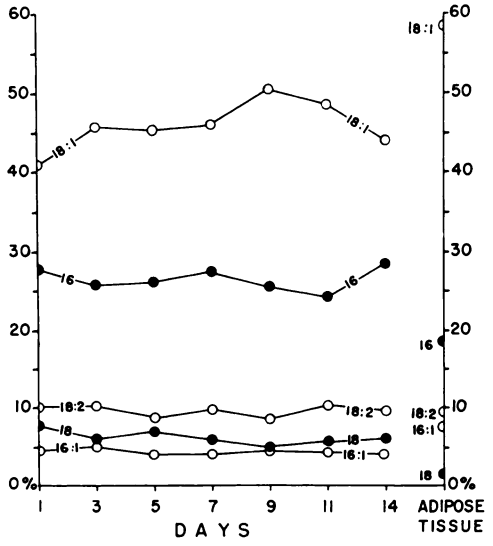

FIG. 3 Plasma free fatty acid composition during fifteen days of fasting in an obese, diabetic, fifty-nine year old woman (EMAC). The fatty acid composition in this subject and in the others under study did not resemble the depot fat composition to a significantly greater degree at the end than at the beginning of the fast (Table 1).

TABLE I

Comparison of Plasma Free Fatty Acids and Glyceride Fatty Acids Before and at the End of Fasting with Adipose Tissue Fatty Acids

Data	Fatty Acid		
	C18:1	C16:0	C18:2
Depot fat	52.3	22.8	9.0
Free fatty acids			
Before fasting	41.0	29.8	9.8
After 12–15 days of fasting	43.0	30.6	9.0
Glycerides			
Before fasting	38.6	29.3	20.1
After 12–15 days of fasting	40.3	32.1	16.4

The rise in arachidonic acid in association with some fall in the linoleic acid level seen in these two subjects was found in each of the subjects under study. In the diabetic man during the six days of fasting C20:4 rose from 4.9 to 8.4 per cent.

Representative findings in total plasma phospholipid fatty acids during starvation are shown in Figures 8 and 9. There is a different distribution of fatty acids as compared to the cholesterol esters, but here too the rise in

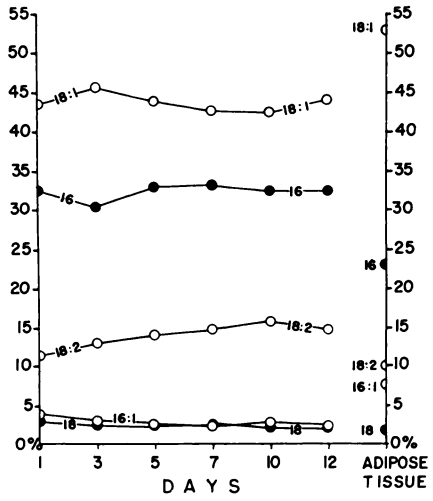

FIG. 4. Plasma glyceride fatty acids during a twelve day fast in an obese forty-one year old woman(EMAS).

arachidonate and fall in linoleate was observed in all subjects studied. The average values for these two acids in plasma cholesterol esters and phospholipids as well as for oleate, palmitate and stearate are shown in Table II. Not shown are the values for C22:6 in the phospholipids. There was an increase during the twelve to fifteen day fast from average values of 2.1 to 3.3 per cent. The increase occurred in all sub-

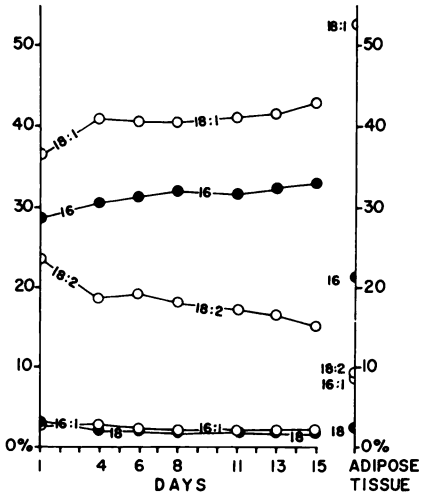

FIG. 5. Plasma glyceride fatty acids during fifteen days of total starvation in an obese fifty-nine year old woman (GMIT). Except for lineoleic acid, the changes are much the same as those observed in subject EMAS (Fig. 4). Also see Figure 11.

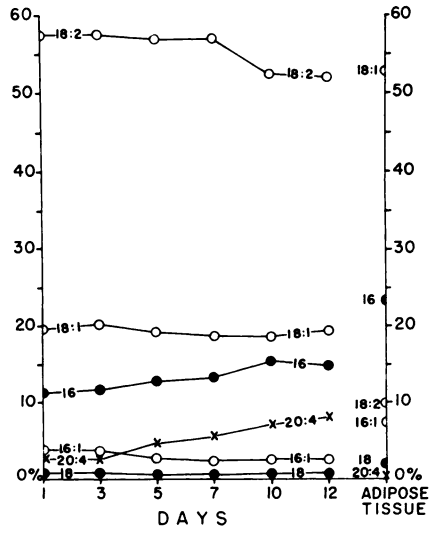

FIG. 6. Plasma cholesterol ester fatty acids during a twelve day fast in an obese forty-one year old woman (EMAS).

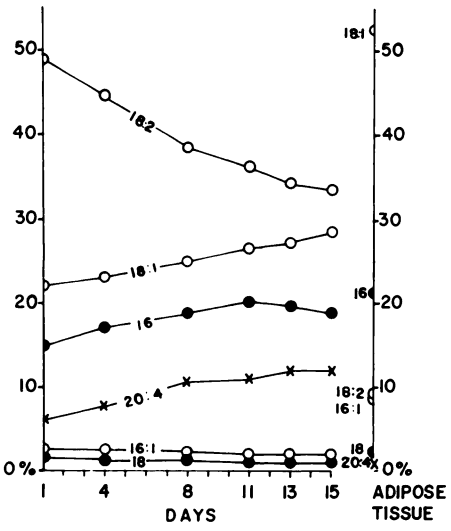

FIG. 7. Plasma cholesterol ester fatty acids during fifteen days of starvation in an obese fifty-nine year old woman (GMIT). The fall in linoleic and rise in arachidonic acid were seen in all subjects studied.

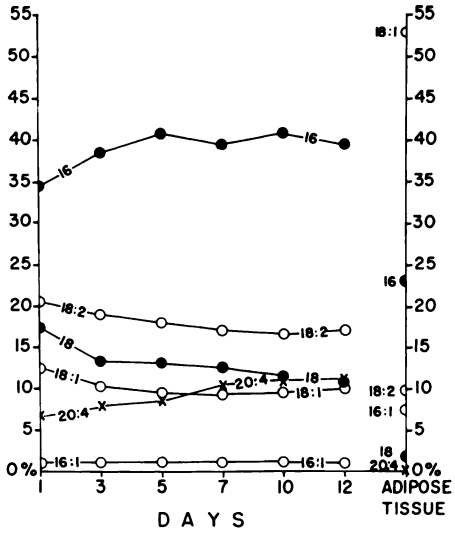

FIG. 8. Plasma phospholipid fatty acids in the course of a twelve day fast in an obese forty-one year old woman (EMAS).

jects and was apparent by the sixth day. (In the diabetic man during six days of fasting, C20:4 rose from 10.2 to 16.0 per cent and C22.6 from 2.4 to 5.8 per cent.)

Characteristic serial chromatograms (through C20:4) for phospholipid fatty acids on the first, eighth and fifteenth days of fasting on one of the subjects are shown in Figure 10.

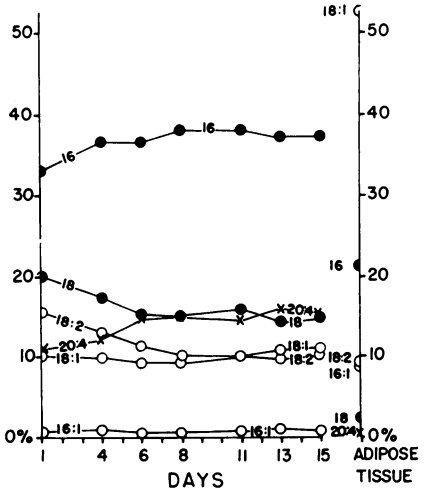

FIG. 9. Plasma phospholipid fatty acids during a fifteen day fast in an obese fifty-nine year old woman (GMIT).

COMMENTS

As previously noted, it was anticipated that during prolonged fasting, the fatty acid pattern of the plasma free fatty acids and glycerides would approach that of the adipose tissue in composition. This did not occur, at least to any major degree. Specifically, in both plasma free fatty acids and glycerides the C18:1

TABLE II

Comparison of Average Plasma Cholesterol Ester and Phospholipid Fatty Acids Before and at the End of Fasting with Adipose Tissue Fatty Acids

Data	Fatty Acid (%)				
	C18:2	C20:4	C18:1	C16:0	C18:0
Depot fat	9.0	0.4	52.3	22.8	2.8
Cholesterol ester					
Before fasting	49.9	4.1	22.6	13.4	1.0
After 12–15 days of fasting	39.8	11.3	23.0	18.6	0.8
Phospholipid fatty acid					
Before fasting	16.5	9.4	12.5	33.7	16.9
After 12–15 days of fasting	11.1	15.0	10.9	38.6	12.7

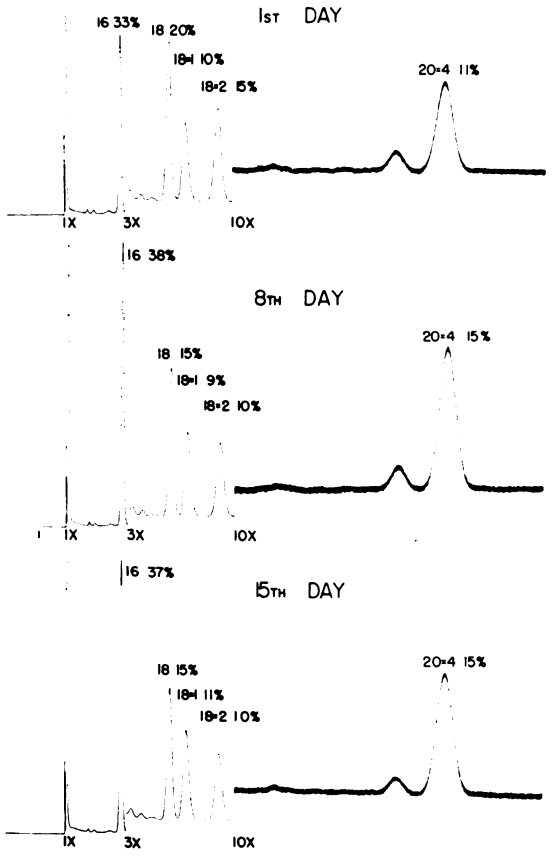

FIG. 10. Actual chromatograms of phospholipid fatty acids on days 1, 8, and 15, of total starvation in an obese fifty-nine year old woman (GMIT). The increase in arachidonic acid is apparent. C22:6, which also increased in all subjects during the fast (see text) is not shown.

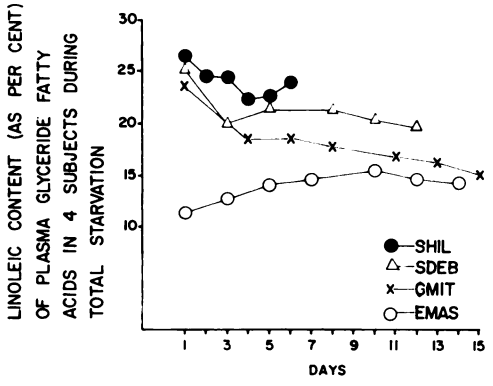

FIG. 11. The concentration of linoleic acid in plasma glycerides decreased in most but not all subjects during the period of starvation.

remains lower and the C16:0 remains higher than in adipose tissue. This might suggest that oleic acid is utilized at a rate exceeding that of palmitic acid. There is some experimental basis for such a concept.[8,9] Since lipogenesis from acetate appears to proceed principally to palmitate, it is also conceivable that during fasting, catabolized amino acids may be contributing at an accelerated rate to the pool of plasma palmitic acid in the free fatty acid and triglyceride fractions. The amount of linoleic acid in the triglyceride fraction was always greater than that in adipose tissue. In some but not all subjects, the level fell considerably during fasting (Fig. 11). Further work using labeled acids will determine whether or not differential net rates of removal and/or oxidation of these acids are present during fasting.

As noted, all subjects had an appreciable fall in linoleate content of plasma cholesterol esters and phospholipids and a concomitant rise in arachidonate. It seems probable that this may be attributable to increased synthesis (probably hepatic) of arachidonate from linoleate with consequent increase in C20:4 in newly synthesized cholesterol esters and phospholipids. Studies with highly purified C14 linoleic acid are currently under way. Why fasting should serve as a stimulus for such a process is not apparent at this time.

SUMMARY AND CONCLUSIONS

It does not appear that the composition of the plasma free fatty acids and triglycerides during fasting is a simple resultant of mobilization from adipose tissue and utilization of all fatty acids at equal rates by peripheral tissues. Changes in the concentration of polyunsaturated fatty acids in the cholesterol ester and total phospholipid fractions suggests increased synthesis (and/or decreased utilization) of C20:4 and C22:6, possibly at the expense of C18:2. The possible biochemical, physiologic and clinical implications of these findings are under study at the present time.

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