Serum Non-Esterified Fatty Acids in Patients with Recent Myocardial Infarctions.*† (24665)

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Triglycerides are frequently elevated in sera of patients with coronary artery disease (1). Since non-esterified fatty acids (NEFA) and triglycerides are closely associated metabolically(2-15) NEFA concentrations were investigated daily in post-absorptive sera from patients who had had myocardial infarctions 10 to 29 days previously.

Methods. Serum NEFA were measured by Dole's method(4,5) with the following alterations: Redistillation of heptane and isopropyl alcohol was discontinued after identical results were obtained with redistilled and undistilled solvents. Solutions of extracted NEFA, stirred with washed nitrogen(5), were titrated with a Rehberg or Gilmont burette(4,5,6) using Nile Blue as the indicator(8). The alkali used for titration was standardized against constant boiling hydrochloric acid. Calculations were made as follows: the observed volume of the upper phase (which exceeds actual volumes of heptane used) was employed as the volume in which titrated NEFA were distributed. The upper phase volumes were checked with every lot of extraction reagents. Such calculations avoid the use of a standard palmitic acid solution which may be inaccurate if crystalline palmitic acid is impure or if temperature alters the volume of the solvent heptane. This method of calculation makes no allowance for the coefficient of distribution of NEFA in the 2 phases of the solvent system. About 150 recovery tests were conducted on heptane solution of palmitic acid alone, or combined with serum or dilutions of Red Cross Albumin to yield concentrations of NEFA throughout the physiological range. NEFA in the upper phase were about 92% of theoretical, even in samples containing more than 1 meq/l. The maximum technical error of the method was less than 0.057 meq/l and is a little higher than data quoted by Dole(4) and Gordon(8) because it includes day-to-day variations. This error is small in comparison with differences in NEFA which have been shown to have physiological significance(2-15). The subjects were 4 non-diabetic individuals (normal post-absorptive blood sugars), otherwise unselected, who had been conducting normal activities until their acute infarcts in July, 1958 just prior to hospitalization (Table I). All were ambulatory during the present studies. After about one month hospitalization all 4 patients returned home in a reasonably healthy state. Changes in weight were not recorded; all patients seemed normally nourished except that C was stocky. After dietary intake had become regular and the effects of heparin treatment on plasma lipids had disappeared, blood was drawn from the antecubital vein each week day morning between 7:15 and 8 a.m. about 12 hours after ingestion of fluids such as fruit juices during the previous evening. Serum NEFA were determined at 24 or 96 hour intervals for 3 to 11 days; serum triglycerides, cholesterol and lipid phosphorus, measured by methods described earlier(1) were estimated in some of the samples for NEFA.

Results. Data on the 4 patients after myocardial infarctions are shown in Table I. All concentrations of NEFA were between 0.203 and 0.592 meq/l which are within the range for normal non-obese non-diabetic young men in a post-absorptive state(5,6). There were only minor variations from day to day in any individual. The greatest difference in NEFA was only 0.328 meq/l for patient A during an interval 15 to 21 days after infarction, when his physical activity was increasing. NEFA of the 4 patients in the hospital were lower

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TABLE 1. Serial Serum Lipids of 4 Patients Having Coronary Artery Disease.

Patient	Days after infarction	NEFA	Triglycerides	Total fatty acid	Cholesterol	Lipid phosphorus
			meq/l		mg/100 ml	
A (A6-23-42) ♂, age 50	11	.207	4.7	12.5	156	8.5
Posterior wall infarction. Regular	12	.207	4.9*	13.3	186	
diet. No anticoagulants.	13	.209				
	15	.203				
	16	.350				
	18	.211	9.2	19.0	190	10.7
	19	.251	8.2	18.2	203	10.6
	20	.441	5.6	15.6	228	9.8
	21	.531	6.2*	16.2	230	
B (49-39-03) ♂, age 66	10	.366	4.1	13.7	238	8.9
Antero-lateral infarction. Regular	11	.491	4.6*	13.9	219	
diet. Heparin on admission and	12	.398	8.8	19.2	211	11.2
next day. Dicoumarol during	13	.592	6.0	15.2	224	8.6
studies.	14	.428				
	18	.492				
	19	.484				
	20	.356	4.5	13.6	212	8.9
	21	.241	4.7	13.6	228	8.0
C (43-50-02) ♂, age 56	18	.369				
Angina 1950-55. Post. infarction	19	.411	18.2	31.4	273	14.0
1955. No angina, no congestive	20	.519	15.8	29.6	295	14.2
heart failure 1956-7/1958. New	21	.591				
post. wall infarction. 1500 cal.,	22	.432				
1200 mg Na for 9 days followed	26	.439				
by regular diet. Heparin first 3	27	.504				
days. Dicoumarol during studies.	28	.578	22.1	39.0	396	16.3
	29	.539	21.6	38.2	397	15.9
D (49-35-19) ♀, age 53	20	.303	6.7	16.1	221	9.2
Ant. infarction 5 days after hospi-	21		7.4	18.3	241	11.0
talization. Digitoxin cont. from	22	.363				
6th day post. infarction. Heparin	23	.379	7.9	18.6	211	11.6
5th through 9th day post. infarc.	24	.349				
Dicoumarol 5th through 23rd day.						
1200 mg Na until regular diet on						
17th day post. infarction.						

* Fatty acids of phospholipids calculated from previous lipid phosphorus.

than unpublished values on 8 ambulatory male out-patients, studied at least 3 months after myocardial infarctions. Normal concentrations of NEFA persisted for all 4 patients (Table I) although in each case the triglycerides were higher than the normal maximum of 6.0 meq/l(1) in at least 2 samples of serum, and were persistently elevated in one male, C. In this brief study concentrations of serum NEFA bore no relationship to the previous myocardial infarction or to the elevation of triglycerides which occurs in this disease(1).

The serum lipid fractions on patients 10 to 29 days after a myocardial infarction furnish further examples of data already reported from this department(1) in which it was found that serum cholesterol and fatty acids often rise during recovery from a myocardial infarction. Lipid concentrations determined soon after an infarction may not be representative of the values for that individual 3 to 4 weeks after the acute episode, (*e.g.*, A & C, Table I). The previous observation(1) that serum triglycerides are more frequently elevated than serum cholesterol following a myocardial infarction is confirmed by the fact that triglycerides were above the maximum of the normal range in at least 2 sera obtained at intervals of 24 hours for all 4 patients although cholesterol was above the normal maximum only in the serum of C.

Recent observations suggest the importance of non-esterified fatty acids as fuel for the myocardium. Bragdon and Gordon(3) found a high content of labelled unesterified fatty acids in the heart, after injection of this ma-

terial into carbohydrate fed rats. Korn has reported that myocardium has a high content of the enzyme lipase(11), but presence of this enzyme in normal plasma has not been proven. If injury such as an infarction results in release of myocardial transaminase into the blood, lipase may also be liberated after an acute infarction. At the time when transaminase concentrations are increased, changes in NEFA concentrations due to lipase would be under the influence both of heparin (if this were prescribed) and of the decreased caloric intake which occurs shortly after an infarction. To avoid these confusing effects on NEFA the present patients were observed only after transaminase would have fallen, and some days after cessation of medication with heparin and resumption of regular intake of food.

Few data have been published concerning NEFA concentrations of one individual studied repeatedly in a post-absorptive state. Both Gordon(8) and Dole(4) observed increases in plasma NEFA during the forenoon when duration of an overnight fast was prolonged. In view of the extremely rapid turnover rate of NEFA(3,11) (2 minutes half life in the dog(2)) it is difficult to appraise the significance of isolated NEFA values. The variation in concentrations of NEFA in arterial and venous plasma found by Gordon (8), may have resulted from changes in supply and demand for NEFA. Our data indicate independence of plasma NEFA and of plasma triglyceride concentrations. Utilization of exogenous triglycerides without obligatory retransport as unesterified fatty acid has been found(16). Constancy of NEFA of our 4 patients, on restricted muscular activity and receiving caloric intake from hospital meals at regular intervals, clearly indicates the importance of evaluating NEFA concentrations in relation to the time since the last meal and the amount of exercise during that interval.

Summary. By a slight modification of Dole's method serum NEFA of 4 patients were measured at 24 hour intervals 10 to 29 days after myocardial infarction. These subjects were in a post-absorptive state. Values varied within a narrow, normal range from 0.203 to 0.592 meq/l. Serum NEFA concentrations were not correlated with serum triglycerides; the latter increased above the maximum for normal males.

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