Reticuloendothelial System Depression in Man After Olive Oil Ingestion (36845)

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(Introduced by B. Benacerraf)

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The ingestion of various lipids including olive oil was recently demonstrated to depress reticuloendothelial system (RES) phagocytosis of colloidal carbon in mice (1). In 1958, Biozzi and co-workers introduced the technique for measuring RES phagocytic function in man employing radioiodinated aggregated human serum albumin (2). This technique has since been used by a number of investigators who have confirmed its safety and precision (3–5).

This report investigates in man the effect on RES function of a suspension of olive oil, prepared for oral administration.

Materials and Methods. ^{125}I labeled microaggregated serum albumin (5.5–6.0 μCi/ml and 25 mg albumin/ml) was generously supplied by the Squibb Institute for Medical Research. This material was used during its first two half-lives in studies to be reported elsewhere. It was then stored under refrigeration to allow further decay of radioactivity. When this had decreased by at least 4 half-lives this now "cold" material was used by adding to 10 ml of it 0.1 ml to 0.2 ml of the commercially available ^{131}I labeled microaggregated serum albumin (Albumatope-H-Squibb). The final mixture had an activity of 4–5 μCi ^{131}I and approximately 25 mg of albumin/ml.

A dose of 2.5 mg of albumin/kg was injected through an 18 gauge pediatric scalp vein needle kept in place in an antecubital vein throughout the procedure. Patency was assured by injection of small amounts of aqueous heparin throughout the procedure. Each patient received about 50 mg of heparin. Blood samples (3 ml) were withdrawn into "Vacutainer" tubes containing EDTA at 5, 10, 15, 20 and 25 min. Approximately 1 wk later, over a 24 hr period, each subject drank 24 oz of a suspension containing 8 oz of olive oil.[1] It was taken in portions of about 4 oz. Three hours after the last portion, the aggregated albumin was again injected. Blood samples were obtained in the same way.

The radioactivity of a 2 ml sample of whole blood was counted for 2 min in a 2 in. sodium iodide (TI) well with a counter-spectrometer and was plotted against time on semilog paper. Straight lines were obtained since all samples were taken within 25 min of injection of the radioiodinated albumin aggregates, when the concentration of unbound ^{131}I liberated by the catabolic activity of the RES on albumin aggregates was minimal.

Phagocytic index (K) was calculated from the formula $K = \log C_1 - \log C_2/T_2 - T_1$ where C is the number of cpm and T is time in minutes. As demonstrated by Biozzi, Benacerraf and Halpern (6), there is constant modification of RES phagocytosis by the increasing concentration of test colloid within the phagocyte and the continually decreasing concentration of the test colloid in the plasma. Thus, the half-time of plasma radioactivity is a less apt index of RES phagocytosis than is the arbitrary K.

The patients participating in this study were hospitalized for various disorders which had been stabilized or resolved. Triglyceride studies were performed on serum samples submitted to Bio-Science Laboratories, Van Nuys, CA.

Results. Table I records the change in

* Deceased.

[1] Commercial olive oil (8 oz) emulsified with 14 oz of water and blended with 2 tbsp of instant coffee, 3 tbsp of cocoa, 1 tbsp of plain gelatin, 5 tbsp of powdered milk and 5 tbsp of sugar.

TABLE I. Effect of Ingested Olive Oil upon the Rate of Blood Clearance of Microaggregated Human Serum Albumin.

Patient	Sex	Age	Underlying disorder (resolved or stabilized)	Phagocytic index (K)	
				Before oil	After oil
R.C.	M	49	Frost bite	.010	.008
G.R.	M	23	Multiple fractures	.023	.020
G.J.	M	32	Pulmonary emboli	.021	.015
L.McG	M	43	Pneumonia	.026	.012
L.M.	M	40	Hemiparesis	.016	.013
T.R.	M	62	Rheumatic heart dis.	.020	.013
J.E.	M	47	Chest pain	.018	.013
E.M.	M	50	Seizure disorder	.014	.010
L.R.	M	48	Osteomyelitis	.015	.012
G.S.	F	76	Hip fractures	.010	.008
S.C.	M	60	Prostatism	.019	.012
F.H.	F	63	Diabetes mellitus	.026	.018
Mean value ± SD				.018 ± .005	.013 ± .004
				$p < .01$	

RES clearance in 12 patients who had drunk the olive oil suspension. It was palatable enough to be consumed without objection if not with great relish. Gastrointestinal distress was not encountered. Depression of the phagocytic index was noted in all patients but to a variable degree. Those with the highest initial clearance rates manifested the most substantial depression.

Table II illustrates the increase in serum triglyceride levels following olive oil ingestion and the considerable lowering of these levels by heparin administered during the course of the clearance tests before and after olive oil ingestion.

Discussion. In the studies reported here, the phagocytic capacity of the RES was measured by plasma clearance of radioiodinated microaggregates of human serum albumin in a group of patients hospitalized for various disorders which had been resolved or stabilized. In our hands as well as those of others (4, 5) the precision of the method is such that there is little variation in results when the test is repeated in an individual under control circumstances. Thus each patient in our series served as his own control. When the measurements were repeated following the ingestion of a palatable emulsion of olive oil, phagocytosis was substantially depressed. Similar results have been obtained by some but not all groups working in animals with lipid-rich diets (1, 7–10). No explanation for the RES depressant effects of lipids has been provided by the present work. It is unlikely that chylomicra still circulating in these patients were phagocytized preferentially to the aggregated albumin, for data from animal experiments reported by Biozzi and coworkers (11) indicate the opposite. Depletion of necessary serum factors is possible but the significance of that issue is still not resolved (12). As heparin has been described as a factor which, in fact, enhances phagocy-

TABLE II. Average Triglyceride Levels in Seven Patients (Normal Range 30–135 mg/100 ml).

Before olive oil ingestion		After olive oil ingestion	
Before heparin	After heparin	Before heparin	After heparin[a]
109	23	171	72

[a] Heparin (50 mg) administered intravenously during the course of each clearance study.

tosis (13), it is important to note that our patients received sufficient heparin during the course of each clearance procedure to result in marked lowering of serum triglycerides levels (Table II).

The important factor in the type of RES inhibition induced by lipids may be interference with cell membrane function. Possibly the globulin moieties of lipoproteins possess binding sites with strong affinities for phagocyte membranes as do certain antibody globulins termed cytophilic antibodies (14). Mouse macrophage phagocytosis is inhibited following exposure to homologous red cells coated with antibodies (15) which presumably bind to the phagocyte membrane via Fc fragment receptors (14) and may inhibit phagocytosis by covering binding sites (15) or by interfering with cell membrane evagination or invagination (16). Perhaps when lipoprotein molecules are circulating in large numbers, these bind RES phagocyte membrane receptors and similarly interfere with membrane function. Evidence for the existence of such macrophage receptors for lipoprotein has recently been described by Werb and Cohn (17).

Summary. Reticuloendothelial system phagocytosis was measured in man by the blood clearance of radioiodinated microaggregated human serum albumin. It was found to be substantially depressed following the ingestion of a palatable emulsion containing 8 oz of olive oil. The mechanism of this effect is unknown but the possibility of interference with phagocyte membrane function is suspected.

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