17097. Oxygen Consumption Studies with Intravenous Infusions of the Combined Fat Emulsion.*

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In previous reports from this laboratory, the results of experimental and clinical investigations of an intravenous fat emulsion combined with protein and glucose were presented.[1-3] The method of preparation of the combined fat emulsion and its effect upon humans were summarized in detail.[3] The present study is concerned with oxygen consumption associated with the intravenous infusion of the combined fat emulsion. Measured changes in oxygen consumption obtained with a variety of other intravenous preparations were made for purposes of comparison and served as control standards. This aspect of energy metabolism was the first of several methods of investigation with a view of obtaining evidence in favor of metabolic utilization of intravenously infused fat.

Method of study. Serial oxygen consumption determinations were conducted in a group of seven surgical patients who received one or more of 6 types of intravenous preparations. The patients, all males ranging in age from 18 to 58 years, were drawn from the surgical service. Because of good emotional stability, they were selected as the most suitable for oxygen uptake studies with the basal metabolism machine. Although these patients were on the surgical service because of a variety of diseases, at the time of testing there were no complicating factors of temperature elevation, active infection, chronic decubitus ulcers or acute organic metabolic disorders. Three different intravenous fat emulsions were studied; Emulsion 1, was a 5% fat emulsion which contained 50 g of coconut oil emulsified with 6% gelatin and provided 450 calories per liter; Emulsion 2, was a 10 per cent fat emulsion which contained 100 g of coconut oil emulsified with 6% gelatin to provide 900 calories per liter and Emulsion 3, always referred to in this paper as the combined fat emulsion, consisted of an homogenate of 10% coconut oil, 5% amigen, 5% glucose and 2% gelatin per liter with a caloric value of approximately 1300 calories. The comparative controls were (a) 5% glucose in normal saline, 200 calories per liter, (b) 6% gelatin solution, caloric value undetermined[4] and (c) 5% amigen and dextrose solution, 350-400 calories per liter.

Each infusion study was started in the morning with the patient in the post-absorptive state after a fasting period of 14 hours. In every case except one, a single liter of test fluid was administered. The duration of the infusion period ranged from 4 to 6 hours with 3 instances of extension up to 8 hours. Serial oxygen consumption determinations were obtained with the Benedict-Roth apparatus and on 2 occasions by the Tissot method. Each infusion study consisted of the determinations of the oxygen consumption level beginning with the pre-infusion period and measured in interval series during the infusion and post-infusion periods. The temperature, pulse, respirations and blood pressure were obtained throughout the study period at hourly intervals. Urine specimens were obtained at regular intervals for the first 14 hours and also at the end of 24 hours. Urinalyses were made for acetone (Rothera's test) and diacetic acid (Gerhardt's test).

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TABLE I.
Oxygen Consumption Changes with Single Liter Intravenous Infusions of 5% Glucose in Normal Saline, of 6% Gelatin Solution, and of 5% Amigen-Dextrose Solution.

Type infusion	PT.		Oxygen consumption changes: Pre-inf.	Infusion period			Post-infusion period	
5% Glucose in N S	W B	at hr	0	2	4		5½	24
		cc/Sq M/min	127	121	117		119	126
		% change	0	—4.8	—7.9		—6.1	—0.4
	J S	at hr	0	2	4		5	
		cc/Sq M/min	123	128	124		116	
		% change	0	+4.0	+0.4		—5.7	
6% Gelatin	W B	at hr	0	2	4	5	7	
		cc/Sq M/min	126	120	123	127	124	
		% change	0	—5.2	—2.2	+0.4	—1.7	
5% Amigen in 5% Dextrose	J G	at hr	0	2	4	6		
		cc/Sq M/min	134	135	148	135		
		% change	0	+0.4	+10.0	+0.4		
		at hr	0	2	6	8	10	12*
	H K	cc/Sq M/min	140	136	156	139	144	163
		% change	0	—2.4	+11.2	—0.4	+3.4	+12.1

* ½ hour after a meal of 350 calories.

TABLE II.
Oxygen Consumption Changes with Single Liter Intravenous Infusions of 5% and 10% Fat Emulsions (50 and 100 g of Coconut Oil Emulsified with 6% Gelatin Solution).

Infusion fat emulsion	PT		Oxygen consumption changes: Pre-inf.	Infusion period			Post-infusion period			
5%	H K	at hr	0	2	4	6	8	10	12*	24
		cc/Sq M/min	152	183	186	179	160	140	178	154
		% change	0	+21.1	+23.4	+18.4	+5.8	—7.0	+18.3	+1.8
	J L	at hr	0	2	6	8	10	12	14	24
		cc/Sq M/min	113	137	145	154	145	132	122	116
		% change	0	+21.5	+27.6	+36.5	+27.6	+16.0	+7.7	+2.8
10%	J L	at hr	0	2	4	6	8	10	12	24
		cc/Sq M/min	129	147	152	173	147	130	129	126
		% change	0	+14.1	+18.0	+34.1	+5.8	+0.4	0	—1.9
	J S	at hr	0	2	4	6	8	10	12	24
		cc/Sq M/min	142	163	154	166	170	139	126	132
		% change	0	+14.4	+7.8	+16.8	+19.2	—2.3	—11.7	—7.0

* ½ hour after a meal of 400 calories.

Results. The oxygen consumption changes obtained with the 6 types of intravenous preparations are summarized in Tables I, II and III. The percentage changes in oxygen consumption during the infusion and post-infusion periods were computed for purposes of comparison with the initial or pre-infusion value taken as the zero level.

Maximal changes in oxygen consumption generally occurred after more than eighty per cent of any preparation had been infused or upon completion of the infusion period. With 5% glucose in normal saline and 6% gelatin infusions, the oxygen uptake values were mainly near the pre-infusion level while the recipients of 5% amigen and dextrose solution showed rises to about 11.0%. The recipients of 5% and 10% fat emulsions showed an increased oxygen consumption to levels ranging from 19.2 to 36.5% above their initial values. Elevations in oxygen consumption levels were usually greatest in recipients of the 10% combined fat emulsion with increases from 42.4 to 49.7%. One subject, FS, who received 2 liters of the 10% combined fat emulsion, was found to have in-

TABLE III.

Oxygen Consumption Change with Single Liter Intravenous Infusions of the 10% Combined Fat Emulsion (10% coconut oil, 5% amigen, 5% glucose and 2% gelatin solution).

PT.		Oxygen consumption changes										
		Pre-inf.	Infusion period				Post-infusion period					
W B	at hr	0	2	4		7						24
	cc/Sq M/min.*	167	221	243		193						152
	% change	0	+32.3	+45.4		+15.8						—9.1
H K	at hr	0	2	4		7						24
	cc/Sq M/min.*	167	209	225		171						152
	% change	0	+25.8	+34.8		+2.7						—9.1
J L	at hr	0	2	4	5	6	8	10	12	14		24
	cc/Sq M/min.	118	169	175	176	162	152	142	135	136		127
	% change	0	+43.8	+49.2	+49.7	+37.3	+28.9	+20.8	+14.9	+16.0		+7.4
S P	at hr	0	2	4	6	8						24
	cc/Sq M/min.	116	159	165	167	137						122
	% change	0	+36.8	+42.1	+43.3	+17.6						+6.4
S P	at hr	0	2	4	6	8	10	12	14			24
	cc/Sq M/min.	122	149	155	176	172	134	133	140			139
	% change	0	+20.2	+25.2	+42.4	+39.0	+8.8	+7.1	+12.6			+12.1
**	at hr	0	1½	3½	5	6¾	9½	12½				24
F S	cc/Sq M/min.	121	155	174	198	192	149	120				121
	% change	0	+28.3	+43.3	+63.9	+57.7	+23.2	—0.6				0
J S	at hr	0	2	4	6	8	10					24
	cc/Sq M/min.	124	148	165	179	178	168					137
	% change	0	+19.8	+33.8	+45.0	+44.1	+36.0					+11.3

* By Tissot method.
** FS received 2 liters.

creased his oxygen uptake to a maximum of 63.9% above his initial level. Another subject, HK was given oral feedings of approximately 350-400 calories at the 12th hour of each of 2 infusion studies as a result of which further elevations in oxygen uptake were again demonstrable.

Urinalysis for acetone and diacetic acid were positive in the intermediate serial samples in 3 patients who received the 5% or 10% emulsion. Tests for acetone were usually 2 and 3 plus in the 4 and 6 hour urine specimens followed by 1 plus to faint traces at 8 hours with negative results for the 10 hour and subsequent specimens. Tests for diacetic acid indicated faint traces only at the height of acetone spillage. Urine specimens were usually negative for ketone bodies in the 24 hour study period in the recipients of the 10% combined fat emulsion. In the latter group, the 4 hour urine specimen was found occassionally to contain a trace of acetone.

Temperature elevations ranging from 99.6 to 100.4° were noted between the tenth and sixteenth hours in the post-infusion period with the combined fat emulsion in the case of JL and SP. With the latter elevations in body temperature correlative secondary rises in oxygen consumption and moderate increases in pulse rate were found to occur. Analysis of temperature, pulse rate, respiration and blood pressure taken in each study at hourly intervals revealed minor fluctuations during the course of any type of infusion without significant findings associative with the oxygen consumption studies.

Comments. Evidence in favor of the metabolic utilization of intravenously infused fat has been reported by many investigators. The respiratory metabolism of human infants in relation to infusions of an homogenized fat emulsion was found to be reflected in increased heat production and alteration in the respiratory quotient. The energy exchange was derived from the combustion of the intravenously injected fat.[5] Other evidence in favor of utilization of intravenously infused fat has been obtained with parenterally administered C_{14} labelled tripalmitin emulsion as a result of which more than 50% of the radioactive isotope was recovered in expired carbon dioxide in a 24 hour study period. Proof was also given of incorporation of the labelled fatty acids into phospholipids.[6] In another experimental study data was presented to show that growing puppies obtained up to 30 per cent of their total energy requirement from daily infusions of a fat emulsion which in combination with a fat free diet provided for positive nitrogen balance and weight and growth gain.[7]

Indications of the metabolic utilization of a 10% combined fat emulsion administered intravenously were obtained by means of studies of oxygen consumption. For proper evaluation of the role of fat contained in the emulsion, 5 and 10% concentrations of the emulsified oil were studied. These studies showed that the increased oxygen consumption was not only correlative with fat as the prime contributing energy factor but that additive concentrations of fat raised significantly the amount of oxygen uptake. The non-fat components of the combined fat emulsion, gelatin, amigen and dextrose, were found to show small increments of change from the initial pre-infusion value. By combination of all the basic constituents with fat into a combined emulsion, the greatest increases in oxygen consumption resulted. Transient ketonuria noted in some of our studies were indicative both of early metabolic utilization and incomplete fat metabolism, the ketogenesis developing during the period of fat plethora.

The Benedict-Roth recording spirometer and the Tissot type apparatus were accepted by us as experimentally adequate for the present investigation. Alterations in tidal air as a possible explanation for increased oxygen consumption has also been eliminated in this study.[8]

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Summary. (1) Sixteen serial oxygen consumption studies were conducted in a group of 7 adult humans who received one or more of 6 types of intravenous preparations.

(2) Maximal increases in oxygen consumption above the initial pre-infusion levels attained their greatest values in recipients of the 10% combined fat emulsion when compared with a variety of intravenous preparations of a lesser caloric or energy value.

(3) With fat as the prime contributing factor to the increased energy value of the 10% combined fat emulsion, it is justifiable to conclude that the intravenously infused fat is utilized for energy production when in part it undergoes oxidative combustions which are ultimately measured in terms of oxygen consumed.

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17098. Effect of Dibenamine on Blood Flow and Cardiac Output in the Dog.

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Since N, N-dibenzyl-β-chloroethylamine (Dibenamine) was first introduced as an adrenergic blocking agent, many reports have been made on various aspects of its pharmacological properties.[1] Evidence has been presented indicating that Dibenamine produces vasodilation as evidenced by an increase in skin temperature,[2] and in dogs subjected to hemorrhage or trauma those pretreated with Dibenamine showed a slightly higher total blood flow than the controls.[3] It also has been reported that Dibenamine has no significant effect on cardiac output,[1] or increases cardiac output,[4] although no data are given on this point. In this report data are presented on the effects of Dibenamine on blood flow and cardiac output.

Methods. With but one exception the dogs were anesthetized with barbital sodium 300 mg/kg, chloralose, 250 mg/kg, was used in one dog. Blood pressure was obtained from a carotid artery with a Hamilton manometer and cardiac output determined from the pressure pulse by the method of Hamilton and Remington.[5] Blood flow was recorded from either a carotid or a femoral artery by means of a rotometer.[6] The anticoagulant used was chlorazol fast pink, 2 cc of an 8% solution per kg. The dose of Dibenamine, 20 mg/kg, when given intravenously (i.v.), was administered slowly over a 5-minute period. In a majority of the dogs the degree of adrenolytic action was tested with epinephrine 30 minutes after the Dibenamine injection. In all cases only a depressor response was elicited.

Results. Table I summarizes the data on those dogs in which cardiac output, blood pressure and blood flow were determined; pressure and flow were measured in 16 additional dogs. In all of the 24 dogs but 7 the blood pressure dropped significantly, 3 of these showed a rise in pressure and in the other 4 the changes were less than 10 mm Hg. The drop in pressure occurred about 20 minutes after Dibenamine was given. Little effect was noted on heart rate with a slight

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