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PARENTERAL NUTRITION. II. THE UTILIZATION OF EMULSIFIED FAT GIVEN INTRAVENOUSLY [1]

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The intravenous administration of various fat emulsions to dogs has been studied in this laboratory (1). Of the emulsions used, one consisting of 15 per cent refined coconut oil stabilized with a purified preparation of soybean phosphatides was found to be well tolerated, and produced only minor pathologic effects after daily infusions for periods of 1 month. In these experiments, amounts of the emulsified fat were used sufficient to give 15 or 16 calories per kgm. of body weight per day. The use of such an emulsion for nutritive purposes would depend on whether or not fat administered in this manner can be efficiently utilized as a source of energy. A study of this problem forms the basis of the present paper.

The utilization of fat given intravenously has been studied by several investigators. Nomura (2) found no decrease in the respiratory quotient of dogs following the infusion of an olive oil-cod liver oil emulsion stabilized with egg phosphatides. This was also found in dogs which had fasted 4 to 8 days previous to the infusion, although the initial respiratory quotients were much lower in this series. Baba (3) fed dogs a meat diet with thyroxin to produce energy deficiency and weight loss. Infusion of this same olive oil-cod liver oil emulsion produced slight decreases in the non-protein respiratory quotient of the magnitude of from 0.75, to 0.70 or 0.71. In depancreatized dogs Baba (4) observed marked decreases in the non-protein respiratory quotient ranging from between 0.69 and 0.71 to the very low values of between 0.59 and 0.64 Partially depancreatized dogs showed a smaller decrease in the respiratory quotient. Murlin and Riche (5) found a decrease in the respiratory quotient of from 0.79 to 0.72, and 0.85 to 0.73, several hours after infusion of a 3 per cent

lard emulsion into dogs. Gordon and Levine (6) observed decreases in the respiratory quotient of from 0.03 to 0.07 following infusion of an olive oil emulsion stabilized with egg phosphatides in a healthy infant, starting with initial respiratory quotients between 0.9 and 1.0. At a control respiratory quotient of 0.8, no significant lowering was produced by infusions of the fat emulsion. No decreases in the respiratory quotient were obtained after infusion of this emulsion into a marasmic infant. In general, it may be concluded that these studies on the effect of intravenous fat emulsions on the respiratory quotient indicate that the fat is utilized, but the evidence is equivocal since the changes are small. It is unfortunate that the respiratory quotient of starvation approaches that of fat metabolism, and thus reduces the value of this criterion of utilization under the conditions in which it is desirable to use fat intravenously: namely, in serious energy deficiency. More definite evidence of utilization should be obtained by other methods of study.

Narat (7) studied starvation survival in 2 pairs of dogs, 1 of each pair receiving by infusion a small amount of an olive oil emulsion stabilized with egg phosphatides. The control dogs died on the 36th and 31st day of starvation, while those receiving the fat infusions survived through the 46th and 45th day respectively. Weight losses were slightly less in the infused dogs. The author concluded from these differences that the fat was utilized. Dunham and Brunschwig (8) injected lard and olive oil emulsions, stabilized with egg phosphatides and "Demal," into 11 dogs receiving an oral food intake furnishing 60 calories per kgm. per day. Urinary nitrogen excretions were not lowered, as was the case with 5 per cent glucose injections. There was no tendency of the depot fat to be displaced toward that of the infused fat with respect to iodine number, saponification number, or melting point. From these results, the authors

concluded that the intravenously administered fat was not utilized.

Since these studies on utilization of the fat have given controversial or at least inconclusive results, it was thought desirable to investigate this matter further. We have used as criteria of utilization, weight maintenance and nitrogen retention on low oral caloric intakes, and also the disappearance of the infused fat from the animal tissues during the infusion period.

EXPERIMENTAL

Four adult mongrel dogs were used in this study. The emulsified fat was infused into the leg veins from a Murphy Drip bottle as previously described (1). Two emulsions were used in the experiments: Emulsion 11M (1) and Emulsion 11MC, identical with Emulsion 11M,

TABLE I

Composition of fat emulsions (11MC and 11M) for intravenous administration

	grams per liter
Water	800
Refined coconut oil	150
Purified soybean phosphatides	27
Na_2HPO_4	6.0
Cholesterol*	4.2
pH of emulsions equals 7.6	

* Omitted in Emulsion 11M.

but containing 2.8 per cent cholesterol[3] dissolved in the coconut oil (0.42 per cent of the emulsion). This latter emulsion appeared to be more stable to autoclaving and standing. The composition of Emulsion 11MC is given in Table I, and its preparation and properties are described in a previous paper (1).

[3] Eastman Kodak Company (from the spinal cords of cattle).

TABLE II

Composition of purified rations

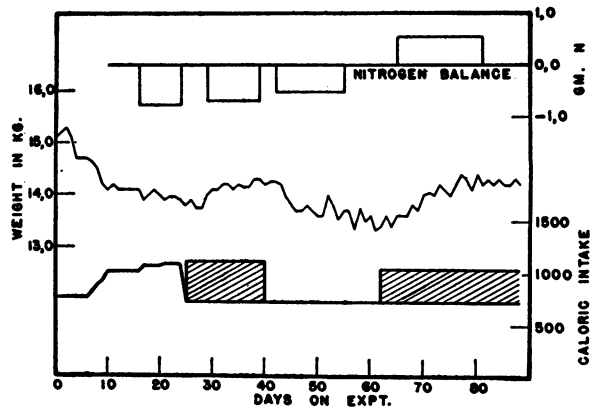|	Ration 1	Ration 2
	per 100 grams	per 100 grams
Sucrose		68 grams
Dextrose	55 grams	
Powdered "Amigen"	16 grams	
Casein (SMA, vitamin-free)		24 grams
Salt mixture*	4 grams	4 grams
Coconut oil	25 grams	
Cod liver oil		2 grams
Haliver oil	50 mgm.	
Liver Concentrate Powder 1–20 (Wilson's)		2 grams
Choline chloride	250 mgm.	250 mgm.
Thiamine and riboflavin, each	0.5 mgm.	0.5 mgm.
Pyridoxine hydrochloride	0.25 mgm.	0.25 mgm.
Calcium pantothenate	2.5 mgm.	2.5 mgm.
Nicotinamide	12.5 mgm.	12.5 mgm.
Mixed tocopherols	10.0 mgm.	10.0 mgm.

* J. Biol. Chem. 1941, 138, 459.

FIG. 1. EXPERIMENT 1. THE EFFECT OF INTRAVENOUS ADMINISTRATION OF FAT EMULSION 11MC ON NITROGEN BALANCE AND BODY WEIGHT OF THE ADULT DOG

Cross hatched areas represent periods of fat infusion.

Experiment 1. A 15.1 kgm. female dog was fed Ration 1, the composition of which is listed in Table II. The ration was calculated to furnish approximately 509 calories per 100 grams. It was supplemented daily with 5 grams of Wilson's Liver Concentrate Powder 1–20, and 9 grams of Cellu Flour, which were added and mixed after each day's ration was weighed out. The ration was fed at varying amounts until an intake just sufficient to maintain weight was obtained (78 calories per kgm., Figure 1). At this point, the amount of coconut oil in the ration was reduced from 25 per cent to 5 per cent, and an amount of the ration given to equal exactly the previous intake of all the other nutrients except fat. The difference in oral intake of coconut oil was then fully made up by the intravenous administration of 290 ml. daily of Emulsion 11MC. This amount of emulsion furnished approximately 390 calories, or 28 calories per kgm. This procedure was continued for 16 days, during which time the weight of the dog was maintained; in fact, there was a slight increase in weight, indicating utilization of the fat administered intravenously, and indicating, also, that the caloric intake was slightly above maintenance. The intravenous administration of fat was then discontinued, and the dog was fed the same amount of the low fat diet for 22 days. This was accompanied by a weight loss, but the nitrogen balance was not significantly different from that observed in the periods before and during the fat infusions. The data on nitrogen balance in this experiment, and in the other experiments reported in this paper, represent an average for the period represented in the diagram, and are determined from combined urine and fecal nitrogen determinations. After this period on the low fat diet, infusion of fat was again started using 239 ml. of Emulsion 11MC per day, which provided 323 calories, or 24 calories per kgm. This produced a striking increase in weight and nitrogen retention, as shown in Figure 1. Thus, it would appear that the fat administered intravenously was definitely utilized. Infusion of the fat emulsion was continued for 27 days, at which time the animal

refused food. At this time (89th experimental day) the blood plasma total cholesterol had reached 476 mgm. per cent, of which 258 mgm. per cent was esterified. Liver function was markedly impaired as measured by poor bromsulfalein elimination, 43 γ of dye per ml. of plasma after 8 minutes, as compared with the normal range of 5 to 20 γ of dye. Prothrombin time (11 seconds) and plasma alkaline phosphatase (126 γ phosphorus liberated per ml. of plasma in 24 hours) were normal. These methods for determining liver function in the dog have been described elsewhere (9). The fat infusions were discontinued and the dog was given milk for 10 days until it would eat the experimental ration. At this time the plasma total cholesterol and esterified cholesterol had dropped to 268 and 134 mgm. per cent respectively. Liver function was almost normal, as measured by brom-sulfalein elimination (20 γ of dye per ml. of plasma) and the dog seemed normal in every respect. The dog was fed ad libitum the purified ration with 25 per cent fat, and gained steadily. In 6 weeks, it weighed 18.4 kgm., and was then given commercial dog ration ad libitum. After 5 months, the dog was sacrified and a post mortem performed. Gross examination revealed no apparent pathology. Microscopic examination showed granulomatous nodular lesions in the lungs as previously described (1), but they were less numerous, and were not as large or as prominent as in the previous animals. Foreign body giant cells were less numerous. There was a marked increase in scar tissue in the nodules. Hemosiderin was present and was both intra- and extracellular. Small scars were occasionally found which were suggestive of the previous presence of nodules. In the spleen, the granulomatous lesions were rare; hemosiderin was present, but in less quantity. In the liver, there was still considerable fat in Kupfer cells of the sinusoids; hemosiderin was present, but again in lesser amounts; and there was no fatty infiltration of the liver cells.

Experiment 2. A 16.6 kgm. male dog was fed Ration 2 (Table II). The ration was calculated to furnish approximately 386 calories per 100 grams. Throughout the experiment the dog received 215 grams of this ration daily, furnishing approximately 830 calories. Nine grams of Cellu Flour were mixed with the ration each day. After 12 days on this ration, during which time the dog lost 1.2 kgm. of weight, daily infusions of Emulsion 11MC were commenced (Figure 2). A total of 47 infusions were given in 48 days, each infusion averaged 239 ml., and the average time of infusion was 166 minutes. These infusions of fat furnished an additional 316 calories per day (approximately 20 calories per kgm.) and during this period there was a gradual gain in weight. Determinations of the total fecal lipid excretion were made before and after the fat infusions were given. The feces excreted in a number of consecutive days were pooled, dried, and weighed, and a sample extracted with chloroform in a Soxhlet extractor for 16 hours. A 5-day sample of feces, collected before the fat infusions were started, had an average daily dry weight of 18.2 grams and of 2.58 grams of chloroform extractable material. After the fat infusions were instituted, the dry weight and chloroform
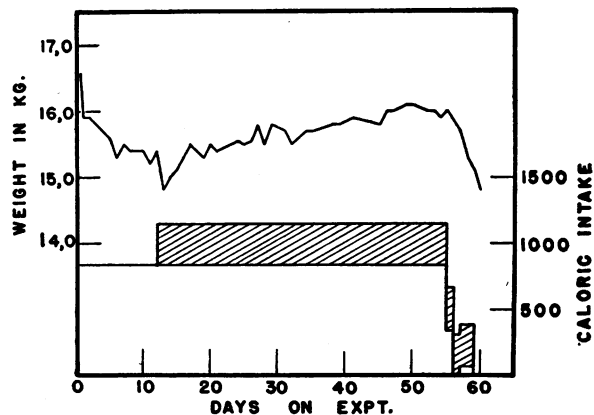

FIG. 2. EXPERIMENT 2. THE EFFECT OF INTRAVENOUS AMINISTRATION OF FAT EMULSION 11MC ON BODY WEIGHT OF THE ADULT DOG

Cross hatched areas represent periods of fat infusion.

extractable material of the feces averaged 17.7 grams and 1.57 grams daily for an 8-day collection period, and 23.0 grams and 2.1 grams for another collection period of 7 days. Hence, it appears that none of the fat administered intravenously was excreted through the intestinal tract. Beginning on the 55th experimental day (44th infusion day) the dog suddenly refused his food, and this produced a marked drop in weight (Figure 2). On the 60th experimental day, the total cholesterol and esterified cholesterol of the blood plasma were 432 and 218 mgm. per cent respectively, and the plasma alkaline phosphatase was slightly elevated (462 γ phosphorus liberated per ml. plasma in 24 hours). The blood hemoglobin was 12.5 grams per cent, the hematocrit was 41.3 per cent, and the plasma protein (Kjeldahl) 4.4 grams per cent. These figures may be compared with representative values in our "laboratory dogs" of 12 to 15 grams per cent for hemoglobin, 38 to 48 per cent for hematocrit, and 4.5 to 6 for plasma protein. The dog was sacrificed for post-mortem examination and complete carcass analysis for fat.

Microscopic examination of the organs demonstrated lesions similar to those previously described (1). Small granulomatous lesions were present in the lungs and spleen, and there was evidence of phagocytosis of fat by cells of the reticulo-endothelial system of the liver and spleen. The content of chloroform extractable material in the liver was found to be 42.3 per cent on the dry weight basis, as compared with normal findings of 10 to 20 per cent; however, the other visceral organs were all found to be in the normal range with regard to chloroform extractable material. It is likely that most of this increase in fat in the liver is due to the presence of phagocytized fat in the macrophages of the liver sinusoids. There was no fatty infiltration of the liver. The gall bladder bile was viscous and seemed inspissated, although the total solids were only 25.9 per cent, which is in the normal range for the dog (10). The bile, however, contained 1120 mgm. per cent cholesterol, which is over 30 times the normal amount for the dog (11).

The fat content of the entire dog was determined in the following manner: The visceral organs including the spleen, liver, lungs, pancreas, kidneys, testes, stomach, esophagus, and washed intestines were weighed, and small aliquots of each dried in an oven at 60° C., ground in a mortar and extracted with chloroform in a Soxhlet extractor for 13 hours. The total lipid content of each organ could then be calculated. The skin was removed from the carcass and weighed, and 200 gram aliquot samples selected, cut into small pieces and dried in an oven at 60° C. The dried skin was then refluxed successively with chloroform, and the chloroform extracts freed from chloroform by distilling off the solvent (hot water bath) first at atmospheric pressure, and finally under reduced pressure to constant weight. The chloroform extractable material obtained in this fashion was then weighed, and the total for the skin calculated. Fat depots were dried in the oven and extracted with chloroform in the same manner. The muscle was stripped from the bones, weighed, and ground in a meat grinder. Suitable aliquots of this were dried and extracted as with the other tissues. An aliquot of the bones (amounting to about ⅛ of the total skeleton) was demineralized in a jar of 2 N HCL. The demineralized bones were then cut into small pieces and dried in the oven. The fat was removed from the black, tarry residue by chloroform extraction. The total fat obtained in these fractions is given in Table III. The saponification numbers and iodine numbers of these fractions were determined by the methods of analysis of the Association of Official Agricultural Chemists (12).

Experiment 3. A 19.1 kgm. male dog was fed Ration 2 (Table II) with 7 to 10 grams of Cellu Flour mixed in with the daily ration. *Ad libitum* feeding was permitted for the first 5 days; from the 6th to the 23rd day the daily ration was restricted to 200 grams (772 calories); and from the 24th to the 57th day, it was further restricted to 160 grams (618 calories). Beginning with the 58th day, and continuing to the end of the experiment, 200 grams of the ration were fed. At both levels of caloric

Experiment 3

Tissue fraction	Total chloroform extractable material	Saponification number	Iodine number	Calculated maximum coconut oil present
	grams			*grams*
I Depot fat	802	217.4	57.9	328
II Skin	393	207.9	63.1	107
III Muscle	558	210.3	62.7	171
IV Bones	404	214.3	66.4	147
V Visceral organs and brain	140			140
Total	2,297			893

Total coconut oil infused: 2,455 grams.
Minimum total coconut oil unaccounted for and presumably metabolized: 1,562 grams. (Coconut oil saponification number, 258.4; iodine number, 11.5).

intake the dog lost weight, and by the 38th day had lost 3.0 kgm. (Figure 3). At this time, daily infusions of Emulsion 11M were started and given for 60 of the next 61 days. An average of 273 ml. of emulsion was infused daily during a period of 163 minutes. The daily caloric intake contributed by the intravenous fat was approximately 368 calories, or 22 calories per kgm. The infusions produced an immediate cessation of weight loss and a gradual recovery of lost weight. By the end of the experiment, over 1 kgm. of body weight had been restored. As shown in Figure 3, the nitrogen balance changed from slight negative balance to nitrogen retention when the additional calories were provided by infusion of fat. As in Experiment 2, determinations of total lipids in the feces were made before and after the fat infusions were started. A 7-day sample of feces, collected before the fat infusions were given, averaged, on a daily basis, 20.6 grams dry weight and 1.12 grams of chloroform extractable material. A 10-day sample of feces prior to giving the fat infusions averaged 20.2 grams dry matter per day and 1.40 grams of chloroform extractable material. These 2

TABLE III

Fat analyses for experiments 2 and 3

Experiment 2

Tissue fraction	Total chloroform extractable material	Saponification number	Iodine number	Calculated maximum coconut oil present
	grams			*grams*
I Depot fat	943	204.5	72.0	198
II Skin	706	206.5	71.6	176
III Muscle and brain	665	211.0	73.3	196
IV Bones	802	212.5	68.1	255
V Visceral organs	136			136
Total	3,252			961

Total coconut oil infused: 1,685 grams.
Minimum total coconut oil unaccounted for and presumably metabolized: 724 grams. (Coconut oil saponification number, 263.5; iodine number, 12.3).
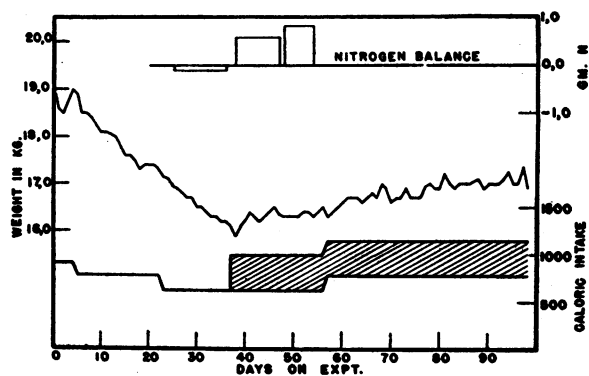

FIG. 3. EXPERIMENT 3. THE EFFECT OF INTRAVENOUS ADMINISTRATION OF FAT EMULSION 11M ON NITROGEN BALANCE AND BODY WEIGHT OF THE ADULT DOG

Cross hatched area represents period of fat infusion.

samples represented the periods of 200 grams and 160 grams daily food intake. After the fat infusions were started, a 10-day sample of feces averaged 17.9 grams dry weight and 1.41 grams chloroform extractable material daily.

The infusions were stopped on the 99th experimental day, at which time the hemoglobin was 10.6 grams per cent, the hematocrit 34 per cent, and the total plasma proteins 5.5 grams per cent. The hemoglobin and hematocrit had decreased from 14.4 and 42 grams per cent respectively, values observed on the 38th experimental day, just before the infusions were started. Liver function was only slightly impaired as measured by bromsulfalein elimination, but normal as judged by .prothrombin time (9.5 seconds), cholesterol and cholesterol ester levels of the plasma (288 and 214 mgm. per cent). At this time the dog was sacrificed for post-mortem examination and complete analysis for fat.

Gross examination at autopsy revealed no significant changes, although histologic examination revealed the same general picture observed with the dog of Experiment 2. The liver showed somewhat more fat in the reticulo-endothelial cells, and contained 47.1 per cent chloroform extractable material on a dry weight basis. Again there was no replacement of liver cells by fat. The small granulomatous lesions in the lungs appeared to be more numerous than in previous experiments.

The complete analysis of the animal for fat was achieved by the same general procedure as described in Experiment 2, but all of the bones and skin were extracted rather than aliquots of these tissues, as was done in Experiment 2. Also the brain was extracted separately, whereas in Experiment 2 it was not extracted, but included in the weight of the muscle fraction. The lipid content of the tissues, together with saponification and iodine numbers, are given in Table III.

Experiment 4. A 16.6 kgm. female dog was given the same ration used in Experiments 2 and 3 (Ration 2, Table II) with 7 to 10 grams of Cellu Flour mixed in with the daily ration. From the 1st to the 17th day, 170 grams of the ration were fed daily; and from the 18th
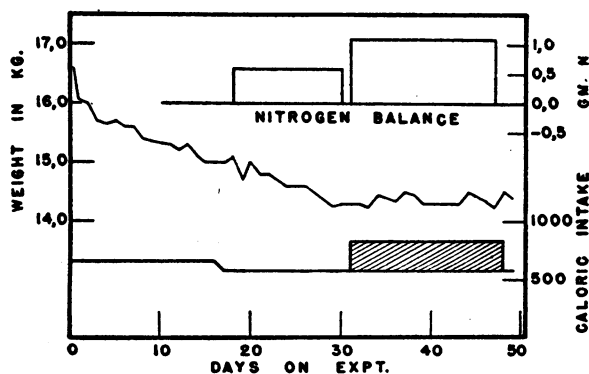

Fig. 4. Experiment 4. The Effect of Intravenous Administration of Fat Emulsion 11M on Nitrogen Balance and Body Weight of the Adult Dog

Cross hatched area represents period of fat infusion.

through the 48th day, 150 grams. These 2 levels of intake furnished 656 and 579 calories per day, neither of which was adequate to maintain weight, and by the 32nd day the dog had lost 2.3 kgm. (Figure 4). Daily infusions of Emulsion 11M were started at this time, and 15 infusions, each averaging 225 ml., were given in the next 18 days. The average time of infusion was 138 minutes, and the daily caloric intake from the intravenous fat was 253 calories, or approximately 17 calories per kgm. As observed in Figure 4, the fat infusions produced a maintenance of weight and an increase in nitrogen retention.

DISCUSSION

The improvement in weight and nitrogen retention produced by infusion of the fat emulsions in these experiments, indicates that the fat is utilized by the dog for energy. The ability of the animal to metabolize this fat is demonstrated by Experiments 2 and 3, in which the lipid material of the entire animal was actually isolated, and found to resemble mammalian fat more than coconut oil, insofar as average length of carbon chain (as indicated by saponification number) and degree of unsaturation (as determined by iodine number) are concerned. If we accept a range of 193 to 198 as the saponification number for mammalian (sheep and beef) fat (13), it is apparent that the carbon chain length averages between 16 and 18, for tripalmitin has a carbon chain of 16 and a saponification number of 209, and tristearin a carbon chain of 18 and a saponification number of 189. Dunham and Brunschwig (8) found an average initial saponification number of 206, with a range of 189 to 234, for fat from 13 dogs. Assuming that the minimum saponification number of the fat of the dogs in Experiments 2 and 3 prior to infusion is that of tristearin, then the maximum coconut oil content of the lipids in the tissues of the dog in Experiment 2 was 0.96 kgm.; and in Experiment 3, 0.89 kgm. (Saponification number of coconut oil used in Experiment 2 was 258.4; of oil used in Experiment 3, 263.5. Table III). These values are substantially below the 1.68 and 2.45 kgm. of coconut oil actually infused into the dogs. Since none of the infused fat was lost by urine or feces, it seems clear that this. unaccounted for coconut oil has been metabolized, at least to a degree to which it is no longer recognizable as such. The possibility of error or artifact entering into such an experiment must be considered. There may have been errors in sampling, but these could

hardly be of such magnitude as to account for the difference in these values. Auto-oxidation of the fats must have been kept to a bare minimum, since the mass of fat isolated from both animals was so surprisingly high. In the case of the dog in Experiment 2, the total fat amounted to 22 per cent of the body weight of the animal; and in Experiment 3, to 14 per cent. We have found only 1 reference in the literature on the total lipid content of the dog (14). This paper dealt entirely with young puppies, and gives a figure of 8.5 per cent of body weight for a 100-day-old pup. The total lipid of the rat varies from 16.2 to 23.3 per cent of the body weight in animals 15 weeks old (15) and it is likely that higher figures might be obtained in older animals. It should be pointed out that in all of the fractions except 1, the great majority of lipid is neutral fat. The exception to this is the lipids of the visceral organs which are high in phospholipid, and for this reason saponification numbers of these extracts were not determined. The total lipid in all of the visceral organs is small, however, as compared with the rest of the body fats, and may be either disregarded or considered as pure coconut oil without influencing the conclusions in either experiment. The phospholipids in the extracts of muscle and bone would be expected to lead to a slight error in the saponification number. It should be pointed out also that much of the lipid determined in these 2 fractions actually belongs under "depot fat," but was not separated as such as a matter of convenience.

Utilization of the infused fat is also suggested by a consideration of the iodine numbers of the fat from the dogs in Experiments 2 and 3. If the iodine numbers of the dog fat prior to infusion may be assumed to lie in the range of 48 to 79, as in the case of sheep and beef fats (13), very little coconut oil (iodine number 11.5 to 12.3) could be present in the fats obtained from the dogs of Experiments 2 and 3, certainly far less than the amounts actually infused (Table III). The reasoning with iodine numbers, however, is hampered by the fact that their values may go well above 100 for dog fat, depending on the ration fed, and other factors. Dunham and Brunschwig (8) found an average iodine number of 95 (range, 69 to 119) in the body fat of 13 dogs reported in their studies. Utilization of the infused fat is indicated by the iodine numbers of the body fats in both experi-

ments, but is actually demonstrated only in the case of Experiment 3.

The experimental results reported in this paper point to the conclusion that the infused coconut oil has been utilized for energy. This is contrary to the conclusions reached by Dunham and Brunschwig (8). They observed no tendency toward nitrogen retention during infusions of their emulsions, in dogs receiving an oral intake of 60 calories per kgm. per day. Their emulsions were toxic, since 9 out of the 24 dogs used in the study died during the infusion periods. It was also noted that the emulsions were hemolytic, and that all of the dogs showed some degree of anemia after the infusions. Nitrogen excretion would be expected to be greater in any toxic condition, and is greater during hemolysis. Phenylhydrazine anemia in dogs is accompanied by increased nitrogen excretion (16) and this is also observed in pernicious anemia in relapse. It is conceivable, therefore, that these factors would tend to hide any nitrogen economy provided for by energy obtained from infused fat. Dunham and Brunschwig (8) also observed that the characteristics of the body fats of the infused dogs, as determined by saponification number, iodine number, and melting point, were not markedly displaced toward those of the infused fats. This is in agreement with our own observations, but they concluded from this that the fat was not utilized. As we have mentioned, failure to account in any way for the infused fat should be good evidence for its metabolism. Failure to metabolize or excrete the fat would result in its deposition somewhere in the tissues, which would result in a displacement of the characteristics of the body fat toward that of the infused fat.

The partial impairment of liver function, and the extensive accumulation of fat in the reticulo-endothelial cells of the liver, observed in the dogs of the first 3 experiments, are interesting in view of our failure to observe these changes in previous infusion experiments with Emulsion 11M (1). It should be pointed out, however, that in the earlier experiments lower intakes of fat per kgm. were used, and also for a shorter experimental period. The addition of cholesterol to the coconut oil (Emulsion 11MC, used in Experiments 1 and 2) appeared to hasten the appearance of liver dysfunction. Determination of sterol excretion in

the feces of the dog of Experiment 2 was carried out on the chloroform extracts of the dried feces obtained for the determinations of the total lipids. Sterols were determined by precipitation with digitonin, and by the Liebermann-Burchard reaction on the saponified extracts. In the period prior to the infusion of fat, the daily excretion of sterols giving the Liebermann-Burchard color reaction, and expressed as cholesterol, was 0.16 gram, and the total sterol precipitated by digitonin was 0.30 gram. The fecal excretion of sterols during the 10th to 13th day of fat infusion, and between the 21st and 25th days of infusion, averaged 0.42 gram cholesterol and 1.48 grams total sterols daily. Thus the dog was excreting approximately all of the infused sterol (about 1.00 gram cholesterol daily) during this stage of the infusion experiment. The cholesterol to coprosterol ratio is roughly in accordance with that found by Schoenheimer (17). It seems clear, therefore, that the earlier appearance of liver impairment in the dogs of Experiments 1 and 2, in which the emulsion containing cholesterol was used (Emulsion 11MC), should not have occurred primarily from inability to excrete the sterol. In addition, there was no apparent difference in the histopathologic appearance of the tissues of the dogs of Experiments 2 and 3. Thus it would seem that no primary toxic effect can be attributed to the cholesterol.

These observations suggest that the earlier appearance of liver dysfunction in Experiments 1 and 2, when Emulsion 11MC containing cholesterol was used, occurs only when failure of liver function accompanying prolonged fat infusions is present. Since the excretion of sterols into the intestinal tract is initiated in the liver, any slight failure of liver function should result in reduced capacity to excrete the infused sterol, and it would be expected to accumulate in the liver and blood. The sterolemia in the dogs of Experiments 1 and 2 has already been mentioned. The cholesterol content of the liver of the dog in Experiment 2 was found to be 23.0 mgm. per gram of dry liver, as compared with the normal range of 9.0 to 16.1 mgm. in the other dogs of the series of fat infusion experiments reported previously (1).

Inasmuch as the impaired liver function observed after prolonged infusion of the coconut oil emulsions is reversible, as shown in Experiment 1,

it might be expected that no impairment of liver function would occur when the emulsions are used over shorter infusion periods, or at smaller daily infusions. In fact, such was found to be the case in our previous studies (1). Since Emulsion 11MC appears to be more stable, the inclusion of the cholesterol would be desirable, provided the emulsion is not used in quantities which would permit the development of any ill effects resulting from cholesterol. Perhaps smaller quantities of cholesterol would produce the desired stabilizing effects on the emulsion without affecting liver dysfunction.

SUMMARY

1. The daily intravenous administration of coconut oil emulsions to dogs receiving an oral ration adequate in all nutritional factors, but inadequate in calories, prevented further weight loss and produced an increase in nitrogen retention.

2. The infused fat is not lost in urine or feces, nor is it deposited as such in the tissues to any marked extent, except in the cells of the reticuloendothelial system.

3. In 2 dogs in which total carcass analysis of fat was performed, it was found that the body lipids were only slightly displaced in their characteristics toward those of coconut oil. A minimum of 0.72 and 1.56 kgm. of coconut oil could not be accounted for in the tissues of these dogs, and hence must have been metabolized during the experimental period. Thus fat given intravenously to the dog is utilized for energy.

4. Infusion of coconut oil emulsions containing 2.8 per cent cholesterol in the emulsified oil (0.42 per cent cholesterol in the complete emulsion) resulted in impairment of liver function, as measured by bromsulfalein elimination, and a cholesterolemia and increased cholesterol content of the liver when infused at amounts sufficient to furnish 20 to 28 calories per kgm. daily for periods of 4 to 6 weeks.

5. These effects appear to be reversible, since liver function and the cholesterol content of the blood returned to normal when fat infusions were stopped.

6. The histopathologic findings previously described following prolonged infusion of fat were also observed.

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