THE EFFECT OF DIETARY TRIGLYCERIDE CHAIN LENGTH ON OBESITY IN RATS FED HIGH FAT DIETS

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ABSTRACT

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By

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There is evidence in a number of investigations that medium chain triglycerides (MCT) may not contribute to the increase in body weight and body fat that is evident when other forms of fat are fed. (Leveille, et al., 1967a; Leveille, et al., 1967b; Harkins and Sarett, 1968b; Kaunitz and Johnson, 1968; Allee, et al., 1972; Stickney and Andrews, 1972; Wiley and Leveille, 1973). The purpose of the present study was to examine some of the parameters of dietary obesity in rats fed high fat diets and to compare the effect of substituting medium chain triglycerides for longer chain fats in these diets. Diets containing 50% fat as Crisco, corn oil or MCT were fed to male Osborne-Mendel rats ad libitum, beginning at 21 days of age, for a period of 12 weeks. At the end of the feeding period six animals from each group were sacrificed for body composition determinations. The right inguinal,

testicular, and perirenal-retroperitoneal fat depots were removed from the remaining six animals, weighed, and utilized for analysis of fatty acid composition.

Total diet consumption by weight in the corn oil-fed animals was decreased by 5% in comparison to the Crisco-fed animals. The rats fed the MCT diet ate 5% less grams of food than the rats fed corn oil. When intakes were adjusted for digestible Kcal per gram of diet, the gap between the total Kcal consumption of rats fed the MCT versus the corn oil and Crisco diets widened. Rats fed MCT consumed 9% less Kcal than the rats fed corn oil over a 12 week period.

In general, growth rates for the three groups seemed to reflect the total energy consumed. Rats fed the Crisco diet attained a final weight of 480 grams while rats fed corn oil reached a final weight of 454 grams. Both groups utilized 16.6 Kcal per gram of weight gain. Rats fed MCT weighed only 369 grams at the end of twelve weeks and utilized 20.3 Kcal per gram of weight gained.

The greatest difference in body composition was found in the amount of body fat. The carcasses of the Crisco and corn oil fed rats contained 27% and 24% fat respectively. In rats fed MCT only 16% of the carcass weight was fat. Animals receiving Crisco or corn oil

diets utilized, respectively, 54 and 62 Kcal per gram of fat gained. MCT fed rats utilized 105 Kcal per gram of body fat gained. Although the rats fed MCT had greater lean body mass expressed as a percent of carcass weight, the total grams of lean body mass found in MCT rats was significantly less than the values obtained for the other two groups.

Fat depot weights also varied among the three diet groups. The decrease in depot weights of the MCT fed rats was very highly significant when compared to depot weights in rats fed the other two diets. There was a 33% decrease in the weights of the inguinal fat depots of the MCT fed rats compared to the same depots in Crisco fed rats when fat depot weights were expressed as a percent of total body weight. There was more than a 50% decrease between the weights of the testicular and perirenal-retroperitoneal fat depots of MCT fed rats compared to the same depots in rats fed Crisco.

Even though 53% of the dietary Kcal were supplied by C_8 and C_{10} fatty acids, and these fatty acids were fed during the period of greatest body growth, only a small increase occurred in these components of adipose tissue.

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REVIEW OF LITERATURE

Fat: Boon or Bane

The ability to store lipid is an adaptive feature of animals which has had considerable survival value. The seasonal lipid stores of migratory birds is only one example of adaptive obesity which allows these small mammals to store enough energy to carry them half across the globe. In the hummingbird, for example, the normal body fat content of 3-10% can increase to 45% within days due to hyperphagia immediately preceding migration (King and Farner, 1965). This fat content exceeds levels normally considered pathological in most animals.

Fat in the form of triglycerides is an ideal storage form of energy for mobile organisms. It has a relatively low density and yet it is high in energy value. Senior (1964) pointed out that even though triglycerides seem to require a number of hydrolysis and resynthesis cycles to be moved across membranes, one cycle of hydrolysis and resynthesis costs only 0.7% of the energy metabolically available from fatty acid oxidation. The hydrolysis and synthesis cycles also permit the organism

to synthesize preferred forms of lipids and to arrange them in suitable configuration. Thus fat is a very unique and necessary component of animal bodies.

The ability to store fat ceases to be an asset and becomes a liability when food is plentiful and strenuous exertion become unnecessary. Americans, in general, have found that the ability to store fat has become a liability in their affluent society. It is estimated that weight control is a major nutritional concern of 20 to 40 million Americans (Wagner, 1970). Obesity is becoming a greater problem in the well-fed, technical societies all over the world. Not only a problem from a cosmetic point of view, obesity has been associated with increased risk of death from cardiovascular and renal disease, diabetes mellitus, cirrhosis of the liver in men, appendicitis, and gallstones (Baird, 1969).

Determination of Obesity

Another major problem associated with obesity is determining who is obese. If obesity is defined as an excess of body fat, then some method of estimating body fat must be used in the diagnosis. Standard height and weight charts are useful, but subjects may have excess adipose tissue and still be normal weight while athletes

may be overweight due to an excess of lean body mass rather than fat. Using hereditary obese mice Alonso and Maren (1955) found that if food intake was restricted so that the obese mice were the same weight as lean controls, the obese mice still possessed an increased amount of body fat. As the weight of lean and obese individuals increased, the obese mice deposited more fat per unit weight gain than the lean controls. Thus body weight per se is a poor indicator of obesity.

A number of standardized definitions of obesity have been proposed (Lebon, 1969). The most common being a body weight which is 20 to 30% above ideal body weight. Others, which try to be more discriminating, include having a Ponderal Index (ht. in inches $\sqrt[3]{\text{wt. in lbs.}}$) less than 12 or having a fat fold thickness greater than 2.5 cm. as measured at the tip of the scapula in man or at the mid triceps region in women. All of these formulae try to approximate total body fat; a difficult measurement to obtain in human subjects. Behnke (1952, 1964) listed other techniques which have been used for determining body composition in live subjects, including metabolic balance studies, roentgen visualization, densiometry, isotope dilution, measurements of exchangeable

electrolytes and gamma emission of K^{40}. Small animal body composition determinations do not present the problems encountered in the determination of body composition in human subjects. Direct analysis can be performed on the animal after sacrifice (Mickelsen and Anderson, 1959).

Etiology of Obesity

The etiology of obesity cannot simply be stated as availability of food and lack of exercise. Although obesity is an ever growing problem in affluent societies the majority of Americans still manage to remain within the norms for body weight. Obesity is caused by more than one factor. Errors in appetite regulation, genetic predispositions and environmental stress, inactivity, as well as psychological disorders have all been implicated as factors in the development of obesity.

Theories of Appetite Control

The theory that "energy in" equals "energy out" is a basic one to all sciences. The definition of simple obesity given in Swift and French (1954) is in terms of an imbalance in food intake and energy expenditure. Factors influencing food intake seem to have received more attention than energy expenditure and a number of theories

of the mechanism of food intake regulation have appeared.

Brobeck (1946) reported that lesions of the hypothalamus produced rapid weight gain in animals. Animals so lesioned often increased their body weight by 15% within 24 hours and continued to gain weight at rates 10 times that of normal animals until a plateau was finally reached. Although there was an indication that these animals were less active than normal and their basal heat production could have been altered, Brobeck attributed the obesity in these animals to their marked hyperphagia. This was one of the first indications that some sort of appetite regulation occurred in the intact hypothalamus. Since then a number of possible theories have been proposed as to the mechanism of hypothalamic regulation of appetite.

Brobeck has proposed a temperature regulation of appetite. In a discussion of this theory (Brobeck, 1955), he stated that body weight itself may not be regulated although food intake, heat loss and activity are directly controlled. Because heat loss is under stricter metabolic controls than either food intake or activity the latter two are changed in relation to the former.

Mayer has proposed a glucostatic regulation of food intake. In a review of this theory (Mayer, 1957) it was stated that the rate of glucose passage in cells of the ventromedial hypothalamus controls food intake. In support of this theory is the fact that goldthioglucose but no other goldthio compounds can selectively destroy the hypothalamus.

Kennedy (1953) found little connection between the hypothalamic center and temperature regulation, but rather, he postulated that it was lipemia which influence food intake. Wide variations in diet composition had little effect on food intake in normal rats suggesting glucose alone could not be the appetite regulator. The limit of food intake was a function of maximal fat assimilation. Other support for this theory came from Liebelt, et al. (1965) who found that there was a "compensatory hypertrophy" of other fat depots when the gonadal depot was removed, suggesting that the adipose tissue itself feeds back to a food intake regulator.

The fact that appetite is well controlled in the normal animal is illustrated in an experiment in which Janowitz and Hollander (1955) varied the intragastric feeding of dogs and recorded their adjustments in oral intake and body weight. Gastric distension was kept

constant and caloric density of the intragastric feeding was varied at 50%, 100% and 175% of the average oral intake of each dog. After the intragastric feeding the dogs were allowed access to food orally. Within five weeks of a change in density of the intragastric feeding, the dogs had adjusted their total food consumption to levels which maintained body weight constant with the 50% feeding, or in the case of the 100% and 150% levels, oral intake dropped to almost nothing.

In a study in rats, Kennedy (1950) reported that normal animals regulated food intake within one week after their diet was adulterated with 50% Kaolin. In the same experiment, hypothalamically lesioned animals required 4 weeks to regulate their food intake and lost considerable weight during this period.

A most interesting study was performed by Hashim and Van Itallie (1965) in which human subjects were asked to consume their total food intake from a specially designed dispensing device. The device recorded the amounts of a liquid diet consumed and the only way the subject could estimate the amount of food eaten was by the number of mouthfuls. Normal weight subjects had little problem regulating intake and maintaining normal weight. Obese subjects, on the other hand, could not

regulate intake and consistently lost weight when fed in this manner. Thus obese human subjects seem to exhibit some of the difficulty regulating food intake seen in rats with hypothalamic lesions. That the hypothalamus is involved with appetite regulation is clear. But as yet the precise mechanism of control, whether glucose, free fatty acids, or temperature is unclear.

Genetic Factors in Obesity

There is a strong correlation between overweight in parents and overweight in their children. Studies have shown that about 10% of children from families of normal weight parents eventually become obese, while 50% of children from families with one obese parent and 80% of children from families with two obese parents become obese (Mayer, 1957, 1965a). Eighty percent of overweight children remain overweight in adulthood (Lloyd, 1969). These data are not conlcusive proof that obesity is hereditary as it is impossible to separate the influence of the home environment in each of these cases.

Mayer (1965a) reviewed a study of identical and fraternal twins and their siblings. There was a definite correlation between weight in identical twins that was absent between fraternal twins or when the twins were

compared with their siblings. It was also reported that sex ratios of offspring were altered when obese x obese, obese x lean, or lean x lean parental unions were compared; thus suggesting a sex linked inheritance pattern for obesity. Body weights of children correlated well with those of their natural parents but when adopted children were examined, there was no correlation between the body weights of the child and those of their adoptive parents.

Animal studies have been helpful in examining the genetic aspects of obesity. The ability to select animals with characteristics under study and breed for the phenotypic expression of these characteristics gives these studies an experimental design unavailable with human subjects. A number of genetic obesities have been isolated in rats and mice. The Zucker rat contains a recessive gene producing spontaneous obesity in animals homozygous for this gene (Zucker, 1965). There are at least four different strains of obese hyperglycemic mice in which the obesity is again a recessive trait expressed in animals homozygous for this trait (Hellman, 1965; Stauffacher, et al., 1965). Even in apparently normal strains of rats it has been possible to selectively breed high and low weight animals until distinctive substrains

have been developed differing in food efficiency, body composition, as well as body weight (Palmer, et al., 1946; Kleiber and Cole, 1950).

By examining the metabolic aberrations in genetically obese animals it may be possible to identify similar metabolic changes in human obesity. Bray (1970) reported on a comparison of obesity in the Zucker obese rats, lean controls, and lean controls with hypothalamic lesions. The Zucker rat and lesioned control reached final body weights 2 times that of the normal control and their food intake was almost 50% greater per day than that of the normal control. Other differences found were a decrease in liver glycogen in the two obese groups, and substantially higher circulating insulin and triglyceride levels. One characteristic of interest that was possessed by the Zucker rat and not by the lesioned control was a slower turnover of radioactive iodine, possibly indicating groups of obese animals were pair fed with controls the Zucker obese rat gained weight more rapidly than the normal or the lesioned control animals. Thus even though the Zucker and hypothalamically lesioned rats had increased ad libitum food intakes there seemed to be other factors contributing to the genetic obesity. Bray also

reported that in human obese subjects there were abnormally low levels of NAD-linked glycerophosphate dehydrogenase and mitochondrial glycerophosphate dehydrogenase. Low levels of these two enzymes seemed inconsistent with the known increase in lipogenesis in obesity but Bray proposed that a decreased activity of the glycerophosphate dehydrogenase cycle could increase the efficiency of oxidative phosphorylation.

Stauffacer, et al. (1965) examined some differences in glucose utilization between obese hyperglycemic mice and lean controls. Both groups were of identical body weight although the obese hyperglycemic mice had an increased amount of body fat. The obese hyperglycemic mice exhibited a decreased incorporation of glucose into diaphragm glycogen and an increased incorporation of glucose into adipose tissue at 1 and 2 months of age. By three months of age the lean controls also had more glucose incorporated into adipose tissue than into diaphragm glycogen.

Besides spontaneous genetic obesity, there is indication that rats and mice may inherit a susceptibility to obesity if placed in nutritionally stressful conditions. Fenton and Dowling (1953) showed that in 2 strains of mice studied, high fat diets (43% fat w/w) produced more rapid.

weight gains than low fat diets. But in one strain diets containing more than 15% fat actually inhibited weight gain. Schemmel, et al. (1970a) also found a difference in weight gain and body composition in seven strains of rats fed a low fat grain diet compared to a 60% (w/w) fat diet.

Hypothalamic lesioning has been said to produce a regulatory obesity as the obesity seems to be caused by simple hyperphagia (Mayer, 1957). Genetic obesities have been termed "metabolic" as they seem to be connected with an inborn error in tissue metabolism (Mayer, 1957). Both models have counterparts in human obesity and both models are being used to examine the complexities of obesity in man.

Inactivity

The traditional view of an obese person as a lazy glutton is based on the laws of thermodynamics, energy intake will equal the energy stored plus "energy output." Mayer (1965b) reported that studies of activity levels in obese adolescent girls showed a 2/3 reduction in activity when they were compared to lean peers. Brobeck (1946) also commented on the lethargy reported in obese animals with hypothalamic lesions. Although it is safe to say that inactivity in these two cases

undoubtedly contributed to the maintenance of obesity; it cannot be ascertained whether inactivity is truly a cause or an effect of obesity.

Psychology of Obesity

In man, the metabolic and physiological aspects of obesity are compounded by the emotional. As Hamburger (1957) states, man has the "non-nutritional" aspect of eating for which to account. Adult appetite is a learned psychological experience associated with love, companionship, religion and all other areas in which food plays a role in society. Miller (1955) expressed the view that hunger cannot be measured by food consumption alone, even in animals. Food consumption is regulated more by a balance of hunger and satiety. Rats with hypothalamic lesions will consume larger amounts of readily available food but they will not work to secure food not readily available. Thus even in lesioned rats, they ate more but were less "hungry" than normals. Monello, et al. (1965) found abnormalities in satiety much more prevalent than abnormal hunger in obese subjects. While non obese women associated feelings of hunger with gastric mobility, Stunkard (1959) found that obese women rarely reported hunger at all even though their periods of

gastric mobility were similar. Hashim and Van Itallie (1965) reported consistant weight loss in obese subjects fed a liquid diet from a feeding machine where the subjects could not see the food or the amount they were consuming.

Although there is no one psychological profile for the obese person there are a number of common psychological problems among the obese. Stunkard and Mendelson (1967) reported a common disturbance of obese subjects was related to body image. The earlier the age of onset of obesity; the more negative the evaluation of their obesity by others; and the presence of other emotional disturbances; tended to create problems, not only in the obese persons' view of themself, but also in their view of others. Bruch (1955) reported that the obese tended to have great fear of starvation. Stunkard (1955, 1957) also warned of the emotional dangers of dieting which could cause severe anxiety and depression in some patients.

It is still not clear how the obese persons' altered feelings of satiety or hunger, their altered response to sensual cues or their disturbed image of themselves and others contributes to the development or

maintenance of their obesity. One aspect is clear, however. The psychological aspects of obesity can only be elucidated by man studying man.

Treatment of Obesity

Again science had looked at a simple energy equation and come to the conclusion that to treat obesity one merely had to cut down energy intake or increase energy output. So reducing diets and exercise clubs were born. Maybe it was indicative of the failure of those two prescriptions that other techniques were tried. Total fasting (Duncan, et al., 1965), bowel by-pass (Sherman, et al., 1965), alterations in dietary composition (Kekwick and Pawan, 1956) and alterations in meal frequency (Young, et al., 1971; Leveille, 1972) are only some of the treatments that have been used in combating obesity. The relative ineffectiveness of most weight reduction programs is reflected in the statistics from Jordan (1973) which stated that attrition rates in clinics range from 20 to 80% of those treated. Only 25% of those who begin therapy lose as much as 20 lbs. and only 5% lose as much as 40 lbs.

Perhaps one aspect of the high rate of failure of weight reduction therapy is due to the total re-education towards food required in patients. A total break

with old eating habits is necessary. But rather than a total change from a familiar diet perhaps a slight remodeling would be more effective.

The average American obtains about 40% of his kilocalories from fat (Pike, 1967). It had been reported that high fat diets can cause obesity in mice and rats (Fenton and Dowling, 1953; Schemmel, et al., 1970a). If dietary fat is a factor in human abesity it may well be wise to investigate substitutes for conventional fats, without their high predisposition toward obesity, and yet able to provide the satiety value and to provide the cooling properties of fat.

Medium Chain Triglycerides: A Review

Progress in the understanding of triglyceride absorption and metabolism has occurred at an impressive pace in the past 30 years. In these investigations it was recognized that all natural fats were not equivalent in chemical or physiological properties. Steinbock, et al. (1936) compared the absorption rates of different fats and found that butter fat exhibited a very rapid initial absorption rate. The shorter, somewhat water soluble fatty acids contained in butter were more rapidly absorbed than the longer chain fatty acids. It became increasingly

apparent that fatty acid chain length was an important variable in triglyceride metabolism.

Long chain fatty acids are the most prevalent fatty acids in natural triglycerides. Stearic ($C_{18:0}$), oleic ($C_{18:1}$), linoleic ($C_{18:2}$), and the higher chain polyenoic fatty acids constitute the majority of naturally occurring fatty acids. Only 5% of naturally occurring fatty acids have carbon chains of less than fourteen (Hashim, 1967). These medium chain fatty acids (MCFA) are found to a small extent in milks and more extensively in kernel oils (Babayan, 1968). Medium chain triglycerides (MCT) are a synthetic oil composed of a random mixture of these saturated fatty acids, eight to ten carbons in length. This review will try to examine some of the unique absorptive and nutritional properties of MCT.

Nutritional Studies

Medium chain triglycerides differ from long chain triglycerides in caloric value. Naturally occurring fats have a caloric value of 9.2 Kcal per gram. MCT yields 8.3 Kcal per gram by bomb calorimetry (Kaunitz, et al., 1958).

Nutritional studies of MCT have been conducted using 10-33% (w/w) of the diet as medium chain or long

chain fats. While Kaunitz, et al. (1958) reported slightly higher food intakes on MCT diets, wiley and Leveille (1973) reported a 5% decrease in food intake in rats consuming MCT when compared to diets containing corn oil or lard. Most investigations agree that MCT-fed animals tend to be lighter in weight than animals fed longer chain fats (Leveille, et al., 1967; Leveille, et al., 1967b; Harkins and Sarett, 1968b; Kaunitz and Johnson, 1968; Allee, et al., 1972; Stickney and Andrews, 1972; Wiley and Leveille, in press). By restricted feeding, weight maintenance requirements were found to be higher for MCT diets than for lard diets (Kaunitz, et al., 1958), and higher than for fat free diets (Kaunitz and Johnson, 1968). The poor growth rates of rats on MCT diets was not related to poor utilization of the fat, as MCT absorption is rapid and more complete than that of long chain fats (Bloom, et al., 1951). Fecal fat losses in rats consuming MCT were found to be slightly lower than those observed for rats consuming longer chain triglycerides (Kaunitz, et al., 1958; Kaunitz and Johnson, 1968; Harkins and Sarett, 1968b).

In studies of carcass composition, rats fed 20% MCT were found to have slightly less carcass fat than rats fed other types of fat (Harkins and Sarett, 1968b).

Catfish fed a 10% MCT diet did not show an increase in carcass lipid above those fed a low fat control diet (Stickney and Andrews, 1972). Harkins and Sarett (1968b) reported a decrease in epididymal fat depot weight in rats fed 20% MCT as opposed to rats fed 20% corn oil.

Physical-Chemical Properties

The physical-chemical properties of medium chain fatty acids are distinct from those of longer chain conventional fatty acids. Medium chain fatty acids exhibit a greater solubility in water; 68 mg/100 ml at 20°C for octanoate as compared to 0.7 mg/100 ml at 20°C for palmitate (Harkins and Sarett, 1968a). The melting point of octanoate is 17°C while that of palmitate is 63°C (Ibid). The most important distinction though, is the manner in which medium chain fatty acids and their triglycerides are metabolized.

Gastric Retention

Gastric retention is influenced by a number of factors not well understood. It is well known, though, that dietary fat tends to increase gastric retention, presumably by influencing the release of an inhibitor of gastric motility from the duodenum (Wiseman, 1964). In

a comparison of the gastric retention of liquid diets containing different fats, a diet containing 4-8% MCT was found to decrease gastric retention of fat when compared to similar levels of longer chain triglycerides (Harkins, et al., 1964). There was no evidence of a selective emptying of the stomach which could have favored evacuation of shorter chain fatty acids.

Hydrolysis and Absorption

Fats are hydrolyzed and absorbed in the small intestine. Hydrolysis depends on bile salts and pancreatic lipase. Medium chain triglycerides are hydrolyzed much more rapidly than long chain triglycerides both in vitro and in vivo (Greenberger, et al., 1966; Hagerman, et al., 1969). The absence of bile has little effect on MCT hydrolysis; and even in the absence of pancreatic lipase some absorption of medium chain fatty acids does occur (Greenberger, et al., 1966; Isselbacher, 1968; Clark, 1968; Hagerman, et al., 1969). An examination of normal intestinal hydrolysis products of trioctanoin and tripalmitin showed more free fatty acids were produced from the trioctanoin and more lower glycerides, especially monoglycerides were produced from the tripalmitin (Greenberger, et al., 1966). This could possibly reflect the greater importance of monoglycerides in the dispersion of long chain hydrophobic fats. Medium chain triglycerides are much less hydrophobic in solution than are long chain

triglycerides. Hoffman (1968) explains the increased rate of MCT hydrolysis and its independence of bile concentrations by the fact that MCT is dispersed in water and in water-bile salt solution at 37°C. Long chain triglycerides are not dispersed in either of these systems. Hoffman proposed that MCT is more rapidly hydrolyzed by pancreatic lipase because of its dispersion in the intestinal lumen. Desnuelle and Lavary (1963) believe that it is the water-lipid interface that is important for lipase activity. The hypothesis being that the lipase must be absorbed at this interface to be active. Although precise K_m values are lacking for the reactions catalyzed by lipases it seems as if there is a preferential hydrolysis of shorter chain fatty acids. Whether this is a function of the larger interface of a more dispersed water-lipid system, or a function of chain length specificity of the lipase reaction has not yet been answered.

In absorption studies it was found that MCT was not absorbed into the lymph as were long chain fats, but rather medium chain fatty acids were absorbed as free fatty acids directly into the portal vein (Borgstrom, 1955; Bloom, et al., 1964; Hashim, et al., 1964). Intestinal acyl CoA synthetase activates shorter chain fatty acids very slowly (Desnuelle and Lavary, 1963). It was postulated that the specificity of the synthetase

determined which fatty acids were esterified in the mucosa and packaged as chylomicrons for transport in the lymph. The medium chain fatty acids were not readily esterified and were thus destined for portal transport to the liver.

Other evidence indicates that triglycerides may be able to enter the portal system. Greenberger, et al. (1966) injected trioctanoin - ^{14}C into normal and irrigated intestinal loops. After 15 minutes the portal blood from the normal loop contained 40.3×10^{-3} dpm/ml; 83% of the label was in the form of free fatty acid and 16% of the label was neutral lipid. In the case of irrigated loops, portal blood label was reduced to 3.8×10^{-3} dpm/ml of which 74% was neutral lipid. Thus, impaired intraluminal hydrolysis of MCT was able to alter the lipid profile of portal blood.

A lipase associated with intestinal cell microsomes and which hydrolyzes trioctanoin but not tripalmitin was described by Playoust and Isselbacher (1964). Even when bile and pancreatic lipase are unavailable intraluminally, the mucosa has a small capacity to hydrolyze absorbed medium chain tri-and lower glycerides. Also, the activity of a MCT-specific lipase and a LCT-specific CoA synthetase favors the formation of free medium chain fatty acids for portal transport.

During MCT absorption there is less chylomicron formation and a slight decrease in intestinal lymph flow. The proportion of medium chain triglycerides in the diet in relation to long chain triglycerides influences the incorporation of medium chain triglycerides into chylomicrons. Using tripelargonin, Lee, et al. (1968) found less than 1% of an oral dose was absorbed into the lymphatic system. As the percentage of long chain triglyceride in the dosage increased, the percentage of MCT found in chyle triglycerides increased. It was not determined whether the MCFA in the chyle were due to an incorporation of these fatty acids into mixed triglycerides with long chain fatty acids. Sylven (1970) found that when MCT was found in the lymph, it was contained in a lower density chylomicron which had a higher amount of cholesterol and lowered triglyceride content. While dietary long chain triglycerides can influence MCT transport, dietary MCT may influence long chain triglyceride absorption. Clark and Holt (1969) demonstrated a 68% inhibition of triolein absorption when intestinal infusion of trioctanoin was maximal.

Harkins and Sarett (1968b) investigated the relationship of fat absorption to protein and calcium absorption in the rat. Fecal excretion of MCT was

decreased below the average levels of five other fats examined, but little difference was seen in the protein or calcium excretion levels for the different diets.

Liver Metabolism

Scheig and Klatskin (1968) compared the hepatic metabolism of 1-^{14}C-octanoate and 1-^{14}C-palmitate in the rat. In vivo studies showed that octanoate produced more water soluble products and less lipid soluble products; while in vitro investigations showed that labeled CO_2 production was greatly increased by octanoate. Examination of incorporation into liver lipids showed that about 50% of both medium and long chain fatty acids were found in the triglyceride fraction, but labeled octanoate was found to a greater extent in unesterified fatty acids and less in the phospholipid fraction when compared to palmitate. Harkins and Sarett (1968b) reported a slight decrease in total liver lipids and cholesterol and an increase in liver phospholipids in rats that had been fed a diet containing MCT. Earlier, Leveille, et al. (1967a; 1967b) had shown in rats and in chicks, the effect of MCT on liver cholesterol levels was a function of changes in the liver-plasma cholesterol pool and was influenced by dietary cholesterol levels.

In rats fed a diet without cholesterol, liver fat and cholesterol decreased only slightly while a large decrease in plasma cholesterol lowered the total pool size considerably. Chicks responded to cholesterol-free diets in the opposite manner. The decrease in liver cholesterol observed in chicks was offset by an increase in plasma cholesterol and pool size remained the same. In both species cholesterol-supplemented MCT diets lowered liver fat and cholesterol with little or no effect on plasma levels. Increases in the liver's ability to lengthen fatty acid chains was reported in the chick and in the rat (Levelille, et al., 1967a; Levelille, et al., 1967b; Scheig and Klatskin, 1968). In vitro studies in the chick had shown that MCT feeding increased acetate-1-^{14}C incorporation into CO_2, fatty acids and cholesterol (Leveille, et al., 1967b). Rat liver showed a decreased incorporation of labeled acetate into cholesterol and no change in acetate incorporation into fatty acid after MCT feeding (Leveille, et al., 1967a). In vitro studies of fatty acid synthesis from glucose indicated an increase in liver synthesis of fatty acids (Wiley and Leveille, 1973). Enzyme activities of glucose-6-phospate dehydrogenase plus 6-phosphogluconate

dehydrogenase were increased after MCT feeding although citrate cleavage enzyme and malic enzyme were depressed to a similar extent when compared to levels in livers from lard or coconut oil fed rats.

Lieber, et al. (1967) found that MCT reduced the increase in hepatic triglycerides seen in diets high in ethanol. The same investigators found that alcohol in the profusion media decreased rat liver CO_2 production from labeled chylomicrons or free fatty acids. When the products of the free fatty acid metabolism were compared, almost all of the palmitate-^{14}C label occurred in hepatic lipids while the octanoate-^{14}C label was found primarily in CO_2. Alcohol in the profusion media increased the amount of both free fatty acids incorporated into hepatic lipids but in no case did octanoate incorporation into hepatic triglycerides exceed 40% of the total label recovered.

Adipose Tissue Metabolism

There is little deposition of medium chain fatty acids in adipose tissue although there is a shift toward increased palmitate and a decrease in tissue linoleate levels (Leveille, et al., 1967a; Harkins and Sarett, 1968b; Kaunitz and Johnson, 1968; Tamir, et al., 1969).

This is understandable in view of the rapid hepatic metabolism of medium chain fatty acids previously discussed. The only significant enrichment of depot fat with medium chain fatty acids was reported by Zurier, et al. (1967). By shunting the portal venous blood directly into the systemic circulation the levels of labeled perlargonin were increased in omental fat depots from zero to 12.4% in one month of feeding a diet in which tripelargonin supplied 30% of the total Kcal. Sham-operated control rats fed the same diet showed only a 3.9% increase in adipose tissue pelargonin. An interesting aspect of this study was the fact that octanoate was not incorporated into adipose tissue to the extent that pelargonin was incorporated; neither after feeding nor after the portal-systemic shunt. Devi, et al. (1969) examined the effect of small and medium chain fatty acids on glucose uptake in rat epididymal adipose tissues and found that only pelargonin (nonanoate) significantly increased glucose uptake by the tissue. Thus it seems as if the odd-carbon chain $C_{9:0}$ fatty acid is more readily incorporated into tissue lipids when compared to the even-chain $C_{8:0}$ or $C_{10:0}$ fatty acids even though the tripelargonin is not normally a component of the tissues or the diet.

Fatty acid synthesis is increased in MCT feeding similar to the increase seen in low fat-high carbohydrate diets both in the rat and in the pig (Leveille, et al., 1967a; Allee, et al., 1972; Wiley and Leveille, 1973). Although there is a small increase in the conversion of acetate to CO_2 in adipose tissue of rats fed MCT, pigs do not show an increase in CO_2 production from acetate. In the pig the activities of malic enzyme and citrate cleavage enzyme are increased, while in the rat only increases in glucose-6-phosphate dehydrogenase and 6-phosphogluconate dehydrogenase could be found in adipose tissue.

Plasma

The levels of a number of plasma constituents are changed in MCT feeding. As was mentioned previously, in the rat, MCT-cholesterol-free diets decrease plasma cholesterol, while in the chicken there is little change in plasma cholesterol levels with MCT-cholesterol-free or MCT-cholesterol-supplemented diets (Kaunitz, et al., 1958; Leveille, et al., 1967a; Leveille, et al., 1967b; Harkins and Sarett, 1968b). Total plasma lipids are decreased in the rat with MCT feeding (Leveille, et al., 1967a; Wiley and Leveille, 1973). In the pig, Allee, et al. (1972)

found plasma cholesterol, free fatty acids, as well as plasma glucose decreased in animals fed MCT. Children fed MCT in the treatment of malabsorption were found to have lower plasma cholesterol and slightly elevated triglyceride levels (Tamir, et al., 1969). MCT diets greatly increased blood ketones in the pig and in the rat reflecting their rapid metabolism in the liver. (Allee, et al., 1972; Wiley and Leveille, 1973). In a study of the effect of MCT in meal-fed rats, Theuer (1971) found that the glucose levels were decreased, the levels of non-esterified fatty acids were increased, and ketones, especially acetoacetate, were elevated prior to meal time. After feeding, total ketones rose much more rapidly and glucose and triglyceride levels dropped faster to pre-feeding levels in the animals fed MCT than in controls.

Clinical Applications

As soon as it was recognized that medium chain triglycerides were absorbed and metabolized differently from long chain, conventional fats, their therapeutic usefulness became apparent. MCT is particularly helpful in the management malabsorption disorders. In children, where a major problem is weight maintenance and adequate nutrition for growth when the intestinal absorptive surface

may be severely reduced, MCT is a good source of utilizable kilo-calories (Gracey, et al., 1970). In diseases of the pancreas, especially cystic fibrosis in children, MCT has been used to reduce the steatorrhea associated with fat malabsorption. MCT has also been used in the nutritional management of children and adults with liver diseases, although liver disorders or large portal-systemic shunts may contraindicate use of MCT. Linscheer, et al. (1970) investigated the reported narcotic effect of medium chain fatty acids in the systemic circulation. After administering a test dose (0.5 g per kg of lean body mass) of MCT to cirrhotic patients and controls, it was discovered that octanoate concentrations in the serum of the cirrhotics was two times the concentration of the controls; and the octanoate recovered in the spinal fluid of cirrhotics was elevated four to five times above control values. Although no narcotic effect of the increased octanoate to the brain was evidence in the cirrhotic patients, reports of narcosis in research animals (Clark, 1968) may indicate caution in the use of MCT in the treatment of patients with severe liver disease.

Freund and Weinsier (1966) used an oral MCT test to measure the ketone response in normal and diabetic subjects. A standard oral dose of 25 ml of MCT

produced a reproducible increase in acetone concentration in end-expiratory air in individual subjects, but a dramatic difference in response was seen between controls and diabetics. The mean ketone response of the diabetics was 2 1/2 times greater than the response of the normal subjects. The ketogenic properties of MCT have also been used in the treatment of epilepsy in children (Medical News, 1971). When a diet containing 60% of the total calories as MCT was administered to a number of young epileptics some types of seisures were reduced in number and severity. MCT was also found to be more acceptable to these children than the conventional 3:1 antiketogenic: ketogenic diet.

INTRODUCTION

The 1970 ten-state nutrition survey reported that obesity was a nutritional problem of considerable importance in the United States. Twenty percent of white adult males, 40% of white adult women, and 50% of black adult women surveyed were classified as obese as determined by skinfold thickness (Ten-State Nutrition Survey, 1968-1970). As obesity is a risk factor in the development of a number of serious diseases including cardiovascular disease and diabetes mellitus (Baird, 1969), the treatment and prevention of obesity become important health objectives.

The laboratory rat is a common model used in studies of regulatory and metabolic obesities. Animal studies permit rigid dietary and environmental control. Comparisons of dietary treatments can be made in a large number of genetically controlled situations. Changes in body composition can be monitored accurately.

There have been indications in the literature that increasing the content of fat in isocaloric diets may increase growth and body fat content in growing rats

(Forbes, et al., 1945a; 1946), increase utilization of dietary nitrogen, and decrease the energy expense of diet utilization for growth (Forbes, et al., 1945b). By feeding a diet in which 85% of the Kcal were supplied by fat, Mickelsen, et al. (1955) produced increased weight gain in rats. Other investigators have shown that high fat diets can produce increases in body fat as well as increases in body weight in rats (Peckham, et al, 1962; Schemmel, et al., 1969; Schemmel, et al., 1970a,b; Schemmel, et al., 1972).

A number of investigators have examined body weight gain and fat accretion in rats utilizing different types of fat (Kaunitz, et al., 1958; Leveille, et al., 1967a; Harkins and Sarett, 1968b). Rats fed medium chain triglycerides (MCT) tend to have lower levels of carcass fat (Harkins and Sarett, 1968b), and lighter fat depots (Harkins and Sarett, 1968b; Kaunitz, et al., 1958). Few investigators, however, have looked at the clinical usefulness of MCT in the treatment of nutitional obesity.

The purpose of the present study was to examine the effect of substituting MCT for conventional fats on some of the parameters of dietary obesity in rats fed diets containing 50% (x/x) fat.

METHODS

Selection and Care of Animals

Forty-two male Osborne-Mendel rats from our breeding colony were weaned at 21 days of age and littermates were divided among three groups. The mean weaning weight of the fourteen animals assigned to a group did not differ; 55 grams for each group. The animals were housed in metal, wire-bottomed cages in a laboratory lighted for 12 hours of each 24 and maintained at a temperature of 23 ± 1°C. Food and water were available ad libitum for a period of 12 weeks. Animals were weighed weekly and food intakes were recorded. Food intakes were recorded from the weight of the food cups before and after refilling. Spillage was minimal but it was also weighed at the time of refeeding and subtracted from intake calculations. At 15 weeks of age the animals were sacrificed.

Diet

Three diets (Table 1) containing 50% fat; utilizing either Crisco, corn oil, or MCT as the major source of

Kilocalories (Kcal); were fed to rats as described above. Long chain triglycerides have a caloric value of 9.2 Kcal per gram while Mct yields only 8.3 Kcal per gram (Kaunitz, et al., 1958). Thus the percentage of Kcal supplied by fat was 73% for the Crisco and corn oil-containing diets and 72% for the diet containing MCT. The diets contained 30% protein. A calcium whey protein concentrate was used as it was able to incorporate more oil into the mixture. The calorie:protein diet ratio of the MCT diet, as calculated from Kcal consumed per gram of dietary protein eaten, was 19.6 compared to a value of 20.3 for the Crisco and corn oil diets. The corn oil diet was included as a control of diet consistency, as it could be possible that the consistency of the diet would influence its acceptibility and consumption by the rat. Five percent Crisco was added to each of the oil-containing diets to improve their consistency. The rat requires 25mg. methyl linoleate per day (Farris, 1949). Corn oil was added to the MCT diet at the 3% level to supply this essential fatty acid. The fatty acid composition of the 3 fats (Table 2) were determined by gas chromatography. The fatty acid

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[1]Our laboratory is especially grateful to Dr. V.K. Babayan for communicating his awareness of the calcium whey protein concentrate to Dr. Olaf Mickelsen. We are grateful to both of these men for their encouragement and continued interest in the usefulness of MCT in human diets.

composition of the 3 diets (Table 3) were then calculated from the total fat content of each diet. This explains the presence of long chain fatty acids in the MCT diet. A difference in color was noted among the feces produced by rats fed the three diets. A one week fecal collection based on weight was made for fat analysis. The feces were dried and fat content was determined by methods similar to tissue fat extraction. The fecal collection did not represent individual animals nor a specific period of time so that digestibility factors could not be determined.

Digestible Kcal per gram of diet were calculated from the values of Merrill and Watt (1955). A value of 8.84 digestible Kcal per gram was used for Crisco and corn oil while values of 4.27 Kcal per gram and 4.03 Kcal per gram were used for protein and cornstarch, respectively. Because MCT is easily hydrolyzed and absorbed, no correction was made for digestibility, and a Kcal value of 8.3 per gram of MCT was used for calculation purposes (Kaunitz, et al., 1958).

Body Composition Analyses

Animals were sacrificed and prepared for body composition analyses by the method of Schemmel, et al. (1969). Aliquots of carcass homogenates were analyzed for

moisture, fat, protein, and ash by methods closely following those of Mickelsen and Anderson (1959). Moisture was determined by drying the aliquots for 48 hours in a vacuum oven under high vacuum and at a temperature of 70°C. Fat from the dried residue was then extracted on a Goldfisch apparatus for 7 hours using ethyl ether as the solvent. The dried, fat-free residues were divided for protein and ash determinations. Protein was calculated from total nitrogen as determined by the micro-Kjeldahl method. Ashing was complete after 12 hours at 500°C.

Fat Depot Weights, Total Triglyceride and Fatty Acid Composition

The left inguinal, testicular, and perirenal-retroperitoneal fat depots were removed according to the method of Schemmel, et al. (1970b). Depots were immediately wrapped in pre-weighed foil, weighed, and stored below 0°C for further analysis.

Total triglyceride of each depot was determined by the method of Ostrander and Dugan (1962). All reagents were reduced by one-half and tissues were macerated in an Omnimixer[1]. Measured aliquots were removed for fatty acid analysis as well as total

[1]Ivan Sorvall, Inc., Newtown, Connecticut.

triglyceride determinations. The latter aliquot was placed in a previously tared flask. Solvents were allowed to evaporate overnight under a hood and flasks were dried for one hour at 60°C before final weighing. Solvents from aliquots for fatty acid analysis were evaporated on a rotary evaporator in a 40°C water bath. Methylation was by the method of Karmen, et al. (1963). Samples were incubated overnight at 60-65°C. The following morning 1 ml. distilled water was added to each sample and they were stored under nitrogen below 0°C.

The methyl esters were prepared for gas chromatography by modifications of the method of Burchfield and Storrs (1962) and Karmen, et al. (1963). Four ml. petroleum ether and 1 ml. distilled water were added to the methylation mixture and the petroleum ether layer was collected. This was repeated three times after which the petroleum ether was washed twice with 1 ml. of distilled water. The petroleum ether was evaporated using a hot plate. Nitrogen was bubbled through the solvent throughout the evaporation to prevent oxidation of the unsaturated fatty acids. The methyl esters were diluted approximately 1:5 with nanograde hexane and loaded into a Hewlett-Packard model 402 gas chromatograph; coating, 5% DEGS; support, Chromosorb W; mesh, 80-100; carrier gas,

Helium; rate, 3.5 at 40psi; program, 130-200°C at 5°C/min. Identification of peaks was by retention time of standard mixture.[1] Calibration was by external normalization of corrected peak area. Measurement of peak areas was by height X width-at-1/2 height.

Statistical Analysis

Analysis of variance and covariance were performed on the MSU Control Data Corporation 3600 computer using the MSU Agricultural Experiment Station STAT series. Scheffé confidence intervals were used in analysis of mean values (Scheffé, 1959).

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[1]Sigma Chemical Co., St. Louis, Missouri.

RESULTS AND DISCUSSION

Diet and Kcal Consumption

Rats fed Crisco ate a mean total of 1122 ± 71 grams of diet over the 12 week feeding period; i.e. weaning to 15 weeks of age; while rats fed corn oil or MCT ate 1073 ± 82 grams and 1014 ± 80 grams, respectively, for the same period (Table 4). Corn oil fed animals ate 5% fewer grams than the rats fed Crisco; while rats fed the MCT diet ate 5% less grams than the rats fed corn oil. The difference in mean values as tested by Scheffé confidence intervals indicated that the Crisco and MCT consumption values were significantly different ($p < 0.025$, Table 4a). Wiley and Leveille (1973) reported a similar percent decrease in food intake in rats fed diets containing 14% (w/w) corn oil or MCT when compared to diets containing lard or coconut oil. Whether these reductions in food intake were a function of food preference, or in the case of the MCT diet, a direct effect of the MCT on appetite because of the increase in blood ketones (Wiley and Leveille, 1973) is not known.

The caloric density of the diets varied due to the variation in caloric density of the constituent fats. The Crisco and the corn oil diets contained 6.1 digestible Kcal per gram, while the diet containing the MCT had a calculated 5.9 digestible Kcal per gram (Table 4). When food intakes were adjusted for the difference in digestible Kcal per gram of diet the gap in intake between the rats fed MCT and those fed Crisco or corn oil widened. The average Kcal intake of the MCT-fed rats was 5985 ± 474 Kcal for the 12 weeks versus intake values of 6842 ± 433 and 6544 ± 498 Kcal for rats fed Crisco or corn oil for the same period (Table 4). The energy intake of rats fed MCT was significantly lower over the 12 week period ($p < 0.025$, Table 4a).

Although no determinations of fat absorption could be made from the fecal collection made; fat content of the feces varied considerably. Feces from animals fed Crisco contained 37.6 grams of fat per 100 grams of dry fecal weight. Feces from corn oil fed animals contained 14.8% fat and fecal fat was 5.7% in rats fed MCT.

It was recognized that variation in energy intake would tend to compound the effects of diet upon the growth rate, if indeed, there were any effects. Ideally it would have been beneficial to regulate food intake so that diet

groups consumed the same amount of Kcal during the feeding period. One problem associated with regulation of food intake in the rat has been that food restriction alters the rat's normal "nibbling" pattern and produces a "meal-eater". Meal-eating in the rat has been shown to increase food efficiency, alter gastro-intestinal tract size, increase glucose utilization, and increase fatty acid synthesis in adipose tissue (Leveille, 1972). In view of these major metabolic alterations it seemed more desirable to follow an ad libitum feeding regime and risk the variation in food and caloric intakes.

Growth Rates

In general, growth rates for the Crisco fed, corn oil fed, and MCT fed rats reflected the total energy consumed (Figure 1). The mean weaning weight of all three groups was 55 grams. Rats fed the Crisco diet attained a final weight of 480 grams, while rats fed corn oil reached a final weight of 454 grams. There was no significant difference in these two rates of gain and both groups utilized 16.6 Kcal per gram of weight gained after weaning. Rats fed MCT weighed only 369 grams at the end of twelve weeks and utilized 20.3 Kcal per gram of weight gained. The MCT fed rats gained weight at a rate

significantly lower than either the Crisco or the corn oil fed animals ($p < 0.005$). Other investigators have indicated that medium chain triglycerides may not be as efficient in producing weight gain as longer chain triglycerides. Harkins and Sarett (1968b) reported that rats fed a diet containing 21% MCT (w/w) for 4 weeks utilized 8.7 Kcal per gram of weight gained compared to 8.2 Kcal per gram when the diet contained corn oil. These two diets produced an 8 gram difference in mean body weight between the two groups. After a period of weight maintenance by restricting food intake, Kaunitz, et al. (1958) reported a 1 Kcal increase in requirement per gram of subsequent weight gain in rats fed MCT versus those fed long chain triglycerides.

Analysis of covariance was used in an attempt to investigate the relative significance of weaning weight, food intake, Kcal intake, and diet on final body weight. By statistically restricting covariates to zero it was possible to test individual factors to indicate if they had a significant effect upon final body weight. When the diets were analyzed in this fashion, with the difference in food and Kcal intake between the diets statistically nullified, there was no significant effect of the diet on final body weight ($p < 0.102$). The variation in food intake

($p < 0.012$) and kcal intake ($p < 0.010$) were much more significant in explaining final body weight. Initial body weight had a significant effect ($p < 0.001$) on final body weight, indicating that if diet and intakes are equal for each animal, the heaviest rats at weaning will be the heaviest rats at sacrifice.

Simple correlation coefficients indicated significant positive correlations between final body weight and diet, as well as food and kcal intake (Table 10).

Body Composition

The greatest difference in body composition among rats fed Crisco, corn oil or MCT was in the amount of body fat. The mean total fat in grams of the Crisco, corn oil, and MCT fed rats were 130.1 ± 29.9, 109.2 ± 21.1, and 61.3 ± 13.7 respectively (Table 5). This means MCT fed rats had 50% less fat in their bodies than did rats fed Crisco or corn oil. Rats fed MCT had less moisture and protein in their bodies than did rats fed Crisco or corn oil (Table 5). This is reflected by their lower body weight. Only ash content showed no difference among rats fed the different diets. Diet composition, obesity or even severe undernutrition have little effect on body ash if animals of the same age and sex are analyzed

(Schemmel, et al., 1969; Pratt and McCance, 1960). Because the MCT fed rats were also lower in total carcass weight, the body composition values were expressed as grams per 100 grams of body weight (Table 6). The carcasses of the Crisco and corn oil fed rats contained a mean value of 26.9 ± 4.5 and 23.9 ± 2.9 grams of fat per 100 grams of body weight. The MCT-fed rats averaged only 16 ± 2.8 grams of every 100 grams of body weight as fat.

Energy utilization was calculated from Kcal consumed per gram of fat gained after weaning. Body composition of male weanling Osborne-Mendel rats as reported by Schemmel, et al. (1969) were subtracted from total body fat of the animals in the present study. Animals receiving Crisco or corn oil diets utilized, respectively, 54 and 62 Kcal per gram of fat gained after weaning; while MCT fed rats utilized 105 Kcal per gram of body fat gained. In a study of the effects of diet and strain in the production of obesity in rats, Schemmel, et al. (1970a) reported that, although ration and strain influenced weight gain equally, the composition of the ration seemed to have more influence on body fat accretion.

Again, the variation in food and Kcal intake could have affected body composition, but it was possible

to account for this statistically. The analysis of covariance routine used allowed for the restriction of designated covariates to zero. Thus it was possible to analyze the covariance of diet and body composition without the effects of food intake, or the covariance of food and energy intakes with body composition ignoring the difference in diet. In this manner it was statistically possible to examine individual factors which could not be separated in the experimental design. Diet, food intake and kcal intake had no statistically significant effect on body composition when these factors were examined individually. Initial body weight was a significant influence on moisture ($p < 0.078$), fat ($p < 0.053$), and protein ($p < 0.098$), but not on ash, when all other factors were excluded. The fact that diet and intake had no statistical significance in determining body composition could merely indicate that diet differences or intake variations alone could not account for changes in body composition; but combinations of these factors may be important.

Percent moisture and protein showed high negative correlations with final body weight while percent body fat had a high positive correlation (Table 11). The same is true when food and kcal intakes were examined.

The relative amount of protein showed negative correlations to food and Kcal intake. It is interesting to note the high negative correlation of percent body moisture to percent body fat (-0.989) which indicates why body moisture is often used to estimate lean body mass.

Fat Depot Weights

Fat depot weights also varied among the three diet groups. The mean inguinal fat depot weight in the MCT fed rats weighed 7.8 ± 2.4 grams while the same depot weighed an average of 15.7 ± 5.3 grams and 12.3 ± 3.4 grams in the Crisco and corn oil-fed animals, respectively (Table 7). The decrease in the inguinal depot weight of the MCT-fed animals was only significant when compared to the depot weight of the Crisco-fed rats (Table 7a). A high standard deviation was seen in the inguinal fat depot weight in individual animals. The standard deviation of the depot weight for rats fed Crisco diets was 33% of the mean value (Table 7). It does not seem possible that this variability was caused by the dissection technique. Schemmel, et al. (1970b) reported only minimal differences in right and left depot weights removed by the technique used in the present study. The inguinal fat depot also was the heaviest fat depot of the 3 weighed in

rats of all three diet groups. Shier and Schemmel (in press) reported that inguinal fat depots tended to be greater in weight than the testicular or perirenal-retroperitoneal depots until the rats reached approximately 20 weeks of age; at which time the perirenal-retroperitoneal depot weight approached that of the inguinal depot and surpassed the weight of the inguinal depot in older rats (Schemmel, et al., 1970b). The amount of subcutaneous fat seemed to be more variable than the amount of intraabdominal fat. The testicular and perirenal-retroperitoneal fat depots gained less weight in rats fed MCT than in rats fed corn oil or Crisco diets. This is likely to be associated with the fact that development of these depots is delayed. Mean weight of the testicular fat depots of MCT fed rats was 2.4 ± 0.4 grams; which was significantly lower ($p < 0.025$) when com-

rats which averaged 8.0 ± 2.6 and 5.4 ± 1.6 grams in weight, respectively. The average weights of the perirenal-retroperitoneal depots were MCT, 3.2 ± 1.1 grams; Crisco, 9.2 ± 2.2 grams; and corn oil, 7.0 ± 2.2 grams, respectively. Mean weight of the perirenal-retroperitoneal depots was also significantly lower in the MCT fed animals

($p < 0.025$) when compared to Crisco or corn-oil fed rats. Even when depot weights were expressed as grams per 100 grams of body weight there was a 33% decrease in the relative weight of the inguinal depot of the MCT-fed rats when compared to the same depot of the Crisco-fed rats (Table 7). The relative weights of the other two depots decreased by over 50% when the values, as percent of body weight, were compared for these two groups. Kaunitz, et al. (1958) had reported that testicular fat depots weighed 0.84 grams per 100 grams of body weight in male Sherman rats fed MCT compared to values of 1.05 grams per 100 grams of body weight for rats fed long chain triglycerides. Harkins and Sarett, (1968b) reported a 2 gram difference between the weights of the epididymal fat depot in MCT and corn oil-fed animals which represented a decrease of 0.3 grams per 100 grams of body weight in the depot of the MCT-fed animals.

Fat depot weights were the only parameters analyzed by restricted covariance in which the diet alone significantly affected the variation in depot weights (inguinal, $p < 0.067$; testicular, $p < 0.083$; perirenal-retroperitoneal, $p < 0.079$). Initial body weight had no effect on fat depot weights when all other factors were

zero. Variation in food and Kcal intakes had no effect on testicular depot weights, while the inguinal and perirenal-retroperitoneal depot weights were affected significantly ($p < 0.03$; $p < 0.08$). All three fat depots showed high positive correlations to final body weight as well as to food and Kcal intake (Table 12).

Fat Depot Triglyceride Content

There was no significant difference in the triglyceride content of the inguinal, testicular, and perirenal-retroperitoneal fat depots of rats fed Crisco, corn oil, or MCT when similar depots were compared among the three groups (Table 8, 8a). There did seem to be a tendency for the intraabdominal depots to contain more fat per 100 grams of tissue (Table 8). Shier and Schemmel (in press) reported less triglyceride per gram of tissue in inguinal depots when compared to testicular or perirenal-retroperitoneal depots, as well as an increase in total triglyceride content of the intraabdominal fat depots with age until values over 90% were reached. Subcutaneous depots never reached triglyceride levels of 90% of tissue weight.

Fat Depot Fatty Acid Composition

Borgstrom (1955) found that medium chain fatty acids were rapidly cleared by the liver and a concentration of 4.7 mg% decanoic acid in the portal blood was reduced to 1.5 mg% in vena cava blood. Leveille, et al. (1967a) found little medium chain fatty acids in the peripheral circulation of rats fed MCT. The review of literature pointed out that other investigators have found little incorporation of MCT into adipose tissue lipids (Leveille, et al., 1967a; Harkins and Sarett, 1968b; Kaunitz and Johnson, 1968; Tamir, et al., 1969). The present study confirmed this fact. Even though 53% of the dietary Kcal were supplied by C_8 and C_{10} fatty acids, and these fatty acids were fed during the period of greatest body growth, only a small increase occurred in these components of adipose tissue (Table 9). It seems as if the relative increase in incorporation of medium chain fatty acids is not easily altered by increasing the dietary level of these fatty acids. In this study where the dietary intake of MCT was very high, as well as in other studies where MCT made up a relatively lower proportion of dietary Kcal (Leveille, et al., 1967a; Harkins and Sarett, 1968b; Kaunitz and Johnson, 1968), there has been a shift toward similar increases of MCT in the fat pads of rodents.

SUGGESTION FOR FURTHER STUDY

Plasma Free Fatty Acids and Triglycerides

One of the important properties of medium chain fatty acids is their rapid and almost complete oxidation by the liver. When the liver's ability to oxidize MCFA is impaired narcosis may be produced by increased plasma free fatty acids entering the spinal fluid and the brain (Linscheer, et al., 1970). Further study on the metabolism of MCT should include post absorption determination of the capacity of the normal liver to clear these free fatty acids from the blood during MCT administration.

Food Preference

The Kcal intake of the MCT diet was considerably lower than either of the other two diets. Whether this decrease was due to a decreased rat preference for the MCT diet, or a direct effect of the MCT diet on appetite should be investiaged further.

Fat Digestibility

Determinations of fat digestibility were not conducted during the present study. The fecal fat content of

the rats fed Crisco, corn oil and MCT diets varied widely. Further study should be done to examine the digestibility of these 3 fats at the high level used in the present study.

Fat Soluble Vitamin Absorption

Relatively little is known of the normal vehicle for the absorption of fat soluble vitamins. The question was raised as to the changes in absorption of nutrients that require fat as an absorption vehicle that might occur during MCT absorption. If medium chain triglyceride absorption differs from normal fat absorption, are the fat-soluble vitamins affected by this change? Kaunitz, et al. (1968) reported less severe testicular damage in vitamin E deficient rats fed MCT when they were compared to deficient rats without MCT in the diet. While investigations are being conducted into the mechanisms of fat-soluble vitamin absorption it must be remembered that all fats are not absorbed in like manner.

Effects on Human Obesity

Animal studies can only give an indication of what may be applied to human situations. The decreased caloric efficiency of MCT and its influence in producing smaller

body weight gains and decreased body fat accretion should be investigated in human subjects.

Clinical use of MCT oils is already widespread as indicated in the literature review. Food products have been developed incorporating MCT oil in place of conventional fats (Schizas, et al., 1967). A clinical study of the effect of the substitution to MCT in human diets would help to establish the effectiveness of MCT as an aid in the treatment of obesity.

CONCLUSIONS

The decreased caloric value of medium chain triglycerides (MCT) decreased the caloric density of the diet containing this fat. Combined with the fact that food intake was lower in the rats fed the MCT diet, their total Kcal intake was significantly lower than the animals fed Crisco or corn oil-containing diets.

Growth rates were similar for the Crisco and corn oil-fed rats over the 12 week feeding period. Rats fed MCT grew slower and reached an average final body weight of 369±20 grams, which was significantly lower than final body weights of animals fed either Crisco or corn oil. Crisco fed animals attained final weights of 480±49 grams while rats fed corn oil weighed 454±36 grams at the end of 12 weeks.

Body composition analyses showed that absolute and relative body fat were decreased in animals fed MCT-diets. The absolute and relative weights of the inguinal testicular and perirenal fat depots were also lower in MCT fed animals while no significant differences were found in

triglyceride content of the depots among animals of the three diets. Inguinal fat depot fatty acid composition showed a slight increase in C_8 and C_{10} fatty acids.

The diet containing 50% MCT did not contribute to the obesity normally found in rats fed a high fat diet. Animals fed MCT contained only 16.5±2.8 grams of fat per 100 grams of body weight, while Crisco-fed rats had 26.9±4.5 grams of fat for every 100 grams body weight and corn oil-fed rats contained 23.9±2.9 grams of fat per 100 grams body weight. It seems that much of this effect could be attributed to the decreased caloric intake of the rats fed the MCT diet. There was, however, a difference in the utilization of dietary Kcal for weight gain among the three diets examined. Rats fed the MCT diet utilized 20.3 Kcal per gram of weight gained while Crisco and corn-oil fed animals utilized 16.6 Kcal per gram of weight gain. This data indicates that MCT may be beneficial in increasing the expense of energy utilization of high fat diets and preventing some of the body weight gain and increase in body fat found in animals raised on such diets.

TABLE 1.--Composition of Rations.

Ingredients	Diets (%)		
	Crisco	Corn Oil	MCT
Fat: Crisco	50.0	5.0	5.0
Corn oil	-	45.0	3.0
MCT[a]	-	-	42.0
Protein[b]	30.0	30.0	30.0
Minerals[c]	5.0	5.0	5.0
Vitamins[d]	1.0	1.0	1.0
Fiber[e]	2.0	2.0	2.0
Antibiotics[f]	0.01	0.01	0.01
Liver Powder	2.0	2.0	2.0
Corn Starch	9.99	9.99	9.99
Kcalories/gram[g]	6.1	6.1	5.9

[a]Purchased from PVO International, Chemical Specialty Div., Boonton, New Jersey.

[b]Protolac, purchased from Borden Industrial Foods Div., New Ulm, Minnesota.

[c]Wesson modified Osborne-Mendel salt mix, purchased from General Biochemicals, Chagrin Falls, Ohio.

[d]A.O.A.C. Vitamin mix purchased from General Biochemicals, Chagrin Falls, Ohio; supplied the following (g/kg of diet): p-aminobenzoic acid, 0.10; B_{12}, (0.1% in mannitol), 0.03; biotin, 0.0004; Calcium pantothenate, 0.04; choline, free base, 2.0, folic acid, 0.002; l-inositol, 0.10, menadione, 0.005; Niacin, 0.04; pyridoxine HCl, 0.04; riboflavin, 0.008; thiamine HCl, 0.005; dextrose, anhydrous, q.s.; (units/kg) Vitamin A, 20,000.00; Vitamin D_2, 2,000.00; Vitamin E Acetate, 100.00.

[e]Cellulose type, purchased from General Biochemicals, Chagrin Falls, Ohio.

[f]Aureomycin (chlortetracycline-HCl, 972 g/mg), generously donated by Lederle Laboratory, American Cyanamid Co., Princeton, New Jersey.

[g] Merrill A. L. and B. K. Watt, 1955, Energy Value of Foods Basis and Derivation. Agricultural Handbook N. 74. Agricultural Research Service U.S.D.A., Washington, D.C.

TABLE 2.--Fatty acid composition of Crisco, corn oil, and MCT. (Values are expressed as percentage of the total fatty acids in the fat)

Fatty Acids	Fats[a]		
	Crisco	Corn Oil	MCT
8:0	-	-	72.0
10:0	-	-	28.0
12:0	-	-	-
14:0	-	-	-
16:0	18.2	9.9	-
16:1	-	-	-
18:0	12.4	1.6	-
18:1	41.5	21.2	-
18:2	27.5	66.2	-
18:3	trace	trace	-
20:0	-	trace	-
20:4	-	-	-

[a]Mean value of samples done in duplicate.

TABLE 3.--Fatty acid composition of Crisco, corn oil, and MCT diets. (Values are expressed as percentage of the total fatty acids in each diet)

Fatty Acids	Diet[a]		
	Crisco	Corn Oil	MCT
8:0	-	-	60.5
10:0	-	-	23.5
12:0	-	-	-
14:0	-	-	-
16:0	18.2	10.9	2.4
16:1	-	-	-
18:0	12.4	2.6	1.3
18:1	41.5	23.2	5.4
18:2	27.5	62.4	6.7
18:3	trace	trace	-
20.0	-	trace	-
20:4	-	-	-

[a]Values calculated from fatty acid composition of the fat and total fat composition of the diet.

TABLE 4.--Dietary intake of male Osborne - Mendel rats fed high fat diets containing Crisco, corn oil, or MCT for 12 weeks; and conversion factors for determining energy and Kcal:protein ratio in the rations.

Diet	Kcal/g.diet[a]	Kcal:Protein[b]	Diet g.	Intake Kcal.
Crisco (14)[c]	6.1	20.3	1122±71[d]	6842±433
Corn oil (14)	6.1	20.3	1073±82	6544±498
MCT (13)	5.9	19.6	1014±80	5985±474

[a]See text for explanation of calculations.

[b]Kcal consumed per gram of protein consumed

[c]Number of rats

[d]Mean ± standard deviation

TABLE 4a.--Scheffé confidence intervals (0.975) for all possible contrasts of mean differences in total diet consumption and total Kcalorie consumption.

	Scheffe Confidence Intervals	
Diets	Diet Intake g	Dietary Intake Kcal.
Crisco vs. Corn oil	48±84[a]	297±512
Crisco vs. MCT	107±86*	856±522*
Corn oil vs. MCT	58±86	559±522*

[a]$\bar{\mu}_1 - \bar{\mu}_2 \pm S\sqrt{MS_e(1/n+1/n)}$

*Significant at $p < 0.025$

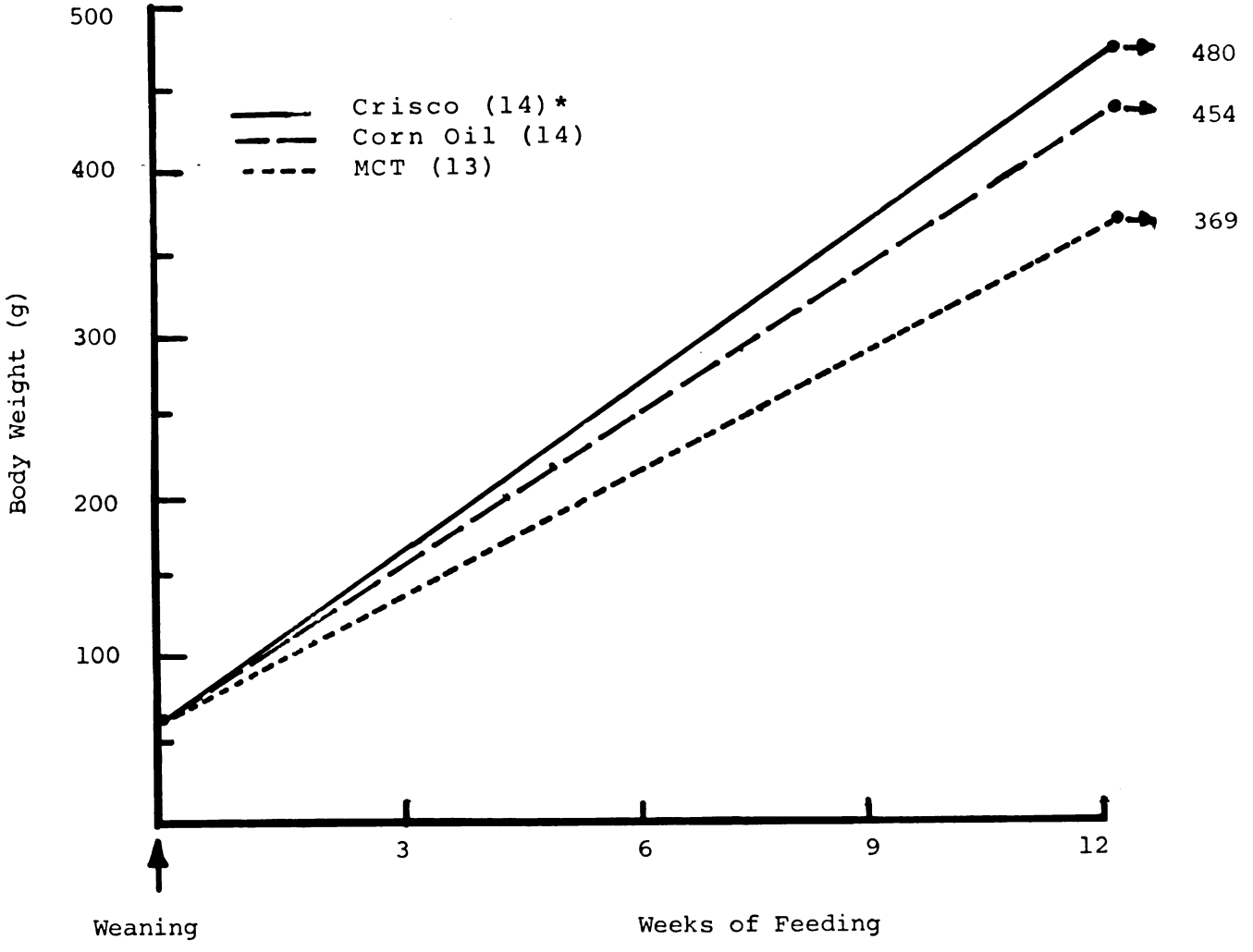

Figure 1.--Mean growth rates of male Osborne-Mendel rats fed high fat diets containing Crisco, corn oil or MCT for 12 weeks from the time of weaning at 21 days of age.

*Number of animals.

TABLE 5.--Absolute body composition of Osborne-Mendel male rats fed high fat diets containing Crisco, corn oil, or MCT for 12 weeks.

Diet	Body Composition				
	Carcass[a] g.	Moisture g.	Fat g.	Protein g.	Ash g.
Crisco (6)[b]	480.4±49.1[c]	253.0±22.2	130.1±29.9	83.5±5.6	11.0±0.3
Corn Oil (6)	454.5±36.3	245.3±13.4	109.2±21.1	84.5±5.0	11.5±0.5
MCT (6)	369.6±20.4	221.2± 4.1	61.3±13.7	74.8±2.4	11.1±0.6

[a] Carcass wt. = live weight - weight of G.I. contents

[b] Number of rats in diet group

[c] Mean ± standard deviation

TABLE 5a.--Scheffé confidence intervals (0.975) for all possible contrasts of mean differences in body composition.

Diet	Scheffé Confidence Intervals				
	Carcass	Moisture	Fat	Protein	Ash
Crisco vs. Corn oil	25.9±65.4[a]	7.7±26.7*	20.9±39.6*	1.0±8.0*	0.5±0.8
Crisco vs. MCT	110.8±65.4*	31.8±26.7*	68.7±39.6*	8.6±8.0*	0.1±0.8
Corn oil vs. MCT	84.9±65.4*	24.1±26.7	47.9±39.6*	9.6±8.0*	0.4±0.8

[a] $\bar{\mu}_1 \pm \bar{\mu}_2 \; S \sqrt{MS_e \; (1/n+1/n)}$

* Significant at $p < 0.025$

TABLE 6.--Relative body composition of Osborne-Mendel male rats fed high fat diets containing Crisco, corn oil, or MCT for 12 weeks.

Diet	Body Composition			
	Moisture g/100g BW[a]	Fat g/100g BW	Protein g/100g dry FFT[b]	Ash g/100g dry FFT
Crisco (6)[c]	52.9±3.4[d]	26.9±4.5	85.9±2.0	11.4±0.8
Corn oil (6)	54.1±2.3	23.9±2.9	84.5±1.6	11.5±0.3
MCT (6)	60.0±2.3	16.5±2.8	86.1±1.7	12.8±0.6

[a]Grams per 100 grams of body weight

[b]Grams per 100 grams of dry, fat-free tissue

[c]Number of rats in each diet group

[d]Mean ± standard deviation.

TABLE 6a.--Scheffé confidence intervals (0.975) for all possible contrasts of mean differences in body composition.

Diets	Scheffé Confidence Intervals			
	Moisture	Fat	Protein	Ash
Crisco vs. Corn oil	1.2±4.8[a]	3.0±6.1*	1.4±3.1	0.1±1.1*
Crisco vs. MCT	7.1±4.8*	10.4±6.1*	0.2±3.1	1.4±1.1*
Corn oil vs. MCT	5.9±4.8*	7.4±6.1*	1.6±3.1	1.3±1.1*

[a]$\bar{\mu}_1 \pm \bar{\mu}_2 \quad S\sqrt{MS_e(1/n+1/n)}$

*Significant at $p < 0.025$

TABLE 7.--Relative inguinal, testicular, and perirenal-retroperitoneal fat depot weights of Osborne-Mendel male rats fed high fat diets containing Crisco, corn oil, or MCT for 12 weeks.

	Fat Depots					
	Inguinal		Testicular		Perirenal-Retroperitoneal	
Diet	g[a]	g/100g BW[b]	g	g/100g BW	g	g/100g BW
Crisco (8)[d]	15.7±5.3[c]	3.3	8.0±2.6	1.7	9.2±2.2	1.9
Corn oil (8)	12.3±3.4	2.7	5.4±1.6	1.2	7.0±2.2	1.5
MCT (7)	7.8±2.4	2.2	2.4±0.4	0.6	3.2±1.1	0.9

[a] Grams

[b] Grams per 100 grams of body weight

[c] Mean ± standard deviation

[d] Number of rats

TABLE 7a.--Scheffé confidence intervals (0.975) for all possible contrasts of mean differences in fat depot weights (grams).

	Scheffé Confidence Intervals		
Diets Compared	Inguinal	Testicular	Perirenal-Retroperitoneal
Crisco vs. Corn oil	3.4±5.9[a]	2.6±2.7	2.3±2.9
Crisco vs. MCT	7.9±6.1*	5.6±2.8*	6.0±3.0*
Corn oil vs. MCT	4.5±6.1	3.1±2.8*	3.8±3.0*

[a] $\bar{\mu}_1 - \bar{\mu}_2 \pm S\sqrt{MS_e(1/n+1/n)}$

* Significant at $p < 0.025$

TABLE 8.--Relative weight of triglyceride in inguinal, testicular, and perirenal-retroperitoneal fat depots of male Osborne-Mendel rats fed high fat diets containing Crisco, corn oil, or MCT for 12 weeks.

	Fat Depot		
	Inguinal g/100g[a]	Testicular g/100g	Perirenal-Retroperitoneal g/100g
Crisco (8)[b]	78.6±5.4[c]	88.7±3.0	88.6±3.2
Corn Oil (8)	75.2±3.0	89.6±4.3	87.3±3.2
MCT (7)	72.5±3.0	83.6±5.4	84.7±3.4

[a]Grams per 100 grams of depot weight

[b]Number of rats

[c]Mean ± standard deviation

TABLE 8a.--Scheffé confidence intervals (0.975) for all possible contrasts of mean differences of relative weight of triglyceride in fat depots.

	Scheffé Confidence Intervals		
Diets	Inguinal	Testicular	Perirenal-Retroperitoneal
Crisco vs. Corn oil	3.4±6.3[a]	0.9±6.6	1.3±4.8
Crisco vs. MCT	6.1±6.3	5.1±6.9	3.9±5.0
Corn oil vs. MCT	2.7±6.5	6.0±7.0	2.6±5.0

[a]$\bar{\mu}_1 - \bar{\mu}_2 \pm S\sqrt{MS_e(1/n+1/n)}$

TABLE 9.--Mean fatty acid composition of inguinal fat depot of male Osborne-Mendel rats fed high fat diets containing Crisco, corn oil, or MCT. (Values are expressed as percent of total fatty acids.)

	Diet		
Fatty Acid	Crisco (8)[a]	Corn oil (8)	MCT (7)
8:0	-	-	< 1
10:0	-	-	2.0
12:0	trace	trace	< 1
14:0	< 1	< 1	< 1
16:0	3.7	3.5	6.7
16:1	2.0	1.1	3.7
18:0	6.7	3.1	7.2
18:1	53.1	34.7	46.1
18:2	33.7	57.2	32.4
18:3	< 1	< 1	< 1
20:0	trace	trace	trace
20:4	trace	trace	trace

[a]Number of depots

TABLE 10.--Simple correlation coefficients for initial weight, food intake, calorie intake, diet and final weight.

	Final wt.	Initial wt.	Food intake	Kcal intake	Diet	Code
	1.000					
Initial weight	0.312*	1.000				
Food intake	0.684*	0.018	1.000			
Calorie intake	0.751*	0.027	0.988*	1.000		
diet	0.689*	0.031	0.501*	0.604*	1.000	
code	0.574*	0.063	0.264	0.385	0.481	1.000

*Significant at $p < 0.01$

TABLE 11.--Simple correlation coefficients for initial weight, food intake, Kcal intake, diet, final weight and percent body composition.

	Final wt.	Initial wt.	Food intake	Kcal intake	Moisture	Fat	Protein	Ash	Diet	code
	1.000									
Initial wt.	0.115	1.000								
Food intake	0.755*	-0.269	1.000							
Caloric intake	0.810*	-0.258	0.989*	1.000						
Moisture	-0.878*	-0.094	-0.706*	-0.762	1.000					
Fat	0.910*	0.077	0.743*	0.796*	-0.989*	1.000				
Protein	-0.886*	-0.037	-0.781*	-0.824*	0.749*	-0.771*	1.000			
Ash	-0.262	0.011	-0.348	-0.351	0.239	-0.221	0.289	1.000		
diet	0.784*	-0.135	0.619*	0.702*	-0.732*	0.784	-0.683*	-0.049	1.000	
code	0.586*	-0.040	0.383	0.490	-0.606*	0.559	-0.614	-0.362	0.500	1.000

*Significant at $p < 0.01$

TABLE 12.--Simple correlation coefficients for initial weight, food intake, Kcal intake, diet, final weight, and weight of the inguinal (ing), testicular (test), and perirenal-retroperitoneal (peri) fat depots.

code	final wt.	initial wt.	food intake	Kcal intake	ing	test	peri	diet	code
	1.000*								
final wt.	0.374	1.000							
initial wt.	0.642*	0.179	1.000						
food intake	0.724*	0.198	0.987	1.000					
calorie intake	0.892*	0.215	0.562*	0.624*	1.000				
ing	0.784*	0.051	0.487	0.571*	0.884*	1.000			
test	0.886*	0.162	0.549*	0.637*	0.902*	0.892*	1.000		
peri	0.667*	0.160	0.419	0.533*	0.650*	0.792*	0.798*	1.000	
diet	0.605*	0.150	0.180	0.308	0.350	0.408	0.475	0.465	1.000

*Significant at $p < 0.01$

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