Ready absorption of medium chain triglyceride in the steatorrhoea syndrome

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The daily diet in England contains 60 to 100 g. of fat, consisting mainly of triglycerides with fatty acid radicals of more than 10 carbon atoms and providing 25 to 40% of the calorie requirements. In an average hospital diet these include about 40% oleic acid, 20 to 25% palmitic acid, and 10 to 12% stearic acid; this composition is similar to that of the average diet of the population (Osborn and Ohlson, 1963; Smits and Wilding, 1965). Long chain fatty acids are not well absorbed in disorders associated with steatorrhoea (Hoagland and Snider, 1943) although the unsaturated compounds are better assimilated than the saturated (Weijers and van de Kamer, 1953). Malabsorption increases with increase in chain length, particularly in conditions with cellular dysfunction of the intestinal mucosa such as coeliac disease and to a lesser degree in pancreatic disease where intraluminal lipolysis is defective (van de Kamer and Weijers, 1961; Fernandes, van de Kamer, and Weijers, 1962).

The replacement of dietary long chain triglycerides by medium chain triglycerides, i.e., in which fatty acids have 8 to 10 carbon atoms, has been studied in a number of clinical conditions (Fernandes, van de Kamer, and Weijers, 1955; Blomstrand, Thorn, and Ahrens, 1958; Hashim, Babayan, and Van Itallie, 1962; Hashim, Roholt, and Van Itallie, 1962; Iber, Hardoon, and Sangree, 1963; Hashim, Roholt, Babayan, and Van Itallie, 1964b; Holt, 1964; Cancio and Menéndez-Corrada, 1964; Pinter, McCracken, Lamar, and Goldsmith, 1964; Holt, Hashim, and Van Itallie, 1965; Kuo and Huang, 1965; Winawer, Broitman, Wolochow, Osborne and Zamcheck, 1966; Zurier, Campbell, Hashim, and Van Itallie, 1966).

This paper reports our findings on the effect of medium chain triglycerides on the daily faecal fat output of six ill patients with steatorrhoea.

MATERIALS AND METHODS

Of the six patients studied, two had coeliac disease confirmed by the accepted diagnostic criteria, including flat jejunal biopsy, abnormal small bowel barium radio-

graphs, etc. Case 3 had extensive diffuse regional enteritis involving most of the small bowel shown radiologically and later confirmed at necropsy, while case 4 had extensive small bowel resection. The fifth case had pancreatic insufficiency confirmed by the secretin test and by examination of the pancreas at laparotomy. The sixth patient had had a total gastrectomy for gastric carcinoma. All were severely ill and confined to bed.

DIET The medium chain triglyceride used was a fractionated coconut oil with a melting point about zero °C. and an iodine value of less than one. Gas chromatographic analyses of the fatty acid component are given in Table I. It is resistant to oxidation and does not easily become rancid. It is more easily miscible with water than long chain triglyceride but unless kept sterile and at a low temperature when mixed with water it tends to ferment owing to bacterial and fungal invasion.

TABLE I
PERCENTAGE FATTY ACID COMPOSITION OF MEDIUM CHAIN TRIGLYCERIDE¹

	Acid	Percentage
C6	Caproic	1
C8	Caprylic	35.8
C10	Capric	55.3
Others (mainly C12)		8.3

¹GLC on 15% Apiezon L. at 155°C.; Pye Argon chromatograph

The test diet contained medium chain triglyceride 110 g., carbohydrate 300 g. (as glucose 250 g. and lactose 50 g. contained in Prosol), protein 125 g. as contained in Prosol, made up to 1.2 to 1.5 litres with water and providing approximately 2,750 calories per day. Prosol contained 1% long chain triglyceride (oleic acid 32%, palmitic acid 25%, stearic acid 15%, and myristic acid 11%) and provided essential minerals and vitamins. Between 50 and 65% of the liquid diet was consumed by the patients during the test period.

Twenty-four-hour faecal collections were diluted to 1,000 ml. and homogenized in an MSE blender and 10 ml. aliquots taken for fat analysis (van de Kamer, ten Bokkel Huinink, and Weijers, 1949) and 20 ml. aliquots for gas chromatography. Faecal fats are reported as three-day running means. Food samples were ground in

a roller mill for several hours, warmed, and homogenized to unit volumes. Recoveries of added medium chain triglyceride to faeces and food showed that van de Kamer's method was satisfactory for determining both medium and long chain triglycerides.

Samples of food and faeces for gas chromatography were saponified and the fats extracted with petroleum ether and absorbed on to alumina after hydrolysis to the free acids: methylation was then achieved with methanolic hydrochloric acid at 37°C. overnight. The methyl esters were analysed with a Pye Argon chromatograph using a 4 foot 15% apiezon L column at 197°C. for long chain esters and 155°C. for medium chain esters. Automatic electronic peak integration was used by means of a digital punch out integrater (Gas chromatography Limited I.E. 165) (Smits, Wilding, and Cooke, 1968).

TEST PROCEDURE In all patients, basal studies were conducted on a normal hospital diet. In three, medium chain triglyceride (40-60 g. daily) was first added to the normal diet for a period of seven to 10 days. In the other three patients this stage was omitted and all patients received the liquid synthetic diet for seven to 10 days when normal diet was resumed except in case 2 to whom a gluten-free diet was given.

RESULTS

The results are summarized in Table II. A typical example of the effect of replacing normal dietary fat by medium chain triglyceride is shown in Figure 1.

CASE 1 Adult coeliac disease, male, storeman, aged 53. Eight-year history with megaloblastic anaemia, impaired B₁₂ absorption (Glass, Boyd, Gellin, and Stephanson,

TABLE II
SUMMARY OF RESULTS SHOWING RANGE AND MEAN OF FAECAL FAT EXCRETION ON NORMAL HOSPITAL AND ON MEDIUM CHAIN TRIGLYCERIDE DIETS¹

Case No.	Diagnosis	Normal Diet		Medium Chain Triglyceride	
		Range	Mean	Range	Mean
1	Coeliac disease	5.8 to 20.0	11.8	1.5 to 6.4	3.2
2	Coeliac disease	17.5 to 42.4	29.7	2.3 to 10.2	4.8
3	Regional enteritis	12.3 to 23.2	20.3	2.0 to 7.2	3.7
4	Massive intestinal resection	11.3 to 20.2	14.7	3.0 to 8.9	5.1
5	Chronic pancreatitis	33.3 to 48.0	42.4	3.0 to 25.3	10.2
6	Total gastrectomy	10.1 to 17.0	13.6	0.6 to 6.2	3.1

¹Results are expressed in g. per day and ranges are three-day running means

1954), and complications including scurvy, gouty polyarthritis, and osteomalacia.

For six days on normal diet, faecal fat ranged from 10 to 20 g. per day (Table II). The addition of medium chain triglyceride (60 to 90 g. per day) for 10 days caused no marked change in the degree of steatorrhoea. When, however, dietary fat was replaced by medium chain triglyceride for 10 days the faecal fat output fell to within normal range, reaching as low as 1.5 g. per day, and containing only small amounts of capric acid (3.7% on day 23). During this period, however, bowel frequency rose to four times daily and also faecal volume from a mean of 250 ml. to 1,000 ml. daily. Resumption of normal diet was accompanied by the return of steatorrhoea.

CASE 2 Adult coeliac disease, female student nurse, aged 21. Short history with 12 kg. weight loss in five months,

FIG. 1. Typical example of effect of medium chain triglyceride diet on faecal fat excretion in case 2 (coeliac disease). In this example normal hospital diet was given for nine days followed by 11 days in which the same diet was continued with the addition of medium chain triglyceride (40 to 60 g. daily) and 11 further days in which dietary fat was virtually completely replaced by medium chain triglyceride. From day 32 onwards the patient received a gluten-free diet. Faecal fat excretion per day expressed in grams as running three-day means.

finger clubbing, severe dependent oedema, hypochromic anaemia with iron and folate deficiency.

Faecal fat excretion (Table II and Fig. 1) varied from 23 to 40 g. while on normal diet for nine days. With the addition of medium chain triglyceride to normal diet for 11 days the faecal fat output remained unaltered but when normal fat was withdrawn there was a dramatic fall. During 11 further days of medium chain triglyceride only mean faecal fat excretion was 3 g. per day of which less than 1% constituted medium chain acids. On the thirty-third day of the experiment the diet was discontinued and, despite a gluten-free diet, faecal fat excretion rose again to more than 30 g. per day. Three months later, faecal fat excretion still averaged 10 g. per day, though she had improved dramatically, gaining 20 lb. in three months. The oedema subsided and serum albumin rose to 4.0 g./100 ml. and globulin 3.0 g./100 ml. respectively. She has resumed her nursing training.

CASE 3 Regional enteritis. Male security officer, aged 55. Six-year history of abdominal pain, hypoproteinaemia, steatorrhoea, and anaemia.

His faecal fat excretion on hospital diet for five days ranged from 21 to 45 g. per day (Table II). From days 6 to 14 the addition of medium chain triglyceride to the diet (40 to 60 g./day) apparently reduced the steatorrhoea due to anorexia caused by adding medium chain triglyceride to the normal diet. From the fourteenth day when he was taking 'M.C.T. diet' only, the faecal fat levels fell dramatically and remained within normal limits. During this time he was consuming 40 to 60 g. of medium chain triglyceride oil per day and the total faecal fatty acid included only 3.7% caprylic acid (C_8) and 2.2% capric acid (C_{10}). On resumption of a normal diet faecal fat rose to 35 g. per day but then gradually resumed its pre-experimental level of 20 to 30 g./day. During pure medium chain triglyceride feeding there was only a slight increase in bowel frequency but a reduction in the volume of faeces.

CASE 4 Intestinal resection. A married West Indian woman aged 22 suffered massive small bowel loss as a result of criminal abortion (Shenoi, Smits, and Davidson, 1966).

Faecal fat output during 14 days' convalescence when appetite was poor and fat intake was approximately 40 g. per day (Table II) varied from 10 to 21 g. per day. Replacement of dietary fat by medium chain triglyceride for eight days (approximately 40 g. daily) resulted in the fall of faecal fat output to normal, though rising slightly above normal on days 16 and 17. On day 19 the faeces, though not containing an abnormal quantity of fat, the latter included 19% capric acid (C_{10}) but only traces of caprylic (C_8). Diarrhoea began to decrease in the latter part of the experimental feeding period.

With the re-introduction of a normal diet but with a reduced fat content (approximately 25 g. long chain triglyceride daily) steatorrhoea returned (maximum 17 g. per day) but then gradually waned.

CASE 5 Chronic pancreatitis. A 62-year-old housewife with intermittent abdominal pain, diarrhoea, malnourishment, and weight loss.

While on a normal ward diet for 14 days without pancreatic extract the faecal fat output ranged from 35 to 50 g. per day (Table II). When dietary fat was replaced for seven days by medium chain triglyceride (65 to 75 g. daily) faecal fat levels fell markedly to within normal limits after four days. On day 19, the faecal fatty acids included only 3.3% caprylic acid (C_8) and 1.2% capric acid (C_{10}), both being detected in amounts of less than 0.5% when on normal diet. On resumption of a normal ward diet gross steatorrhoea returned (up to 40 g. daily faecal fat).

CASE 6 Total gastrectomy. A 70-year-old retired brick-layer had undergone total gastrectomy for carcinoma of the stomach nine months previously.

On normal hospital diet for nine days, though with reduced intake (less than 40 g. fat per day), daily faecal fat output varied from 10 to 19 g. per day (Table II). When replaced by the medium chain triglyceride diet for 10 days (mean 50 g., range 30 to 70 g. daily), faecal fat excretion became normal and only traces of medium-chain acids were detected in the faeces. When normal diet was resumed on the 17th day faecal fat excretion increased immediately (range 17 to 35 g. daily).

DISCUSSION

Normal dietary fat is largely absorbed via the lymphatics of the gut (Munk, 1880; Munk and Rosenstein, 1891; Frank, 1898; Bloor, 1912-13; 1913-14; Freeman and Ivy, 1935; Verzár and McDougall, 1936) and medium chain fatty acids via the portal blood (Raper, 1912-13; Hughes and Wimmer, 1932) though these points were controversial for some time (Frazer, 1946, 1947). Further work, however, has confirmed the validity of the earlier contentions (Bloom, Chaikoff, Reinhardt, Entenman, and Dauben, 1950; Reiser, 1950; Reiser and Bryson, 1951; Bloom, Chaikoff, Reinhardt, and Dauben, 1951b; Bloom, Chaikoff, and Reinhardt, 1951a; Chaikoff, Bloom, Stevens, Reinhardt, and Dauben, 1951; Kiyasu, Bloom, and Chaikoff, 1952; Borgström, 1955). Analysis of human portal blood from abdominal wall anastomotic veins (Sherlock and Walshe, 1948; Bean, Franklin, Embick, and Daum, 1951) and from cannulated human thoracic ducts (Blomstrand and Ahrens, 1958; Blomstrand, Dahlback, and Linder, 1959; Blomstrand and Dahlback, 1959, 1960; Blomstrand, Gürtler, and Werner, 1965) has further confirmed these hypotheses, though some long chain fatty acids may be absorbed via the portal vein (Gallagher, Webb, and Dawson, 1965).

Chain length undoubtedly governs fatty acid metabolism (Kirschner and Harris, 1961) and originally it was thought that medium chain triglyceride was absorbed as fatty acid before passing into the portal blood (Bloom *et al.*, 1951a). Chain length is

inversely proportional to the rate of intraluminal lipolysis (Desnuelle and Savarry, 1963) and medium chain triglyceride is more easily split not only in the liver but also within the mucosal cell (Desnuelle and Savarry, 1963). In the presence of adequate pancreatic lipase splitting is virtually complete (Hashim, Bergen, Krell, and Van Itallie, 1964a), but is impaired in its absence (Valdivieso and Schwabe, 1965b). The latter also maintain the necessity for bile salts for the absorption of medium chain triglyceride (Valdivieso and Schwabe, 1965a) though because of greater solubility it is likely that bile salts are less important for micelle formation with medium chain fatty acids. Within the mucosal cell medium chain fatty acids are poorly reesterified (Borgström, 1960) due to the absence of the necessary enzyme system (Dawson and Isselbacher, 1960; Senior and Isselbacher, 1960; Ailhaud, Sarda, and Desnuelle, 1962). After absorption into the mucosal cell partially lipolyzed medium chain glycerides are hydrolyzed further instead of being reesterified (Tidwell and Johnston, 1961; Senior and Isselbacher, 1963; Gelb and Kessler, 1963; Hashim *et al.*, 1964; Wood, Imaichi, Knowles, Michaels, and Kinsell, 1964). Furthermore, medium chain triglyceride is well absorbed unsplit and is lipolyzed within the mucosal cell into fatty acid components, whereas unsplit long chain triglyceride is poorly absorbed (Playoust and Isselbacher, 1964).

There is evidence therefore that medium chain triglyceride can be absorbed both split and unsplit. In cases 1 and 2, both with coeliac disease and probably in case 3 with extensive regional enteritis, intracellular mechanisms are likely to be disturbed, so that the action of pancreatic lipase within the lumen may have been necessary to ensure normal absorption of medium chain triglyceride. In case 5, however, it was absorbed well in the absence of pancreatic lipase and in the presence of normal cellular function, in contradiction to the observation made by Valdivieso and Schwabe (1965b) in rats. After total or partial gastrectomy the reason for steatorrhoea is less well understood, though the altered anatomy is probably a major factor. Vagotomy can result in impairment of bile salt production (Fields and Duthie, 1965) and both acid and enzyme hydrolysis of triglyceride can occur in the intact stomach (Bank, Krut, Marks, Bronte-Stewart, and Uys, 1964). In gastrectomy a large proportion of unsplit long chain triglyceride reaches the absorptive section of the small intestine, but as in case 6, this matters little with medium chain triglyceride, as it is absorbed almost completely and presumably lipolyzed within the cell. In case 4 good absorption of medium chain triglyceride was evident in a normal upper small intestine but in which the total absorption area was insufficient to absorb long chain triglyceride adequately.

In addition, since the ileum was completely lost, impaired resorption of bile salt would contribute to deficient absorption of long chain triglyceride (Lack and Weiner, 1961). Furthermore though absorption of long chain triglyceride normally takes place in the proximal jejunum (Bergström, Borgström, and Carlsten, 1954; Borgström, Dahlqvist, Lundh, and Sjövall, 1957; Booth, Alldis, and Read, 1961), medium chain triglyceride has been shown to be absorbed from the large bowel (Lindscheer, Castelli, Moore, Patterson, and Chalmers, 1964).

Gas chromatographic analysis of the total faecal fatty acids during medium chain triglyceride feeding in the six patients studied confirmed that only small proportions of medium chain acids were excreted in all but the patient with only 4 foot 6 inches of residual small bowel where 19% of total fatty acids appeared as capric acid (C_{10}) on the day studied. In this patient there was in fact slight steatorrhoea, at least during the early part of feeding medium chain triglyceride, possibly a reflection of the much reduced total available absorptive area. The faecal long chain fatty acid patterns during medium chain triglyceride feeding must reflect the endogenous fatty acid excretion, except for the small contribution of unabsorbed long chain triglyceride in the source of protein used.

The possible nutritional value of medium chain triglyceride was first noted by Powell (1930, 1932) and later by Schön, Gey, Strecker, and Weitzel (1955). Medium chain fatty acids are carried via the portal blood to the liver where they are rapidly oxidized to two carbon compounds (Hashim *et al.*, 1964a), and increased B-hydroxybutyric acid and acetone appear in the blood (Schön, Lippach, and Gelpke, 1959). Butyric acid in the diet is not incorporated into body fat (Lebedeff, 1883; Leube, 1895; Zuntz, 1901; Eckstein, 1929; Powell, 1932) but fatty acids from ten-carbon compounds upwards are incorporated (Powell, 1932; Visscher, 1946). Some medium chain may therefore be resynthesized to long chain triglyceride (Popják, French, Hunter, and Martin, 1951; Popják, French, and Folley, 1951; Brady and Gurin, 1950).

The primary value of medium chain triglyceride lies, therefore, in its ready absorption and the provision of calories. Kaunitz, Slanetz, Johnson, Babayan, and Barsky (1958) estimated the calorific value of a similar medium chain triglyceride preparation to be 8.3 calories per g. Thus it provides twice as many calories per unit weight as carbohydrate, and, by partially replacing long chain triglyceride in the diet, may decrease the frequency of bowel action in steatorrhoea conditions. It is possible, though this requires further study, that the absorption of fat-soluble vitamins may be facilitated. The practical

value of the material remains a problem. Despite its minimal oily taste, regular taking is likely to fail because of increasing distaste. It can be used for frying but smokes easily, browns poorly, and its flash point is low. It can be incorporated in stews and similar dishes and also in pastry, though experience has shown the latter to become hard if not baked immediately after preparation. Cakes made with it, though quite edible, tend to soften after a few days. It forms a good basis, however, for many sauces.

Experiments with flavoured oil and water emulsions have been disappointing owing to rapidity of saphrophytic growth when mixed with water and kept at room temperature. Further mixtures need to be tried in an attempt to find a suitable preparation for long-term dietary supplementation. Such a preparation would be of value not only in malnutrition associated with steatorrhoea but also in other causes because of its simplicity and ease of digestion.

SUMMARY

Six patients with steatorrhoea caused by five different proven aetiologies are described. In each case dietary replacements of long and medium chain triglyceride resulted in immediate cessation of steatorrhoea. Current concepts regarding fat digestion and absorption, with particular reference to chain length, are reviewed and discussed. Further long-term study will be necessary to confirm the practical value of medium chain triglyceride in the steatorrhoea syndrome.

We are grateful to Mr. J. A. Williams, Ch.M., F.R.C.S., for permission to study case 6; also to the dietary departments of Birmingham General Hospital for assistance, and particularly to Mr. J. Anson, pharmacist, for preparing the special medium chain triglyceride diets. We are especially indebted to Dr. R. Gaddie, F.R.C.S., Ph.D. for the help of members of the Department of Biochemistry. We are indebted to Mrs. D. Banks for experiments with medium chain triglyceride cookery. One of us (B.J.S.) is in receipt of a grant from United Birmingham Hospitals Endowment Fund.

REFERENCES

- Ailhaud, G., Sarda, L., and Desnuelle, P. (1962). Formation d'hydroxymates d'acides gras à longues chaînes par une fraction subcellulaire de muqueuse intestinale. (Formation of hydroxymates of long-chain fatty acylhydroxamates by a subcellular fraction of intestinal mucosa). *Biochim. biophys. Acta (Amst.)*, **59**, 261-272.
- Bank, S., Krut, L. H., Marks, I. N., Bronte-Stewart, B., and Uys, P. J. Le R. (1964). Hydrolysis of fat by human gastric juice. *Gut*, **5**, 480-484.
- Bean, W. B., Franklin, M., Embick, J. F., and Daum, K. (1951). Absorption studies using portal anastomotic veins. *J. clin. Invest.*, **30**, 263-273.
- Bergström, S., Borgström, B., and Carlsten, A. (1964). On the mechanism of intestinal fat absorption in the cat. *Acta physiol. scand.*, **32**, 94-98.
- Blomstrand, R., and Ahrens, E. H., Jr. (1958). The absorption of fats studied in a patient with chyluria. II. Palmitic and oleic acids. *J. biol. Chem.*, **233**, 321-326.
- , and Dahlback, O. (1959). Gas-liquid chromatography of human lymph fatty acids after feeding C14-labelled fats. *Acta Soc. Med. upsalien*, **64**, 177-184.
- , — (1960). The fatty acid composition of human thoracic duct lymph lipids. *J. clin. Invest.*, **39**, 1185-1191.
- , —, and Linder, E. (1959). Asymmetric incorporation of linoleic acid-1-C14 and stearic acid-1-C14 into human lymph lecithins during fat absorption. *Proc. Soc. exp. Biol. (N.Y.)*, **100**, 768-771.
- , Gürtler, J., and Werner, B. (1965). Intestinal absorption and esterification of 14C-labelled fatty acids in man. *J. clin. Invest.*, **44**, 1766-1777.
- , Thorn, N. A., and Ahrens, E. H., Jr. (1958). The absorption of fats, studied in a patient with chyluria I. Clinical investigation. *Amer. J. Med.*, **24**, 958-966.
- Bloom, B., Chaikoff, I. L., and Reinhardt, W. O. (1951a). Intestinal lymph as pathway for transport of absorbed fatty acids of different chain lengths. *Amer. J. Physiol.*, **166**, 451-455.
- , —, and Dauben, W. G. (1951a). Participation of phospholipids in lymphatic transport of absorbed fatty acids. *J. biol. Chem.*, **189**, 261-267.
- , —, Entenman, C., and Dauben, W. G. (1950). The quantitative significance of the lymphatic pathway in transport of absorbed fatty acids. *Ibid.*, **184**, 1-8.
- Bloor, W. R. (1912-1913). On fat absorption. *Ibid.*, **11**, 429-434.
- (1913-1914). On fat absorption. III. Changes in fat during absorption. *Ibid.*, **16**, 517-529.
- Booth, C. C., Alldis, D., and Read, A. E. (1961). Studies on the site of fat absorption. II. Fat balances after resection of varying amounts of the small intestine in man. *Gut*, **2**, 168-174.
- Borgström, B. (1955). Transport form of 14C-decanoic acid in porta and inferior vena cava blood during absorption in the rat. *Acta physiol. scand.*, **34**, 71-74.
- (1960). In *Lipid Metabolism*, edited by K. Bloch, p. 138. J. Wiley, New York.
- , Dahlqvist, A., Lundh, G., and Sjövall, J. (1957). Studies of intestinal digestion and absorption in the human. *J. clin. Invest.*, **36**, 1521-1536.
- Brady, R. O., and Gurin, S. (1950). The biosynthesis of radioactive fatty acids and cholesterol. *J. biol. Chem.*, **186**, 461-469.
- Cancio, M., and Menéndez-Corrada, R. (1964). Absorption of medium chain triglycerides in tropical sprue. *Proc. Soc. Exp. Biol. (N.Y.)*, **117**, 182-185.
- Chaikoff, I. L., Bloom, B., Stevens, B. P., Reinhardt, W. O., and Dauben, W. G. (1951). Pentadecanoic acid-5-C14: its absorption and lymphatic transport. *J. biol. Chem.*, **190**, 431-435.
- Dawson, A. M., and Isselbacher, K. J. (1960). The esterification of palmitate-1-C14 by homogenates of intestinal mucosa. *J. clin. Invest.*, **39**, 150-160.
- Desnuelle, P., and Savary, P. (1963). Specificities of lipases (Review). *J. Lipid Res.*, **4**, 369-384.
- Eckstein, H. C. (1929). The influence of diet on the body fat of the white rat. *J. biol. Chem.*, **81**, 613-628.
- Fernandes, J., van de Kamer, J. H., and Weijers, H. A. (1955). The absorption of fats studied in a child with chylothorax. *J. clin. Invest.*, **34**, 1026-1036.
- , —, — (1962). Differences in absorption of the various fatty acids studied in children with steatorrhea. *Ibid.*, **41**, 488-494.
- Fields, M., and Duthie, H. L. (1965). Effect of vagotomy on intraluminal digestion of fat in man. *Gut*, **6**, 301-310.
- Frank, O. (1898). Zur lehre von der Fettresorption. *Z. Biol.*, **36**, 568-593.
- Frazer, A. C. (1946). The absorption of triglyceride fat from the intestine. *Physiol. Rev.*, **26**, 103-119.
- (1947). The absorption of fat from the intestine. *Chem. Ind.*, pp. 379-382.
- Freeman, S., and Ivy, A. C. (1935). The synthesis of neutral fat by the intestine of diabetic dogs. *Amer. J. Physiol.*, **114**, 132-136.
- Gallagher, N., Webb, J., and Dawson, A. M. (1965). The absorption of 14C oleic acid 14C triolein in bile fistula rats. *Clin. Sci.*, **29**, 73-82.
- Gelb, A. M., and Kessler, J. I. (1963). Effect of fatty acid structure on esterification by the small intestine in vitro. *Amer. J. Physiol.*, **204**, 821-824.

- Glass, G. B. J., Boyd, L. J., Gellin, G. A., and Stephanson, L. (1954). Uptake of radioactive vitamin B12 by the liver in humans: test for measurement of intestinal absorption of vitamin B12 and intrinsic factor activity. *Arch. Biochem.*, **51**, 251-257.
- Hashim, S. A., Babayan, V. K., and Van Itallie, T. B. (1962). Treatment of chyluria with a medium chain triglyceride. (Abstract). *Amer. J. clin. Nutr.*, **10**, 351.
- , Bergen, S. S., Jr., Kreli, K., and Van Itallie, T. B. (1964). Intestinal absorption and mode of transport in portal vein of medium chain fatty acids. (Abstract). *J. clin. Invest.*, **43**, 1238.
- , Roholt, H. B., Babayan, V. K., and Van Itallie, T. B. (1964). Treatment of chyluria and chylothorax with medium-chain triglyceride. *New Engl. J. Med.*, **270**, 756-761.
- , and Van Itallie, T. B. (1962). Pancreatogenous steatorrhea treated with medium chain triglyceride. (Abstract). *Clin. Res.*, **10**, 394.
- Hoagland, R., and Snider, G. G. (1943). Digestibility of certain higher saturated fatty acids and triglycerides. *J. Nutr.*, **26**, 219-225.
- Holt, P. R. (1964). Dietary treatment of protein loss in intestinal lymphangiectasia. The effect of eliminating dietary long chain triglycerides on albumin metabolism in this condition. *Pediatrics*, **34**, 629-635.
- , Hashim, S. A., and Van Itallie, T. B. (1965). Treatment of malabsorption syndrome and exudative enteropathy with synthetic medium chain triglycerides. *Amer. J. Gastroent.*, **43**, 549-559.
- Hughes, R. H., and Wimmer, E. J. (1935). The absorption of soluble, volatile fatty acids. *J. biol. Chem.*, **108**, 141-144.
- Iber, F. L., Hardoon, E., and Sangree, M. H. (1963). Use of eight and ten carbon fatty acids as neutral fat in the management of steatorrhea. (Abstract). *Clin. Res.*, **11**, 185.
- Kaunitz, H., Slanetz, C. A., Johnson, R. E., Babayan, V. K., and Barsky, G. (1958). Nutritional properties of the triglycerides of saturated fatty acids of medium chain-length. *J. Amer. Oil Chem. Soc.*, **35**, 10-13.
- Kirschner, S. L., and Harris, R. S. (1961). The effects of chain length on the metabolism of saturated fatty acids by the rat. *J. Nutr.*, **73**, 397-402.
- Kiyasu, J. Y., Bloom, B., and Chaikoff, I. L. (1952). The portal transport of absorbed fatty acids. *J. biol. Chem.*, **199**, 415-419.
- Kuo, P. T., and Huang, N. N. (1965). The effect of medium chain triglyceride upon fat absorption and plasma lipid and depot fat of children with cystic fibrosis of the pancreas. *J. clin. Invest.*, **44**, 1924-1933.
- Lack, L., and Weiner, I. M. (1961). In vitro absorption of bile salts by small intestine of rats and guinea pigs. *Amer. J. Physiol.*, **200**, 313-317.
- Lebedeff, A. (1883). Woraus bildet sich das Fett in Fällen der akuten Fettbildung? Experimenteller Beitrag zur Kenntniss der Leber und MilCHFette. *Pflügers Arch. ges. Physiol.*, **31**, 11-59.
- Leube, W. (1895). Ueber die subcutane Ernährung. *Verh. Kongr. inn. Med.*, **31**, 418-432.
- Lindscheer, W. G., Castelli, W. P., Moore, E. W., Patterson, J. F., and Chalmers, T. C. (1964). Absorption and plasma concentrations of octanoic acid in cirrhosis. (Abstract). *J. clin. Invest.*, **43**, 1280.
- Munk, I. (1880). Zur Kenntniss der Bedeutung des Fettes und seiner Componenten für den Stoffwechsel. *Virchows Arch. path. Anat.*, **80**, 10-47.
- , and Rosenstein, A. (1891). Zur Lehre von der Resorption im Darm-nach Untersuchungen an einer Lymph (Chilus)-fistel beim Menschen. *Ibid.*, **123**, 230-279.
- Osborn, M. O., and Ohlson, M. A. (1963). Fatty acids in hospital menus. *J. Amer. diet. Ass.*, **43**, 533-536.
- Pinter, K. G., McCracken, B. H., Lamar, C., Jr., and Goldsmith, G. A. (1964). Fat absorption studies in various forms of steatorrhea. *Amer. J. clin. Nutr.*, **15**, 293-298.
- Playoust, M. R., and Isselbacher, K. J. (1964). Studies on the intestinal absorption and intramucosal lipolysis of a medium chain triglyceride. *J. clin. Invest.*, **43**, 878-885.
- Popják, G., French, T. H., and Folley, S. J. (1951). Utilization of acetate for milk-fat synthesis in the lactating goat. *Biochem. J.*, **48**, 411-416.
- , —, Hunter, G. D., and Martin, A. J. P. (1951). Mode of formation of milk fatty acids from acetate in the goat. *Ibid.*, **48**, 612-618.
- Powell, M. (1930). Metabolism of tricaprylin and trilaurin. *J. biol. Chem.*, **89**, 547-552.
- (1932). The metabolism of tricaprln. *Ibid.*, **95**, 43-45.
- Raper, H. S. (1912-1913). Experiments bearing on the functions of the liver in the metabolism of fats. I. *Ibid.*, **14**, 117-134.
- Reiser, R. (1950). Conjugated Linoleic acid in rat tissue lipids after ingestion as free acid and as triglyceride. *Proc. Soc. exp. Biol. (N. Y.)*, **74**, 666-669.
- , and Bryson, M. J. (1951). Route of absorption of free fatty acids and triglycerides from the intestine. *J. biol. Chem.*, **189**, 87-91.
- Schön, H., Gey, F., Strecker, F. J., and Weitzel, G. (1955). Stoffwechselversuche mit Fettsäuren mittlerer Kettenlänge. III. Fütterungsversuche mit Laurinsäure-estern. *Hoppe-Seylers Z. physiol. Chem.*, **301**, 143-155.
- , Lippach, I., and Gelpke, W. (1959). Stoffwechseluntersuchungen mit einem Mischglycerid der Fettsäuren mittlerer Kettenlänge. I. I. Untersuchungen über die Veränderungen des Ketonkörpergehaltes von Blut und Urin nach Zufuhr der Mischglycerides. (Metabolic studies with a mixed glyceride of fatty acids with medium chain length. II. Investigations on the changes of the Ketone body content of blood and urine after administration of the mixed glycerides.) *Gastroenterologia (Basel)*, **91**, 199-213.
- Senior, J. R., and Isselbacher, K. J. (1960). Activation of long-chain fatty acids by rat-gut mucosa. *Biochim. biophys. Acta (Amst.)*, **44**, 399-400.
- , — (1963). Demonstration of an intestinal monoglyceride lipase; an enzyme with a possible role in the intracellular completion of fat digestion. *J. clin. Invest.*, **42**, 187-195.
- Shenoi, P. M., Smits, B. J., and Davidson, S. (1966). Massive removal of small bowel during criminal abortion. *Brit. med. J.*, **2**, 929-931.
- Sherlock, S., and Walshe, V. (1948). The use of a portal anastomotic vein for absorption studies in man. *Clin. Sci.*, **6**, 113-123.
- Smits, B. J., and Wilding, P. (1965). Personal communication.
- , —, and Cooke, W. T. (1966). Faecal fatty acid spectra in steatorrhoea syndromes. To be published.
- Tidwell, H. C., and Johnston, J. M. (1961). Glyceride glycerol utilization in triglyceride formation. *Arch. Biochem.*, **93**, 546-549.
- Valdivieso, V. D., and Schwabe, A. D. (1965a). Factors influencing the absorption of a medium chain triglyceride. I. The role of bile in the intraluminal phase of absorption. *Gastroenterology*, **48**, 331-335.
- , — (1965b). Factors influencing the absorption of a medium chain triglyceride. II. The role of pancreatic juice in the intraluminal phase of absorption. *Ibid.*, **43**, 336-341.
- van de Kamer, J. H., ten Bokkel Huinink, H., and Weijers, H. A. (1949). Rapid method for the determination of fat in feces. *J. biol. Chem.*, **177**, 347-355.
- , and Weijers, H. A. (1961). Malabsorption syndrome. *Fed. Proc.*, **20**, (suppl. 7), 335-344.
- Verzár, F., and McDougall, E. J. (1936). *Absorption from the Intestine*. Longmans, London.
- Visscher, F. E. (1946). Storage of hendecanoic acid in the white rat. *J. biol. Chem.*, **162**, 129-132.
- Weijers, H. A., and van de Kamer, J. H. (1953). Coeliac disease. III. Excretion of unsaturated and saturated fatty acids by patients with coeliac disease. *Acta Paediat. (Uppsala)*, **42**, 97-112.
- Winawer, S. J., Broitman, S. A., Wolochow, D. A., Osborne, M. P., and Zamcheck, N. (1966). Successful management of massive small-bowel resection based on assessment of absorption defects and nutritional needs. *New Engl. J. Med.*, **274**, 72-78.
- Wood, P., Imaichi, K., Knowles, J., Michaels, G., and Kinsell, L. (1964). The lipid composition of human plasma chylomicrons. *J. Lipid Res.*, **5**, 225-281.
- (1900). Ueber die Herkunft der Flüchtigen Fettsäuren in der Butter. *Arch. Physiol. (Lpz.)*, **382**-384.
- Zuntz, N. (1901). *Z. Untersuch. Nahr.-u. Genussmitt.*, **4**, 126-127.
- Zurier, R. B., Campbell, R. G., Hashim, S. A., and Van Itallie, T. B. (1966). Use of medium-chain triglyceride in management of patients with massive resection of the small intestine. *New Engl. J. Med.*, **274**, 490-493.