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Utilization of Glycerol-C^{14} for Intestinal Glyceride Esterification: Studies in a Patient with Chyluria *

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Ingested long chain triglycerides are hydrolyzed to partial glycerides and free fatty acids in the intestinal lumen, but the extent of intraluminal hydrolysis is still in dispute (2). After digestion and absorption into the intestinal mucosa, re-esterification of the fatty acids is necessary before incorporation into chylomicra, which pass into the intestinal lymphatics. Favarger and Gerlach originally considered that mucosal esterification of fatty acids occurred by a mechanism that was a reversal of lipolysis (3). Subsequent studies indicated that a more complex system of synthesis was involved (4). In addition, glycerol, liberated within the intestinal lumen by hydrolysis, was not believed to be a substrate for glyceride-glycerol synthesis, for when C^{14}-labeled glycerol and free fatty acids or triglycerides were fed to rats, little labeling of either intestinal mucosal lipids (5, 6) or lymph triglycerides was observed (7). Subsequent studies in the rat revealed, however, that 7 to 31% of glycerol-C^{14} fed intraduodenally could be recovered in chyle glycerides (8). The recent demonstration of an active glycerokinase in the rat intestinal mucosa (9) supports the concept that glycerol may be a precursor for intestinal esterification with fatty acids.

The present studies were performed in a patient with chyluria of 30 years duration secondary to filariasis who demonstrated a partial chylous fistula into the genitourinary tract. The patient was fed a mixture of glycerol-C^{14} and long chain fatty acids by intestinal tube. Examination of the chylous lipids excreted in the urine allowed a quantitative estimation of the incorporation of the exogenous labeled glycerol into intestinal lymph lipids.

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Materials and Methods

Clinical features. The subject, a 63-year-old Puerto Rican male, was admitted to St. Luke's Hospital with a 30-year history of chyluria. Complete clinical data on this patient have been published (10). Lymphography revealed tortuous dilated intra-abdominal lymphatics with communications from the cisterna chyli and para-aortic lymph glands to the left kidney and bladder (10). Cystoscopy showed a fistula in the region of the bladder neck.

Before these studies the patient had been maintained on formula feedings, and while ingesting only long chain fats (C16 to C18 triglycerides), excreted in the urine fat amounting to 3.5 to 14% (mean, 8.5%) of the daily fat intake. When maintained on a medium chain fat formula (C6 to C10 triglycerides), the chyluria virtually disappeared (11).

Procedure. For at least 12 days before the studies, the patient had received formula feedings consisting of a homogenized mixture of dextrose, casein, and medium chain triglycerides and was excreting less than 0.1% of this ingested fat in the urine. He was allowed only water for 14 to 16 hours before administration of the glycerol-fatty acid mixture. A polyethylene tube was passed into the jejunum just distal to the ligament of Treitz. Twenty ml of a solution containing the test substances was instilled over a period of 10 minutes and the lumen of the tube washed out several times with a total of 40 ml of tap water. The jejunal tube was then removed and the patient allowed to drink water ad libitum. Formula feedings containing medium chain triglycerides as the fat source were begun again after 3 hours. The patient was instructed to empty his bladder completely after 1, 2, 4, 8, and 24 hours, and all urine passed at these times was collected and frozen immediately. Twenty-four hour stool collections were also frozen immediately.

Study A. The solution administered consisted of 10 g of oleic acid,[1] 1.67 g of glycerol containing 9.6 μc glycerol-

[1] Gas liquid chromatography of the oleic acid revealed that only 72.3% was C18:1. The remaining fatty acids included 13.2% C16:1, 5.0% C14:1, 4.3% C18:2, and small quantities of C16:0, C18:0, and C14:0. 90.9%

1,3-C^{14} [2] (SA, 0.53 μc per mmole), and 2.5 g of sodium taurocholate.[3] This solution was homogenized just before administration. The patient tolerated the instillation well but did have some diarrhea during the first study. For this reason the concentration of taurocholate was reduced during the second study.

Study B. The solution consisted of 10 g of palmitic acid [1] containing 25 μc of palmitic acid-H_3,[4] 1.67 g glycerol containing 25 μc of glycerol-2-C^{14} (SA, 1.38 μc per mmole), 1 g of sodium taurocholate, and 1 ml of Tween 80 (polyoxyethylene sorbitan mono-oleate) to assist in homogenization just before administration.

Methods. Duplicate samples of urine were lyophilized or reduced in volume under vacuum, and the lipid was extracted with 20 vol of chloroform-methanol (2:1) by the technique of Folch, Lees, and Sloan Stanley (13). The chloroform layer was evaporated under N_2, taken up in petroleum ether, and washed with saline until no further C^{14} activity appeared in the saline layer. Portions of the petroleum ether fraction were kept for isotope counting. Other samples were saponified with alcoholic KOH, acidified, and extracted with petroleum ether, and the organic solvent layer was separated for counting. After alkaline hydrolysis, the water layer, containing the lipid-glycerol, was neutralized, evaporated, and reconstituted with water. A portion of this fraction was counted. To the remainder was added unlabeled glycerol, the mixture treated with periodic acid, and the formaldehyde from the glycerol carbons 1 or 3 isolated as the formaldimedone (14). After washing, the precipitate was dissolved in the dioxane scintillating mixture and counted. For comparison, the original glycerol-C^{14} was treated in the same way.

In study B, when the lipid labeling was appreciable, the lipid classes were separated by silicic thin layer chromatography (solvent system, hexane: ethyl ether: acetic acid, 89:10:1) or by silicic acid column chromatography using the method of Hirsch and Ahrens (15). The column effluents and solvent eluted spots were evaporated under N_2, reconstituted with petroleum ether, and samples kept for isotopic counting. Other portions were quantitated by infrared spectroscopy (16). The phospholipid content was also determined chemically by the technique of Youngburg and Youngburg, (17).

The fatty acid content of the individual urinary collections was determined in duplicate by the method of Pikaar and Nijhof (18). The fatty acid pattern of these lipid extracts was determined by gas liquid chromatography.

The C^{14} counts were measured in a liquid-scintillation spectrometer (Packard Tri-Carb 314X). The counting solutions used for the lipid and water soluble fractions were prepared as described previously (19). Internal standards were used in all quenched samples.

Some water soluble counts appeared in the urinary collections, but attempts to identify all the labeled materials were unsuccessful. No glucose was detected, and no significant counts were noted in phosphorylated glucose intermediates or ketoacids. Paper chromatography revealed the presence of little glycerol-C^{14} in the urine.

Calculation of glycerol-C^{14} incorporation into lipid-glycerol. Less than 2% of the C^{14} appeared in the 24-hour fecal collection, and this was subtracted for estimation of the glycerol-C^{14} absorbed. Less than 1% of the C^{14} in the lipid extracts was found in the fatty acid fraction after alkaline hydrolysis.

The total lipid glycerol present in the urinary collections was assessed by calculating the moles of glycerol in the lipid fractions, assuming a mean molecular weight for fatty acids of 270. Calculation of the mean molecular weight of fatty acids of individual samples measured by gas liquid chromatography indicated that in no sample did the molecular weight of fatty acids excreted deviate by more than 5% from this figure. The percentage of incorporation of labeled glycerol was estimated from measurement of the quantity of glycerol-C^{14} present and calculation of the total lipid glycerol content of each fraction.

Results

The 24-hour urinary excretion of lipid amounted to 11.7% and 8.4% of the administered dose of long chain fat in studies A and B, respectively. These figures are in agreement with the results of previous studies in this patient which suggested that only a partial lymphatic-urinary fistula existed and that most of the chylous lipids passed into the thoracic duct. Whether the lymphatics of some areas of the small intestine drained into the urinary tract preferentially or a fraction of the total mixed chyle was diverted could not be ascertained. The radiological appearance after lymphography suggested, however, that several fistulous connections did drain the region of the cisterna chyli just below the diaphragm, where mixed intestinal lymph would be found. The highest concentration of lipid was found in urinary specimens excreted between 1 and 4 hours after

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of the palmitic acid was C16:0 (6.8% C18:1, 1.8% C16:1). Oleic acid, palmitic acid, and glycerol were obtained from Fisher Scientific Co., Fairlawn, N. J.

[2] Glycerol-1,3-C^{14} and glycerol-2-C^{14} were obtained from New England Nuclear Corp., Boston, Mass.

[3] Obtained from K & K Laboratories, Inc., Jamaica, N. Y., and checked for purity by glass paper chromatography (12) and thin layer chromatography. Less than 1% unconjugated bile salts were present, but there was over 20% contamination with glycocholate and small quantities of other conjugated bile salts.

[4] At the conclusion of Study B, 10% of the palmitic acid-H_3 administered was found to be water extractable and was a major contaminant of nonlipid fractions of the urine. For this reason the results of palmitate-H_3 incorporation into urinary lipids were omitted.

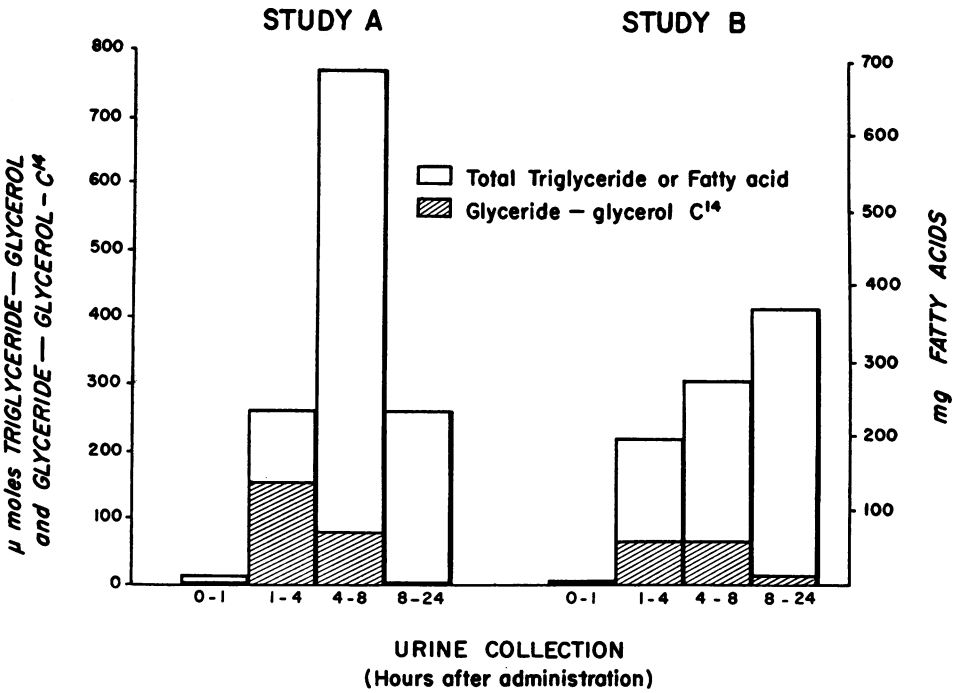

FIG. 1. THE EXCRETION OF FATTY ACIDS, CALCULATED TRIGLYCERIDE-GLYCEROL, AND GLYCERIDE-GLYCEROL-C^{14} OF INDIVIDUAL URINARY SPECIMENS. Triglyceride-glycerol was calculated from the chemical estimations of total fatty acid content and on the assumption that 90% of fatty acids excreted were triglycerides. Urinary lipid-glycerol-C^{14} was calculated from the specific activity of administered glycerol-C^{14} and based upon a mean mol wt of 270 for fatty acids present (see text).

ingestion, but considerable quantities were excreted for at least 24 hours (Figure 1). When oleic acid was fed, 80% of the total lipid excreted appeared within the first 8 hours after feeding, whereas only 55% appeared in this period when palmitic acid was administered.

Fatty acid pattern of urinary lipids. The fatty acid pattern of the urinary lipid differed significantly from the fatty acids fed (Table I). Because of the impurity of the oleic and palmitic acid administered, the dilution of these lipids by other fatty acids was difficult to quantitate. Urinary lipid extracts within the first 4 hours, when the concentration of lipid was greatest, most closely resembled the pattern of the fatty acids fed, whereas after this time, the percentage of lipid excreted that was measured as palmitic or oleic acid fell strikingly. As most lipid excreted appeared after 4 hours (Figure 1), at least 50% dilution of administered fat can be estimated. Such changes in fatty acid pattern could have occurred as a result of conversion of the lipid fed to other fatty acids, which has not been demonstrated in the intestine, or more likely, as a result of dilution by endogenous intestinal lipids. When glycerol incorporation into urinary lipids was calculated in these studies, both administered and endogenous fatty acids were assumed to be available for esterification with glycerol. No fatty acids with chain length below C12 were detected in the chylous urine.

Glycerol-C^{14} incorporation into total urinary lipid. Only 0.7 to 1.2% of glycerol-C^{14} administered appeared in the urine in the 24-hour collection. However, the fraction of administered fatty acids passing through the mesenteric lymphatic fistula during this time was very small. To quantitate the glycerol incorporation into the chylous lipid excreted in the urine, the total glycerol content of these lipids was calculated, the C^{14} label measured, and the specific activity obtained. In this way the percentage of the urinary glyceride-glycerol derived from the exogenously administered glycerol-C^{14} was calculated in each

TABLE I

Fatty acid pattern of fatty acids extracted from urinary specimens after administration of glycerol-C^{14} and oleic or palmitic acid

	Study A					Study B				
	Major fatty acids					Major fatty acids				
	16:0	16:1	18:0	18:1	18:2	16:0	16:1	18:0	18:1	18:2
Original fat administered	trace	13	trace	72	4	91	2	7	trace	trace
Urine collection (hours)										
1–2	7	12	4	62	6	72	3	6	9	4
2–4						64	5	5	12	6
4–8	13	10	4	58	8	44	4	11	29	8
8–24	26	5	8	31	17	29	3	9	29	20

specimen. In the first experiment, no separation into lipid classes was attempted. To calculate the total urinary glyceride-glycerol in Figure 1, two assumptions were made: first that 90% of the lipid excreted in the urine was present as triglycerides, a figure quoted for the incorporation of exogenous lipid into the thoracic duct lymph (20), and second, that the labeled glycerol was present only in the triglyceride fraction. As seen in Table II, neither assumption was correct, as only about 77% of the total fatty acids were excreted as triglycerides. In addition, Table III demonstrates that labeling of other lipid fractions occurred. Recalculation of the results of total lipid-glycerol incorporation in study B, as performed for study A (Figure 1), indicates that the results (in urinary specimens 2 to 4, 4 to 8, and 8 to 24 hours) were almost identical. For this reason the calculation of glycerol incorporation in total glycerides shown in Figure 1 has been accepted.

TABLE II

Fatty acid content of lipid fractions extracted from urinary specimens after administration of glycerol-C^{14} and oleic acid

Urine collection after administration	Lipid fraction	Total fatty acid	% of total
hours		*μmoles*	%
1–2	Triglyceride	0.76	
2–4	Triglyceride	567.0	76.9
	Free fatty acid	44.0	6.0
	Cholesterol ester	36.4	4.9
	Phospholipid	30.0	12.2
	Total	737.4	100.0
4–8	Triglyceride	750.0	77.9
	Free fatty acid	57.7	6.0
	Cholesterol ester	57.8	6.0
	Diglyceride	16.0	1.7
	Monoglyceride	12.6	1.3
	Phospholipid	68.0	7.1
	Total	962.1	100.0
8–24	Triglyceride	987.0	76.2
	Free fatty acid	83.0	6.4
	Cholesterol ester	99.0	7.6
	Diglyceride	33.6	2.6
	Monoglyceride	*	
	Phospholipid	94.0	7.2
	Total	1,297.0	100.0

* Although some monoglycerides were detected by infrared spectroscopic analysis, no accurate determination was possible because of contamination with silicic acid.

After the oleic acid mixture was fed, 17.9% of the lipid-glycerol present in the 24-hour urine collection was found to be labeled, whereas 15.7% was labeled after palmitic acid administration. The percentage of labeling (namely, specific activity of lipid-glycerol-C^{14}) was highest during the first 4 hours when the concentration of urinary lipid was greatest and the fatty acid pattern of the lipid most closely resembled that of the fat administered (Figure 1). In fact, in study A in the 1- to 4-hour collection, over 59% of the urinary lipid-glycerol was calculated to be labeled, in contrast to the urinary collection after 8 hours, where as little as 0.5% lipid-glycerol labeling occurred in spite of the continuation of considerable lipid excretion. This striking difference is most probably related to rapid absorption from the intestinal lumen of water-soluble glycerol as compared to the fatty acids fed. As a result, the amount of glycerol-C^{14} available for esterification with lipid is greatest shortly after administration. This supposition is supported by the greater occurrence of glycerol-C^{14} incorporation in study A despite the greater total excretion of lipid because most of the fat appeared in the urine within the first 8 hours. These data clearly show that a considerable percentage of lymph lipid-glycerol

can be derived from exogenously administered glycerol.

Glycerol-C^{14} incorporation into lipid fractions of urine. When the urinary lipids in study B were fractionated by silicic acid chromatography, over 95% of the glycerol-C^{14} was found in the triglyceride fraction, but some labeling of the other lipid fractions was noted (Table III). The specific activity of the glycerol-C^{14} in phospholipids was only 10 to 17% of that in triglycerides. Although only small quantities of mono- and diglycerides appeared, labeling of monoglycerides was virtually absent, whereas significant diglyceride labeling occurred. Spectrometric and chemical analysis of these specimens revealed that about 76 to 78% of the total fatty acids was present as triglycerides, a figure significantly less than that reported for thoracic duct lymph (20). About 7 to 12% was noted in phospholipids, 6% as free fatty acids, 6 to 8% as cholesterol esters, and small quantities as mono- and diglycerides. These results suggest that while preferential incorporation of glycerol into triglycerides occurred under the conditions of the study, there was essentially none into monoglycerides.

TABLE III

Total lipid-glycerol and glycerol-C^{14} incorporated into lipid fractions extracted from urinary specimens after administration of glycerol-C^{14} and oleic acid

Urine collection	Lipid fraction	Total lipid glycerol*	Lipid-glycerol-C^{14}†	Lipid-glycerol labeled
hours		*μmoles*	*μmoles*	%
1–2	Triglyceride	0.25	0.105	41.3
2–4	Triglyceride	189.0	58.2	30.8
	Phospholipid	45.0	1.34	3.0
	Total	234.0	59.54	25.4
4–8	Triglyceride	250.0	56.2	22.5
	Diglyceride	8.0	0.82	10.3
	Monoglyceride	12.6	0.08	0.6
	Phospholipid	34.0	1.29	3.8
	Total	304.6	58.39	19.2
8–24	Triglyceride	329.0	14.04	4.2
	Diglyceride	16.8	0.14	0.8
	Monoglyceride	‡	0	0
	Phospholipid	47.0	0.26	0.6
	Total	392.8	14.44	3.7

* Calculated from the spectrometric and chemical estimations and based upon a mean mol wt of 270 for fatty acids present.

† Calculated from the specific activity of glycerol-C^{14} administered and C^{14} counts measured in each lipid fraction.

‡ Although some monoglycerides were detected by infrared spectroscopic analysis, no accurate determination was possible because of contamination with silicic acid.

TABLE IV

Distribution of C^{14} activity in aqueous extract of lipid-glycerol from fractional urinary specimens measured by precipitation as the formaldimedone

	Glycerol-C^{14} administered	Total lipid glycerol	Formaldimedone precipitated	Glycerol-C^{14} activity in terminal C	
				Theoretical*	Actual
	cpm	*cpm*	*cpm*	%	%
Study A					
Glycerol-1,3-C^{14}	15,646		8,034	50	51.3
1–4 hours		9,880	5,335		54.0
4–8 hours		2,431	1,256		51.7
Study B					
Glycerol-2-C^{14}	22,077		112	0	0.5
2–4 hours		4,516	164		3.6
4–8 hours		6,100	110		1.8
8–24 hours		6,450	135		2.0

* The theoretical percentage of C^{14} activity precipitable was calculated using the assumption that glycerol carbons 1 and 3 would be precipitated as the formaldimedone. Glycerol-1,3-C^{14} would have random labeling of either carbon 1 or 3.

Quantitation of C^{14} label in the terminal carbon of urine glyceride-glycerol. Glycerol could have been converted to α-glycerophosphate within the intestinal mucosa and been incorporated intact into lipid-glycerol. In addition, glycerol could have been metabolized in the intestine or liver through pyruvate and the tricarboxylic acid cycle and the label reincorporated into glucose and α-glycerophosphate. If significant metabolism by such a pathway had occurred, rearrangement of glycerol-C^{14} labeling in the lipid-glycerol would have been expected. However, as shown in Table IV the arrangement of labeled carbons in the lipid-glycerol closely resembled that in the glycerol-C^{14} administered. Alternatively, glycerol could have been converted directly to glucose in the intestine or liver and then have been remetabolized to dihydroxyacetone phosphate and α-glycerophosphate before esterification in the intestinal mucosa with available fatty acids. This pathway would not have resulted in rearrangement of the C^{14}-labeled glycerol. Glycerol metabolism by the intestinal mucosa has been observed *in vitro* (8, 19) but in amounts much smaller than glucose.

Free glycerol absorbed from the intestinal lumen is transported to the liver, and rapid hepatic metabolism to CO_2 occurs (21). Any glycerol-C^{14} converted to glucose would have been diluted by the large endogenous pool. Buchs and Fa-

varger (6) in their studies of the incorporation of free glycerol-C^{14} into intestinal lipids in rats were unable to detect significant labeling when the material was given orally in large doses (200 mg per kg). In addition, when glucose C^{14} or glycerol-C^{14} was administered intravenously to rabbits by the same investigators, there was eightfold greater labeling of intestinal lipids after the injection of glycerol. These observations would make it unlikely that 10 to 20% of glycerol-C^{14} given orally could be incorporated into lymph triglycerides by prior conversion to glucose in the liver.

Discussion

The studies in this chyluric patient clearly demonstrate that exogenous glycerol can be incorporated into esterified lipids of the chyle in man. They confirm experiments in intact rats and in rat and hamster intestinal slice preparations (8, 19) that also showed glycerol incorporation into chyle or mucosal lipids. Although less than 20% of the lipid-glycerol excreted in the urine in 24 hours was labeled, in fractional urine collections as much as 60 and 41% were incorporated. These experiments are in disagreement with those of earlier workers (5–7) who failed to show glycerol incorporation when the labeled compound was fed with fatty acids and triglycerides by mouth or stomach tube to rats. This discrepancy is probably because glycerol may be absorbed from the stomach (22) and water-soluble substances may leave the stomach more rapidly than fat (23). In addition, glycerol may be absorbed by the intestinal mucosa and pass into the portal vein more rapidly than fat is absorbed even when they are administered together. The observations in this patient that glycerol incorporation was far greater during the first 4 hours of urine collection and when oleic acid was more rapidly absorbed support this contention.

Significant quantities of glycerol are liberated in the intestinal lumen by triglyceride hydrolytic digestion, but the extent of reutilization of this glycerol by the mucosa for glyceride synthesis is difficult to assess. The intestinal absorption of monoglycerides has been demonstrated (24, 25), and Senior and Isselbacher have shown that monoglycerides act as acceptors of fatty acid acyl CoA fragments to form triglycerides (26). In their studies utilizing subcellular fractions, monoglyceride esterification occurred when palmityl-CoA was present in excess; the physiological significance of a monoglyceride acylase is therefore uncertain. Studies of intestinal dipeptide and disaccharide splitting enzymes have revealed that these exist mainly at the mucosal cell border (27, 28), and final hydrolysis is felt to occur at this site followed by the absorption of the hydrolyzed amino acids and monosaccharides. A similar mechanism for monoglycerides could be postulated, but this is unlikely, as both monoglyceride lipase and fatty acid acylase are in greatest concentration in the microsomal fraction and not in the cell membrane (26, 29). Although pancreatic lipase rapidly liberates the fatty acid ester bond at the two primary (α and α_1) hydroxyl groups of triglycerides, hydrolysis of monoglycerides occurs slowly (30), whereas the lipase of the intestinal mucosa readily breaks down monoglycerides (31). Thus the fatty acid and glycerol moieties of monoglycerides may be presented to the intestinal mucosa concurrently and the condition for glyceride-glycerol resynthesis established. Although esterification of intestinal lipids with absorbed free glycerol occurs, the mechanism and extent of resynthesis of glycerol released by intracellular hydrolysis of monoglycerides may not be the same. At this time the amount of monoglycerides that may act as fatty acid acceptors, or glucose or glycerol that provides the glyceride-glycerol skeleton during mucosal triglyceride synthesis, is not known.

The inability of previous workers to demonstrate glycerol incorporation into intestinal lipids and the assumption that no glycerol reutilization occurred have been used to calculate the extent of intraluminal triglyceride lipolysis and intact glyceride absorption by the intestine. In these investigations, triglycerides labeled in both the glycerol and fatty acid moieties were fed and the percentage of glycerol labeling of lymph triglycerides measured. Assuming no intestinal glycerol reutilization, the amount of glycerol labeling was equated with the percentage of glyceride absorption so that as much as 50 to 75% of glycerides was felt to be absorbed intact (7, 32, 33). In the present studies, 20 to 60% of the chyle lipids recovered during the first 8 hours of collection was labeled. As rapid intestinal absorption

of free glycerol occurs, it is unlikely that significant quantities remained available for intestinal esterification after 8 hours. Thus, if synthesis of intestinal glycerides with hydrolyzed glycerol does occur to this extent, the validity of the calculations for intact glyceride absorption is in doubt and the extent of intraluminal hydrolysis underestimated.

The fatty acid patterns of lipids extracted from the urine during these studies were significantly different from those administered and suggested considerable dilution by endogenous fatty acids. Turner has shown that appreciable quantities of phospholipids are secreted in bile (34), and fat may have been secreted into the intestinal lumen from the pancreas and intestinal wall. In addition, glycerides may have been synthesized from existing fatty acids within the mucosal cell. Studies attempting to quantitate the contribution of endogenous lipid to the chyle lipids are being undertaken in this patient.

Although the majority of the glycerol-C^{14} that was incorporated into lipid-glycerol appeared in the triglyceride fraction, significant amounts appeared in phospholipids and partial glycerides. Only 10 g of exogenous long chain fat was administered in these studies, however, and may have been incorporated into the mucosal lipids in an unusual fashion. Essentially no monoglyceride labeling occurred, although the diglycerides were labeled and small but significant amounts of monoglycerides were detected. The studies of Skipski, Morehouse, and Deisel (25) using double-labeled lipids also suggested that, as the specific activity of deuterated monoglyceride-glycerol extracted from the intestinal mucosa was the same as that in the absorbed monoglyceride, no incorporation into this fraction of free unlabeled glycerol or glucose occurred. Dawson and Isselbacher (4) first demonstrated in the intestinal mucosa a pathway for fatty acid incorporation into triglycerides similar to that described by Kennedy (35) in the liver in which α-glycerophosphate reacts with two fatty acid-CoA fragments to form phosphatidic acid, which is in turn dephosphorylated to diglyceride. Monoglycerides are not formed by this system. Although glucose was used as an α-glycerophosphate precursor in their studies, a similar system is probably involved using glycerol as a precursor (9). The failure to detect monoglyceride labeling in this patient suggests that a pathway in which glycerol is first phosphorylated may be operative for intestinal glyceride synthesis in man.

Summary

Two studies of glycerol-C^{14} incorporation into chyle lipids have been performed in a patient with chyluria. After the intraluminal administration of a glycerol-C^{14} and fatty acid mixture, between 15 and 18% of the lipid-glycerol excreted in the urine in 24 hours was found to be labeled, and as much as 59.5% incorporation was calculated in one urine specimen. The C^{14} labeling of the excreted glyceride-glycerol was almost identical to that fed, suggesting that incorporation occurred without extensive prior metabolism of glycerol.

Glycerol-C^{14} was incorporated mainly into triglycerides of chyle, but significant labeling of other lipid fractions was observed. No labeling of monoglycerides occurred, indicating that glycerol was not incorporated into this fraction.

The urinary lipid fatty acid pattern differed significantly from the pattern of fatty acids administered, implying considerable dilution with endogenous lipids.

These studies suggest that glycerol released in the intestinal lumen during triglyceride hydrolysis may be reutilized for glyceride synthesis in the mucosa. Should this occur, the validity of previous calculations of the extent of intestinal glyceride absorption is in question.

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