

# Efficacy of Different Triglycerides in Total Parenteral Nutrition for Preventing Atrophy of the Gut in Traumatized Rats

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**ABSTRACT.** *Background:* The efficacy of different fat emulsions as components of a total parenteral nutrition (TPN) regimen on the integrity of the gut was assessed in traumatized rats. With the release of the short-chain fatty acids butyric or propionic acid during the hydrolysis of a structured triglyceride containing butyric acid (C4-L-C4-TG) or the  $\beta$ -oxidation of nonanoic acid from trinonanoin (C9TG), respectively, the infusion of these two triglycerides was supposed to reveal positive effects against the TPN-induced atrophy of the intestine. *Methods:* After 3 days of fiber-free liquid diet, rats were traumatized (laparotomy) and catheterized. Afterwards they received equicaloric TPN that delivered 1008 kJ (241 kcal)/kg of body weight per day and 30% nonprotein calories as fat emulsion. The four fat emulsions tested in four groups of six animals contained either long-chain triglycerides (LCT), medium-chain triglycerides (MCT)-LCT (1:1), C9TG/LCT (1:1) or C4-L-C4-TG. Animals of a control group were infused with

isovolemic 0.9% NaCl solution and were offered oral standard chow. *Results:* After 7 days of MCT/LCT administration, the mass-to-length ratio of the total small bowel as well as the masses of mucosa/submucosa and muscularis/serosa in 10-cm segments of the distal half of the small bowel were significantly higher than that found in the other TPN groups or not different from controls. Histometric measurement of the villus height in the ileum revealed no statistically significant differences from controls for the rats of the MCT/LCT and C4-L-C4-TG groups. In the colon, no statistically significant differences between TPN groups were found for either parameter. *Conclusions:* Within the tested fatty substrates the MCT/LCT fat emulsion revealed less structural impairments in the distal half of the small bowel regarding mucosa/submucosa (mass and villus height), but also muscularis/serosa (mass).

Normally, the gastrointestinal barrier is highly effective in preventing translocation of the gut microorganisms into systemic circulation. However, subsequent to stress of thermal injury, major trauma, surgery, or immunosuppression this barrier of the human gut becomes impaired or even breaks down.<sup>1,2</sup> Additionally, these patients regularly receive total parenteral nutrition (TPN), which has been shown to lead *per se* to atrophy of the gut mucosa after a few days, followed by a relatively high rate of bacterial translocation.<sup>3-6</sup> Sepsis of "undefined origin" can be the dangerous result.<sup>1,7</sup>

In TPN with the lack of stimuli by oral food intake, the prevention of bacterial translocation is concentrated on isolated nutrients that reveal a positive effect toward the maintenance of normal intestinal structure and function. Different nutrients like short-chain fatty acids (SCFAs), glutamine, glutamine peptides, nucleotides, and arginine are under discussion.<sup>2,8</sup> Usually, the SCFAs acetic, propionic, and butyric acid are products of the microbial fermentation of dietary fibers in the large bowel. Especially, butyric acid is recognized as the predominant energy substrate for colonocytes *in vitro*.<sup>9</sup> Moreover, mixtures of SCFAs were also shown to reveal a trophic effect on the

mucosa of the small and large bowel when administered as sodium salts either parenterally or by colonic infusions.<sup>10-14</sup> Although these forms of applications seem less suitable for practical purposes, administration of triglycerides within TPN, which would release SCFAs by triglyceride hydrolysis or  $\beta$ -oxidation of their fatty acid components, should be a tolerable and practicable measure. It was shown in rabbits that infusion of a high doses of trinonanoin (C9TG) gives rise to plasma propionic acid; additionally, plasma acetic and butyric acid concentrations increased.<sup>15</sup> On the other hand, butyric acid as component of a structured triglyceride should be easily released in the plasma and transported to the cells. Consequently, in this study the effects of these two triglycerides on the integrity of the rat intestine should be compared with a control group receiving standard chow and saline infusions. For the small knowledge even about the effects of "usual" fat emulsions on morphologic alterations in the intestine during TPN of a traumatized organism, long-chain triglyceride (LCT) and medium-chain triglyceride (MCT)-LCT fat emulsions were administered in two further groups of animals.

## MATERIALS AND METHODS

Thirty male, sexually mature Wistar rats (270 to 320 g) were housed in metabolic cages (5 per cage) and fed a fiber-free liquid diet (Nutricomp F, B. Braun Melsungen AG, Melsungen, Germany) for 3 days to minimize the effects of residual fiber in the intestinal tract. On the 4th

day the rats underwent standardized laparotomy and placement of the subcutaneous part of the swivel apparatus (Instech Laboratories Inc, Plymouth Meeting, PA). After surgery, the animals were put into individual metabolic cages and isotonic NaCl solution (0.9%; B. Braun Melsungen AG) was infused. From afternoon (4 PM) of day 4 until morning (8 AM) of day 5 administration of the TPN started with a half dose. Continuous infusion (24 h/d) of TPN solution as given in Table I lasted from the morning of the first postoperative day (POD, day 5) until the morning of the 8th POD (day 12).

Postoperatively, the rats were randomly assigned to five groups (6 animals each). Four groups received an equicaloric TPN regimen differing only in the kind of fat emulsion. As fat compounds either LCT, MCT/LCT (1:1, wt/wt), trionanoin (C9TG)/LCT (1:1, wt/wt) emulsions, or an emulsion containing butyric acid in the sn-1,3 position of glycerol and a fatty acid of commercially available soya oil in sn-2 position (C4-L-C4-TG) were supplied. Thirty percent of the nonprotein energy of the TPN regimen was provided as fat (Table I). For the animals of the control group, NaCl solution (0.9 %) was infused corresponding to the TPN volume. For energy and nutrient supply, isoca-

loric amounts (conferring to the TPN regimen) of the standard chow ssniff R/M 10 (ssniff GmbH; Soest, Germany) were offered to the control animals. The calculation of the total infusion volume, the amount of standard food, and the volume of liquid diet was based on the individual body weights on day 1. Water was given *ad libitum* to all rats during the whole study. The infusions were administered by means of infusion pumps (Perfusor Secura FT; B. Braun Melsungen) and the swivel system.

Every day in the morning the animals were weighed and the wounds were mopped up with a disinfectant solution; no other medication was applied. On the 8th POD the animals were anesthetized and maximal amount of blood was drawn by puncture of vena cava inferior. EDTA plasma samples were stored at  $-25^{\circ}\text{C}$  until analysis of SCFA concentrations. After extraction<sup>16</sup> SCFAs were determined by means of gas chromatography (flame ionization detector [FID]), using pivalic acid as internal standard (all chemicals were purchased from Sigma-Aldrich Chemie GmbH, Deisenhofen, Germany). SCFAs were separated with a Permabond FFAP column (50 m  $\times$  0.25 mm inner diameter; Macherey Nagel, Düren, Germany), installed in an HP 5890 gas chromatograph with a FID (Hewlett Packard,

TABLE I  
TPN regimen

Nutrient preparations*	Amount of nutrients (g) <sup>†</sup>	Energy supply		Infusion volume (mL) <sup>‡</sup>	Infusion rate (mL) <sup>‡</sup>
		kJ <sup>†</sup>	Kcal <sup>†</sup>		
Glucose (50% wt/wt) <sup>§</sup>	36.8	586	140	73.7	3.07
Amino acids (15% wt/wt) <sup>  </sup>	9.4	157	38	62.5	2.60
Fat emulsions (20% wt/wt) <sup>¶</sup>					
LCT <sup>**</sup>	6.7	251	60	31.6	1.32
MCT/LCT (1:1, wt/wt) <sup>††</sup>	7.0	251	60	33.2	1.38
C9TG/LCT (1:1, wt/wt) <sup>‡‡</sup>	7.0	251	60	33.2	1.38
C4-L-C4-TG	7.7	251	60	36.5	1.52
$\Sigma$ Energy		1008	241		
Sodium chloride (5.85%)				15.0	0.63
K-/Mg-L-asparaginate (24.3%)				4.0	0.17
Potassium phosphate (9.6%)				6.0	0.25
Calcium (10%)				1.0	0.04
Cholin chloride (20%)				0.5	0.02
Solution of water-soluble vitamins <sup>§§</sup>				1.3	0.05
Trace element solution <sup>   </sup>				1.3	0.05
$\Sigma$ LCT				196.8	8.20
$\Sigma$ MCT/LCT				198.4	8.27
$\Sigma$ C9TG/LCT				198.4	8.27
$\Sigma$ C4-L-C4-TG				201.7	8.40

TPN, total parenteral nutrition; LCT, long-chain triglyceride; MCT, medium-chain triglyceride; C9TG, trionanoin; C4-L-C4-TG, triglyceride emulsion containing butyric acid in the sn-1,3 position of glycerol and a fatty acid of commercially available soya oil in the sn-2 position.

\*All preparations were from B. Braun Melsungen AG, Melsungen, Germany.

<sup>†</sup>Values are per kg body weight per day.

<sup>‡</sup>Values are per kg body weight per hour.

<sup>§</sup>Glucose 50; Braun.

<sup>||</sup>Aminoplasmal: 15% E without carbohydrates.

<sup>¶</sup>In 100 mL: 2.5 g glycerol, 1.2 g phospholipids from egg yolk as emulsifier.

<sup>\*\*</sup>Endolipide 20%.

<sup>††</sup>Lipofundin MCT 20%.

<sup>‡‡</sup>Emulsified together.

<sup>§§</sup>In 5 mL: 3 mg thiaminhydrochloride, 3.6 mg Na-riboflavin-5-phosphate, 40 mg nicotic acid amide, 4 mg pyridoxin hydrochloride, 16.5 mg Ca pantothenate, 113.3 mg Na ascorbate, 60  $\mu\text{g}$  biotin, 0.4 mg folic acid, 5  $\mu\text{g}$  cyanocobalamine.

<sup>|||</sup>In 5 mL: 3 mg Zn, 0.5 mg Cu, 0.01 mg Cr, 0.2 mg Mn.

Taufkirchen, Germany). After identification of the substances by retention times, quantification was made concerning "relative response factors." The concentrations of  $\beta$ -hydroxybutyrate and acetoacetate in the plasma were determined enzymatically.<sup>17,18</sup>

After blood sampling, the intestine from the pylorus to the anus was rapidly excised, carefully freed of its mesenteric fat, and rinsed in cold saline. The bowel was transected at the ileocecal and cecocolonic junction and after rinsing with NaCl solution the weight and length of the small intestine and large intestine (without cecum) were measured. All length determinations were done with fixed tension of 10 g. The small intestine was transected at its half length to get comparable segments for the middle jejunum between animals with different length of the small bowel. Segments of 0.5-cm length were taken from the distal duodenum (B), the middle of jejunum (F), the distal ileum (L), and the colon transversum (N) and fixed in formaldehyde solution (4%, phosphate-buffered) for histologic and histometric examination. Villus height (duodenum, jejunum, and ileum) and mucosal height (colon) were determined by light microscope after paraffin embedding and staining with hematoxylin and eosin. Using an ocular micrometer, 10 measurements were made per intestinal segment; mean values were calculated for further statistical procedures.

Ten 10-cm segments of the gut were taken under 10 g of tension, in the following, indicated with the capital letters A through M: A, duodenum; C and D, proximal jejunum; E, G, and H, middle of jejunum; I and J, distal jejunum; K, ileum; and M, colon. The segments were opened longitudinally, rinsed in NaCl solution, and blotted dry. The mucosa and submucosa were completely removed by scraping with a glass slide. By weighing of the segments before and after scraping the mass of mucosa/submucosa could be calculated. The mucosal-submucosal scrapings were stored at  $-25^{\circ}\text{C}$  until analysis of protein,<sup>19</sup> RNA,<sup>20</sup> and DNA.<sup>21</sup>

The results are expressed as means  $\pm$  SEM. Statistical analysis was performed with SPSS, Version 6.0 (SPSS Inc, Chicago, IL). After analysis of variance (one-factorial model) comparisons of means were made with the Student-Newman-Keuls test (snk-test) at an  $\alpha$ -level of 5%.

## RESULTS

During the TPN period mean body weight of the rats decreased up to 8% of the initial weight without showing statistically significant differences between all groups. At the end of the study, mean wet weights of the small bowel and of the colon/rectum were significantly lower in all rats of the TPN groups when compared with controls; between TPN groups no differences could be found. If the weight was related to the length of the small bowel, the rats of the MCT/LCT group revealed a significantly higher mean than animals of the other TPN groups (Fig. 1). No differences between groups were found for the weight per length in the colon/rectum due to a similar decrease in length and wet weight in all TPN groups.

As can be seen in Figure 2, the animals of the MCT/LCT group revealed the highest masses for the mucosa/submucosa as well as for the muscularis/serosa in the 10-cm segments of the small bowel of all TPN rats. Especially, in

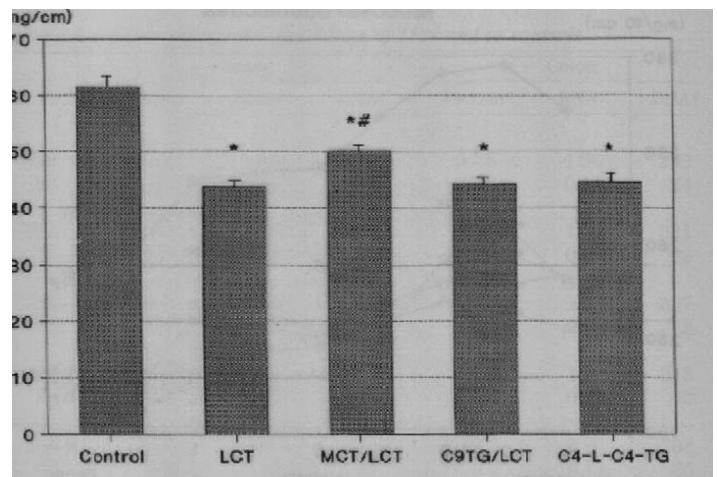


FIG. 1. Mass per length of the small bowel (mg/cm, mean  $\pm$  SEM) of traumatized rats ( $n = 6/\text{group}$ ) after 7 days of TPN with different types of fat emulsions and in controls (0.9% NaCl, standard chow). \*Significantly different mean compared with control; #significantly different mean compared with all other TPN groups; snk-test,  $p \leq .05$ .

the distal area of the small bowel the differences in the weight of mucosa/submucosa between MCT/LCT animals and controls further decreased and were no longer statistically significant (segments E and H through K). Also mean weights of muscularis/serosa were highest in the MCT/LCT group when compared with the other TPN groups (statistical significance for the segments I through K) and less different from controls (missing statistical significance between MCT/LCT and control group in the segments A and H).

In the investigated parts of the large bowel no significant differences between all groups were measured for the wet weight of mucosa/submucosa; however, mean masses of muscularis/serosa were significantly lower in all TPN groups compared with controls without differences between TPN groups (Fig. 3).

The histologic examination of the gut mucosa showed no impairments in animals from any group, but with histometric evaluation of the villus height in the small bowel a statistically significant decrease in all TPN groups compared with controls was obtained in the duodenum (Fig. 4). In the ileum, the MCT/LCT and the C4-L-C4-TG groups showed no significant differences in mean villus height compared with controls. Mean results of the histometric examination of mucosal height in the colon of all TPN groups were not significantly different from controls.

Mean protein and RNA values in the mucosa/submucosa of the 10-cm segments of the duodenum and jejunum were decreased in all TPN groups compared with the control group (Table II). The differences were no longer statistically significant in the ileum, where the highest values of all TPN groups could be found for the animals of the MCT/LCT group. When calculating the ratio of RNA to protein, mean values of all groups were not statistically distinguishable. Mean DNA concentrations of mucosa/submucosa in all investigated parts of the small bowel showed a high range of variability (see SEM values) and revealed no statistical difference between all groups (with exception of

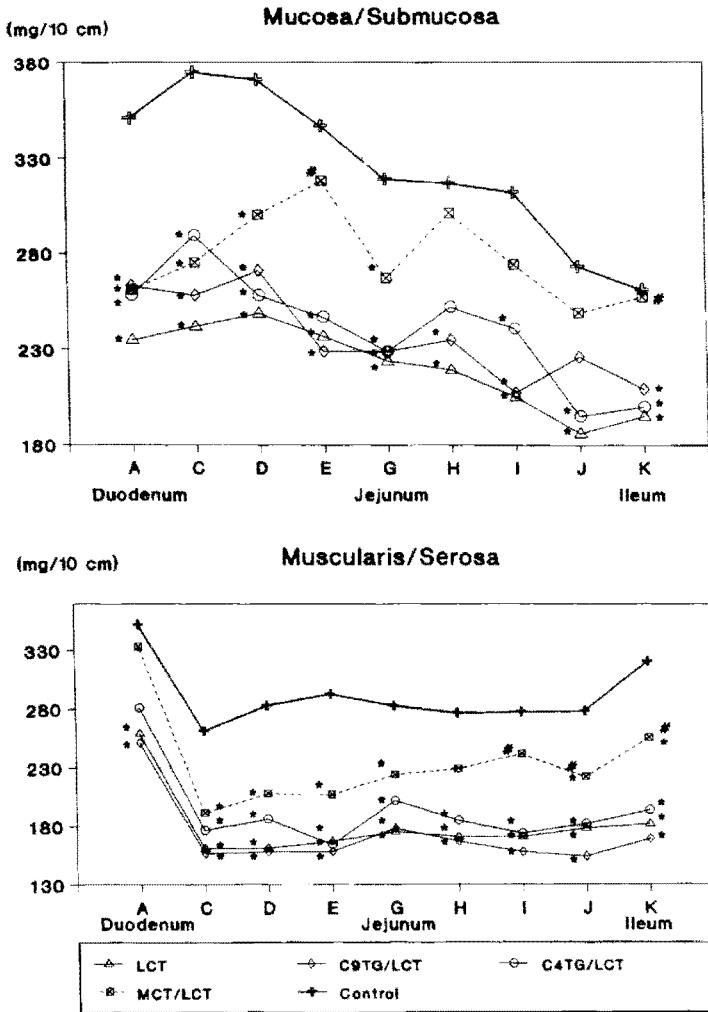


Fig. 2. Mass of mucosa/submucosa and muscularis/serosa of 10-cm segments (mg/10 cm, mean) in the small bowel of traumatized rats (n = 6/group) after 7 days of TPN with different types of fat emulsions and in controls (0.9% NaCl, standard chow). \*Significantly different mean compared with control; #significantly different with mean compared with all other TPN groups; snk-test,  $p \leq .05$ . Capital letters indicate 10 cm-segments; for explanation see text.

MCT/LCT vs control in the ileum; Table II). For the colon, mean results of the protein, RNA, and DNA analysis in the mucosa/submucosa were not significantly different between all groups.

Plasma butyric acid concentrations in the C4-L-C4-TG group were significantly increased after 7 days of TPN infusion compared with the other TPN groups and with controls (Table III). Additionally, this was the only TPN group in which mean plasma acetic acid concentration was not statistically distinguishable from controls. For the animals of the C9TG/LCT group no increase in plasma SCFA concentrations could be observed.

The animals of the MCT/LCT group revealed the highest plasma  $\beta$ -hydroxybutyrate concentrations with  $0.23 \pm 0.12$  mmol/L; for the LCT, C9TG/LCT and C4-L-C4-TG groups plasma concentrations of  $0.05 \pm 0.01$ ,  $0.08 \pm 0.04$ , and  $0.13 \pm 0.06$  mmol/L were measured, respectively. Mean acetoacetate concentrations in all TPN groups were below 0.05 mmol/L.

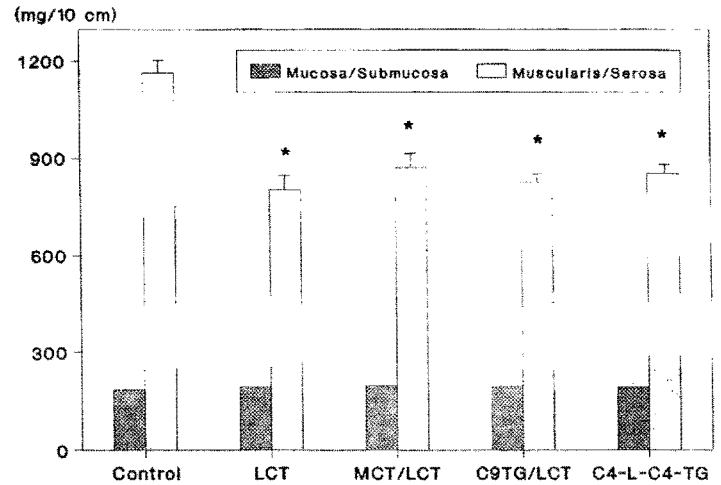


Fig. 3. Weight of mucosa/submucosa and muscularis/serosa (mg/10 cm, mean  $\pm$  SEM) in the colon of traumatized rats (n = 6/group) after 7 days of TPN with different types of fat emulsions and in controls (0.9% NaCl, standard chow). \*Significantly different mean compared with control; snk-test,  $p \leq .05$ .

### DISCUSSION

Because of the proven trophic effect of SCFAs on the intestinal mucosa, the two fat emulsions C4-L-C4-TG or C9TG/LCT were supposed to reveal a distinctly less impaired intestine after 7 days of TPN when compared with the other fat emulsions. However, the results of some gut parameters investigated indicate an effect of the MCT/LCT fat emulsion, which is the opposite of this hypothesis. Moreover, not as much the villus-mucosal height, but the masses of mucosa/submucosa and muscularis/serosa in the (distal) small bowel, showed a smaller decrease when the MCT/LCT fat emulsion was administered. Between the

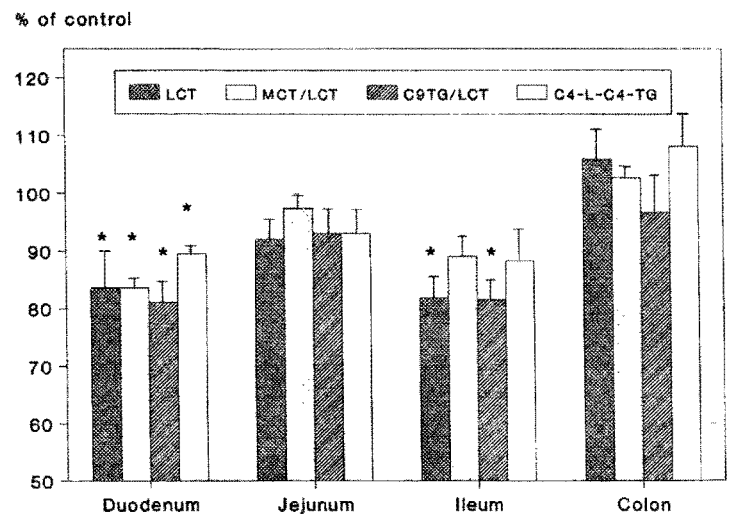


Fig. 4. Mucosal villus height ( $\mu$ m, mean) in the duodenum, jejunum, and ileum as well as mucosal height in the colon of traumatized rats (n = 6/group) after 7 days of TPN with different types of fat emulsions, expressed as percent of the controls (0.9% NaCl, standard chow). \*Significantly different mean compared with control; snk-test,  $p \leq .05$ .

TABLE II  
Concentrations of protein, RNA, and DNA in the mucosa and submucosa of traumatized rats after 7 days of TPN and in controls

Group (n = 6/group)	Duodenum			Middle of jejunum			Ileum			Colon		
	Protein*	RNA†	DNA‡	Protein*	RNA†	DNA‡	Protein*	RNA†	DNA‡	Protein*	RNA†	DNA‡
Control												
Mean	62.5	3.67	400	37.3	2.72	317	24.4	2.85	413	17.8	1.36	292
SEM	3.0	0.22	34	2.6	0.28	23	2.6	0.51	50	1.8	0.14	24
LCT												
Mean	41.3‡	2.26‡	367	28.2‡	1.71‡	362	19.9	1.66	328	22.1	1.38	321
SEM	2.7	0.09	23	1.1	0.07	17	1.1	0.05	33	2.2	0.08	22
MCT/LCT												
Mean	38.7‡	2.01‡	298	26.2‡	1.78‡	331	23.9	2.66	227‡	20.5	1.73	337
SEM	2.1	0.09	19	1.4	0.15	59	1.4	0.20	21	2.1	0.12	72
C9TG/LCT												
Mean	40.3‡	2.40‡	350	23.5‡	1.84‡	344	20.0	2.12	283	17.9	1.33	318
SEM	3.8	0.17	28	1.4	0.22	26	1.4	0.27	28	1.8	0.10	20
C4-L-C4-TG												
Mean	40.1‡	2.03‡	318	23.1‡	1.52‡	316	19.1	2.16	331	18.2	1.80	253
SEM	3.0	0.15	22	1.8	0.07	50	1.8	0.40	40	3.2	0.15	35

For abbreviations, see Table I. TPN contained different types of fat emulsions; controls received standard chow (0.9% NaCl).

\*Values are expressed in mg/10 cm.

†Values are expressed in mg/10 cm and  $\mu$ g/10 cm for RNA and DNA, respectively.

‡Significantly different means compared with control;  $p \leq .05$ , snk-test.

other TPN groups (LCT, C9TG/LCT, and C4-L-C4-TG) no distinct differences could be found in this study, but all showed atrophic changes when compared with the control group. With missing differences in mean small bowel villus height of the TPN groups, the higher 10-cm segment masses in the MCT/LCT group should mainly result from less atrophic gut muscle tissues. The differences in the protein and RNA contents between groups were in good agreement with the differences in the wet weights of mucosa/submucosa (Table II, Fig. 2). In the ileum, for example, similar results for protein and RNA concentration were obtained for the MCT/LCT and the control groups, whereas no statistically significant differences in mucosal-submucosal wet weight between these groups existed.

A positive dose-dependent effect of MCT given enterally to rats on jejunal mass and jejunal mucosal protein synthesis already has been described.<sup>22</sup> Also, in a hepatectomy model (rats) with parenteral nutrition, jejunal mucosal protein content and protein synthesis increased with increasing proportion of MCT, whereas no effect was found in a trauma model (femoral fracture).<sup>22</sup> The authors concluded that the effects of MCT depend on the metabolic state.

The observed effects of parenterally administered MCT may be the result of a faster hydrolysis, cellular uptake, and  $\beta$ -oxidation when compared with LCT emulsions.<sup>23,24</sup> Especially, the higher ketone body formation with infusion of MCT/LCT fat emulsions<sup>23</sup> would provide an explanation, because ketone bodies were shown to reveal a favorable effect on the mucosa of jejunum and colon.<sup>25,26</sup> In the present study the higher plasma concentration of  $\beta$ -hydroxybutyrate on the 8th postoperative day in the MCT/LCT group was not statistically different from the means in the other TPN groups. However, a protein-sparing effect of MCT vs LCT in catabolic states is documented even without significant elevations of plasma ketone bodies.<sup>23,27</sup> Because visceral protein is one of the first protein sources used in catabolic conditions, a protein-sparing effect of MCT toward gut muscle tissues seems reasonable, and speculation can be made about the consequences for the focused problem of bacterial translocation (eg, higher

secretory immunoglobulin A). In studies with enteral MCT administration, mucosal brush border membrane bound enzyme activities and absorptive function was shown to be better maintained than with LCT.<sup>28,29</sup>

Other investigators have focused on effects of different nutrients on the muscularis/serosa of the intestine. In the present experiment similar changes in the masses of mucosa/submucosa and muscularis/serosa were shown indicating an advantage of the MCT/LCT emulsion also for the muscularis in the distal jejunum and ileum (Fig. 2). However, it has to be pointed out that in the duodenum (Fig. 2, segment A) the mass of the muscularis/serosa was not reduced in the animals of the MCT/LCT group, whereas the decrease in mucosal-submucosal mass was highest in this gut region for all TPN groups. Speculations about possible implications can not be given.

The expected positive effect of the trinonanoic-containing fat emulsion on intestinal integrity should mainly proceed from propionic acid/propionyl CoA released during  $\beta$ -oxidation of nonanoic acid. In the present study no increase in propionic acid or other SCFA concentrations was measured in the plasma after C9TG/LCT infusion as found in a previous experiment<sup>15</sup> in which a much higher dose of C9TG was infused (33% vs 12% of total daily energy). Propionyl CoA must have been released intracellularly, but the main release probably was in the liver, which is the most important organ for MCT metabolism.<sup>23</sup> This would indicate that the previously measured increase in plasma

TABLE III  
Concentrations of acetic, propionic, and butyric acid in the plasma of traumatized rats after 7 days of TPN and in controls

Group (n = 6/group)	Acetic acid ( $\mu$ mol/L)	Propionic acid ( $\mu$ mol/L)	Butyric acid ( $\mu$ mol/L)
Control	746.8 $\pm$ 169.5	21.9 $\pm$ 7.3	34.1 $\pm$ 15.3
LCT	338.7 $\pm$ 85.7*	7.6 $\pm$ 1.0	2.7 $\pm$ 0.3
MCT/LCT	270.2 $\pm$ 19.7*	7.8 $\pm$ 1.3	4.3 $\pm$ 0.4
C9TG/LCT	302.7 $\pm$ 33.8*	11.5 $\pm$ 1.6	3.6 $\pm$ 0.8
C4-L-C4-TG	499.3 $\pm$ 92.3	14.0 $\pm$ 1.7	148.0 $\pm$ 73.7*

Values are means  $\pm$  SEM. For abbreviations, see Table I. Controls received standard chow (0.9% NaCl).

\*Significantly different mean compared with control;  $p \leq .05$ , snk-test.

SCFAs can be seen as a consequence of overloading. However, utilization of even-numbered MCTs in tissues other than the liver has been demonstrated,<sup>23</sup> and it seems unlikely that nonanoic acid should not be metabolized in the gut cells. Theoretically, with the given C9TG doses more propionic acid should have been provided to the organism than parenterally administered by Koruda and coworkers,<sup>11</sup> showing the trophic effect of Na salts of SCFAs on the gut mucosa.

Although after a 7-day infusion of triacetin-LCT (1:1) a reduced atrophy of the intestinal mucosa was found in comparison with LCT administration,<sup>30</sup> mean plasma acetate concentrations were lower (<300  $\mu\text{mol/L}$ ) than obtained in the C4-L-C4-TG group of the present experiment (499  $\mu\text{mol/L}$ , Table III). For the investigations that showed a positive effect of parenteral or intracecal infusion of SCFAs on gut integrity, no data on plasma SCFA values were available.<sup>10-14</sup> With respect to the molar ratio of parenteral SCFAs (acetate:propionate:butyrate = 36:15:9) administered by Koruda and coworkers,<sup>11</sup> higher plasma values of propionic acid should have been reached in that study compared with the present one with a plasma ratio of 36:1:11. Butyrate, the preferred oxidative fuel of colonocytes,<sup>9,31,32</sup> improved colonic and even ileal mucosal parameters after intracolonic infusion in coecetomized rats fed a fiber-free elemental diet.<sup>12</sup> However, the investigated parameters of the ileum and the colon in the C4-L-C4-TG group revealed no distinct differences to the other TPN groups in spite of a theoretically much higher supply of butyrate to the colonocytes via systemic circulation. The questions arising are whether by the IV route butyrate is not as effective as shown with intracolonic instillation and whether a certain ratio of the three main SCFAs is necessary for revealing protective effects on the mucosa of the small intestine; the latter suggestion would not be in accordance with the favorable results found after parenteral triacetin administration.<sup>30</sup>

In conclusion, after MCT/LCT administration structural impairments in the distal half of the small bowel were smallest within TPN groups referring to the mucosal villus height and the masses of mucosa/submucosa as well as muscularis/serosa. However, further testing of the MCT/LCT fat emulsion by means of functional parameters is needed to clarify possible consequences of the results shown for the problem of bacterial translocation. In the proximal small bowel and the colon no distinct differences between the tested fat emulsions could be found.

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#### REFERENCES

- Epstein MD, Banducci DR, Manders EK: The role of the gastrointestinal tract in the development of burn sepsis. *Plast Reconstr Surg* 90:524-531, 1992
- Langkamp-Henken B, Glezer JA, Kudsk KA: Immunologic structure and function of the gastrointestinal tract. *NCP* 7:100-108, 1992
- Shou J, Lappin J, Minnard EA, et al: Total parenteral nutrition, bacterial translocation, and the host immune function. *Am J Surg* 167:145-150, 1994
- Alverdy JC, Aoye E, Moss GS: Total parenteral nutrition promotes bacterial translocation from the gut. *Surgery* 104:185-190, 1988
- Spaeth G, Berg RD, Specian RD, et al: Food without fiber promotes bacterial translocation from the gut. *Surgery* 108:240-247, 1990
- Deich EA, Xu DZ, Naruhn MB, et al: Elemental diet and IV-TPN-induced bacterial translocation is associated with loss of intestinal mucosal barrier function against bacteria. *Ann Surg* 221:299-307, 1995
- Sigurdsson GH: Is translocation of bacteria and endotoxin from the gastrointestinal tract a source of sepsis in critically ill patients? *Acta Anaesthesiol Scand* 39 (Suppl 105):11-19, 1995
- Grant JP: Nutritional support in critically ill patients. *Ann Surg* 220:610-616, 1994
- Rombeau JL, Kripke SA: Metabolic and intestinal effects of short-chain fatty acids. *JPEN* 14 (Suppl):181S-185S, 1990
- Koruda MJ, Rolandelli RH, Settle RG, et al: Effect of parenteral nutrition supplemented with short-chain fatty acids on adaptation to massive small bowel resection. *Gastroenterology* 95:715-720, 1988
- Koruda MJ, Rolandelli RH, Zimmaro Bliss D, et al: Parenteral nutrition supplemented with short-chain fatty acids: Effect on the small bowel mucosa in normal rats. *Am J Clin Nutr* 51:685-689, 1990
- Kripke SA, Fox AD, Berman JM, et al: Stimulation of intestinal mucosal growth with intracolonic infusion of short-chain fatty acids. *JPEN* 13:109-116, 1989
- Friedel D, Levine GM: Effect of short-chain fatty acids on colonic function and structure. *JPEN* 16:1-4, 1992
- Sakata T, von Engelhardt W: Stimulatory effect of short chain fatty acids on the epithelial cell proliferation in rat large intestine. *Comp Biochem Physiol* 74A:459-462, 1983
- Linseisen J, Wolfram G: Odd-numbered medium-chain triglycerides (trimonanoin) in total parenteral nutrition: Effects on parameters of fat metabolism in rabbits. *JPEN* 17:522-528, 1993
- Björkman C, Forslund K: Volatile fatty acids in adult and young ruminants: An evaluation of a gas chromatographic method. *J Dairy Sci* 69:998-1003, 1986
- Williamson DH, Mellanby J: d-(-)-3-Hydroxybutyrate. IN *Methoden der Enzymatischen Analyse*. Bd. II, Bergmeyer HU (ed). Verlag Chemie GmbH, Weinheim, Germany, 1970, pp 1772-1775
- Mellanby J, Williamson H: Acetacetat. IN *Methoden der Enzymatischen Analyse*. Bd. II, Bergmeyer HU (ed). Verlag Chemie GmbH, Weinheim, Germany, 1970, pp 1776-1779
- Kresze G-B: The biuret method. IN *Methods of Enzymatic Analysis*, Vol. II, Bergmeyer HU (ed). Verlag Chemie, Weinheim, Germany, 1983, pp 86-88
- Fleck A, Begg D: The estimation of ribonucleic acid using ultraviolet absorption measurements. *Biochim Biophys Acta* 108:333-339, 1954
- Giles KW, Myers A: An improved diphenylamine method for the estimation of deoxyribonucleic acid. *Nature* 206:93, 1965
- Schwartz S, Farriol M, Garciaarumi E, et al: Effect of medium chain triglycerides (MCT) on jejunal mucosa mass and protein synthesis. *Gut* 35 (Suppl):S39-S41, 1994
- Bach AC, Storck D, Meraiti Z: Medium-chain triglyceride-based fat emulsions: An alternative energy supply in stress and sepsis. *JPEN* 12:82S-88S, 1988
- Metges CC, Wolfram G: Medium- and long-chain triglycerides labeled with <sup>13</sup>C: A comparison of oxidation after oral or parenteral administration in humans. *J Nutr* 121:31-36, 1991
- Kripke SA, Fox AD, Berman JM, et al: Inhibition of TPN-associated intestinal mucosal atrophy with monoacetoacetin. *J Surg Res* 44:436-444, 1988
- Kripke SA, Fox AD, Berman JM, et al: Inhibition of TPN-associated colonic atrophy with  $\beta$ -hydroxybutyrate. *Surg Forum* 39:48-50, 1988
- Iwasa Y, Ogoshi S, Iwasa M, et al: The effect of triacetyl emulsion on protein turnover in scald burn rats. *Nutrition* 6:107-113, 1990
- Weinberg LM, Pusateri JPJ, Levine GM: Comparison of different caloric substrates (MCT, LCT and dextrose) on intestinal adaptation of the rat. *Gastroenterology* 96:1514-1520, 1989
- Takase S, Goda T: Effect of MCT on brush border membrane-bound enzyme activity in rat small intestine. *J Nutr* 120:969-976, 1990
- Karlstad MD, Killeffer JA, Bailey JW, et al: Parenteral nutrition with short- and long-chain triglycerides: Triacetin reduces atrophy of the small and large bowel mucosa and improves protein metabolism in burned rats. *Am J Clin Nutr* 55:1005-1011, 1992
- Roediger WEW: Utilization of nutrients by isolated epithelial cells of the rat colon. *Gastroenterology* 83:424-429, 1982
- Frankel WL, Zhang W, Shing A, et al: Mediation of the trophic effects of short-chain fatty acids on the rat jejunum and colon. *Gastroenterology* 106:375-380, 1994