

# Prospective Evaluation of Faecal Fatty Acid Excretion in Short Bowel Syndrome in Newborns

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● Short bowel syndrome (SBS) in the newborn results in limited intestinal absorptive capacity, leading especially to fatty acid (FA) malabsorption. It is unknown whether adaptation occurs in time in FA absorption, and whether this adaptation is chain-length dependent. The aim of the present study was to prospectively evaluate FA absorption and excretion during SBS in the newborn. Twenty-one neonates who underwent small bowel resection (of variable length) for various reasons (necrotizing enterocolitis, intestinal atresia, meconium peritonitis, cloacal extrophy, etc) were studied. Eight neonates had SBS, defined as a small bowel remnant of less than 50% of the original small bowel length related to gestational age. The mean remaining small bowel length in the SBS group was 34% (24% to 42%). The non-SBS control group consisted of 13 neonates who had only minor small bowel resections. The mean remaining bowel length for the non-SBS group was 95% (70% to 100%). The results show that the total fractional excretion of FA (FE-FA) at 2 weeks and 1, 2, 3, and 4 months postsurgery was  $51\% \pm 37\%$ ,  $33\% \pm 24\%$ ,  $51\% \pm 65\%$ ,  $53\% \pm 27\%$ , and  $7\% \pm 2\%$  in patients with SBS, versus  $12\% \pm 8\%$ ,  $24\% \pm 10\%$ ,  $9\% \pm 3\%$ ,  $8\% \pm 3\%$  and  $17\% \pm 14\%$  in the non-SBS controls, respectively ( $P < .05$  by ANOVA). There appeared to be an amelioration in time in FA absorption, especially in the SBS group, after 3 months. FE-FA was chain-length related, being considerably less for C10 and C12 than for C14 and longer amounts. An amelioration of absorption occurred in the SBS patients, especially with the longer-chain FA. On the basis of the study data, the authors conclude that in the initial adaptation phase shorter chain lengths are better absorbed than longer chain lengths; however, in the latter FA group, substantial adaptation occurs with time.

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**INDEX WORDS:** Short bowel syndrome, intestinal tract, adaptation, neonate, fatty acids.

**S**HORT BOWEL SYNDROME (SBS) occurring after massive intestinal resection is characterized by severe diarrhea, malabsorption, negative nitro-

gen balance, and body weight loss, primarily as a result of a drastic decrease in intestinal absorptive surface.<sup>1,2</sup> The adaptive response in the remaining small and large intestine is marked by hyperplastic villi, with parallel increases in segmental mucosal DNA, RNA, protein, and weight.<sup>3-6</sup> Mucosal adaptation ultimately results in diminution of malabsorptive nutritional losses.<sup>2,7</sup> The intestinal adaptation is achieved by the interaction of various factors for which the presence of enteral substrate is very important.<sup>8,9</sup> Because the outcome after major bowel resection in the neonatal period depends primarily on the time needed for adaptation of the bowel,<sup>10</sup> it is of utmost importance to achieve enteral autonomy as soon as possible. Depending on the composition of the luminal content, mucosal growth can be enhanced.<sup>11-15</sup>

Of the individual dietary components, it has been suggested that long-chain triglycerides (LCT) may be especially potent promoters of small intestinal mucosal cell proliferation.<sup>14,16-18</sup> However, because fat malabsorption is common in these patients,<sup>19,20</sup> supplying medium-chain triglycerides (MCT) instead of LCT is a standard practice. The reason for this is that MCT are hydrolysed more rapidly by pancreatic lipase than are LCT<sup>21</sup> and are transported principally by the portal vein to the liver for oxidation rather than through the intestinal lymphatic vessels, which are used by LCT.<sup>22</sup>

Because little is known about the adaptation that occurs with time in MCT- and LCT-derived fatty acid (FA) malabsorption and about whether this malabsorption/adaptation is chain-length dependent, we conducted a prospective study that evaluates FA absorption and excretion in neonates with SBS and neonates who underwent minor small bowel resection.

## MATERIALS AND METHODS

### Patients

Twenty-one neonates had undergone intestinal resection, of variable length, as a consequence of various underlying diseases. The diagnoses were necrotizing enterocolitis (NEC),<sup>10</sup> jejunal atresia (3), meconium peritonitis (non-cystic fibrosis) (3), cloacal extrophy (2), Hirschsprung's disease (1), multiple atresia (1), and obstruction ileus (non-cystic fibrosis) (1). Fifteen patients were born prematurely (before 37 weeks' gestation).

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The patients were divided into two groups. Eight had SBS (SBS group), defined as a loss of more than 50% of the original small bowel as related to gestational age.<sup>23</sup> The mean remaining small bowel length related to gestational age in this group was 34% (range, 24% to 42%). Thirteen patients had only minor small bowel resections (non-SBS group), and served as controls. Their mean remaining small bowel length related to gestational age averaged 95% (range, 70% to 100%).

In the SBS group (n = 8), five patients had an ileostomy; in the non-SBS group (n = 13), nine patients had an ileostomy and one had a colostomy. As reported earlier,<sup>24</sup> the intestinal continuity in these groups of patients was reestablished after an average of approximately 100 days after the initial operation. Growth was recorded regularly. Patient data are summarized in Table 1.

### FA Intake, Excretion, and Analysis

The patients participated in a prospective evaluation of nutritional intake of FA and faecal excretion of FA. The protocol was begun after 2 weeks of recovery and stabilization of the patient and after informed consent was obtained from the parents or caretakers. During a 72-hour period, enterostomy fluid or faeces were collected for analysis at week 2 and 1, 2, and 3 months postoperatively, and subsequently one-time 24-hour faeces were collected at 4, 6, and 12 months postoperatively. FA intake was calculated from the amount of food intake of a specific formula and the FA content of that formula. FA excretion was calculated from enterostomy fluid or faecal collections and from the FA concentrations. For FA analysis, the total stool sample was homogenized and the volume determined. Then, a representative sample was taken, which was analyzed by use of gas chromatography.<sup>25</sup> Intake and excretion of FA were calculated in food and faeces (respectively) for the total of all FA and for chain lengths C10, C12, C14, C16, and C18. The fractional excretion was calculated as:

$$100 \times \frac{\text{FA output}}{\text{FA input}}$$

as a measure of the FA malabsorption of the gut.

### Statistical Analysis

Data are presented as mean  $\pm$  SEM. *P* values of less than .05 were considered significant. Statistical analyses were performed with the SPSS/PC+ statistical software package on a standard personal computer.<sup>26</sup> For analysis of the main effects of group and time as well as their interactions, analysis of variance (ANOVA) was used. For time effects within groups, the one-way ANOVA was used. Both ANOVA procedures were run for the entire study

Table 1. Characteristics of Patients

	SBS	NON-SBS
No. of patients	8	13
Mean gestational age (wk)	35.2 (range, 28 to 40)	33.7 (range, 29 to 42)
Male:female ratio	5:3	8:5
Enterostomy	5 Ileostomy	9 Ileostomy 1 Colostomy
Mean weight at start of protocol (g)	2,610 $\pm$ 480	2,500 $\pm$ 380
Mean weight at age 4 mo (g)	3,950 $\pm$ 490	4,500 $\pm$ 280
Mean remaining small bowel length (%)	34 (range, 24 to 42)	95 (range, 70 to 100)

Table 2. Faecal Fatty Acid Excretion in SBS and Non-SBS Patients

	No. of Months After Surgery						
	½	1	2	3	4	6	12
FE TOT							
SBS	51 $\pm$ 37	33 $\pm$ 24	51 $\pm$ 65	53 $\pm$ 27	7 $\pm$ 2	3 $\pm$ 0	5
CON	12 $\pm$ 8	24 $\pm$ 10	9 $\pm$ 3	8 $\pm$ 3	17 $\pm$ 14		2
FE C10							
SBS	9 $\pm$ 5	8 $\pm$ 4	5 $\pm$ 8	15 $\pm$ 14	1 $\pm$ 1	2 $\pm$ 1	1
CON	1 $\pm$ 1	9 $\pm$ 7	0 $\pm$ 0	1 $\pm$ 1	5 $\pm$ 5		0
FE C12							
SBS	10 $\pm$ 4	17 $\pm$ 18	51	24 $\pm$ 14	2 $\pm$ 1	0 $\pm$ 0	1
CON	11 $\pm$ 11	9 $\pm$ 8	32	1 $\pm$ 1	10 $\pm$ 10		
FE C14							
SBS	53 $\pm$ 75	72	75	49	8 $\pm$ 3	2 $\pm$ 0	6
CON	17 $\pm$ 17	27 $\pm$ 5	8	9 $\pm$ 6	12 $\pm$ 9		2
FE C16							
SBS	77 $\pm$ 50	44 $\pm$ 24	61 $\pm$ 63	87 $\pm$ 46	16 $\pm$ 4	5 $\pm$ 1	14
CON	19 $\pm$ 10	38 $\pm$ 15	69 $\pm$ 67	18 $\pm$ 10	24 $\pm$ 14		6
FE C18							
SBS	60 $\pm$ 37	41 $\pm$ 24	58 $\pm$ 69	82 $\pm$ 47	8 $\pm$ 3	3 $\pm$ 0	2
CON	17 $\pm$ 10	37 $\pm$ 17	5 $\pm$ 2	7 $\pm$ 2	18 $\pm$ 15		1

NOTE. If the number of determinations is less than 3, no SEM is given.

Abbreviations: SBS, patients with short bowel syndrome; CON, patients with non-short bowel syndrome; FE TOT, faecal fractional excretion of total of all fatty acids; FE C10, C12, C14, C16, and C18, faecal fractional excretion of fatty acids with (respectively) 10, 12, 14, 16, and 18 carbon atoms.

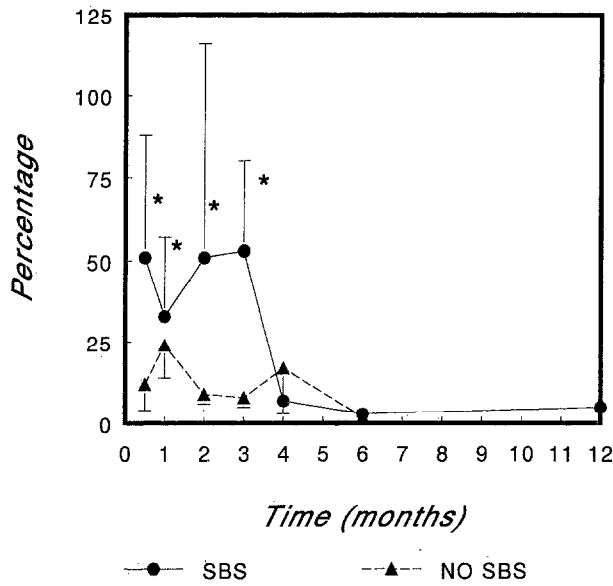
period as well as for various shorter intervals. For clarity, only the results of the total study period and the time span between 2 weeks and 3 months postsurgery will be discussed. Differences between groups at individual time points were tested nonparametrically using the Mann Whitney U test. (Because the latter test did not yield additional valuable information, it will not be discussed further.)

## RESULTS

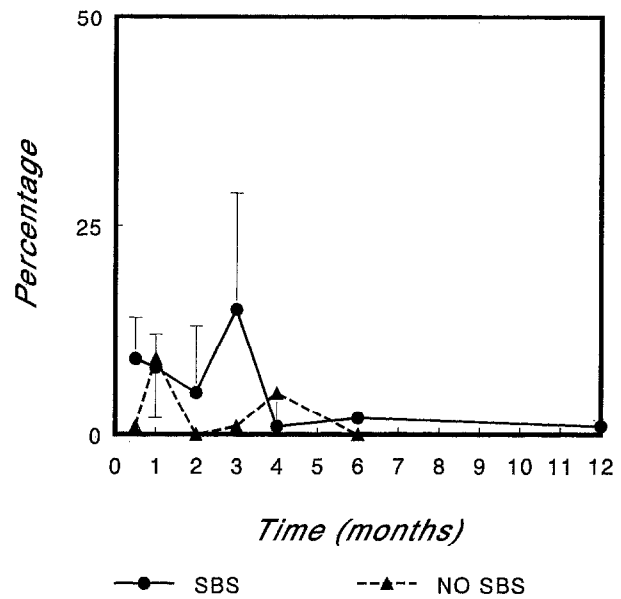
Patient characteristics are summarized in Table 1. The SBS and non-SBS groups are comparable with the exception of the mean remaining bowel length, which was 34% (24% to 42%) and 95% (70% to 100%), respectively.

In Table 2, the fractional faecal FA excretion in SBS and non-SBS patients is shown. Data are presented as mean  $\pm$  SEM. The results show that total FA fractional excretion at 2 weeks and 1, 2, 3 and 4 months postsurgery was 51%  $\pm$  37%, 33%  $\pm$  24%, 51%  $\pm$  65%, 53%  $\pm$  27%, and 7%  $\pm$  2% in SBS patients and 12%  $\pm$  8%, 24%  $\pm$  10%, 9%  $\pm$  3%, 8%  $\pm$  3%, and 17%  $\pm$  14% in non-SBS controls, respectively. Statistical analysis (ANOVA) for the period between 2 weeks and 3 months postsurgery showed a significant difference between the curves (Fig 1).

With respect to the fractional faecal FA excretion of the individual chain lengths, the following results were obtained. For C10 and C12 FA, the fractional



**Fig 1.** Fractional faecal fatty acid excretion for the total of all fatty acids in patients with short bowel syndrome (n = 8; bowel remnant length, 34% ± 3%; dots) compared with patients operated on for similar conditions but with near-normal gut remnant (n = 13; gut remnant length, 95% ± 4%; triangles). Statistical significance ( $P < .05$ ; ANOVA analysis between 2 weeks and 3 months) is indicated by the asterisks.



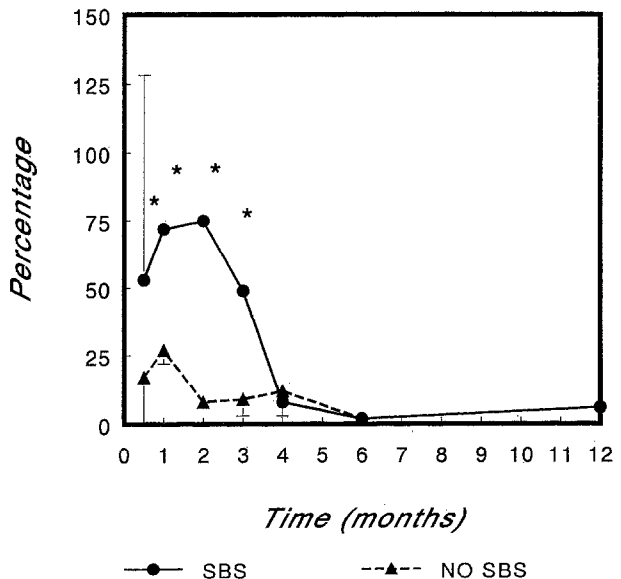
**Fig 2.** Fractional faecal fatty acid excretion for C10 chain length fatty acids in patients with short bowel syndrome (n = 8; bowel remnant length, 34% ± 3%; solid circles) compared with patients operated on for similar conditions but with near-normal gut remnant (n = 13; gut remnant length, 95% ± 4%; triangles). There were no significant differences.

faecal excretion did not differ significantly for the two patient groups, and ranged, at the observed time points, between 1% ± 1% and 24% ± 14%, with a few exceptionally high values. In neither the C10 nor the C12 group of FA was there a significant difference between the curves (ANOVA analysis for the period between 2 weeks and 3 months as well as for all other time ranges). For the C10 FA, this is depicted in Fig 2. For the C14, C16, and C18 FA, the fractional faecal excretion ranged from 40% to more than 80% in the SBS group, and was significantly higher (ANOVA analysis) in SBS patients in the first 3 months postsurgery. The values from 4 months postsurgery onward did not differ significantly. The curves of C14 and C18 fractional faecal FA excretion are shown in Figs 3 and 4.

**DISCUSSION**

In the present study we found that FA absorption (as assessed by the measurement of fractional FA excretion in stools) in neonates with SBS is dependent on FA chain length and on the time between evaluation and initial small bowel resection. The shorter chain lengths, especially C10 and C12, are absorbed almost completely from the time enteral nutrition is begun. The longer chain lengths are malabsorbed for at least 12 weeks after surgery. From our data it appears that there is a separation point in

the absorption in SBS neonates, between FA of up to 12 carbon atoms (MCT) and FA of 14 or more carbon atoms (LCT). The results confirm those of animal studies in which the absorption of dietary fat contain-



**Fig 3.** Fractional faecal fatty acid excretion for C14 chain length fatty acids in patients with short bowel syndrome (n = 8; bowel remnant length, 34% ± 3%; dots) compared with patients operated on for similar conditions but with near-normal gut remnant (n = 13; gut remnant length, 95% ± 4%; triangles). Statistical significance ( $P < .05$ ; ANOVA analysis between 2 weeks and 3 months) is indicated by the asterisks.

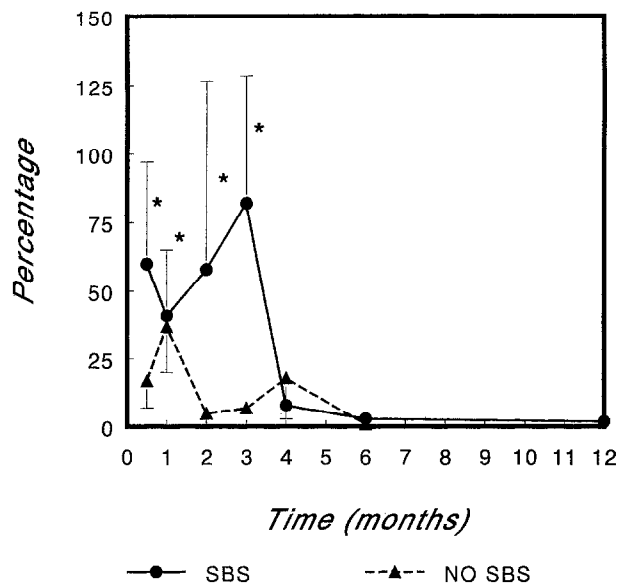


Fig 4. Fractional faecal fatty acid excretion for C18 chain length fatty acids in patients with short bowel syndrome ( $n = 8$ ; bowel remnant length,  $34\% \pm 3\%$ ; dots) compared with patients operated on for similar conditions but with near-normal gut remnant ( $n = 13$ ; gut remnant length,  $95\% \pm 4\%$ ; triangles). Statistical significance ( $P < .05$ ; ANOVA analysis between 2 weeks and 3 months) is indicated by the asterisks.

ing LCT and MCT was evaluated and it was shown that MCT are more rapidly hydrolysed and absorbed in the intestinal lumen than are LCT.<sup>22</sup> The proximal small bowel being the preferred side of MCT absorption and the mid and distal small bowel being the preferred side of LCT absorption might explain why there is a difference in fractional faecal FA excretion between the SBS and non-SBS groups.

Although the advantage of MCT from the standpoint of rate of absorption in SBS has been well documented,<sup>21,27</sup> little is known about the effect of the remaining colon on FA (mal)absorption and about the effect of LCT versus MCT on mucosal adaptation.

In the present study there appeared to be a rapid decrease in the malabsorption of C14 and longer FA chains, and thus enhanced adaptation between 3 and 4 months postsurgery. This coincides with the closure of enterostomies around this time.<sup>24</sup> The sudden amelioration in the absorption of the longer FA after 3 months might be attributable true adaptation in the small bowel remnant in the SBS group. Alternatively, this might be related to the inclusion of the colon in the intestinal stream after closure of enterostomies, with or without a terminal ileal segment and the ileocecal valve. Regardless of this adaptation or its explanation, the data provide evidence that it might be better to give MCTs instead of LCTs during the first 3 months after resection.

Morin et al<sup>14</sup> reported that, in rats, morphological mucosal hyperplasia (as determined by measurement of mucosal protein and DNA content) was greater after LCT feedings than after MCT feedings. Vanderhoof et al<sup>13</sup> confirmed these results in rats and added the observation that mucosal function improved after the use of LCT feedings, as demonstrated by enhanced leucine uptake in the distal small bowel and enhanced sucrase activity in the proximal small bowel in the animals subjected to small bowel resection. To clarify the relative enterotrophic actions of different triglycerides, Jenkins and Thompson<sup>28</sup> gave rats five different oils in mixed diets and compared the effects on the overall mass of the small intestine and on the distribution of mass along the small intestine. Subsequently, the enterotrophic effects of bolus doses of LCT and MCT were compared. They found that LCT and MCT differed in their regional effects on cell proliferation; all four LCT-rich diets increased mucosal mass and cell proliferation maximally in the mid small intestine, whereas MCT diets had the greatest effect proximally. When the LCT and MCT diets were given as boluses, the differences disappeared. The authors suggested that the enterotrophic effect of bolus MCT is the result of accelerated transit causing the release in the distal small bowel of an enterotrophic peptide that enhanced the overall trophic effect to the small bowel. It is noteworthy that the infusion of MCT directly into the human ileum causes a release of enteroglucagon,<sup>29</sup> which has been proposed as an enterotrophic hormone.<sup>30</sup>

In summary, it is possible that LCT-rich diets have a positive effect on adaptation after small bowel resection. However, the issue is whether this positive LCT effect outweighs the physiological advantages of MCT. From our clinical data and the results of animal studies, it remains unclear which form of triglycerides (MCT or LCT) should be used in SBS patients. One animal study has addressed this question, comparing the relative effects of diet mixtures containing either 50% MCT/50% LCT or 100% LCT.<sup>31</sup> It was shown that the diet that contained 50% MCT/50% LCT led to a higher increase in the mucosal mass and protein content. It was found that the mixed diet determined the most appropriate lipid content and composition in the brush-border membrane.<sup>32</sup> There were no deleterious effects of the mixed diet on the activities of sucrase, lactase, or aminopeptidase.<sup>33</sup>

On the basis of our data and the literature cited, it is our opinion that the enteral diet of neonates with SBS should contain a mixture of MCT and LCT, to combine the physiological advantages of MCT with

the positive effects of LCT on adaptation and the maintenance of a sufficient supply of essential FAs (C18 provided by the LCT component). Otherwise, detrimental changes in intestinal morphology and membrane lipid composition could occur as a result of essential FA deficiency in the diet.<sup>34-36</sup> Furthermore, avoiding enterostomies certainly enhances rehabilitation. If no reanastomosis is performed, then it should be considered to reinfuse proximal enterostomy output in the distal enterostomy to include the remaining small bowel and colon in the adaptation process.<sup>35,36</sup>

A prospective clinical trial that compares the effects of a mixed MCT/LCT diet to those of an LCT diet in neonates with SBS is warranted. To enhance the enterotrophic effects, these diets should be given as a bolus.<sup>37</sup>

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