Published in final edited form as:

J Pediatr. 2015 July ; 167(1): 35–40.e1. doi:10.1016/j.jpeds.2015.02.053.

Necrotizing Enterocolitis and Central line Associated Blood Stream Infection Are Predictors of Growth Outcomes in Infants with Short Bowel Syndrome

Bram P. Raphael, M.D.^{1,2}, Paul D. Mitchell, M.S.³, Darryl Finkton, B.A.², Hongyu Jiang, Ph.D.³, Tom Jaksic, M.D., Ph.D.⁴, and Christopher Duggan, M.D., M.P.H.^{1,2}

¹Center for Advanced Intestinal Rehabilitation, Boston Children's Hospital, Harvard Medical School, Boston, MA, USA 02115

²Division of Gastroenterology, Hepatology and Nutrition, Boston Children's Hospital, Harvard Medical School, Boston, MA, USA 02115

³Clinical Research Center, Boston Children's Hospital, Harvard Medical School, Boston, MA, USA 02115

⁴Department of Surgery, Boston Children's Hospital, Harvard Medical School, Boston, MA, USA 02115

Abstract

Objectives—To describe the natural history of growth patterns and nutritional support in a cohort of infants with short bowel syndrome (SBS), and characterize risk factors for suboptimal growth.

Study design—Retrospective chart review of 51 infants with SBS followed by our intestinal rehabilitation program. Weight and length data were converted to age, sex and gestational age-standardized weight-for-age Z-scores (WAZ) and length-for-age Z-scores (LAZ).

Results—Median (25thile, 75thiles) age at enrollment was 8.3 (0.9, 14.6) weeks, and follow-up duration was 10 (8, 13) months, including both inpatient and outpatient visits. Both WAZ and LAZ followed a U-shaped curve, with median for newborns (WAZ = −0.28 and LAZ = −0.41), a nadir at age 6 months (−2.38 and −2.18) and near recovery by age 1 year (−0.72 and −0.76). Using multivariable regression analysis, diagnosis of NEC was independently associated with significant decrements of WAZ (−0.76±0.32, *P*=0.02) and LAZ (−1.24±0.32, *P*=0.0001). 2 central line associated bloodstream infections (CLABSIs) was also independently associated with a decrease in WAZ (−0.95±0.33, *P*=0.004) and LAZ (−0.86±0.32, *P*=0.007).

Conclusions—In a cohort of infants with SBS, we observed a unique pattern of somatic growth, with concomitant deceleration of both WAZ and LAZ and near recovery by 1 year. Inflammatory conditions (NEC and CLABSIs) represent potentially modifiable risk factors for suboptimal somatic growth.

Corresponding Author: Bram P. Raphael, M.D., Division of Gastroenterology, Hepatology and Nutrition, 333 Longwood Avenue, Fourth floor, Boston, MA 02115, Phone: 617-355-6439, Fax: 617-730-4722, bram.raaphael@childrens.harvard.edu.

The authors declare no conflicts of interest.

Short bowel syndrome (SBS) is a condition where significant small intestine deficit leads to malnutrition, dehydration, and electrolyte depletion.¹ Parenteral nutrition (PN) is the mainstay of treatment for this condition when nutritional requirements cannot be met by enteral feeds.² Over time, intestinal adaptation allows for greater absorption, weaning of PN and enteral feeding advancement.³ The most common etiologies in infants are necrotizing enterocolitis (NEC), intestinal atresia, midgut volvulus and gastroschisis.^{4,5} The prognosis of patients with SBS depends upon the underlying disease, residual small bowel length, presence of ileocecal valve, presence of colon, and associated complications.² The goal of nutritional therapy is to optimize linear growth and lean mass accrual as well as to achieve appropriate developmental milestones. There have been limited studies to address what constitutes adequate nutrition in patients with SBS, and anecdotal evidence suggests that some children require very high amounts of parenteral and/or enteral energy intake to attain normal growth rates.

Infants with SBS are particularly vulnerable to poor somatic growth. During infancy, energy requirements for growth are at a post-natal high, even in healthy individuals. SBS is associated with metabolic stress as noted by variability in resting energy expenditure⁶, intestinal malabsorption, as well as co-morbidities of prematurity, all of which can significantly compromise growth. With advances in management, the weight-for-age Z-score (WAZ) for children with SBS has improved slightly but remain abnormally low.⁷ At 18 to 22 months, seventy-four percent of very low birth weight preterm infants with surgical SBS were reported to have either weight, length or head circumference less than 10th percentile.⁸ In older children, weaning of PN has been shown to negatively impact WAZ.⁹ It is unknown if a similar pattern is seen in infants, even though this the period when the majority of patients are weaned from PN.³ The aim of this retrospective study was to describe growth patterns in infants with SBS, as well as characterize risk factors for suboptimal growth.

Methods

Following institutional review board approval, we carried out a retrospective medical record review of patients followed between January 2003 and December 2008 at Boston Children's Hospital's Center for Advanced Intestinal Rehabilitation (CAIR). CAIR is a multi-disciplinary program involving intestinal failure specialists in pediatric gastroenterology, surgery, nutrition, nursing, pharmacy and social work.¹⁰ Included were children ages 0 to 6 months at initial hospitalization, with a diagnosis of SBS (a malabsorptive state resulting from congenital or acquired gastrointestinal disease leading to dependence on PN for at least 90 days) and who required PN for at least 30 days during initial hospitalization. We excluded subjects with fewer than 30 days of inpatient nutritional intake data to review.

Data collected included demographic factors (date of birth, sex, race/ethnicity, zip code), medical/surgical history (gestational age, birth weight, diagnoses leading to SBS, intra-operatively measured residual small bowel length, presence of ileocecal valve), laboratory studies (international normalized ratio, direct bilirubin, total bilirubin, alanine aminotransferase [ALT], albumin, and serum citrulline). Anthropometrics (weight, length) and nutritional intake (enteral and PN intake) were collected weekly on the same day of the

week. When measurements were not available on the assigned day, the measurement closest to that day within the same week was chosen. A digital scale accurate to 1 gram was used to measure weight, and a length board accurate to 0.1 cm was used to measure length. Each central line-associated bloodstream infection (CLABSI) was recorded (date of positive cultures and organisms) and were classified according to Centers for Disease Control and Prevention definitions.¹¹ Clinical data was collected from inpatient and outpatient encounters up until age 1 year. An encounter was defined where nutrition intake and anthropometric measurements were available. We recorded the type, concentration and volume of parenteral dextrose, amino acids and lipids received. We also recorded the type, concentration and volume of enteral feeds. Patients were considered PN-independent after two or more consecutive weeks without PN. PN duration was calculated as the difference between the last PN date recorded (or end of study) and the entry date, accounting for any gaps in PN administration.

Dietitians used recommended dietary allowances to devise energy intake recommendations, and titrated PN and EN prescriptions for appropriate weight gain and clinical events. Enteral nutrition was advanced as tolerated according to our standard feeding algorithm.¹² Enteral feeds with breast milk were preferred, if available. Otherwise amino acid-based formulas were used. Feeds advanced typically by increments of 10 ml/kg/day with close monitoring ostomy/stool output.^{12,13}

WAZ and length-for-age Z-score (LAZ) were calculated using World Health Organization 2000 growth charts.¹⁴ For infants with gestation-corrected postnatal age less than 0, we calculated WAZ according to available published data.¹⁵ The percentage of enteral energy intake was calculated as the amount of dietary energy intake derived by enteral routes divided by the total energy intake multiplied by 100. Patients weaned from PN were assigned 0 parenteral energy intake. Cholestasis was defined as the occurrence of serum direct bilirubin greater than 2.0 mg/dL on two separate measurements at least one week apart. Coagulopathy was defined as at least one occurrence of INR greater than 1.5.

We reviewed WAZ, LAZ and weight-for-length raw data. We excluded points 6 Z-scores higher or lower than the median as suggested by WHO macro.¹⁶ We also excluded points increasing or decreasing from baseline greater or less than 2 Z-scores within a 30-day window, as these likely resulted from measurement error. Categorical data were summarized with frequency counts and percentages, and continuous data were summarized as median and quartiles (25%ile, 75%ile) unless otherwise specified. A generalized estimating equation, using an empirical sandwich estimator,¹⁷ was used to investigate the independent association of demographic, underlying etiology of short bowel syndrome, gastrointestinal anatomical features, nutritional, and medical factors with WAZ and LAZ over the first year of life. The relation of outcomes both WAZ and LAZ with age was curvilinear and was therefore modeled as the square of age (measured in weeks since birth). In subsequent regression analyses of association between predictors and growth outcomes (WAZ or LAZ), the strong non-linear age effect was always adjusted. Central line associated bloodstream infections (CLABSI) was dichotomized to reflect a location shift between 0–1 and 2–7 CLABSI observed in scatterplots. Univariable correlates of growth (adjusted for non-linear age) were investigated and those significant at $P < 0.10$ were considered collectively in a

multivariable model. Backwards elimination was then used to obtain a final multivariable model. All tests of significance were two-sided, and comparisons at $P < 0.05$ were considered statistically significant. Statistical analysis and graphical presentation of the data were conducted with SAS (Cary, NC).

Results

Fifty-one infants (27 male; median age at enrollment 8.3 (0.9, 14.6) weeks) with SBS were studied over 10 (8, 13) months (Table I). Thirty-nine subjects (85%) had low, very low or extremely low weight at birth. Among the 22 subjects ages 0–1 month at the first study week, only one (5%) was receiving any enteral nutrition. Baseline anthropometric measurements were within normal range. The median intra-operative residual bowel length was 57 (30, 77) cm, and 18 (40%) had the ileocecal valve resected.

Median PN duration was 4.8 (2.8, 8.3) months. Cholestasis occurred in 38 (75%). Thirty (59%) subjects were treated with intravenous fish oil emulsion, Omegaven (Fresenius Kabi AG, Bad Homburg, Germany). Thirty-four infants (67%) had at least one central line associated bloodstream infection. Thirty-three (65%) were weaned off PN during the study. None of the patients in this cohort was referred for intestinal transplantation. The survival rate was 50/51 (98%) during the study period.

Figure 1 depicts the parenteral and enteral energy intakes in all subjects over the first year of life. Total energy intake remained approximately 100 kcal/kg/day throughout the period. Up until post-natal age 10 months, there was an upward trend for enteral energy intake. Enteral energy intake became the predominant source at 6–7 months old.

There were 1,179 weekly anthropometry measurements collected. After excluding 18 (1.5%) of Z-score measurements due to suspected error or non-physiologic measures and restricting to the first year of life, 1,125 (95%) WAZ scores and 512 (43%) LAZ remained for analysis. Figure 2 illustrates growth rates during the first year of life. WAZ and LAZ both followed a distinctive U shaped curve. The median WAZ was highest for newborn children at -0.28 , and decreased steadily for every additional month until 6.4 months-old with a nadir at -2.38 . Thereafter, the median WAZ increased with each additional month of age, reaching -0.72 at 1 year. Similarly, the median LAZ was highest for newborn children at -0.41 , and decreased steadily for every additional month of age until 6.3 months-old with a nadir at -2.18 . Thereafter, the median LAZ increased with each additional month reaching -0.76 at 1 year. The fitted regression curve for WAZ followed the equation $-0.36 - 0.15 \times \text{Age(weeks)} + 0.003 \times \text{Age(weeks)}^2$ and was statistically different from zero ($P = 0.001$) at each 1 month interval except 0. The fitted regression curve for LAZ followed the equation $-0.47 - 0.13 \times \text{Age(weeks)} + 0.002 \times \text{Age(weeks)}^2$ and was statistically different from zero ($P = 0.001$) at each 1 month interval except 0. Weight-for-length Z-score was not associated with age (data not shown). Restricting analysis to the 22 infants less than age 1 month at baseline and followed for the full 12 months, WAZ and LAZ followed analogous curves, which corroborated our findings (Figure <>; available at www.jpeds.com).

Table II describes univariable correlates of WAZ and LAZ scores adjusting only for age. Older gestational age was associated with greater LAZ ($P=0.002$), and male sex and low birth weight were associated with lower LAZ and WAZ, respectively ($P<0.05$). NEC was associated with lower WAZ ($P=0.04$) and lower LAZ ($P=0.002$). Two or more CLABSI episodes and increased total energy intake were each associated with lower WAZ ($P=0.005$ and $P=0.002$, respectively) and lower LAZ ($P=0.04$ and $P=0.02$, respectively). There was no observed relationship between growth and race/ethnicity, household income (proxy by zip code), residual bowel length, ileocecal valve preservation, number of inpatient weeks, parenteral and enteral energy intake, protein intake, or severity or presence of liver disease.

The results of multivariable regression analysis are shown in Table III. Total energy intake, NEC and two or more CLABSI were independently associated with both lower WAZ and LAZ. For every 100 kcal/kg/day increase in total energy intake, we observed a median (95% CI) decrease in WAZ and LAZ of -1.01 ($-1.48, -0.54$) and -0.55 ($-1.07, -0.04$), respectively. WAZ was -0.76 ($-1.38, -0.14$) lower, and LAZ -1.24 ($-1.86, -0.61$) lower, in subjects with NEC compared with those without NEC. For subjects with two or more CLABSI episodes, we observed a decrease in WAZ and LAZ of -0.95 ($-1.59, -0.03$) and -0.86 ($-1.49, -0.24$), respectively.

NEC was associated with both low birth weight and gestational age. All subjects with NEC were below normal weight at birth, compared with 72% among subjects without NEC ($P = 0.01$); likewise, median gestational age was lower among subjects with NEC compared with those without (25.0 (24.0, 29.0) versus 35.0 (32.0, 36.0), $P < 0.0001$). When substituted in the model for NEC, subjects with low birth weight were independently associated with WAZ, with median (95% CI) -1.51 ($-2.31, -0.72$). A similar effect was not found for LAZ after adjusting for total energy intake and presence of CLASBI; however, each additional week of gestational age was independently associated with a median (95% CI) increase of 0.15 ($0.08, 0.21$) LAZ when substituted in the model for NEC. The effect of substituting gestational age for NEC in the WAZ model was small, 0.06 ($-0.004, 0.13$), and not statistically significant.

Discussion

In this retrospective study, we reviewed the growth and nutritional intakes of 51 infants with SBS during the first year of life. We found that infants exhibited a unique pattern of suboptimal growth with a nadir in WAZ and LAZ simultaneously around age 6 months. In this cohort, two or more CLABSI and NEC were both independently associated with decreased somatic growth. Other predicted risk factors, such as socio-economic status, residual bowel length, severity of liver disease, and others were not associated with these altered growth patterns.

A particularly novel finding was WAZ and LAZ following a U shaped curve during the first year of life. WAZ and LAZ decelerated symmetrically until age 6 months, and thereafter, symmetrically accelerated. This differs from the pattern seen customarily in malnutrition or severe malabsorption where weight deceleration occurs faster than length. It more closely resembles patterns seen in children with chronic inflammatory conditions affecting their

small intestine, including tropical enteropathy or Crohn's disease.^{18,19} In fact, we found that SBS secondary to NEC, one of the most severe types of intestinal inflammation, was a significant risk factor for decreased growth measurements. Hintz et al similarly reported that surgical NEC was associated with substantial growth delay.²⁰ Another common source of intestinal inflammation seen in SBS is small bowel bacterial overgrowth.²¹ It is postulated that adaptation leads to intestinal dilation and ensuing stasis, which in turn creates a favorable milieu for bacterial proliferation and inflammation.²² This intestinal inflammation with elevation in IL-6 might negatively affect the growth hormone-IGF axis²³. TNF-alpha elevation may also increase protein catabolism, as in Crohn's disease²⁴. Although our study did not directly measure intestinal inflammation or bacterial overgrowth, our previous experience in these children suggest that these are common phenomena that could potentially contribute to the suboptimal growth patterns we observed.²¹

CLABSI represent a systemic type of inflammation that might also affect somatic growth, and in fact we observed an association with poorer WAZ and LAZ. This is an important finding in that, unlike other predictors, CLABSI represent a potentially modifiable risk factor. More study is deserved in how interventions aimed at reducing CLABSI, including ethanol locks and better teaching methods of caregivers, might impact somatic growth.

Our multivariable analysis also found that total energy intake was inversely associated with WAZ and LAZ. This somewhat paradoxical finding is likely because additional nutrition support was provided to the smallest infants in an effort to fuel catch-up growth. In contrast to existing literature,^{8,25,26} we did not find that weaning from PN was associated with worsening growth patterns, but we note that our follow-up period was limited to the first 12 months of life.

This cohort was unique in that a majority was exposed to intravenous fish oil emulsion. Intravenous fish oil emulsion has been used at intestinal rehabilitation programs through a compassionate-use protocol to treat PN associated liver disease (PNALD).²⁷⁻³⁰ Interestingly, anti-inflammatory properties are proposed as a mechanism in reducing PNALD. A study of 18 infants treated with intravenous fish oil emulsion did not suggest an effect on WAZ³¹. Another modality used for PNALD is intravenous lipid restriction.^{32,33} Rollins et al reported in a study of 28 surgical infants treated with intravenous lipid restriction that there was a negative impact on somatic growth.³⁴ We did not observe an effect of various intravenous lipid strategies on somatic growth in the present study, but it was not powered to detect differences. The potential effect of intravenous fish oil emulsions and intravenous lipid restriction on somatic growth deserves further study.

Previous studies focused specifically on the growth outcomes after the inciting intestinal injury.^{8,25,26} There has been less attention on growth patterns during the immediate time after the intestinal injury. This is a critical period to study, because undesirable effects on somatic growth may have lasting effect.⁸ Olieman et al observed that adults with SBS had significantly lower height-for-age Z-score than target height.³⁵ Future studies should address the lasting effects of infant SBS growth patterns on adult nutritional status and long-term health.

There are some limitations to our study. We collected the data retrospectively from a medical record review. Because head circumferences were infrequently recorded, we did not include this important growth measure as part of this analysis. We did not collect clinical exam findings of ascites or edema that could have contributed to weight fluctuations. Mid parental heights were not available for analysis. We also did not have available measures of body composition, such as muscle and fat mass. Gains in WAZ and LAZ may not always represent accrual of lean mass, as body composition measurements are not part of standard care.³⁶ Future studies might follow these measures prospectively, as tools such as dual-energy X-ray absorptiometry (DXA) and air-displacement plethysmography are increasingly available.

The strengths of this study include its inclusion of a large number of anthropometric measures in a moderately-sized cohort of infants with SBS, as well as its fair reflection of the SBS general population.⁴ We observed the expected severity of disease in terms of residual small bowel length and PNALD prevalence.³⁷

In summary, in a cohort of infants with SBS, we observed growth measurements that followed a U-shaped curve with a nadir around 6 months-old. This is a distinctive pattern of somatic growth that has not been described before. Our findings also suggest that frequency of CLABSI is potentially an important modifiable risk factor for poor somatic growth.

Acknowledgments

Supported by the National Institutes of Health (T32DK007477-25 [to B.R.] and 1K24HD058795 [to C.D.]).

We thank the entire CAIR team for their expert care of the patients.

Abbreviations

CLABSI	Central line-associated bloodstream infections
LAZ	Length-for-age Z-score
NEC	Necrotizing enterocolitis
PN	Parenteral nutrition
PNALD	Parenteral nutrition associated liver disease
SBS	Short bowel syndrome
WAZ	Weight-for-age Z-score

References

1. O'Keefe SJ, Buchman AL, Fishbein TM, Jeejeebhoy KN, Jeppesen PB, Shaffer J. Short bowel syndrome and intestinal failure: consensus definitions and overview. *Clin Gastroenterol Hepatol*. 2006; 4:6–10. [PubMed: 16431298]
2. Duro D, Kamin D, Duggan C. Overview of pediatric short bowel syndrome. *J Pediatr Gastroenterol Nutr*. 2008; 47(Suppl 1):S33–6. [PubMed: 18667916]

3. Squires RH, Duggan C, Teitelbaum DH, et al. Natural history of pediatric intestinal failure: initial report from the Pediatric Intestinal Failure Consortium. *J Pediatr*. 2012; 161:723–8. e2. [PubMed: 22578586]
4. Andorsky DJ, Lund DP, Lillehei CW, et al. Nutritional and other postoperative management of neonates with short bowel syndrome correlates with clinical outcomes. *J Pediatr*. 2001; 139:27–33. [PubMed: 11445790]
5. Vargas JH, Ament ME, Berquist WE. Long-term home parenteral nutrition in pediatrics: ten years of experience in 102 patients. *J Pediatr Gastroenterol Nutr*. 1987; 6:24–32. [PubMed: 3098947]
6. Duro D, Mitchell PD, Mehta NM, et al. Variability of resting energy expenditure in infants and young children with intestinal failure-associated liver disease. *J Pediatr Gastroenterol Nutr*. 2014; 58:637–41. [PubMed: 24361903]
7. Olieman JF, Tibboel D, Penning C. Growth and nutritional aspects of infantile short bowel syndrome for the past 2 decades. *J Pediatr Surg*. 2008; 43:2061–9. [PubMed: 18970941]
8. Cole CR, Hansen NI, Higgins RD, Ziegler TR, Stoll BJ. Very low birth weight preterm infants with surgical short bowel syndrome: incidence, morbidity and mortality, and growth outcomes at 18 to 22 months. *Pediatrics*. 2008; 122:e573–82. [PubMed: 18762491]
9. Miyasaka EA, Brown PI, Kadoura S, Harris MB, Teitelbaum DH. The adolescent child with short bowel syndrome: new onset of failure to thrive and need for increased nutritional supplementation. *J Pediatr Surg*. 2010; 45:1280–6. [PubMed: 20620332]
10. Modi BP, Langer M, Ching YA, et al. Improved survival in a multidisciplinary short bowel syndrome program. *J Pediatr Surg*. 2008; 43:20–4. [PubMed: 18206449]
11. Horan TC, Andrus M, Dudeck MA. CDC/NHSN surveillance definition of health care-associated infection and criteria for specific types of infections in the acute care setting. *Am J Infect Control*. 2008; 36:309–32. [PubMed: 18538699]
12. Brenn, M.; Gura, K.; Duggan, C. Intestinal Failure. In: Sonnevile, K.; Duggan, C., editors. *Manual of Pediatric Nutrition*. 5. Shelton: People's Medical Publishing House; 2014.
13. Gosselin KB, Duggan C. Enteral nutrition in the management of pediatric intestinal failure. *J Pediatr*. 2014; 165:1085–90. [PubMed: 25242686]
14. Grummer-Strawn LM, Reinold C, Krebs NF. Use of World Health Organization and CDC growth charts for children aged 0–59 months in the United States. *MMWR Recomm Rep*. 2010; 59:1–15. [PubMed: 20829749]
15. Olsen IE, Groveman SA, Lawson ML, Clark RH, Zemel BS. New intrauterine growth curves based on United States data. *Pediatrics*. 2010; 125:e214–24. [PubMed: 20100760]
16. WHO [Internet]. WHO child growth standards SAS macro (version 3.2.2). [updated January 2011; cited September 2012]. Available from: http://www.who.int/childgrowth/software/readme_sas.pdf
17. Zeger SL, Liang KY. Longitudinal data analysis for discrete and continuous outcomes. *Biometrics*. 1986; 42:121–30. [PubMed: 3719049]
18. Prendergast AJ, Rukobo S, Chasekwa B, et al. Stunting is characterized by chronic inflammation in Zimbabwean infants. *PLoS One*. 2014; 9:e86928. [PubMed: 24558364]
19. Kanof ME, Lake AM, Bayless TM. Decreased height velocity in children and adolescents before the diagnosis of Crohn's disease. *Gastroenterology*. 1988; 95:1523–7. [PubMed: 3181677]
20. Hintz SR, Kendrick DE, Stoll BJ, et al. Neurodevelopmental and growth outcomes of extremely low birth weight infants after necrotizing enterocolitis. *Pediatrics*. 2005; 115:696–703. [PubMed: 15741374]
21. Gutierrez IM, Kang KH, Calvert CE, et al. Risk factors for small bowel bacterial overgrowth and diagnostic yield of duodenal aspirates in children with intestinal failure: a retrospective review. *J Pediatr Surg*. 2012; 47:1150–4. [PubMed: 22703785]
22. Kaufman SS, Loseke CA, Lupo JV, et al. Influence of bacterial overgrowth and intestinal inflammation on duration of parenteral nutrition in children with short bowel syndrome. *J Pediatr*. 1997; 131:356–61. [PubMed: 9329409]
23. De Benedetti F, Alonzi T, Moretta A, et al. Interleukin 6 causes growth impairment in transgenic mice through a decrease in insulin-like growth factor-I. A model for stunted growth in children with chronic inflammation. *J Clin Invest*. 1997; 99:643–50. [PubMed: 9045866]

24. Thomas AG, Miller V, Taylor F, Maycock P, Scrimgeour CM, Rennie MJ. Whole body protein turnover in childhood Crohn's disease. *Gut*. 1992; 33:675–7. [PubMed: 1612486]
25. Colomb V, Dabbas M, Goulet O, Talbotec C, Corriol O, Ricour C. Prepubertal growth in children with long-term parenteral nutrition. *Horm Res*. 2002; 58(Suppl 1):2–6. [PubMed: 12373005]
26. Goulet O, Baglin-Gobet S, Talbotec C, et al. Outcome and long-term growth after extensive small bowel resection in the neonatal period: a survey of 87 children. *Eur J Pediatr Surg*. 2005; 15:95–101. [PubMed: 15877257]
27. Ekema G, Falchetti D, Boroni G, et al. Reversal of severe parenteral nutrition-associated liver disease in an infant with short bowel syndrome using parenteral fish oil (Omega-3 fatty acids). *J Pediatr Surg*. 2008; 43:1191–5. [PubMed: 18558205]
28. Calhoun AW, Sullivan JE. Omegaven for the treatment of parenteral nutrition associated liver disease: a case study. *The Journal of the Kentucky Medical Association*. 2009; 107:55–7. [PubMed: 19263944]
29. Premkumar MH, Carter BA, Hawthorne KM, King K, Abrams SA. High rates of resolution of cholestasis in parenteral nutrition-associated liver disease with fish oil-based lipid emulsion monotherapy. *J Pediatr*. 2013; 162:793–8. e1. [PubMed: 23164314]
30. Puder M, Valim C, Meisel JA, et al. Parenteral fish oil improves outcomes in patients with parenteral nutrition-associated liver injury. *Ann Surg*. 2009; 250:395–402. [PubMed: 19661785]
31. Gura KM, Lee S, Valim C, et al. Safety and efficacy of a fish-oil-based fat emulsion in the treatment of parenteral nutrition-associated liver disease. *Pediatrics*. 2008; 121:e678–86. [PubMed: 18310188]
32. Sanchez SE, Braun LP, Mercer LD, Sherrill M, Stevens J, Javid PJ. The effect of lipid restriction on the prevention of parenteral nutrition-associated cholestasis in surgical infants. *J Pediatr Surg*. 2013; 48:573–8. [PubMed: 23480915]
33. Cober MP, Killu G, Brattain A, Welch KB, Kunisaki SM, Teitelbaum DH. Intravenous fat emulsions reduction for patients with parenteral nutrition-associated liver disease. *J Pediatr*. 2012; 160:421–7. [PubMed: 21982303]
34. Rollins MD, Ward RM, Jackson WD, et al. Effect of decreased parenteral soybean lipid emulsion on hepatic function in infants at risk for parenteral nutrition-associated liver disease: a pilot study. *Journal of pediatric surgery*. 2013; 48:1348–56. [PubMed: 23845629]
35. Olieman JF, Penning C, Spoel M, et al. Long-term impact of infantile short bowel syndrome on nutritional status and growth. *Br J Nutr*. 2012; 107:1489–97. [PubMed: 21917192]
36. Mehta NM, Raphael B, Guteirrez IM, et al. Comparison of body composition assessment methods in pediatric intestinal failure. *J Pediatr Gastroenterol Nutr*. 2014; 59:99–105. [PubMed: 24614122]
37. Squires RH, Duggan C, Teitelbaum DH, et al. Natural History of Pediatric Intestinal Failure: Initial Report from the Pediatric Intestinal Failure Consortium. *J Pediatr*. 2012; 161:723–8. [PubMed: 22578586]

Figure 1.
Median parenteral and enteral energy intake in 51 infants (1129 follow-up observations) with surgical short bowel syndrome over the first year of life.

Figure 2.

Weight- and length-for-age Z-scores in 51 infants (1125 WAZ follow-up observations; 512 LAZ follow-up observations) with surgical short bowel syndrome over the first year of life. Shown is the fitted regression curve superimposed over median (IQR) at each week of age.

Figure 3.
All visits for each subject, with a closed dot (●) indicating on PN, and an open circle (○) indicating off PN. Subjects are ordered by decreasing time in the study.

Age (months)	0-1	1-2	2-3	3-4	4-5	5-6	6-7	7-8	8-9	9-10	10-11	11-12
Subjects	2	7	16	22	31	34	33	30	30	20	22	27
Observations	2	13	31	36	52	43	51	45	40	25	23	30

Figure 4.

Weight-for-length Z-scores in 51 infants (391 WLZ follow-up observations) with surgical short bowel syndrome over the first year of life. Weight-for-length Z-scores are unavailable for preterm infants. Shown is the fitted regression curve superimposed over median (IQR) at each week of age.

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Figure 5. Weight- and length-for-age Z-scores restricted to 22 infants (570 WAZ follow-up observations; 249 LAZ follow-up observations) with surgical short bowel syndrome over the first year of life. Shown is the fitted regression curve superimposed over median (IQR) at each week of age.

Table 1

Baseline clinical characteristics of 51 infants with short bowel syndrome.

Characteristic	Median (IQR) or n (%)
Demographic	
Age (weeks)	8.3 (0.9–14.6)
Male sex	27 (53%)
Gestational age (weeks)	31 (25–35)
Household income (n=50)	\$44,668 (\$35,513–61,790)
Birth weight category (n=46)	
Extremely low birth weight (<0.5 kg)	15 (33%)
Very low birth weight (0.5–1.5 kg)	8 (17%)
Low birth weight (1.6–2.5 kg)	16 (35%)
Normal birth weight (>2.5 kg)	7 (15%)
Race/Ethnicity (n=46)	
Caucasian	27 (59%)
Asian	2 (4%)
Black	7 (15%)
Latino	3 (7%)
Other	7 (15%)
Diagnoses leading to parenteral nutrition dependence	
Necrotizing enterocolitis	25 (49%)
Intestinal atresia	17 (33%)
Gastroschisis	13 (25%)
Malrotation or midgut volvulus	5 (10%)
Hirschsprung's disease	1 (2%)
More than 1 diagnosis	10 (20%)
Anatomical characteristics	
Residual small bowel length, cm (n=36)	57 (30–77)
Ileocecal valve resected (n=45)	18 (40%)
Citrulline level (n=8)	12 (8–20)
Nutritional characteristics	
Total energy intake, kcal/kg/day	73 (56–88)
Protein intake, grams/kg/day	2.5 (1.7–2.9)
Subjects with any enteral energy intake	12 (24%)

Table 2

Regression analysis of association of weight- and length-for-age Z-scores, adjusted for age.

Variable	WAZ		LAZ	
	Est (SE)	P	Est (SE)	P
<i>Demographic</i>				
Gestational age	0.05 (0.04)	0.18	0.13 (0.04)	0.002
Male sex	−0.76 (0.38)	0.06	−0.82 (0.40)	0.04
Birth weight <2.5 kg	−1.73 (0.43)	0.02	−1.24 (0.55)	0.06
Caucasian race/ethnicity	0.18 (0.43)	0.67	0.19 (0.45)	0.67
Household income by ZIP code (per \$10,000)	0.08 (0.08)	0.34	0.13 (0.08)	0.11
<i>Surgical</i>				
Diagnosis of necrotizing enterocolitis	−0.78 (0.36)	0.04	−1.17 (0.35)	0.002
Residual bowel length (per 10 cm)	0.007 (0.08)	0.93	0.002 (0.066)	0.97
Ileocecal valve resected	0.23 (0.42)	0.59	0.15 (0.39)	0.70
<i>Medical</i>				
2 central line associated bloodstream infections	−0.99 (0.35)	0.005	−0.79 (0.38)	0.04
Number of weeks as inpatient	−0.03 (0.02)	0.15	−0.02 (0.02)	0.31
Cholestasis or coagulopathy ^I	−0.59 (0.36)	0.13	−0.28 (0.46)	0.54
<i>Nutritional</i>				
Total energy intake (per 100 kcal/kg/day)	−1.31 (0.31)	0.002	−0.95 (0.36)	0.02
Parenteral energy intake (per 100 kcal/kg/day)	−0.11 (0.44)	0.80	0.08 (0.40)	0.84
Enteral energy intake (per 100 kcal/kg/day)	−0.45 (0.30)	0.15	−0.38 (0.28)	0.19
Protein intake, grams/kg/day	0.03 (0.12)	0.78	−0.03 (0.10)	0.75
Percentage enteral energy intake (%)	−0.22 (0.39)	0.57	−0.06 (0.33)	0.85
Omegaven exposure	0.41 (0.31)	0.20	0.02 (0.32)	0.95
Weaned from PN during study	0.54 (0.39)	0.18	0.38 (0.41)	0.36

^I Cholestasis defined as direct bilirubin >2 on 2 separate measurements at least 2 weeks apart. Coagulopathy defined as at least one occurrence of INR greater than 1.5.

Table 3

Multivariable predictors of Z-scores after accounting for age (weeks).

Variable	WAZ		LAZ	
	Est (SE)	P	Est (SE)	P
Total energy intake (per 100 kcal/kg/day)	−1.01 (0.24)	<0.0001	−0.55 (0.26)	0.03
Necrotizing enterocolitis	−0.76 (0.32)	0.02	−1.24 (0.32)	0.0001
2 central line associated bloodstream infections	−0.95 (0.33)	0.004	−0.86 (0.32)	0.007