INTESTINAL REHABILITATION AND TRANSPLANTATION
WORKING TOGETHER TO CHANGE THE LIVES OF CHILDREN AND ADULTS WITH INTESTINAL FAILURE

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Disclosures

- I am a primary investigator in a Shire sponsored clinical trial of teduglutide
- I act as a consultant and lead clinical investigator for Zealand Pharma who make glepaglutide
Intestinal Failure

- Inability to maintain nutrition and hydration solely with your own intestines
Not enough bowel
- gastroschisis, NEC, intestinal atresia, volvulus

Enough bowel, but doesn’t work
- MVID, aganglionosis
- pseudoobstruction
SBS in Adults

Not enough bowel
- Catastrophic
  - Vascular accidents, volvulus, internal hernias, surgical injury, trauma
- Non-catastrophic
  - desmoid tumours, multiple resections, Crohn’s, fistulas

Enough bowel, but doesn’t work
- Recurrent obstructions/adhesions
- Dysmotility syndromes
- Radiation enteritis
GOAL
Take 100% of food and water by mouth

REHABILITATION

TRANSPLANTATION

RISKS?

Taking nothing by mouth

Complementary not contradictory
Who would you transplant?

- Failure of TPN
  - PN-associated liver failure
  - Thrombosis of ≥2 central veins
  - ≥2 episodes/yr severe sepsis esp. fungemia
  - Unreconstructable GI tract
Isolated Intestine  Combined liver-pancreas-intestine
Liver - Small Bowel Transplant
Patient survival following primary intestinal transplant

- **~80% 1-year**
- **~60% 5-year**
In what circumstances is rehab possible?
“Many of the truths we cling to depend on our point of view”
Successful Rehabilitation in Pediatric Ultrashort Small Bowel Syndrome

Benjamin J. Fantone, MD, MS,1 David F. Merot, MD, MPH, FRCP(C),2 Brandi D. Huben, RN,3 Ryan F. Frisher, MD,1 Bordi K. Gerhardt, RN, BSN,4 Wendy J. Grant, MD,5 Alan N. Langer, DO,5 and Waldin E. Okuno-Teyma, MD5

Objective: To examine treatment outcomes in pediatric patients with ultrashort small bowel (USSB) syndrome in an intestinal rehabilitation program (IRP).

Study design: We reviewed IRP records for 2001-2011 and identified 28 children with USSB (<0.5 cm of small bowel). We performed univariate analysis using the Fisher exact test and Wilcoxon rank-sum test to compare characteristics of children who achieved parenteral nutrition (PN) independence with infants who achieved enteral nutrition and those who did not. Growth, nutritional status, and hepatic laboratory test results were compared from the time of enrollment to the most recent values using the Wilcoxon signed-rank test.

Results: Of the 28 patients identified, 27 (96%) survived. Almost one-half (48%) of these survivors achieved PN independence with their native bowel. The successfully rehabilitated patients were more likely to have an intact colon and esophageal valve (p = .01). Significant improvements in new leading, total bilirubin, and height and weight z-scores were seen in all patients, but mean hepatic transaminase levels did not improve in the nonrehabilitated patients.

Conclusion: Enrolment in an IRP provides an excellent probability of survival for children with USSB. The presence of an intact esophageal valve and colon are positively correlated with rehabilitation in this population, but without these, PN dependence can be resolved in less than 2 years. The USSB population can achieve reduced PN dependence in 1 year, improvement in PN-associated liver disease, and enhanced growth with the aid of an IRP. J Pediatr 2013;163:361-6.

See editorial, p 1243

Short bowel syndrome, the most common cause of intestinal failure in the pediatric population, is characterized by an inability of the gastrointestinal tract to absorb sufficient nutrients and water to maintain adequate hydration, nutrition, and ultimately growth, secondary to loss of surface area. Growth, nutritional status, and ultimately survival are strongly associated with improved survival in these children.12 Ultrashort bowel syndrome (USSB) syndrome has been definitively defined as 20 cm or less of remaining small bowel.2 Massive resections leading to USSB syndrome have been reported in the literature for several years,3 although in the past the outcomes of these patients have been documented in case reports and small case series.4-11

The concept of rehabilitation patients with USSB syndrome began with the development of parenteral nutrition (PN) and nasoenteric diet since the evolution of parenteral nutrition and enteral nutrition forms the feeding foundation.12 The development of these technologies has fostered the idea of nutritional adaptation, which strives to enable the remaining gut to undergo compensatory changes, including intestinal hypertrophy, villus lengthening, and increase in crypt depth.2 This concept has been termed the intestinal adaptive response.12 These series have been instrumental in assessing nutritional adaptation in children with USSB syndrome. It is the recently introduced concept of intestinal adaptation in children with USSB syndrome. It is the recently introduced concept of intestinal adaptation in children with USSB syndrome that has been instrumental in assessing nutritional adaptation in children with USSB syndrome.12

Children with USSB syndrome after an initial resection are considered to have higher mortality and less chance of achieving enteral autonomy compared with those with low remaining bowel.12 Because of the prolonged period of parenteral nutrition dependence, the primary care provider is often concerned about the development of PN-associated liver disease (PNALD), which further reduces the potential for enteral autonomy.12 USSB in children has been considered an indication for terminal small intestinal transplantation, but this goal has not been achieved.

USSB in infants has been considered an indication for terminal small intestinal transplantation, but this goal has not been achieved. USSB in infants has been considered an indication for terminal small intestinal transplantation, but this goal has not been achieved.
<table>
<thead>
<tr>
<th></th>
<th>Group</th>
<th>Adapted</th>
<th>Non-adapted</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Number</strong></td>
<td>27</td>
<td>56% (15)</td>
<td>44% (12)</td>
<td></td>
</tr>
<tr>
<td><strong>Male</strong></td>
<td>67% (18)</td>
<td>67% (10)</td>
<td>67% (8)</td>
<td>1</td>
</tr>
<tr>
<td><strong>Prematurity</strong></td>
<td>85% (23)</td>
<td>87% (13)</td>
<td>83% (10)</td>
<td>0.77</td>
</tr>
<tr>
<td><strong>Transplant</strong></td>
<td>41% (3)</td>
<td>13% (2)</td>
<td>8% (1)</td>
<td>0.67</td>
</tr>
<tr>
<td><strong>Mean SBL (cm)+/-SD</strong></td>
<td>13 +/- 4.1</td>
<td>12.9 +/- 3.8</td>
<td>13.1 +/- 4.7</td>
<td>0.95</td>
</tr>
<tr>
<td><strong>ICV</strong></td>
<td>44% (12)</td>
<td>60% (9)</td>
<td>25% (3)</td>
<td>0.05</td>
</tr>
<tr>
<td><strong>Colon intact</strong></td>
<td>44% (12)</td>
<td>60% (9)</td>
<td>25% (3)</td>
<td>0.05</td>
</tr>
<tr>
<td><strong>1° Diagnosis</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NEC</td>
<td>22% (6)</td>
<td>27% (4)</td>
<td>17% (2)</td>
<td>0.53</td>
</tr>
<tr>
<td>Gastrochisis</td>
<td>22% (6)</td>
<td>7% (1)</td>
<td>42% (5)</td>
<td>0.0258</td>
</tr>
<tr>
<td>Malrotation/Volvulus</td>
<td>19% (5)</td>
<td>27% (4)</td>
<td>8% (1)</td>
<td>0.1711</td>
</tr>
<tr>
<td>Intestinal Atresia</td>
<td>22% (6)</td>
<td>20% (3)</td>
<td>25% (3)</td>
<td>0.7578</td>
</tr>
<tr>
<td>Omphalocele</td>
<td>11% (3)</td>
<td>12% (2)</td>
<td>8% (1)</td>
<td>0.7275</td>
</tr>
<tr>
<td>Vascular Disease</td>
<td>4% (1)</td>
<td>7% (1)</td>
<td>0</td>
<td>0.288</td>
</tr>
<tr>
<td><strong>1° Anastomosis</strong></td>
<td>56% (15)</td>
<td>67% (10)</td>
<td>42% (5)</td>
<td>0.18</td>
</tr>
<tr>
<td><strong>Mean Time in Program (mo)+/-SD</strong></td>
<td>36.5 +/- 25.6</td>
<td>45.2 +/- 28.8</td>
<td>25.6 +/- 16.1</td>
<td>0.019</td>
</tr>
<tr>
<td>Lengthening Procedure</td>
<td>52% (14)</td>
<td>53% (8)</td>
<td>50% (6)</td>
<td>0.88</td>
</tr>
<tr>
<td><strong>2nd STEP</strong></td>
<td>30% (8)</td>
<td>40% (6)</td>
<td>17% (2)</td>
<td>0.17</td>
</tr>
<tr>
<td><strong>3rd STEP</strong></td>
<td>19% (5)</td>
<td>27% (4)</td>
<td>8% (1)</td>
<td>0.17</td>
</tr>
<tr>
<td><strong>4th STEP</strong></td>
<td>4% (1)</td>
<td>0</td>
<td>8% (1)</td>
<td>0.31</td>
</tr>
<tr>
<td><strong>Mean Time on TPN (mo)+/-SD</strong></td>
<td>26.1 +/- 15.7</td>
<td>24.1 +/- 14.7</td>
<td>28.5 +/- 17.1</td>
<td>0.328</td>
</tr>
</tbody>
</table>
Reconnection surgery in adult post-operative short bowel syndrome < 100 cm: is colonic continuity sufficient to achieve enteral autonomy without autologous gastrointestinal reconstruction? Report from a single center and systematic review of literature

A. LAURO1, R. CIROCCHI1, N. CAUTERO1, A. DAZZI1, D. PIRONI1, F.M. DI MATTEO2, A. SANTORO2, L. PIRONI2, A.D. PINNA3

Summary: Reconnection surgery in adult post-operative short bowel syndrome < 100 cm: is colonic continuity sufficient to achieve enteral autonomy without autologous gastrointestinal reconstruction? Report from a single center and systematic review of literature.

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Introduction
In adults, the massive resection of small bowel leaving less than 150 cm of intestine results in malabsorption and diarrhea and defines the short bowel syndrome (SBS). Small bowel length inferior to 100 cm is highly predictive of postoperative intestinal failure and total parenteral nutrition (TPN) dependency. Most adults with 75 cm will achieve enteral independence after 5 years of TPN, probability of permanent intestinal failure is > 90% for this group of patients (1-2).

After massive small bowel resection, enteral parenteral nutrition is not feasible. Three (out of 108 screened papers) randomized controlled trials with 116 adult patients were identified showing weaning from TPN (20%, 42%, and 70% respectively) after reconnection surgery without autologous gastrointestinal reconstruction: median rate of 35% (51 patients), mean rate of 54.1 years (53.8% (AV)), 39.2% with a high output enterostomy, with TPN dependence up to 90%. By performed jejuno-ileo-colic anastomosis (SBS type III) in 53.8% of cases and jejuno-colic anastomosis (SBS type II) in 80.5% (116 adult patients), enteral autonomy was achieved in 81% and 89% after a maximum period of 1 year without/without regular reliance on TPN (100%) and oral intake in 100% of cases. A subtotal small bowel length of at least 75 cm, even if reconnected to segments of remaining colon, is associated with a lower dependence of TPN supply. Lengthening (8) or segmental reversal (9-11) procedures have been proposed in recent years in order to prolong the transit time of bolus and increase the absorptive capacity of remaining bowel. After massive small bowel resection, jejuno-ileo-colic anastomosis (SBS type II) or better a jejuno-ileo-colo-nic anastomosis (SBS type III) show improved absorption capacity with time, after a proper period of intestinal rehabilitation, whereas patients with end-terminal jejunostomy without colon (SBS type I) do not, and the presence of remaining colon is associated with a lower dependence of TPN supply. Lengthening (8) or segmental reversal (9-11) procedures have been proposed in recent years in order to prolong the transit time of bolus and increase the absorptive capacity of remaining bowel. After massive small bowel resection, jejuno-ileo-colo-nic anastomosis (SBS type III) show improved absorption capacity with time, after a proper period of intestinal rehabilitation, whereas patients with end-terminal jejunostomy without colon (SBS type I) do not, and the presence of remaining colon is associated with a lower dependence of TPN supply. Lengthening (8) or segmental reversal (9-11) procedures have been proposed in recent years in order to prolong the transit time of bolus and increase the absorptive capacity of remaining bowel.
Why?

- Institutional acceptance
- Not multidisciplinary - TRANSDISCIPLINARY
- Continual evaluation of progress
- Public presentation of results and outcomes
- Cross-pollination with other programs
# Line Care

<table>
<thead>
<tr>
<th>OLD</th>
<th>NEW</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pull lines when infected</td>
<td>Treat through, only pull if persistently (+) cultures</td>
</tr>
<tr>
<td>Rotate line sites</td>
<td>Rewire lines, reuse good sites, repair broken lines</td>
</tr>
<tr>
<td>Standard dressings</td>
<td>Biopatch - chlorhexidine-impregnated sponge</td>
</tr>
<tr>
<td>Heparin locks</td>
<td>Ethanol locks</td>
</tr>
</tbody>
</table>
Ethanol locks

- Use with ethanol-compatible lines (i.e. broviac, but not PICC or port)
- 1-2 ml standard volume
- Dwell minimum 2 hours, ideally at least 4h, up to 24h

Tauroolidine locks in future?
Lipid management

Impact of Fish Oil-Based Lipid Emulsion on Serum Triglyceride, Bilirubin, and Albumin Levels in Children With Parenteral Nutrition-Associated Liver Disease

SANG I. LEE, CLARISSA VALIM, PATRICK JOHNSTON, HAU D. LI, JONATHAN MEISEL, DANIELLE A. ARSENAULT, KATHLEEN M. GURA, AND MARK PUDER

Omegaven
Lipid Minimization

Omegaven

No Omegaven!!
SMOF (Soy MCT Olive Fish)

Introducing a new lipid emulsion option for adults in the U.S.
Intestinal growth factors

- Long-acting analogues of glucagon-like peptide 2
- Teduglutide (Gattex)
  - Daily subcutaneous injection
  - RCT - 20% reduction in TPN volume
  - Continued improvement over time
- Side effects: cramping, fluid retention, altered medication absorption
Surgery

- Early surgery to restore continuity
- Recognize when you are “stuck”
- Deal with dilation
* 48 year old man with distention, pain, vomiting, TPN use past few years
Long Segment Tapering Enteroplasty
Enterocutaneous Fistulas
Intestinal growth factors

Teduglutide
trial complete in pediatrics
?FDA approval this year?

Glepaglutide
Trial beginning now, first
North American patient
next week
Microbiome

The sum of the microbiota and their habitat

- You have 10e13 cells BUT you support 10e14 microorganisms
  - YOU ARE 10 X MORE SOMETHING ELSE THAN YOURSELF!
Intestinal rehab and transplant work together

We should strive to make intestinal transplant unnecessary for most children and adults

What seems true today may well prove false tomorrow
Hope.