Short Bowel Syndrome

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Feldman's GastroAtlas online
Overview

- Definition/Incidence of Intestinal Failure
- Intestinal Physiology
- Etiology and Pathophysiology
- Intestinal adaptation
- Medical Management – rehabilitation
- Surgical Management
- Intestinal transplantation

Intestinal Failure: Definition

- A condition in which inadequate digestion and/or absorption of nutrients leads to malnutrition and/or dehydration
- Inability of the native gastrointestinal tract to provide nutritional autonomy

Incidence and Prevalence

- 3-4/million in western countries eventually develop intestinal failure
- Occurs in ~ 15% of pts undergoing intestinal resection
  - ~ 3% occur from massive resection
  - ~ 1/4 from multiple sequential resections
- ~70% pts with SBS are d/c from the hospital & ~ 70% of these remain alive one year later
- Improved Survival is due to ability to deliver long-term nutritional support

Causes of Intestinal Failure: Major Categories

- Loss of bowel length
- Loss or absence of bowel function
- Unresectable tumors

References:
- Thompson JS. J Gastrointestinal Surg 2000; 4: 101-4
- Meisng B. et al Gastroenterology 1996; 117:1045-50
**Short Bowel Syndrome (SBS)**

- Defined as loss of ≥2/3 of small bowel (remnant of <200 cm)
  
  Wilmore DW, Best Pract Res Clin Gastroenterol 2003;17:895

- “Functional” definition? (Fecal energy loss)

- Most common condition resulting in intestinal failure

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**Pathophysiology**

- **INTESTINAL REMNANT LENGTH** is the primary determinant of outcome but quality also important

  - Resection of up to ½ of the SB is usually well tolerated
  
  - SBS is most likely to develop in patients losing > 2/3 length of SB.

  - Adults likely to require long-term TPN:
    - <50 cm small bowel AND colon
    - <100 cm small bowel AND NO colon

  - Children likely to require long-term TPN:
    - <30 cm small bowel

  - Presence of ileocecal valve is highly advantageous
    - Due to presence of ileum, prevention of bacterial reflux

  D’Baise JK et al, Am J Gastroenterol 2004;99:1388

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**Normal Intestinal Function**

- Duodenum
  - 1500 mL

- Jejunum
  - 7000 mL

- Ileum
  - 1500 mL

- Saliva
  - 9000 mL

- Bile
  - 1000 mL

- Pancreatic secretion
  - 1000 mL

- Gastric secretion
  - 1000 mL

- **Mucosal resistance**
  - Very leaky
  - Very leaky
  - Moderately leaky

- **Na absorptive mechanism**
  - Na-nutrient
  - Na-H exchange
  - Electrogenic Na

- **Specialized absorption**
  - Ca
  - Fe

- **Bile salts**
  - Vitamin B12

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**Intestinal Growth**

- **Small intestine**
  - Greatest growth velocity during last trimester
  - Term ~275cm

- **Colon**
  - 30-40cm at birth
  - 1.5-2.0m in adult

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Feldman’s GastroAtlas online
Stages Following Massive Resection

- Large fluid/electrolyte losses (weeks)
- Fewer fluid and electrolyte problems; need for nutritional support (months/year)
  - TPN weaning?
- Intestinal adaptation

Intestinal Adaptation

- Muscular hypertropy
  - Increased bowel diameter
  - Increased wall thickness
- Mucosal hyperplasia
  - Crypt cell proliferation
  - Increased number of enterocytes
  - Villous hyperplasia
- Lengthening

Intestinal Adaptation

- Dependent on enteral nutrients
- May take 1-2 years
- Ileum adapts for macronutrient absorption
- Blunted adaptation: Active Crohn’s, radiation enteritis, carcinoma, pseudoobstruction

Intestinal adaptation-Mechanisms

- Hormonal mediators
  - Growth hormone
  - Glucagon like peptides
  - Enteroglucagon
  - Neurotensin
  - Peptide YY
  - Insulin-like growth factor
- Luminal factors
  - Glutamine
  - Polyamines
  - Epidermal growth factor
  - Trefoil peptides
  - Short chain fatty acids
  - Long chain fatty acids
Medical Management

- Early management: Critically ill in post-op setting
  - Control of sepsis, maintenance of fluid and electrolyte balance
  - TPN is required early
  - Initiation of enteral feeds when possible
  - Fluid and electrolytes losses are high in post-op period management can be challenging

- For pts that survive the early phase, goals are to maintain adequate nutritional status and prevent complications

- MAINTENANCE OF NUTRITIONAL STATUS BECOMES THE PRIMARY GOAL

SBS: Medical Management

- Fluid and electrolytes
  - Oral rehydration solution
  - Antisecretory agents (PPI)
  - Antimotility agents
    - Lomotil, Imodium, tincture of opium
  - Supplemental IV fluids may be required in addition to TPN
- Micronutrients

Medical Management -Dietary Management-

- Pts should eat more than usual (hyperphagic)
- Small meals throughout the day and/or tube feeds
- Pts with colonic continuity should eat complex CHO with starch, non-starch polysaccharides and soluble fibers (not absorbed by SB).
  - Colon ferments these carbs → butyrate (fuel)
  - 500-1000 Kcals can be absorbed from colocytes
  - Amount of energy absorbed is proportional to the length of the residual colon and may increase with adaptive response to resection
  - Medium chain triglycerides can be absorbed in the colon

SBS-other consequences

- Gastric acid hypersecretion
- Metabolic bone disease
  - Calcium deficiency
  - Renal calculi
    - Hyperoxaluria
  - Liver disease
  - Cholelithiasis
  - Bacterial overgrowth
    - D-lactic acidosis
    - Neurologic syndrome
SBS: Pharmacologic Options

- Antisecretory, antimotility agents
- Antibiotics for overgrowth
- Growth hormone?
- Glucagon-like peptide II (Gattex)
- Glutamine supplementation of feeds

Glucagon like peptide 2

- Proglucagon-derived peptides
  - Synthesized in L cells
- Tissue specific post-translational processing of proglucagon in the intestine liberates PGDPs
- Highly localized expression of GLP-2 receptor in intestinal epithelium

Teduglutide (Gattex)

Randomised placebo-controlled trial of teduglutide in reducing parenteral nutrition and/or intravenous fluid requirements in patients with short bowel syndrome

Jeppesen et al. Gut. 2011;60:902-14
How to feed

- CONTINUOUS ENTERAL FEEDINGS ARE ADVANTAGEOUS
  - Via NG or GT
  - Constant saturation of carrier transport proteins
  - Take full advantage of absorptive surface area available
- Older children have better capacity to regulate gastric emptying

How to feed

- ADVANCE SLOWLY
  - Concentration vs. volume
- Small quantities of oral feedings
  - Scheduled at least 2-3 times per day
  - Stimulate suck swallow
  - Minimize feeding aversion

Home Parenteral Nutrition

- TPN should be compressed volume and time of infusion. (preferably over night)
- Tapered over 30-60 min to avoid hypoglycemia.
- Complications;
  - Avoid line sepsis (0.3/ year)
  - Line thrombosis

Jeppesen et al. Gut. 2011;60:902-14

Woolf GM et al. Gastroenterology 1983; 84:823-8
**PN complications**

- Catheter related:
  - Sepsis
  - Access
  - Venous thrombosis
  - Occlusion
  - Migration

- Metabolic:
  - Liver disease
  - Biliary stones
  - Metabolic bone disease
  - Trace element and/or vitamin deficiency

**PNALD**

- Biochemical elevations in:
  - Serum aminotransferases
  - Alkaline phosphatase, GGT
  - Bilirubin

- Histologic changes
  - Steatosis
  - Steatohepatitis
  - Cholestasis
  - Cirrhosis

- May improve with decreased lipid infusion and/or switch to Omega-3 enriched lipids

**SBS: Surgical Management**

- Ostomy closure
- Restoration of bowel continuity
- Bowel lengthening and tapering procedures

**Surgical Management**

- Dilated segments of bowel with ineffective peristalsis are associated with:
  - bacterial overgrowth
  - secretory diarrhea
  - mucosal inflammation
  - increased malabsorption
  - increase risk of liver disease

- Aims:
  - Increase total length of small bowel, prevent stasis in dilated segment
Surgical Management

- Experimental animal models:
  - Constriction of intestinal valve or sphincter
  - Denervation of intestinal segments

- Human Experience:
  - Reversing segments of intestine
    - Antiperistaltic “physiologic valve”
  - Bowel lengthening procedures:
    - Bianchi – longitudinal lengthening
    - STEP – serial transverse enteroplasty

Increasing Absorptive Surface Area

Serial Transverse Enteroplasty (STEP)

- Pt selection: Dilated intestinal segment, bacterial overgrowth.
- Stapler is from Alternating directions.
- Less complicated than Bianchi Procedure.
- Improves absorptive capacity in ~90% pts.
- Complications:
  - Leak and obstruction ~20%
• Infant < 12 mos
• 60/74 consecutive days of PN during first year of life
• 272 infants enrolled
• Follow up data – median 25.7 months

The impact of multi-disciplinary intestinal rehabilitation programs on the outcome of pediatric patients with intestinal failure: A systematic review and meta-analysis
Jennifer D. Stanger, Carol Oliveira, Christopher Blackmore, Yann Avitzur, Paul W. Wales*

• Implementation of an IRP results in
  – Reduction in septic episodes
  – Increase in patient survival (22 -> 42%)

SBS: Management

• Remedial surgery
• Nutritional support
• Medication
• Transplantation

Implementation of an IRP results in
– Reduction in septic episodes
– Increase in patient survival (22 -> 42%)
Medicare Criteria for Failure of Parenteral Nutrition

- Impending or overt liver failure
- Thrombosis of 2 or more central veins
- 2 or more episodes of systemic sepsis per year
- Episode of line-related fungemia, septic shock or ARDS
- Frequent episodes of severe dehydration

Fishbein TM et al. Gastroenterology 2003;124:615

Types of Transplants

Total intestinal transplants in the US

Graft survival among intestinal transplant recipients transplanted in 2006, by age: deceased donors

Causes for Transplantation in Current Era (Children)

Causes for Transplantation in Current Era (Adults)

UCSF Program

- Multidisciplinary team
- Outpatient and inpatient
- Intestinal rehabilitation
- TPN management
- Intestinal transplantation
- Gastric neurostimulator for refractory gastroparesis
Goals

- Anticipate physiology based on residual anatomy
- Promote intestinal adaptation
  - Nutritional management
  - Medical management
  - Surgical management
- Assess complications
  - Bowel dilatation
  - Liver disease
  - Recurrent sepsis
- Early evaluation for transplantation

UCSF Program

Nursing
Betsy Haas-Beckert
Claudia Praglin

Nutrition
Viveca Ross

Pharmacy
David Quan

Gastroenterology
Sue Rhee

Surgery
Sang-Mo Kang

UCSF Program
877-sm-bowel
(877-762-6935)

Fax referrals: 415-353-8917
### IN 1.10 Characteristics of patients on the intestinal transplant waiting list on December 31, 2001 & December 31, 2011

<table>
<thead>
<tr>
<th>Level</th>
<th>2001 N</th>
<th>2011 N</th>
<th>2001 %</th>
<th>2011 %</th>
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<tr>
<td>0-5</td>
<td>64</td>
<td>126</td>
<td>49.5%</td>
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<td>6-11</td>
<td>40</td>
<td>66</td>
<td>28.4%</td>
<td>24.4%</td>
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<tr>
<td>12-17</td>
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<td>20</td>
<td>16.1%</td>
<td>16.1%</td>
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<tr>
<td>18-24</td>
<td>12</td>
<td>29</td>
<td>15.4%</td>
<td>16.4%</td>
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<tr>
<td>25-34</td>
<td>15</td>
<td>10</td>
<td>11.1%</td>
<td>10.1%</td>
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<tr>
<td>35-44</td>
<td>9</td>
<td>5</td>
<td>6.3%</td>
<td>5.6%</td>
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<td>45-54</td>
<td>0</td>
<td>3</td>
<td>1.1%</td>
<td>1.1%</td>
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<td>55+</td>
<td>0</td>
<td>0</td>
<td>0.0%</td>
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<table>
<thead>
<tr>
<th>Age</th>
<th>2001 N</th>
<th>2011 N</th>
<th>2001 %</th>
<th>2011 %</th>
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<tbody>
<tr>
<td>Male</td>
<td>85</td>
<td>115</td>
<td>53.1%</td>
<td>42.4%</td>
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<td>Female</td>
<td>75</td>
<td>110</td>
<td>46.9%</td>
<td>57.6%</td>
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<thead>
<tr>
<th>Race</th>
<th>2001 N</th>
<th>2011 N</th>
<th>2001 %</th>
<th>2011 %</th>
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<tbody>
<tr>
<td>White</td>
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<td>102</td>
<td>63.8%</td>
<td>61.4%</td>
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<tr>
<td>Black</td>
<td>34</td>
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<td>21.3%</td>
<td>17.7%</td>
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<td>Hispanic</td>
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<td>100</td>
<td>6.9%</td>
<td>10.5%</td>
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<td>Asian</td>
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<td>7</td>
<td>1.9%</td>
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<td>Other</td>
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<td>0.6%</td>
<td>5.9%</td>
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<table>
<thead>
<tr>
<th>Primary cause</th>
<th>2001 N</th>
<th>2011 N</th>
<th>2001 %</th>
<th>2011 %</th>
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<tbody>
<tr>
<td>Necrotizing enterocolitis</td>
<td>25</td>
<td>40</td>
<td>15.0%</td>
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<td>Congenital</td>
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<td>45</td>
<td>23.8%</td>
<td>16.6%</td>
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<td>Other</td>
<td>50</td>
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<td>31.3%</td>
<td>31.6%</td>
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<td>Pseudo- obstruction</td>
<td>9</td>
<td>16</td>
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<td>5.9%</td>
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<tr>
<td>Entero- jejunos</td>
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<td>1</td>
<td>1.3%</td>
<td>0.4%</td>
</tr>
<tr>
<td>Other</td>
<td>36</td>
<td>78</td>
<td>22.5%</td>
<td>28.8%</td>
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<th>Transplant status</th>
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<th>2011 N</th>
<th>2001 %</th>
<th>2011 %</th>
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<tr>
<td>Listed for kidney</td>
<td>147</td>
<td>197</td>
<td>51.9%</td>
<td>46.3%</td>
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<tr>
<td>Listed for liver</td>
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<td>13</td>
<td>10.4%</td>
<td>6.7%</td>
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<tr>
<td>Active</td>
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<td>29</td>
<td>8.1%</td>
<td>15.7%</td>
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<tr>
<td>Inactive</td>
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<td>96</td>
<td>40.6%</td>
<td>42.8%</td>
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<td>Time on waitlist</td>
<td>&lt;1 y</td>
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<td>52.1%</td>
<td>31.7%</td>
</tr>
<tr>
<td>1-3</td>
<td>27</td>
<td>18.9%</td>
<td>22.5%</td>
<td></td>
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<tr>
<td>3+</td>
<td>18</td>
<td>11.3%</td>
<td>12.5%</td>
<td></td>
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<td>Medical urgency status</td>
<td>51</td>
<td>56.5%</td>
<td>58</td>
<td>60.2%</td>
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<tr>
<td>Inactive</td>
<td>20</td>
<td>10.8%</td>
<td>18.8%</td>
<td></td>
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<tr>
<td>Total</td>
<td>160</td>
<td>100.0%</td>
<td>271</td>
<td>100.0%</td>
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