**OVERVIEW**

- Definition and causes of Short Bowel Syndrome (SBS)
- Assessment of SBS and Intestinal Failure (IF) patients
- Complications of SBS and IF
- Management of SBS and IF

**INTESTINAL FAILURE**

1. Failure of digestion and absorption
2. Inability of the intestinal tract to maintain an adequate nutritional status and fluid/electrolyte balance
3. It is the result of a loss or absence of sufficient functional intestinal absorptive surface area

**DISCLOSURES**

- Dr. Segovia has no conflicts of interest related to this discussion
INTESTINAL FAILURE

- It is an anatomical and functional definition
- Usually occurs in patient who have undergone extensive resection of the small bowel
- It can occur in patients who have undergone no resection but have significant intrinsic disease: celiac sprue, carcinoid, pseudo obstruction, Crohn’s disease

SHORT BOWEL SYNDROME

- Most common cause of intestinal failure
- Defined as having <200cm of small intestine
- Remaining bowel length necessary to prevent parenteral nutrition dependence is:
  - 100 cms in the absence of intact / functional colon
  - 60 cms in the presence of functional colon
  - 35 cms in the presence of full functional colon
- Jejunal resection is better tolerated than ileum resection

SBS - DEMOGRAPHICS

- Recent study in 2013 limited to patients with SBS (N = 268)
  - Median age of 52.5 (range: 18–89) years
  - Majority was female patients (52%)
  - Mean ± SD body mass index of 20.7 ± 3.9 kg/m² at baseline
  - Most patients (67%) had jejuno-colic anastomoses; 18% had end jejunostomies and 15% had jejuno-ileo-colic anastomoses

CAUSES OF SBS - CHILDREN

<table>
<thead>
<tr>
<th>Condition</th>
<th>USA</th>
<th>CANADA</th>
<th>FRANCE</th>
<th>INTERNATIONAL</th>
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</thead>
<tbody>
<tr>
<td>Atresia</td>
<td>30%</td>
<td>30%</td>
<td>39%</td>
<td>23%</td>
</tr>
<tr>
<td>Volvulus</td>
<td>10%</td>
<td>10%</td>
<td>24%</td>
<td>24%</td>
</tr>
<tr>
<td>Gastrochisis</td>
<td>17%</td>
<td>12.5%</td>
<td>14%</td>
<td>14%</td>
</tr>
<tr>
<td>NEC</td>
<td>43%</td>
<td>35%</td>
<td>14%</td>
<td>27%</td>
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</table>
CAUSES OF IF / SBS - ADULTS

<table>
<thead>
<tr>
<th>IATROGENIC</th>
<th>ISCHEMIC</th>
<th>INFILTRATIVE</th>
<th>OBSTRUCTIVE</th>
<th>FUNCTIONAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blunt trauma</td>
<td>Arterial embolism</td>
<td>Dermoid tumors</td>
<td>Adhesive</td>
<td>Pseudo-obstruction</td>
</tr>
<tr>
<td>Penetrating trauma</td>
<td>Venous occlusion</td>
<td>Carcinoid</td>
<td>Internal hernia</td>
<td>BID</td>
</tr>
<tr>
<td>Operative mishap</td>
<td>Low flow/shock</td>
<td>Amyloidosis</td>
<td>Radiation enteritis</td>
<td>Bacterial Overgrowth</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Malignancy</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

SBS in Bariatric Surgery Patients
- Obstruction due to adhesions
- Internal hernias and volvulus
- Incarcerated incisional hernia
- Mesenteric ischemia
- Complications in bypassed intestine

TYPES OF SHORT BOWEL SYNDROME

TYPES OF INTESTINAL RESECTION

SURVIVAL
Depends on the remnant small bowel length, the reason for resection and the presence or absence of colon

Higher survival rates reported for patients with SBS secondary to radiation therapy for abdominal and pelvic malignancies: 83% at 1 year and 68% at 5 years
FACTORS AFFECTING OUTCOMES

<table>
<thead>
<tr>
<th>Factor</th>
<th>Favorable</th>
<th>Unfavorable</th>
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</thead>
<tbody>
<tr>
<td>Extent of Resection</td>
<td>&lt;80%</td>
<td>&gt;80%</td>
</tr>
<tr>
<td>Site of Resection</td>
<td>Jejunum</td>
<td>Ileum</td>
</tr>
<tr>
<td>Ileocecal Valve</td>
<td>Present</td>
<td>Absent</td>
</tr>
<tr>
<td>Colon</td>
<td>Present</td>
<td>Absent</td>
</tr>
<tr>
<td>Underlying Disease</td>
<td>Absent</td>
<td>Present</td>
</tr>
<tr>
<td>Age</td>
<td>Adult</td>
<td>Extremes of Age</td>
</tr>
<tr>
<td>Time from Onset</td>
<td>&lt;1 year</td>
<td>&gt;1 year</td>
</tr>
</tbody>
</table>

ASSESSMENT OF PATIENTS WITH SBS

- Complex situation
- Requires a multidisciplinary approach
- The health provider should understand: cause of SBS / IF; reasons for feeding intolerance; intestinal anatomy; patient’s nutritional status; recognize complications

COMPONENTS OF AN INITIAL EVALUATION

- History and Physical Examination
- Determine anatomy: BE, UGIS, endoscopy
- US abdomen and UUEE with dopplers
- Bone health
- Nutritional assessment
- Liver biopsy – if indicated
- Psychological evaluation

NUTRITIONAL ASSESSMENT

- Weight / BMI
- Parenteral and enteral intake
- Symptoms: diarrhea, vomiting, bloating
- Labs: electrolytes, albumin, PT, Vit B12, fat soluble vitamins
- Serum citrulline: <20 umol/L is associated with permanent IF

M. Cristina Segovia, M.D.
ASSESSMENT OF COMPLICATIONS

- Diarrhea
- Fluid / Electrolytes abnormalities
- Malnutrition
- Bacterial overgrowth
- Intestinal failure associated liver disease (IFALD)
- Metabolic complications
- Anemia
- Bone demineralization
- Renal stones
- Peptic Ulcer Disease
- Cholelithiasis
- Difficulty concentrating
- Chronic pain
- Substance abuse
- Weakness
- Low body temperature
- Impaired growth
- Impaired sexual development
- Premature aging
- Poor quality of life

COMPLICATIONS (cont.)

- Hypotension and early kidney failure because of water and sodium deficiencies
  - More likely with colonic resection
- Magnesium deficiency
  - Fatigue
  - Depression
  - Muscle weakness and dysfunction
  - Cardiac arrhythmias / seizures
- Increased risk for infection and impaired wound healing
  - Vitamins A, C and zinc, copper and selenium deficiencies

COMPLICATIONS - Cholelithiasis

- Pathogenesis incompletely understood
  - Interruption of enterohepatic circulation of bile acids results in a reduced hepatic bile acid secretion and altered composition, becoming supersaturated with cholesterol
  - Diminished enteric hormonal stimulation of gallbladder contraction may lead to biliary stasis and subsequent biliary sludge

BOWEL ANATOMY
MANAGEMENT OF SBS AND IF

• Intestinal rehabilitation: close follow up with dietitian
• Meet caloric and nutritional requirements via an alternate route (parenteral nutrition)
• Humoral factors in intestinal adaptation
• Autologous reconstruction of the GI tract (pediatrics)
• Intestinal replacement (transplantation)

MANAGEMENT OF SBS

EARLY | LATE
--- | ---
Fluid and Electrolyte Stabilization | Dietary Assessment
Early Initiation of TPN | Continued electrolyte surveillance
Antimotility / Antisecretory Agents | Monitor trace elements
Initiate Enteral Nutrition as tolerated | Supplement fat soluble vitamins and Vit B12
Periodic Nutritional Assessment | Attempt to wean off TPN

BASIC PRINCIPLES OF NUTRITION

• Avoid malnutrition
• If the bowel works, use it
• Avoid overfeeding
• The route, timing and type of nutritional formulation are more important than the amount
• Role of nutritional support is to limit protein wasting and to supply essential nutrients

ENTERAL NUTRITION

• Main limitation to successful oral-enteral nutrition is the fluid and electrolyte losses

• Normal physiology:
  a) Gastric emptying
  b) Small bowel transit
  c) Colon
  d) Unique functions of the ileum
DIETARY MODIFICATIONS IN SBS

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Type I</th>
<th>Type II</th>
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</thead>
<tbody>
<tr>
<td>Oxalate restriction</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Lactose restriction</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Fat restriction</td>
<td>Ad lib</td>
<td>Low normal</td>
</tr>
<tr>
<td>Soluble fiber</td>
<td>Consider</td>
<td>Important</td>
</tr>
<tr>
<td>Electrolytes</td>
<td>ORS solution, calcium, and salt</td>
<td>ORS solution</td>
</tr>
<tr>
<td>Low FODMAP diet</td>
<td>Not helpful</td>
<td>Consider</td>
</tr>
</tbody>
</table>

FODMAP fermentable oligo- and mono-saccharides and polyols. ORS oral rehydration solution.

SUPPLEMENTATION IN SBS

- Zinc gluconate 100 g/d
- Selenium 60 - 100 g/d
- Vitamin A 10,000 IU/d
- 1,25 OH Vitamin D 0.25 – 0.5 g/d
- Vitamin E 1200 IU/d
- Calcium gluconate 1500 mg/d
- Vitamin B12 monthly injection

PHARMACOLOGIC MANAGEMENT IN SBS

FACTORS AFFECTING MEDICATION ABSORPTION IN SBS

- Change to the total surface area, permeability and integrity of the intestinal epithelia
- Change in orocecal transit time
- Impact on dissolution and release of the drug from the formulation
- Loss of the specific absorptive area in the bowel where the medication is routinely absorbed
- Loss of specific enzymes or epithelial transport proteins needed to activate the drug
- Location of the bowel that acts as the site of action for the medication
- Health of the remaining bowel
- Magnitude of intestinal adaptation
- Other factors that alter intestinal architecture leading to impaired absorption
INTESTINAL ADAPTATION

• The small intestine has a perpetually proliferating and differentiating epithelium

• Ability to regenerate and adapt to the loss of functional surface area

• Adaptive response: crypt cell hyperplasia, villus lengthening, increased absorptive capacity

• Mechanism has been poorly elucidated

INTESTINAL ADAPTATION (cont.)

TOTAL PARENTERAL NUTRITION (TPN)

1 year survival for patients treated with TPN is 90%, 70% at 3 years and 63% at 5 years

Long term therapy is associated with complications: catheter related, metabolic, organ dysfunction

Average annual cost of home TPN administration $150,000

OUTCOMES WITH TPN DEPENDENCY

AFFECTING SURVIVAL

• Age >60 at institution of TPN

• Jejuno-ileal length <50cms

• Dysmotility

• Radiation enteritis

• Longer treatment

AFFECTING REHABILITATION

• Jejuno-ileal length <50cms

• Absence of ileo-cecal valve

• Mucosal disease

• Dysmotility

• Abdominal wall defect in children
### ADVERSE EFFECTS OF TPN

<table>
<thead>
<tr>
<th>CATHETER RELATED</th>
<th>TOXICITIES</th>
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<tbody>
<tr>
<td>Bloodstream Infection</td>
<td>Aluminum</td>
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<tr>
<td>Infectious “metastasis”</td>
<td>Chromium</td>
</tr>
<tr>
<td>Central venous thrombosis</td>
<td>Manganese</td>
</tr>
<tr>
<td>Loss of venous access</td>
<td></td>
</tr>
</tbody>
</table>

### ADVERSE EFFECTS OF TPN (cont.)

<table>
<thead>
<tr>
<th>BILIARY / HEPATIC</th>
<th>RENAL / SKELETAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sludge / Gallstones</td>
<td>Hyperoxaluria</td>
</tr>
<tr>
<td>Gallbladder Dysmotility</td>
<td>Kidney Stones</td>
</tr>
<tr>
<td>Acalculous Cholecystitis</td>
<td>Chronic kidney disease</td>
</tr>
<tr>
<td>Steatosis</td>
<td>Impaired Tubular Function</td>
</tr>
<tr>
<td>Cholestasis</td>
<td>Osteopenia / Osteoporosis</td>
</tr>
<tr>
<td>Fibrosis / Cirrhosis</td>
<td>Osteomalacia</td>
</tr>
</tbody>
</table>

### INTESTINAL FAILURE-ASSOCIATED LIVER DISEASE (IFALD)

- Persistent elevation of liver function tests
- 50% of children and 30% adults have evidence of IFALD after 4-12 weeks of TPN
- It typically presents as cholestasis in children and steatosis in adults
- Increases morbidity / mortality in patients waiting for small bowel transplants

### POSTULATED MECHANISMS FOR IFALD

#### STEATOSIS

- Excess calories in TPN
- Choline deficiency
- Essential fatty acid deficiency
- Carnitine deficiency

#### CHOLESTASIS

- Lack of enteral stimulation
- IV lipid infusion
- IV amino acids infusion
- Taurine deficiency
- Methionine
- Genetic predisposition
**HUMORAL FACTORS IN INTESTINAL ADAPTATION**

- Glucagon-like peptide 2 (GLP-2) analogue – Teduglutide
- Somatotropin
- Epidermal growth factor
- Transforming growth factor-alpha
- Keratinocyte growth factor
- Insulin-like growth factor-1

**GLUCAGON-LIKE PEPTIDE 2**

- Stimulates intestinal growth
- Up regulates villus height in the small intestine
- Increases crypt cell proliferation
- Decreases enterocyte apoptosis
- Prevents intestinal hypoplasia resulting from TPN

**TEDUGLUTIDE**

- Pivotal 24 week, phase III double blind placebo controlled study
- Endpoint: 20-100% TPN volume reduction from baseline at week 20 and maintained at week 24
- 63% (teduglutide) vs 30% (placebo) achieved endpoint
- Mean TPN volume reduction was 4.4 L/week vs 2.3L/week at week 24
- Most common side effects: headaches (35%), nausea (31%), abdominal pain (25%)
- Screen for colon polyps before initiation and after one year on the drug

**TEDUGLUTIDE – STEPS 2**

- Graph showing reduction in TPN volume over time with TEDUGlutide treatment.
SURGICAL MANAGEMENT OF SHORT BOWEL SYNDROME

AUTOLOGOUS RECONSTRUCTION OF THE GI TRACT

Operations to Correct Slow Transit
- Consider the possibility of structural, partial obstruction, fistulas, or anastomotic leakage; diagnose and treat accordingly.
- Creation of valves

Operations to Improve Intestinal Motility With Dilated Bowel
- Tapering enteroplasty
- Longitudinal intestinal lengthening and tailoring (Bianchi-LTE procedure)
- Serial transverse enteroplasty (STEP)
- Intramesenteric placement

Operations to Slow Intestinal Transit in the Absence of Bowel Dilatation
- Sequential reversal of the small bowel (SNHB)
- Hypoactive colonic incontinence

Operations to Increase Mesenteric Surface Area
- Sequential anastomotic lengthening
- Controlled tissue expansion

STEP

INTESTINAL TRANSPLANTATION

- For nearly three decades considered forbidden organ for transplant:
  - Susceptibility of graft to ischemia
  - High risk of rejection
  - Bacterial translocation

- Survival significantly improved over the last decade due to:
  - Novel immunosuppression protocols
  - Improved post-operative management
  - Surgical innovations
INTESTINAL TRANSPLANTATION (cont.)

• 1988 – First successful isolated intestinal transplant by Deltz in Germany (56 month survival)
• 1988 – First successful liver and intestinal transplant by Grant in Canada
• 2001 – Accepted by CMS as therapeutic option for patients with intestinal failure

INDICATIONS

• Irreversible intestinal failure (IF) patients who:
  a) Require ongoing parenteral nutrition (PN)
  b) Complications of parenteral nutrition
  c) High risk of death if the native gut is not removed (unresectable mesenteric tumors)

CRITERIA FOR FAILURE OF TPN

• Imminent or evident liver failure of PN-induced liver injury
• Thrombosis or at least two central vein
• Two or more episodes of line sepsis per year that require hospitalization
• Single episode of line-related fungemia, septic shock or acute respiratory distress
• Recurrent episodes of severe dehydration despite intravenous fluid supplementation

INDICATIONS IN CHILDREN

<table>
<thead>
<tr>
<th>Indication</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Necrotizing Enterocolitis</td>
<td>12%</td>
</tr>
<tr>
<td>Gastroschisis</td>
<td>22%</td>
</tr>
<tr>
<td>Intestinal Atresia</td>
<td>8%</td>
</tr>
<tr>
<td>Short Gut</td>
<td>8%</td>
</tr>
<tr>
<td>Intestinal Inflammation</td>
<td>6%</td>
</tr>
<tr>
<td>Microvillus Inclusion</td>
<td>6%</td>
</tr>
<tr>
<td>Pseudo-obstruction</td>
<td>9%</td>
</tr>
<tr>
<td>Re-Tx</td>
<td>7%</td>
</tr>
<tr>
<td>Other</td>
<td>3%</td>
</tr>
<tr>
<td>Male bowel obstruction</td>
<td>1%</td>
</tr>
<tr>
<td>Female bowel obstruction</td>
<td>1%</td>
</tr>
<tr>
<td>Other</td>
<td>4%</td>
</tr>
<tr>
<td>Vodradil</td>
<td>17%</td>
</tr>
<tr>
<td>Duodenal Obstruction</td>
<td>1%</td>
</tr>
<tr>
<td>Hirschsprung's disease</td>
<td>7%</td>
</tr>
<tr>
<td>Other</td>
<td>3%</td>
</tr>
<tr>
<td>Malabsorption</td>
<td>3%</td>
</tr>
<tr>
<td>Other</td>
<td>3%</td>
</tr>
</tbody>
</table>

INTESTINAL TRANSPLANTATION: Diagnosis, Management and Transplantation. Langnas et al. 2008
INDICATIONS IN ADULTS

DEMOGRAPHICS

ISOLATED SMALL BOWEL TRANSPLANT

MULTIVISCERAL TRANSPLANTATION

In the absence of liver disease, an isolated small bowel transplant procedure is performed.

In the presence of liver disease, the liver and intestine are transplanted en bloc with the pancreas and duodenum, with or without the stomach, depending on the intra-abdominal status of the recipient.
POSTOPERATIVE COMPlications

- Technical complications- incidence is about 9% (bleeding, thrombosis, anastomotic leaks)
- Infections
- Rejection
- Graft versus Host Disease (about 7%)
- Post-transplant lymphoproliferative Disorder
- Graft pancreatitis
- Bowel obstruction
- Recurrent disease

ACUTE REJECTION

- About 40 – 50% moderate / severe rejection in the first month
- Mortality with severe rejection is 25-45% at 6 months
- Graft loss occurs in virtually all patients with severe rejection despite aggressive immunosuppressive therapy
- Manifests as increased stoma output, fever, abdominal pain, distention and ileus
- Also predisposes to sepsis from bacterial translocation and fungal infections
- Early diagnosis is extremely important
- Patients who had isolated bowel transplant are at higher risk

NORMAL ALLOGRAFT

ACUTE REJECTION

CHRONIC REJECTION

Occurs in about 8%

Risk factors include
- Isolated intestinal transplant
- Acute rejection within the first month
- Increased number and higher grade of acute rejection episodes
- Older recipient age
- Definitive diagnosis by full thickness biopsy of the allograft usually after removal
Graft and Patient Survival

- One year graft survival: 80%
- One year patient survival: 85 – 90%
- Survival at 5, 10 and 15 years: 60, 40 and 30%
- Multiple readmissions are not unlikely

Future Directions

- Advances in immunosuppression
- Tolerogenic protocols
- Earlier referrals for transplant
- Multivisceral Transplant for
  - Metastatic neuroendocrine tumors
  - Cirrhosis with portomesenteric thrombosis
  - Unresectable retroperitoneal tumors

Summary

- Short bowel syndrome is a relatively rare entity that needs to be approached in a multidisciplinary fashion
- Enteral nutrition should be introduced as soon as possible
- The small bowel has a great ability to adapt
- There is ongoing and great opportunity for research
- Small bowel transplant (isolated or multivisceral) is the last resort - outcomes are improving