Healthline VOLUME 21

Coram®* Continuing Education Program

Short Bowel Syndrome

Short bowel syndrome (SBS) is a significantly debilitating condition that can have a number of causes. SBS occurs when the body is without sufficient intestinal surface area to support adequate absorption of fluids, electrolytes, macronutrients (such as proteins, carbohydrates, and fats), and micronutrients (such as vitamins, minerals, and trace elements) with a normal or supplemented oral or enteral diet. SBS is a rare condition. Each year, SBS affects about three in every million people.[1]

Common causes of SBS are listed in Table 1. In most cases, an SBS diagnosis can be made when the patient has fewer than 200 cm, or less than 50%, of functional small intestine, without a functioning colon (or fewer than 60 cm if a functional colon is present).[3] Normal adult small intestinal length is about 400 to 600 cm. Since nearly 90% of nutrient absorption occurs in the first 100 to 150 cm of the small intestine, intestinal surface layer loss in this area often results in malabsorption.[4] With malabsorption, patients suffer from symptoms such as diarrhea, steattorhea, severe malnutrition and dehydration, fatigue, osteopenia, electrolyte imbalances, and weight loss. Parenteral nutrition support (PN) and/or intravenous (IV) fluids may be required, on an intermittent or long-term basis.

Importantly, not all patients with significant loss of small bowel develop SBS. Factors that impact development of the condition include:

- Original length of small bowel,
- Specific section of the intestine that is lost,
- Length of the remaining bowel and colon,
- Age of the patient,
- Presence or absence of the ileocecal valve (the valve between the ileum of the small intestine and the cecum of the large intestine that controls the rapidity of the flow of small bowel contents into the colon),
- Functionality of the remnant bowel, and
- Degree of adaptation of remaining bowel.

Anatomical and Functional Review

The small intestine is made up of three major anatomical parts — the duodenum, jejunum, and ileum. Intestinal villi, which are microscopic finger-like projections that absorb nutrients as food passes by, line the walls of the entire small intestine, increasing the surface area of the intestinal lining. The increased surface area gives the small intestine the ability to absorb the greatest amount of digestive products. In fact, the majority of digestive products never make it to the distal end of the small intestine because of the absorptive effectiveness in the proximal section.

The duodenum, which makes up the first 25 to 30 cm of the small intestine (and is rarely involved in resection), is the preferred site of absorption for iron and folate, as

Table 1: Common Causes of SBS[2]

Adults
• Crohn's disease • Cancer and damage to the intestine caused by treatment • Mesenteric vascular accidents • Trauma • Recurrent intestinal obstruction
Children
• Necrotizing enterocolitis • Intestinal atresias • Congenital short small bowel • Gastroschisis • Meconium ileus or peritonitis • Gastroschisis or Omphalocele

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well as fat-soluble and B vitamins, and selenium. Pancreatic enzymes and bile salts enter the intestine here to mix with food, the essential first step in food breakdown and absorption. Most digestion of protein, fat, and carbohydrates takes place in the duodenum and in the first three feet of the jejunum.

The jejunum is the second portion of the small bowel and measures 200 to 300 cm (6 to 10 feet) in length. The primary nutrients absorbed in the jejunum include calcium, folate, vitamins A, D, E, and K, sodium, fatty acids, phosphorus, copper, magnesium, zinc, chromium, water, and carbohydrates. Extensive jejunal resection leads to carbohydrate malabsorption. The undigested carbohydrates produce osmotic diarrhea that draws water into the intestine, resulting in large-volume watery diarrhea that may place a patient at higher risk for dehydration. The jejunum is also the site responsible for primary drug absorption.

In the ileum, which is 300 to 400 cm (10 to 13 feet), motility is much slower, allowing for more nutrient contact time with the mucosa and thus greater absorption. It is also the site of absorption of bile salts and vitamin B-12. Importantly, ileal resection is the least tolerated from a nutritional standpoint, in part because of the increased nutrient contact time, but also because the ileum can adapt somewhat and help compensate for jejunal loss. Neither the duodenum nor the jejunum can take on the absorptive functions of the ileum.

The ileocecal valve controls the amount of ileal contents in the colon (large intestine). It also slows the passage of these contents into the colon, again allowing for important nutrient contact time. In addition, the ileocecal region possesses specific absorptive functions and plays a crucial role in the regulation and integration of postprandial gastrointestinal (GI) motility and secretions. If the ileocecal valve is preserved, intestinal transit is slowed, which allows more time for nutrient absorption.

The colon (large intestine) is the final segment of the GI tract. The colon is about 160 cm (about 5 feet) in length. It is highly adaptable and can increase its absorptive capacity three- to five-fold, which is essential with an absent small bowel. The presence, decreased length, or total absence of the colon impacts the patient's absorptive quality and capacity. See Table 2.

Table 2: Bowel Continuity

With Colon
• Increased absorption of water • Increased absorption of sodium • Increased metabolization of carbohydrates to short-chain fatty acids (the preferential "food" for cells in the colon to help promote cell growth and enhanced nutrient absorption) • Risk: Increased oxolate crystals
Without Colon
• Electrolyte depletion • Dehydration • Inability to produce calories from fiber

Intestinal Adaptation

While most SBS patients have a lifelong dependency on parenteral nutrition (PN) post-diagnosis, there are patients for whom sufficient intestinal adaptation ultimately allows for weaning from PN. Intestinal adaptation refers to the time it takes for the GI tract to adjust to the damage that has been done to it; this adjustment is essentially the resumption of the GI tract's absorptive function. It is described in three phases, occurring over a course of 12 to 24 months: the acute phase, the adaptation phase, and the maintenance phase.

Acute Phase

The acute adaptation phase begins immediately after bowel resection and can last up to three months. Within days, the bowel starts to compensate for a reduction in the surface area by:

- Increasing the length and diameter of the remaining bowel,
- Causing villous hypertrophy, cellular hyperplasia, and formation of crypts (depressions within the GI tract lumen), and
- Altering motility and hormonal responses.

Functional adaptation (increased brush border enzyme activity and decreased gastrointestinal motility) also occurs to promote fluid and nutrient absorption. The ultimate effect is to maximally increase the remaining luminal absorptive capacity. During this time, however, patients often present with severe

diarrhea (or high ostomy output) and extremely poor absorption. The potential for life-threatening dehydration and electrolyte imbalances is real. PN is almost universally required to maintain fluid and electrolyte balance and meet nutritional needs.

Adaptation Phase

The adaptation phase typically begins within 48 hours of small bowel resection and lasts up to two years. This is the most active phase, during which 90% of bowel adaptation occurs as the body continues to increase the surface area of the remaining intestine, again via villous hyperplasia, enteric cellular hypertrophy, and increased crypt depth.[5,6] Intestinal dilatation and lengthening also continue. PN remains an essential form of nutrition throughout this phase as well. Trials of modified oral or enteral feedings are essential to maintain intestinal integrity and enhance absorptive capabilities.

During the adaptation phase, as calories, protein, vitamins, fluids, and electrolytes are increasingly absorbed by the intestine, reduction of these components in a patient's PN prescription may be indicated. As their intestine adapts and they are able to support their nutrition needs via an oral or enteral diet (at least partially), patients may be able to reduce their overall number of daily PN infusion hours, or have "PN-free" days.

Maintenance Phase

At some point, the absorptive capacity of the intestine reaches its maximum potential. Some patients will have achieved and be able to maintain nutritional and metabolic homeostasis with oral feeding. However, most patients will not have gained the necessary absorptive capacity to be sustained with oral feeding and will require PN indefinitely.

Nutritional Management

The American Gastroenterological Association has developed guidelines surrounding nutrition for the SBS patient.[7] According to the guidelines, healthcare goals for treating SBS are to ensure adequate hydration, ensure the provision of adequate macronutrients and micronutrients, prevent complications associated with both short- and long-term malnutrition, and, in children, promote growth. Adult PN recommendations include approximately 20 to 35 kcal/kg/day. Carbohydrates and lipids should be limited to ≤ 7 g/kg/day and 1.0 g/kg/day, respectively. To prevent fatty acid deficiency, approximately 1% to 2% of total calories should come from linoleic acid, and 0.5% from alpha-linolenic acid. Finally, PN should provide 186 mg/kg/day of essential amino acids, or 25% to 30% of total protein intake.[8]

Patients with significant fluid loss—typically more than 2.5 to 3 liters/day—may require oral rehydration solution (ORS). ORS, such as CeraLyte®, WHO formula, or Pedialyte®, not only replaces fluid losses from diarrhea, but also provides sodium, potassium, and carbohydrates. Water alone, which promotes sodium losses, is not recommended.

Table 3: Vitamin and Mineral Supplementation for Patients with Short Bowel Syndrome Weaning From Parenteral Nutrition[9]

Nutrient	Strength	Dose
Vitamin B12	1000 µg	Injection once monthly
Vitamin A	25,000 IU	1 tablet PO daily
Vitamin D	1000 IU	1 tablet PO daily
Vitamin E	400 IU	1 tablet PO daily
Calcium	500- to 600-mg tablet	1–2 tablets PO TID
Magnesium lactate	8-mg tablet	1–2 tablets PO TID
Magnesium gluconate	1000-mg tablet (or liquid)	1–3 tablets PO TID
Potassium chloride	20-mg tablet	1–2 tablets PO daily
Phosphate	250-mg package	1 package PO TID
Sodium bicarbonate	650-mg tablet	1 tablet PO TID
Chromium	100-µg tablet	1–2 tablets PO TID
Copper	3-mg tablet	1–2 tablets PO daily
Selenium	200-µg tablets	1 tablet PO daily
Zinc sulfate	220-mg tablet	1–3 tablets PO daily

Vitamin and mineral supplementation is recommended as listed in Table 3. Of course, vitamins and minerals must be monitored routinely, and supplementation prescribed according to individual patient needs.

Oral Intake

Oral intake should be encouraged regardless of absorptive ability in order to promote the oral and GI stimulation necessary for intestinal hyperplasia. Oral stimulation also promotes the release of both growth factor and regulatory peptides, which deliver nutrients to GI cells. In addition, oral intake is

important for infants and children in order to help prevent food aversion. When oral intake becomes better tolerated and some absorption is evident (weight gain with no change to PN or tube feeding therapy), nutrients may need to be provided at 1.5–2 times the usual estimated needs to account for malabsorption.[8,9,10] Consistent compliance to oral rehydration solutions (ORS) are also an important component to successful independence from enteral and parenteral therapy.

Enteral Therapy

To attain sufficient nutritional intake, SBS patients may require enteral therapy (tube feeding), which they typically take via continuous or nocturnal feedings as tolerated. Initially, trophic or low-volume enteral "drip" feeds (very slow enteral feedings) are often required to stimulate bowel function. If the patient has an intact colon, soluble fiber-containing formulas can be used. If a standard formula is not tolerated by the patient, a peptide-based or elemental formula may work. Potential complications associated with tube feeding include issues with the feeding tube itself, such as displacement, clogging, and site infection, and issues with the formula, including symptoms of intolerance (nausea, vomiting, and diarrhea).

Parenteral Therapy

Most SBS patients require PN, at least at the outset. Patients who achieve sufficiently increased absorptive capacity through the adaptation process may be weaned off of PN in a year or two. Weaning is more likely if the remnant bowel is longer than 100 cm with the colon removed, or longer than 60 cm with the colon intact.[11,12] Some patients may require intermittent PN three to four times per week. Potential complications associated with long-term PN administration include hepatic dysfunction, catheter-related bloodstream infections, metabolic bone disease, and potential lack of venous access. Home PN therapy is also costly, with an average annual cost of $75,000 to $122,000 for solution and supplies.[12]

Complications from PN therapy can be reduced, and hospitalization avoided, by proactive clinical management from an experienced interdisciplinary nutrition support team.[13] An average of $4,100 per-patient cost savings can also be achieved through Home Nutrition Support Team management.[13]

Potential Complications

Patients with SBS are at significant risk for numerous therapy-related and physiologic complications. Patients on long-term PN are at risk for osteoporosis and metabolic bone disease, hyperglycemia, hypoglycemia, hypocalcemia, hypomagnesemia, and vitamin D deficiency. D-lactic acidosis may develop when colonic bacteria ferment unabsorbed nutrients into an atypical form of lactic acid, which can lead to altered mental status, slurred speech, and ataxia. Deficiencies of electrolytes, vitamins, and minerals are ongoing risks and monitoring is essential. Catheter-related bloodstream infections (CRBSIs) and PN-related liver disease are serious potential problems that contribute significantly to morbidity and mortality in SBS patients.

Patients who have a colon are at risk for calcium oxalate kidney stones. Oxalates typically bind with calcium in the digestive system; however, malabsorption often prevents this binding, and the oxalates are then absorbed by the colon and transported to the kidneys. In the kidneys, calcium and oxalates can bind together and cause renal stones. Volume depletion, metabolic acidosis, and hypomagnesemia also compound the risk for renal stones.

Medication Management

Antidiarrheals are often used to slow gut motility, allowing for increased absorptive capacity and decreased fluid output. These agents may be prescribed starting with the mildest agent at the lowest recommended dose and increasing as necessary. Some SBS patients will require doses that are higher than recommended due to malabsorption.

Table 4: Medical Treatment of SBS[14]

Treatment Goal	Medications
Slow transit time, decrease diarrhea	Anti-diarrheals Narcotics Bile salt binders Pancreatic enzymes
Decrease GI secretions	H2 receptor antagonists Proton pump inhibitors Somatostatin analogues
Treat bacterial overgrowth	Antibiotics Probiotics Prokinetics
Improve colonic absorption	Glutamine
Growth intestinal absorption	Growth hormone

Gastric hypersecretion can occur for six months or longer following small bowel resection, especially when the jejunal surface is lost. This causes an increased volume of secretions from the stomach to pass into the small bowel, resulting in a decrease in the pH of the upper GI tract. To treat this, proton pump inhibitors are often prescribed. Hydrochloric acid (H2) blockers are indicated to reduce gastric acidity.

Octreotide (Sandostatin®), a somatostatin analogue, is occasionally prescribed to reduce gastric, biliary, and pancreatic secretions and to slow gastrojejunal transit time. Octreotide is given subcutaneously, three times a day, 30 minutes prior to a meal.

Bile salts are produced in the liver and flow through the bile ducts into the intestine where they are needed for fat digestion. Ursodiol is a naturally occurring bile salt that, when taken as a medication, replaces some of the bile salts lost due to SBS and promotes fat digestion. Ursodiol is FDA-approved for the following indications:

- Dissolving cholesterol gallstones
- Preventing gallstone formation during rapid weight loss
- Treating primary biliary cirrhosis

If a patient has an intact colon and loss of ileum (where bile salts are absorbed), bile salts produced by the liver may "pour" into the colon, resulting in colonic mucosal irritation and diarrhea. Cholestyramine is a bile salt binder that may be used to mitigate the cathartic effect of unabsorbed bile salts on the colon.

In patients who retain their colon but not their ileocecal valve, the risk of bacterial regurgitation from the colon into the remaining small bowel may be significant. Antibiotics may be used sparingly to prevent small-bowel bacterial overgrowth and minimize the likelihood of bacterial resistance.

Investigation continues into the use and benefit of pharmacologic agents such as glutamine (a preferred amino acid of intestinal cells) to help maintain the structural integrity of the small intestine, and growth hormone to promote small intestinal cellular growth to enhance absorption. The growth hormone somatropin (Zorbtive™) is FDA-approved for use in combination with glutamine, although outcomes have been mixed. The most recent entrant into the medication pool for SBS is teduglutide (Gattex®), which was approved by the FDA in 2012 as an ultra-orphan drug for the treatment of SBS. Teduglutide contains a novel, recombinant analogue of human glucagon-like peptide 2 (GLP-2), a natural protein that plays a role in stimulating growth of the lining of the small intestine and increasing absorption. This agent has been shown to reduce some dependence on PN in adults with SBS.[14]

Surgical Intervention

Various surgical options have been attempted to improve transit time in SBS patients, with an overall success rate of approximately 50%.[16] Today, however, two procedures predominate. The Bianchi procedure for intestinal lengthening divides one loop of the bowel into two segments longitudinally, creating two parallel segments of smaller diameter, which are then connected to add length. The result is greater small bowel surface area and slower motility, which are important for increasing fluid and nutrient absorption. With serial transverse enteroplasty (STEP), the small bowel is stapled into V-shapes on alternating sides, decreasing bowel width and increasing its length. Food moves more slowly through the repaired bowel, allowing for greater absorption.

Intestinal Transplantation

For a subset of patients, therapy-related complications may progress to the point where the only remaining option is an intestinal transplant (or a liver-intestinal transplant, in the case of actual or impending liver failure). Candidacy evaluation may be indicated if the patient presents with such clinical situations as:

- Impending or overt liver failure due to HPN-induced liver injury,
- Thrombosis of the major central venous channels—jugular, subclavian, and femoral veins,
- Frequent line infection and sepsis, or
- Frequent episodes of severe dehydration despite intravenous fluid supplement in addition to HPN.

Approximately 139 intestinal transplants were performed in the United States in 2014. Survival for the transplanted SBS patient at 1 year, 3 years and 5 years is reported at 77.3%, 59.8%, and 47.0%, respectively.[16] ♦

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Self-Assessment Quiz: Short Bowel Syndrome

LEARNING GOAL

To understand the clinical complexities and treatment options for short bowel syndrome.

LEARNING OBJECTIVES

At the end of this program, the reader will be able to:

1. Describe the pathophysiology of and risk factors associated with short bowel syndrome.
2. Discuss the key physiologic changes and needs during the three phases of intestinal adaptation.
3. Discuss the rationale for treatment strategies.

SELF-ASSESSMENT QUESTIONS

In the Quiz Answers section on the next page, fill in the correct answer for each question. To obtain two (2.0) contact hours toward CE credit, the passing score is 100%. Return your Self-Assesment Quiz to Coram via email or fax. See the next page for details on how to return your quiz. Please allow approximately seven days to process your test and receive your certificate upon achieving a passing score.

1. **The majority of nutrient absorption occurs in:**
   a. The first 100–150 cm of the small intestine
   b. The last 100–150 cm of the small intestine
   c. The first 100–150 cm of the large intestine
   d. The last 100–150 cm of the large intestine

2. **All patients with a significant loss of small intestine will develop short bowel syndrome.**
   a. True
   b. False

3. **Intestinal adaptation can occur in patients with short bowel syndrome, reducing or eliminating the need for PN.**
   a. True
   b. False

4. **PN is required during the acute phase of intestinal adaptation.**
   a. True
   b. False

5. **The primary adaptive response of the small intestine during adaptation is:**
   a. Slowed GI motility
   b. Increased GI motility
   c. Increased surface area of the remaining intestine

6. **Long-term PN is rarely needed for patients throughout the maintenance phase.**
   a. True
   b. False

7. **Oral intake should be avoided in the SBS patient on long-term PN.**
   a. True
   b. False

8. **Concomitant medications for SBS treatment may include all of these EXCEPT:**
   a. Antidiarrheals
   b. Proton-pump inhibitors
   c. H2 blockers
   d. Antibiotics
   e. GI stimulants
   f. Bile salts

9. **Teduglutide (Gattex®) is an analogue of a natural protein that plays a role in:**
   a. Stimulating growth of the lining of the small intestine
   b. Increasing absorption of the small intestine
   c. Reducing some dependence on PN in adults
   d. All of the above
   e. A and C

10. **Surgical intervention may include:**
    a. The Bianchi procedure for intestinal lengthening
    b. Serial transverse enteroplasty (STEP) to decrease bowel width and increase bowel
    c. Intestinal transplantation
    d. All of the above
    e. A and B

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QUIZ ANSWERS

Fill in the key below with the correct answers to receive 2.0 Continuing Education credits.*

1.	a	b	c	d	e	f	g
2.	a	b	c	d	e	f	g
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5.	a	b	c	d	e	f	g
6.	a	b	c	d	e	f	g
7.	a	b	c	d	e	f	g
8.	a	b	c	d	e	f	g
9.	a	b	c	d	e	f	g
10.	a	b	c	d	e	f	g

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