

Short Bowel (Gut) Syndrome

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Learning Objectives

- Define SBS
- Normal function of small bowel
- Clinical Manifestation and Diagnosis
- Management
- Updates

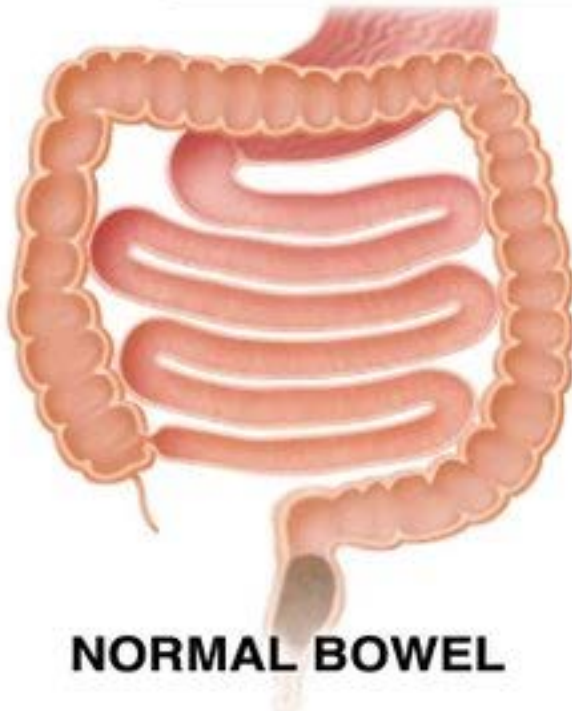
Basic Definition

- A malabsorption disorder caused by the surgical removal of the small intestine, or rarely it is due to the complete dysfunction of a large segment of bowel.
- Most cases are acquired, although some children are born with a congenital short bowel.

SHORT BOWEL SYNDROME - Jane Doe

Short bowel syndrome results in malabsorption of water, electrolytes, macronutrients and micronutrients

Schematic
view



NORMAL BOWEL



JANE'S BOWEL

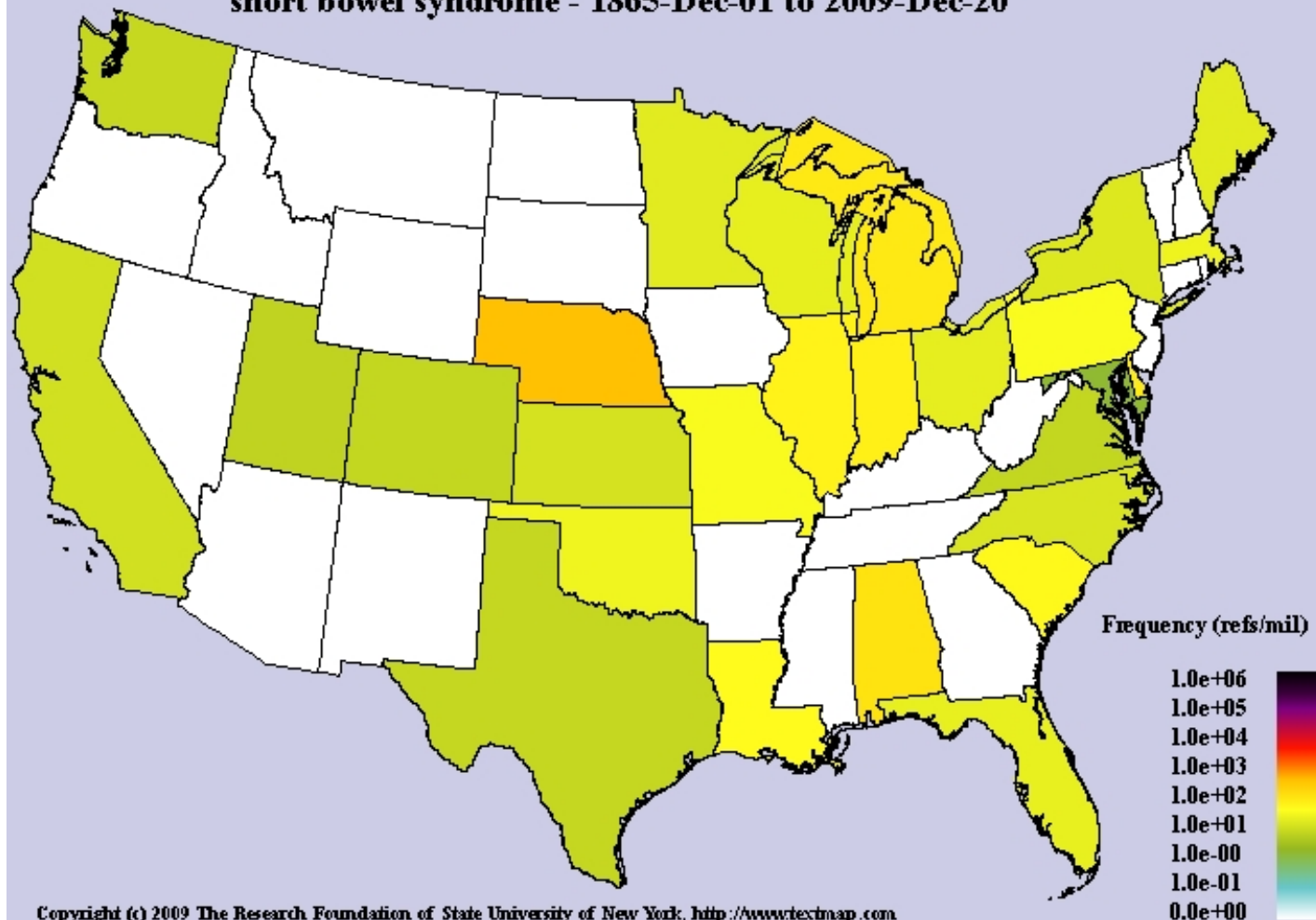
Intestinal Failure

- SBS is the most common cause of intestinal failure, the state in which an individual's GI function is inadequate to maintain his/her nutrient and hydration status w/o intravenous or enteral supplementation.
- In addition to SBS, diseases or congenital defects that cause severe malabsorption, bowel obstruction, and dysmotility (eg, pseudo-obstruction) are causes of intestinal failure.

Causes of SBS

- surgical resection for Crohn's disease
- Malignancy
- Radiation
- vascular insufficiency
- necrotizing enterocolitis (pediatric)
- congenital intestinal anomalies such as atresias or gastroschisis (pediatric)

short bowel syndrome - 1865-Dec-01 to 2009-Dec-20

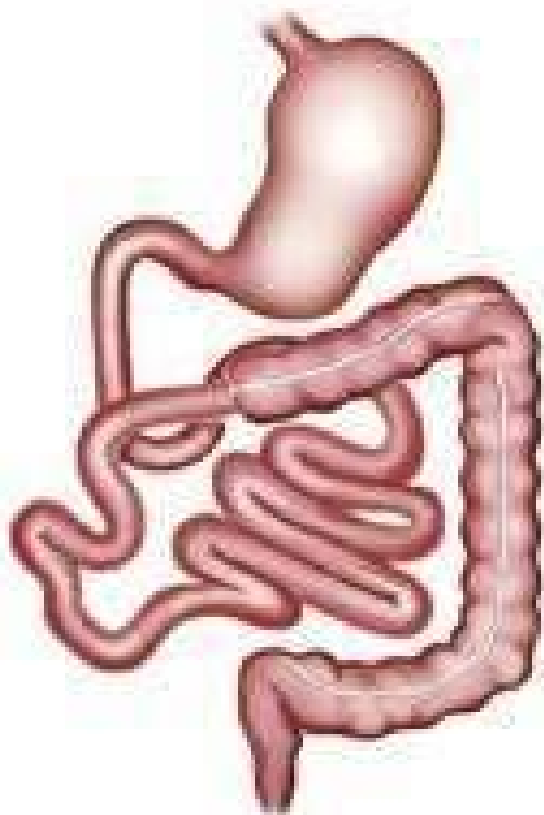


Length as a Determinant of Intestinal Function

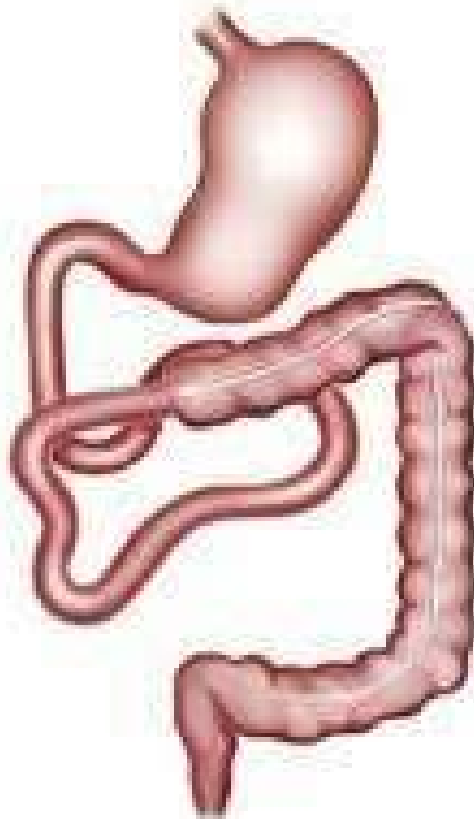
- The length of the small intestine is an important determinant of intestinal function
- Infant normal length is approximately 125 cm at the start of the third trimester of gestation and 250 cm at term
- <75 cm are at risk for SBS
- Adult normal length is approximately 400 cm
- Adults with residual small intestine of less than 180 cm are at risk for developing SBS; those with less than 60 cm of small intestine (but with a colon) are unlikely to achieve independence from parenteral nutrition

Other Factors

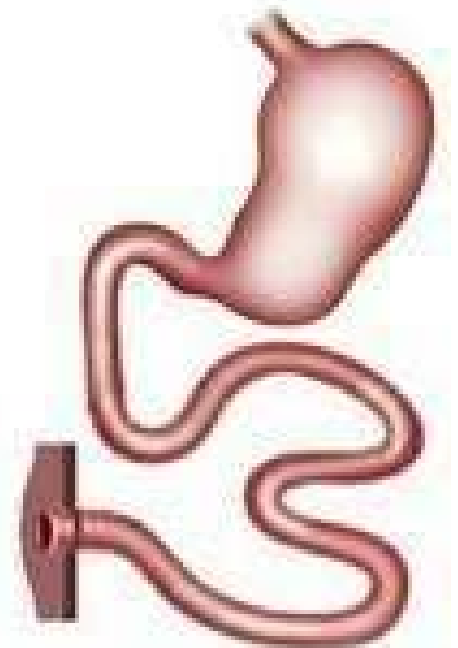
- site of intestinal resection
- presence or absence of the ileocecal valve
- presence or absence of colon
- gradual process of intestinal adaptation after surgical resection
- intestinal motility (such impairment in gastroparesis, colonic inertia, or gastroschisis)



Ileocolonic
anastomosis



Jejunocolonic
anastomosis



End-jejunostomy

Normal Physiology

- Each segment of small bowel has unique absorption properties and differences in their ability to adapt s/p resection
- Mechanisms of adaptation include lengthening of the intestinal villi and small bowel dilation
- Most intestinal adaptation occurs in the ileum

Metabolite Absorption Sites

Dude Is

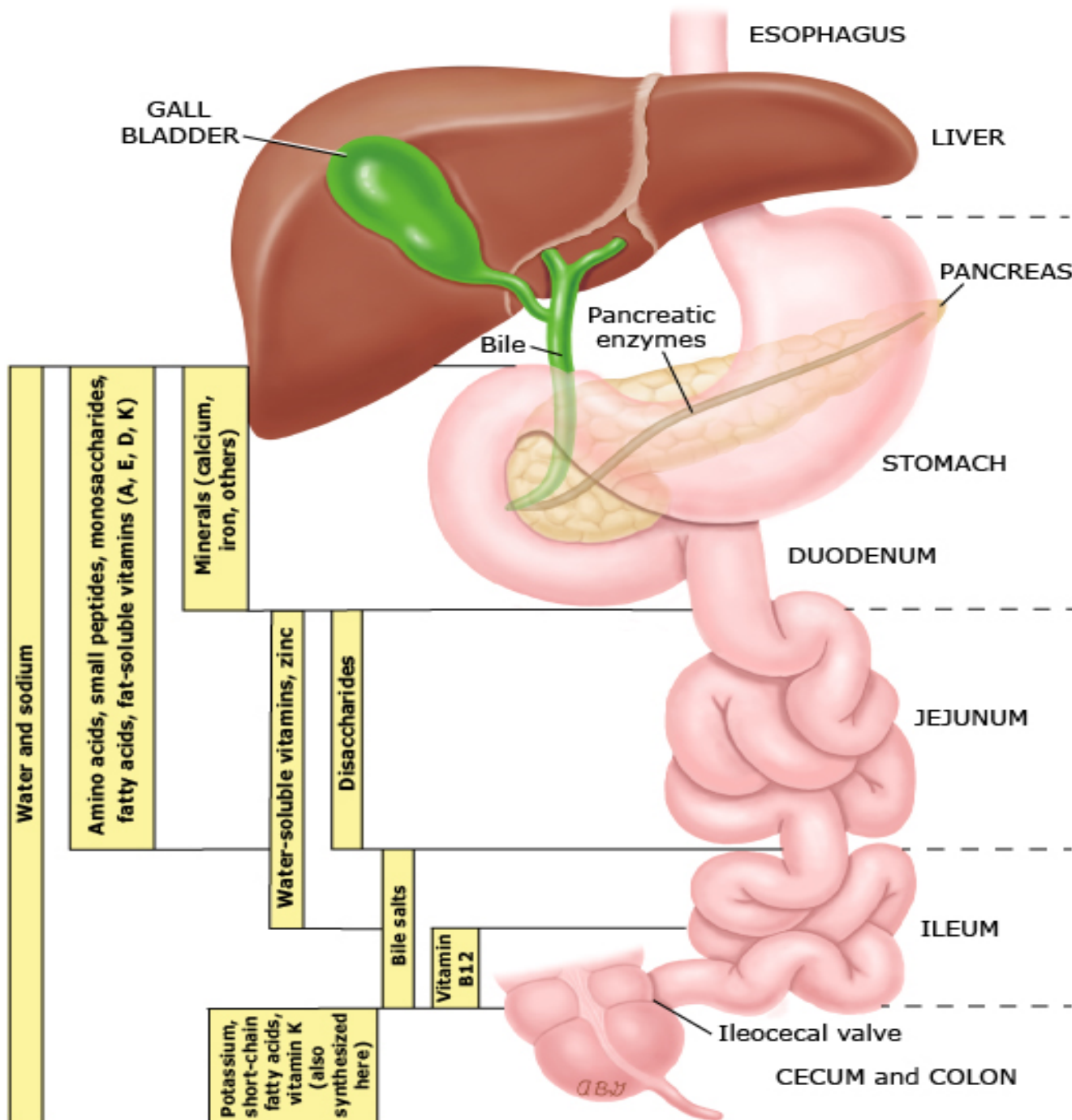
Just Feeling

Ill, Bro

Duodenum – Iron

Jejunum – Folate

Ileum – B12



Normal Jejunum Physiology

- **Jejunum**
 - long villi, large absorptive surface, highly concentrated digestive enzymes, and many transport carrier proteins
 - the primary digestive and absorptive site for most nutrients (Fat soluble vitamins A, D, E, K, other water soluble vitamins, minerals, disaccharides, water, and sodium)
 - when resected, a temporary reduction in absorption of most nutrients occurs

Normal Ileum Physiology

- **Ileum**
 - Having residual ileum is advantageous because of its specialized functions and the greatest capacity for adaptation when compared to jejunum
- **Absorption of Vit B12 bound to IF**
 - vitamin B12 malabsorption tends to occur if more than 60 cm of ileum is resected
 - resection of >100 cm leads to disruption of the enterohepatic circulation, resulting in bile salt deficiency and fat malabsorption

Ileum Physiology Continued

- **Bile acid absorption**
 - malabsorption of bile acids leads to a compensatory increase in their production by the liver, but losses can exceed production.
 - The diminished bile acid pool can further exacerbate malabsorption of fat and fat-soluble vitamins.
 - The increased passage of bile acids into the colon may induce a colonic secretory diarrhea (choleretic enteropathy)
 - Malabsorption of bile acids also causes excessive absorption of oxalate, leading to hyperoxaluria and possible kidney stone formation.

Normal Physiology

- Ileal brake

Unabsorbed lipids reaching the ileum cause delay in gastric emptying (the "ileal brake"), which is beneficial because it facilitates absorption of nutrients within the small intestine, and is mediated by hormones secreted by the ileum including peptide YY . Ileal resection may be associated with loss of this compensatory mechanism, which may contribute to the diarrhea observed in SBS.

- Fluid absorption

The ileum normally reabsorbs a large portion of the fluid secreted by the jejunum during the digestive process, particularly in response to hypertonic feedings. If a substantial part of the ileum is resected, fluid and electrolyte loss will occur. Such patients often cannot tolerate large bolus feedings or to feedings containing high concentrations of rapidly digested foods

- A 42-year-old woman with long-standing Crohn's disease of the small bowel which has been complicated by recurrent jejunal and ileal strictures is admitted with recurrent nausea and vomiting. She underwent ileal resection 10 years ago and a proximal jejunal resection 5 years ago. She has been maintained on infliximab 5 mg/kg ever since her last surgery. Computed tomography enterography confirms a 10-cm long strictured segment of distal jejunum with significant proximal bowel dilation. A nasogastric tube is placed and she is kept n.p.o., but after 48 hours, she has had no improvement. She is seen by general surgery and surgical resection of her distal jejunal stricture is recommended.

Which of the following is most likely to occur in the immediate post-operative period in this patient?

- A. Hypersecretion of gastric acid
- B. Hypogastrinemia
- C. Hypokalemia
- D. Hypomagnesemia
- E. Hypophosphatemia

Loss of the Ileocecal Valve

- The IC valve is an important barrier to reflux of colonic material from the colon into the small intestine. It also helps to regulate the passage of fluid and nutrients from the ileum into the colon
- Loss of the IC valve is usually considered to be a negative predictor of the ability to wean a patient from parenteral nutrition, however some studies suggest other factors.

Loss of IC valve is not independent predictor of small bowel transit, the risk of bacterial overgrowth, or the likelihood of weaning from parenteral nutrition

Instead, small bacterial overgrowth was related to small intestinal length and the presence of ileal peristalsis, and these factors were the primary predictors of the likelihood of weaning from parenteral nutrition,

Loss of the Colon

- Role in absorption of water, electrolytes, and short-chain fatty acids
- Loss of the colon in combination with extensive small bowel resection is poorly tolerated and is likely to lead to dehydration and electrolyte depletion.
- These patients usually require long-term TPN . The colon also helps to slow intestinal transit and stimulate intestinal adaptation.
- The colon can absorb up to 15 percent of energy requirements, primarily in the form of fermented carbohydrates; in patients with SBS on a high-carbohydrate diet, the colon can absorb as much as 50 percent of energy requirements

Loss of Colon

- The colon can absorb up to 15 percent of energy requirements, primarily in the form of fermented carbohydrates; in patients with SBS on a high-carbohydrate diet, the colon can absorb as much as 50 percent of energy requirements
- high carbohydrate feeding has the advantage of being absorbed in the colon in patients with SBS and retained colon
disadvantage is diarrhea
- The retained colon undergoes adaptation after small bowel resection, with gradual increases in enterocytes and other cells, and in gut hormones including peptide YY

Nutrient Effects

- Enteral feeding is the mainstay of therapy (induces ileal adaptation)
- Various nutrients effect intestinal adaptation
- These include the amino acids, arginine and glutamine, and medium- and long-chain triglycerides.
 - TBD in Management Section

Histologic Changes

Control



TPN



SBS



Management

- Assess likelihood of resuming an oral diet
 - Intact colon? Presence of IC valve? Jejunal length > 200 cm? Which segments of small bowel remain?
- Anticipate Consequences
 - Cholereic enteropathy, gastric acid hypersecretion, fat malabsorption, fat soluble vitamin malabsorption, other vitamins and minerals malabsorption, protein malabsorption
 - Drug absorption, enteric coated may not be well absorbed
- Screen, treat, and replace as needed

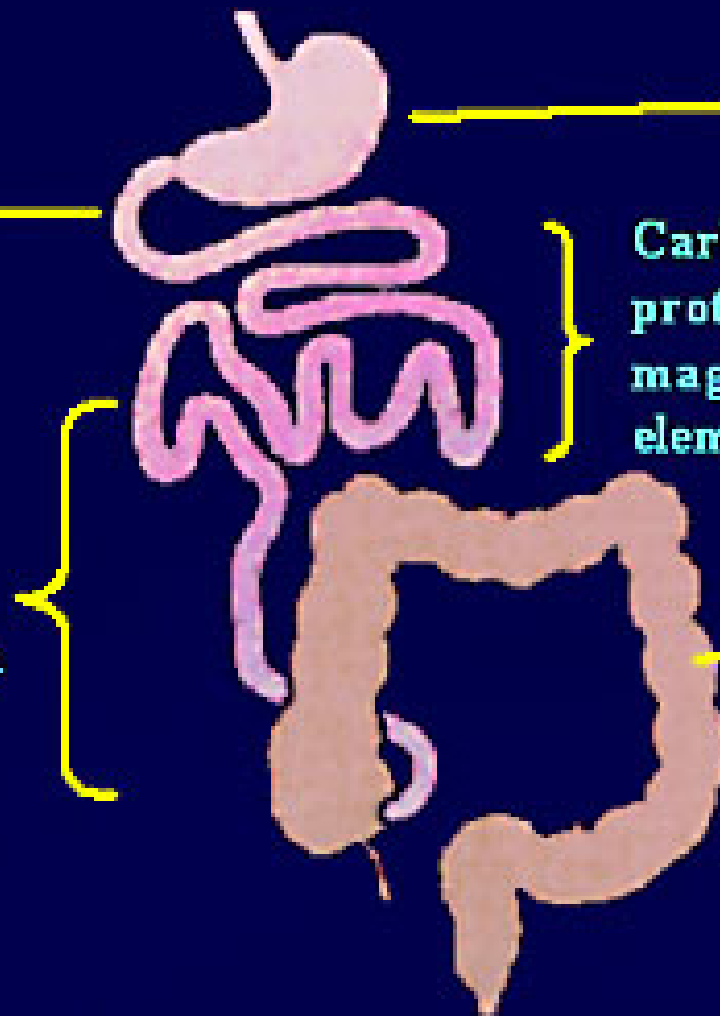
Beginning of
food breakdown

Iron and folate

Carbohydrates, fats,
proteins, calcium,
magnesium, trace
elements and vitamins

Same as jejunum,
but distal ileum is
specific for vitamin
B12 and bile salts

Water,
electrolytes,
and short
chain fatty
acids



Early Management

- Fluid and electrolyte replacement predominates
- Begin enteral feeding once patient stabilizes
- Antidiarrheals may help
- Octreotide (recommended by some authorities) can reduce digestive secretions but increases the risk of gallstones and tachyphylaxis develops.
- It should be used with caution and only in late stages of therapy (after approximately two years when intestinal adaption has been achieved)

Pharmacologic Therapy

- Acid production (Hypersecretory state)
 - octreotide, H2 blockers, PPI's
 - Octreotide reduces fluid losses but also diminishes splanchnic protein synthesis, which can interfere with the process of adaptation, increases small bowel transit time, but tachyphylaxis often develops
 - Octreotide predisposes patients to the development of gallstones for which they are already at high risk.
- Decrease Stool Output
 - Loperamide often results in a decrease in stool output and may be useful in patients without small bowel bacterial overgrowth.
 - Thickening agents are sometimes used but they are primarily carbohydrates, which can act as a prebiotic for intestinal bacteria and thereby exacerbate bacterial overgrowth.

- A 62-year-old man with presented with an acute abdomen and subsequently underwent a 100 cm distal ileal resection with ileocolonic anastomosis to remove infarcted intestine secondary to an embolus in the distal superior mesenteric artery. There was no evidence for mesenteric atherosclerosis or hypercoagulable state, but he was found to have new onset atrial fibrillation. He developed a marked diarrhea and a 10 kg weight loss since resuming his normal diet post-operatively. His stool is noted to have the characteristics of steatorrhea with a positive qualitative fecal fat stain.

Which of the following is the most likely explanation for his change in bowel habits and weight loss?

- A. Chronic mesenteric ischemia
- B. Bile acid effects on small intestine mucosa
- C. An increase in small intestinal secretion
- D. Recurrent embolic disease
- E. Reduction in luminal bile salt concentration.

Growth Factors

- May hasten adaptation and enhance mucosal growth beyond the normal limits of adaptation.
- Glucagon-like peptide-2 – Glucagon-like peptide-2 (GLP-2) an enteroendocrine peptide released in response of luminal nutrients, initiates and maintains small bowel adaptive responses to resection and improves nutrient absorption

Teduglutide- GLP 2 analogue

- It has been demonstrated to modestly reduce the volume and number of days of TPN required by patients with SBS with intestinal failure [
- In a phase III randomized controlled trial, 86 patients with short bowel syndrome with intestinal failure were randomized to teduglutide (0.05 mg/kg/day) or placebo for 24 weeks.
- Patients treated with teduglutide had a 20 percent reduction in the volume of parenteral support as compared with placebo (63 versus 30 percent)
- In a 28-week extension, 83 patients were assigned to treatment with teduglutide (0.05 mg/kg/day or 0.10 mg/kg/day) or placebo for 24 weeks. At week 52, a 20 percent reduction in the volume of parenteral support was noted in patients treated with both teduglutide doses of 0.05 mg/kg/day and 0.10 mg/kg/day (68 and 52 percent).
- The most common side effects were headache (35 percent), nausea (31 percent), and abdominal pain (25 percent). Adverse effects led 13 percent of patients to withdraw from the study.

Enteral Feeding

- Most enteral feeds are high in carb content and those with retained colon can handle these best given ability to absorb short chain fatty acids (Ensure)
- Protein hydrolysate diets often contain a higher, more physiologic percentage of fat and are frequently better tolerated (Peptamen 1.5 or Vitale)
- Fiber supplementation also may be helpful by enhancing adaptation via increased short-chain fatty acid production and providing an additional calorie source in patients with a reasonable amount of colon.

Less Helpful Supplementation

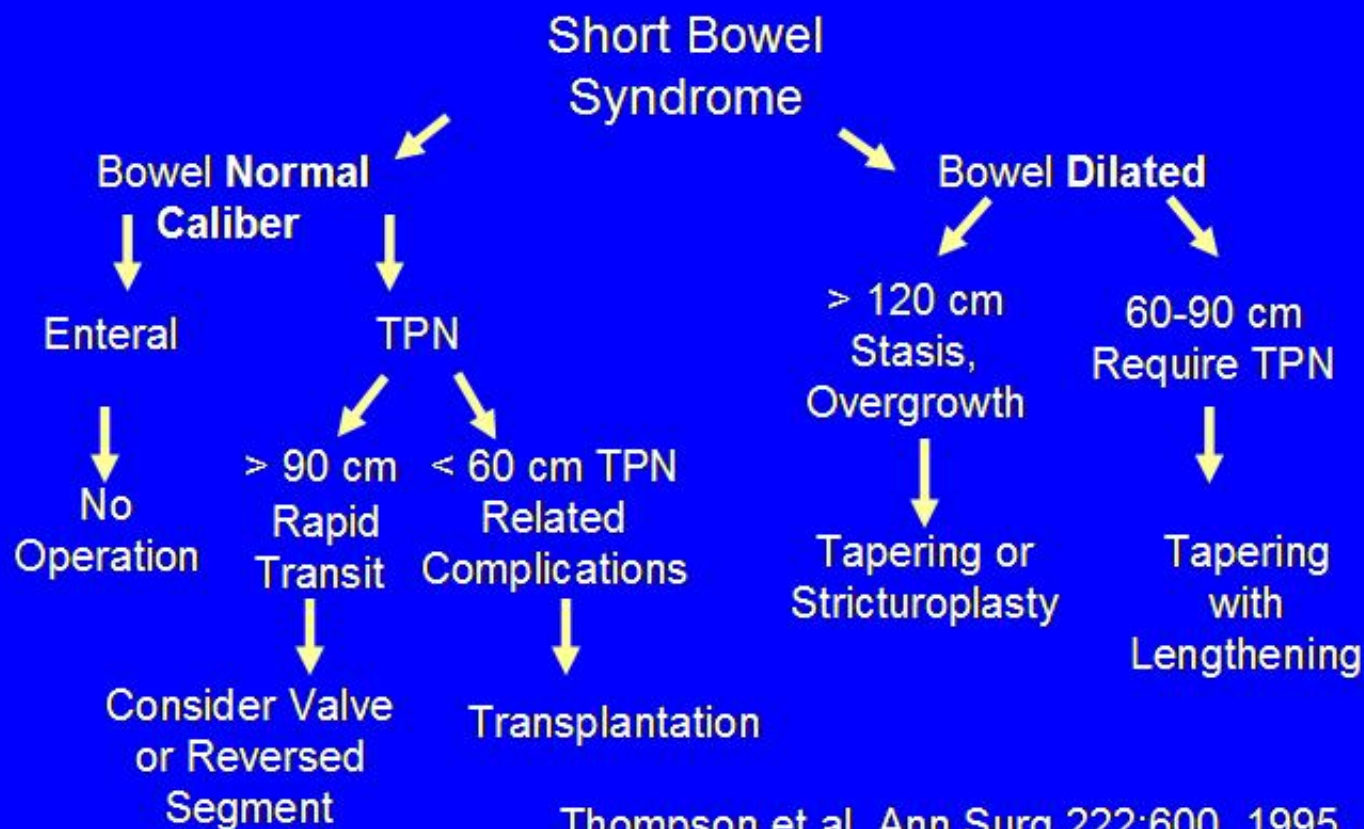
- Medium chain TG's frequently given because better absorbed in the presence of bile acid and pancreatic insufficiency, however lower caloric density and greater osmotic load makes this less efficacious in SBS (most have normal bile acid and pancreatic enzyme levels)
- Lactulose is generally well tolerated
- Pancreatic enzymes rarely help fat malabsorption

Frequency of Feeding

- Important to adaptation
- Small frequent or continuous feeding recommended as opposed to large bolus and infrequent feedings
- NG, NJ, DHT, gastrotomy, any source of enteral feeding recommended



SURGICAL MANAGEMENT OF SBS



Thompson et al. Ann Surg 222:600, 1995

Enteral Feeding

- Small frequent feedings (every two to three hours in adults).
- A reasonable mixture of protein, carbohydrates and fats; ideally, 40 percent of the patient's caloric intake should be provided in the form of fat.
- Avoidance of hypertonic beverages (eg, sodas and fruit juices).
- Avoidance of high carbohydrate feedings; those with simple carbohydrates often result in sudden osmotic fluid losses and dehydration and all forms of carbohydrate increase bacterial proliferation.

Ileum Resection Treatment

- Patients with limited ileal resection (<100 cm) can resume intake of solid food in the late postoperative phase. Specific issues to be addressed include secretory diarrhea due to bile salt malabsorption, and fat and vitamin B12 malabsorption.
- [Cholestyramine](#) will often improve diarrhea associated with bile salt malabsorption. Lack of improvement suggests that bile salt malabsorption is probably not the principal cause of diarrhea.
- Documented vitamin B12 malabsorption with low serum cobalamin concentrations requires life-long vitamin B12 supplementation. This is usually accomplished with monthly intramuscular injections; however, experience with a nasal preparation of vitamin B12 looks encouraging

Nutrient Deficiency

- The risk of nutrient deficiency is greatest during and after the transition to enteral feeding
- Serum levels of calcium, magnesium, zinc, [selenium](#), and the fat soluble vitamins (A, D, E, and K) should be monitored every three months.
- Replace as needed

A 44-year-old female with a history of short bowel syndrome presents to the office with complaints of a scaly red rash on her face, groins and hands and progressive alopecia.

What is the most likely etiology?

- A. Vitamin B12 deficiency
- B. Zinc deficiency
- C. Vitamin D deficiency
- D. Copper deficiency
- E. Vitamin E deficiency

Glutamine and Growth Hormone

- Glutamine, growth hormone, and high complex carb diet combination has been shown in a RCT to allow enteral nutrition in patients who had been TPN dependent
- This is not consistent in other RCT
- There was modest improvement in electrolyte absorption but no effect on small bowel morphology, stool losses, or macronutrient absorption occurred
- Both Gluatmine and Growth Hormone alone show no benefit

Adaptability

- **Jejunum -modest adaptive changes**
 - most changes are functional (changes in transport and enzyme activity) rather than structural (changes in absorptive area)
 - Studies suggests these changes can be induced by oral feeding, treatment with insulin-like growth factor 1, topical application of benzalkonium chloride, or administration of exogenous thyroid hormone during the hypothyroid phase of SBS
- **Ileum –significant adaptive changes, moreso than jejunum**
 - most changes are functional (changes in transport and enzyme activity) rather than structural (changes in absorptive area)
 - Studies suggests these changes can be induced by oral feeding in humans
 - Other studies in rats suggests treatment with insulin-like growth factor 1, topical application of benzalkonium chloride, or administration of exogenous thyroid hormone during the hypothyroid phase of SBS may be benefetial

Infant Risk of TPN dependent IBS

- In one series of infants with SBS due to surgical resection during the neonatal period, the likelihood of achieving independence from parenteral nutrition was more than 60 percent for infants with residual small intestine length >38 cm, as compared with 7 percent in those with residual small intestine length <15 cm [5].
- In a separate series, the probability of weaning from parenteral nutrition for infants with at least 50 cm of small intestine was 88 percent after 12 months, and 96 percent after 24 months [6].
- For infants with less than 50 cm of small intestine, the probability of weaning was 23 percent after 12 months, 38 percent after 24 months, and 71 percent after 57 months.
- Infants in this series were treated at a center with expertise in intestinal rehabilitation, and many were treated with fish-oil based lipid emulsions to protect the liver from intestinal failure-associated liver disease.

New Predictor of TPN Dependency

- **Citrulline concentrations**
- Measurement of plasma citrulline concentrations (a non-protein amino acid produced by intestinal mucosa) has been proposed to predict permanent versus transient intestinal failure
- In a study of 57 patients with nonmalignant short bowel syndrome who were followed for at least two years, a level <20 micromol/L identified patients destined to have permanent intestinal failure with positive and negative predictive values of 95 and 86 percent, respectively.
- A study in children with SBS demonstrated that plasma citrulline levels were strong predictors of parenteral nutrition and correlated well with a patient's recorded bowel length. Cutoff level here was 15 micromol/L
- One study demonstrated that a **citrullinemia stimulation test with oral L-glutamine** may offer even greater predictive capacity of severity of intestinal failure but confirmatory studies are lacking

SMALL BOWEL TRANSPLANTATION

- Small bowel transplantation has been advocated for certain patients with short bowel syndrome who are not candidates or have developed complications from long-term parenteral nutrition and in whom adequate adaptation cannot occur.

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