

# Short Bowel Syndrome

## Medical Management & Intestinal Rehabilitation

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# Discussion Outline

- Overview of SBS
- Normal gut physiology
- Short bowel pathophysiology
- Medical Management
  - Nutrition support
  - Pharmacotherapy
  - Trophic hormones

# Short Bowel Syndrome

- Malabsorptive syndrome due to functional and/or anatomic loss of extensive small bowel
- Incidence and prevalence unclear
  - Estimates based on The Oley Foundation Home TPN Registry (1992)
    - 40,000 home TPN patients each year
    - 26% had short bowel syndrome

# SBS: Etiologies

- **Adults**

- Mesenteric vascular accidents
- Crohn's disease
- Radiation enteritis
- Trauma
- Recurrent intestinal obstruction
- Volvulus

- **Children**

- Necrotizing enterocolitis
- Intestinal atresia
- Volvulus
- Extensive agangliosis
- Gastroschisis
- Congenital short bowel
- Meconium peritonitis

# SBS: Clinical Features

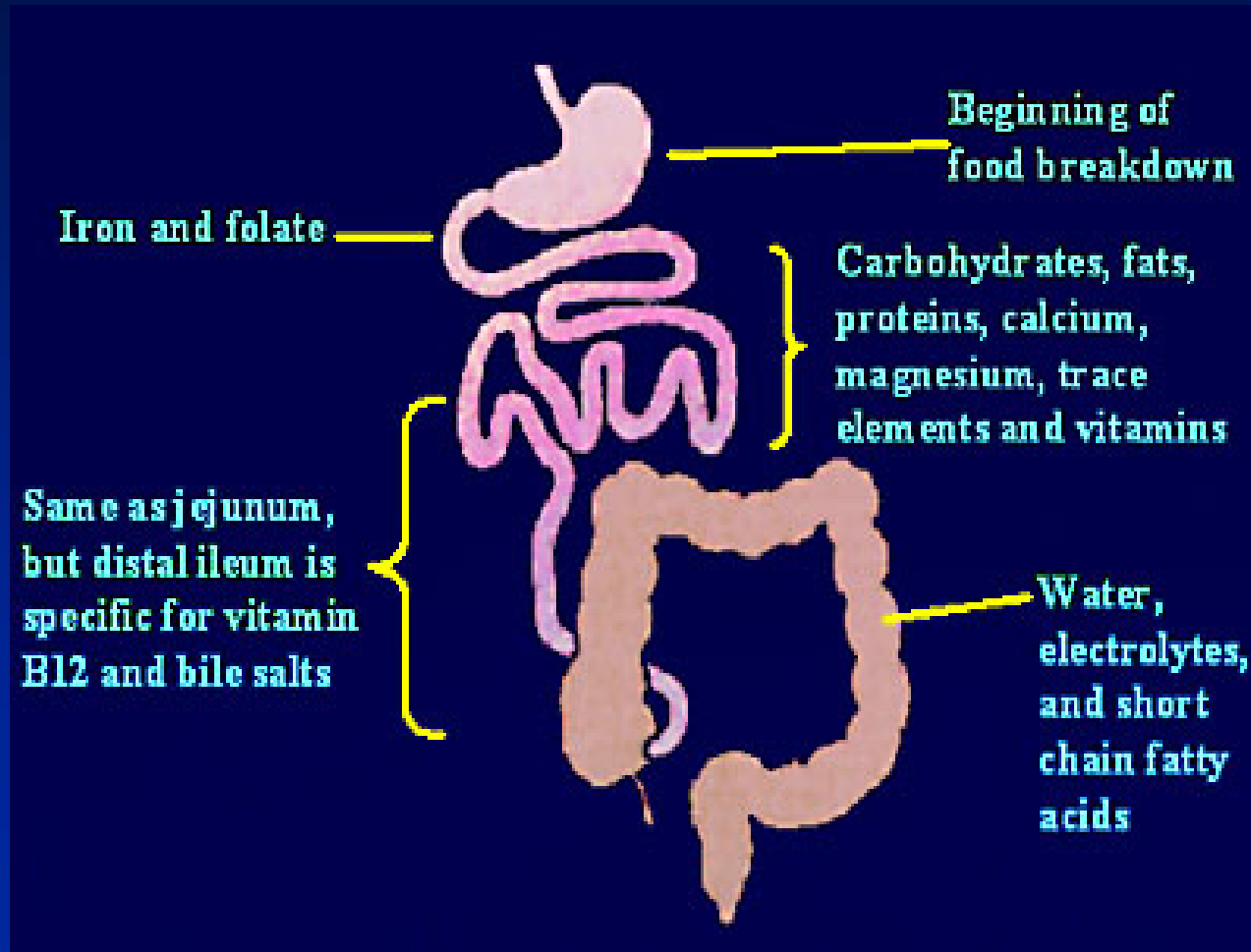
- Diarrhea
- Dehydration
- Electrolyte abnormalities
- Malnutrition
  - Weight loss
  - Vitamin deficiencies
  - Mineral deficiencies
- Complications
  - Peptic ulcer disease
  - Kidney stones
  - Gallstones
  - Small bowel bacterial overgrowth
  - Metabolic bone disease
  - Treatment related
    - Line infections
    - Hepatic dysfunction

# Gut Physiology & Pathophysiology

# The Healthy Intestine

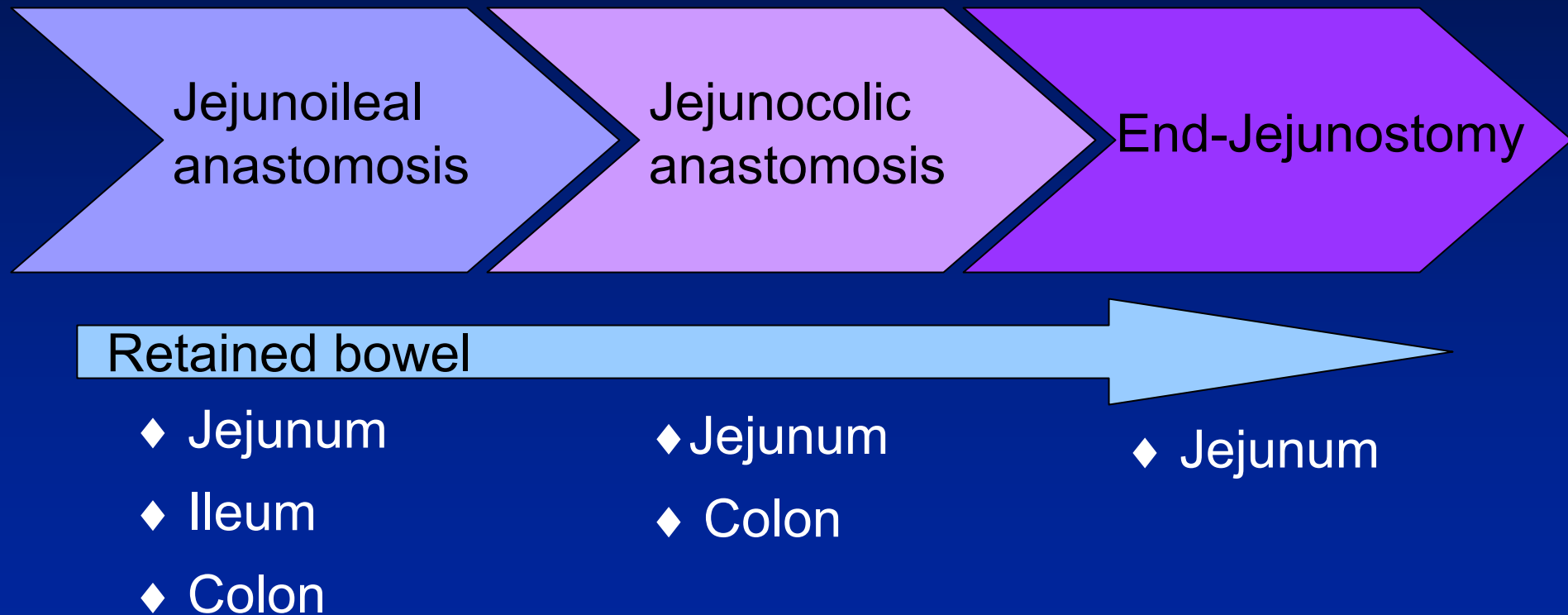
- **Small bowel:** 6 meters (3-8 m) or 20 feet
  - Duodenum 25 cm
  - Jejunum 2.5 m
  - Ileum 3.5 m
- **Colon:** 1.5 meters or 5 feet

# The Healthy Intestine





# The Shortened Intestine



# The Shortened Intestine

- Retained bowel anatomy determines functional capacity
  - Length of small bowel remaining
  - Health of small bowel remaining
  - Presence of colon and ileocecal valve
  - Type of small bowel and its capacity to adapt

# The Shortened Intestine

- Cutoff values of small bowel lengths separating transient and permanent TPN dependence
  - End enterostomy: 100 cm
  - Jejunocolic: 65 cm
  - Jejunoleocolic: 30 cm

# Intestinal Adaptation

- **Structural changes**
  - Macroscopic
    - dilation, thickening, lengthening
  - Microscopic
    - Villus: increase height & diameter
    - Crypt: elongation
    - Lifecycle: increase proliferation, decrease apoptosis
- **Functional changes**
  - Slowed transit to promote absorption
  - Increased carb & protein absorption per unit length
  - Up-regulation of sodium/glucose transporter

# Intestinal Adaptation

**Control**



**TPN**



**SBS**



# Intestinal Adaptation

- Factors affecting intestinal adaptation
  - Remaining anatomy
    - Adaptive capacity of ileum > jejunum
  - Luminal nutrients
    - Hyperplasia via contact
    - Stimulates trophic hormone secretion
    - Stimulation of trophic pancreaticobiliary enzymes
  - Hormones & growth factors
    - Growth hormone, GLP-2, enteroglucagon

# SBS: Treatment Options

```
graph LR; A[Intestinal Rehab] --> B[Surgical Augmentation]; B --> C[Long-term TPN]; C --> D[Intestinal Transplant];
```

**Intestinal  
Rehab**

**Surgical  
Augmentation**

**Long-term  
TPN**

**Intestinal  
Transplant**

# Intestinal Rehabilitation



# Intestinal Rehabilitation

- The process of restoring enteral autonomy and decreasing TPN dependence
- Rehab modalities
  - Diet, nutrition support
  - Fluids/electrolytes
  - Pharmacotherapy
  - Growth hormones

# Intestinal Rehab: Diet

- Caloric needs increase by at least 50%
  - Absorb only 1/2 to 2/3 of energy consumed
- Maximizing absorption
  - Meal pattern
    - 5 to 6 small, calorically-dense meals
    - Separate liquids and solids
  - Meal composition

# Intestinal Rehab: Diet

- Diet composition:
  - Depends on presence/absence of colon
  - **Colon present: Increase complex carbs**
    - Soluble fiber & starches pass undigested into colon
    - Fermentation by bacteria yields SCFA
    - SCFA absorbed by colon, salvaging 310-740 kcal/d
  - **Colon absent: Less carbs, more fat**

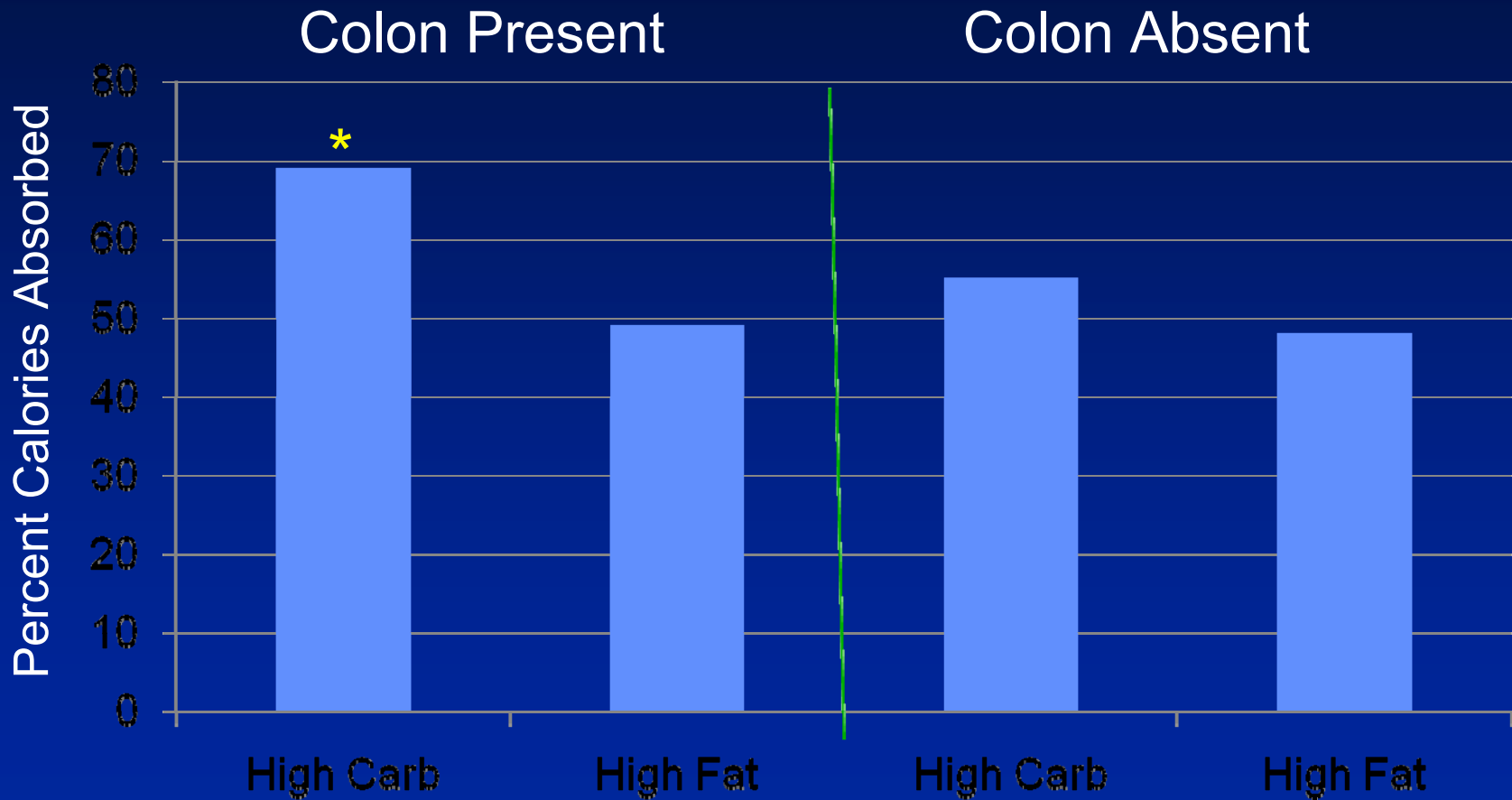
# Intestinal Rehab: Diet

	<b>Colon present</b>	<b>Colon absent</b>
<b>Carbohydrate</b>	<ul style="list-style-type: none"><li>• 50-60% of kcal</li><li>• Complex carbs</li></ul>	<ul style="list-style-type: none"><li>• 40-50% of kcal</li><li>• Complex carbs</li></ul>
<b>Fat</b>	<ul style="list-style-type: none"><li>• 20-30% of kcal</li><li>• MCT/LCT</li></ul>	<ul style="list-style-type: none"><li>• 30-40% of kcal</li><li>• LCT</li></ul>
<b>Protein</b>	<ul style="list-style-type: none"><li>• 20-30% of kcal</li></ul>	<ul style="list-style-type: none"><li>• 20-30% of kcal</li></ul>

MCT medium chain triglycerides, LCT long chain triglycerides

Complex carbs = starches (pasta, rice, potatoes, bread)

# Intestinal Rehab: Diet



# Intestinal Rehab: Diet

- Food Choices
  - Carbohydrates:
    - Avoid simple sugars, favor complex carbs

## Simple Carbs

Regular soda  
Juices  
Candy  
Cakes, cookies, pies  
Ice cream

## Complex Carbs

Pasta  
Rice  
Potatoes  
Breads  
Cereals

# Intestinal Rehab: Diet

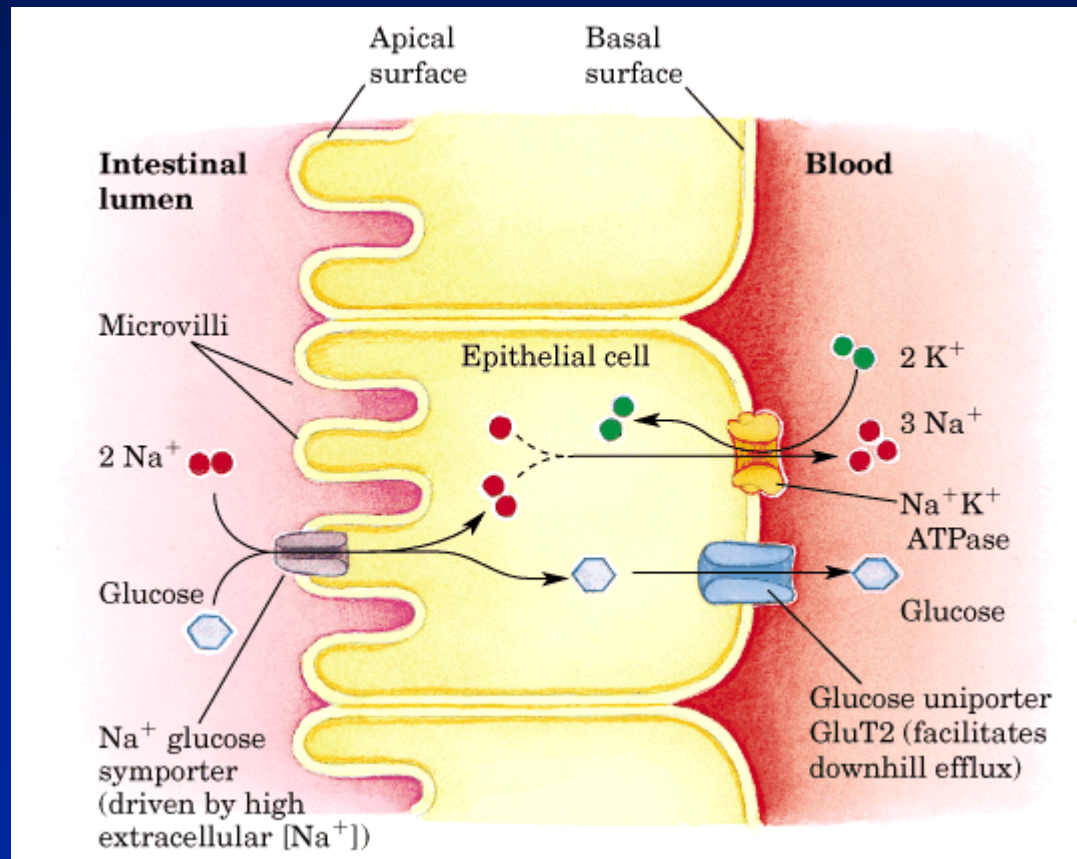
- Food Choices
  - Dairy products
    - Lactose intolerance may be a problem
    - If symptomatic, substitute lactose free products
  - Fruits and vegetables
    - Gradual introduction
    - Well cooked veggies, peeled fruits

# Intestinal Rehab: Fluids

- Avoid hypotonic fluids (water)
- Focus on **oral rehydration solutions**
  - Balanced ratio of salt and sugar
    - Sodium: 70-90 mMol/L
    - Sugar: 20 g/L
  - Products
    - WHO-ORS
    - Rice based formulas (Ceralyte)
    - G2 plus ½ tspn of salt per liter



# Intestinal Rehab: Fluids



# Intestinal Rehab: Fluids

- Home Recipe for ORS
  - 1 Liter of Water
  - 4 tablespoons of sugar
  - $\frac{3}{4}$  teaspoon of salt
  - Sugar free artificial sweetner
  - Optional:
    - 1 tspn baking powder (1/2 tspn baking soda)
    - $\frac{1}{2}$  tspn of 20% potassium chloride

# Intestinal Rehab: Fluids

- Fluid intake
  - Sip throughout the day, do not guzzle
  - Separate from meals
  - Set volume targets
    - 1-2L per day to start, titrate as needed

# Intestinal Rehab: Medications

- Antidiarrheals
  - Opiates
  - Octreotide
  - Pancreatic enzymes
  - Bile acid sequestrants, supplements
  - Clonidine

# Antidiarrheals: Opiates

Medication	One dose	Typical dose
Loperamide (Imodium)	1 tab = 5 ml = 2mg	1-2 tabs 4x per day
Diphenoxylate atropine (Lomotil)	1 tab = 5 ml = 2.5 mg	1-2 tabs 4 x per day
Codeine	1 tab = 15-60 mg	15-30 mg 3-4 x per day
Tincture of opium (DTO)	0.3 ml = 6 drops	6-20 drops (0.3 – 1ml) 4x per day

**Timing of medication:  
30 min before meals and at bedtime**

# Acid Suppressive Therapy

- Indication
  - Acid hypersecretion after major resection increases risk of ulcers
  - Excess acid impairs fat digestion & absorption

- Agents

## PPIs

Omeprazole  
Esomeprazole  
Lansoprazole  
Rabeprazole

## H2 RAs

Famotidine  
Ranitidine

# Pancreatic Enzymes

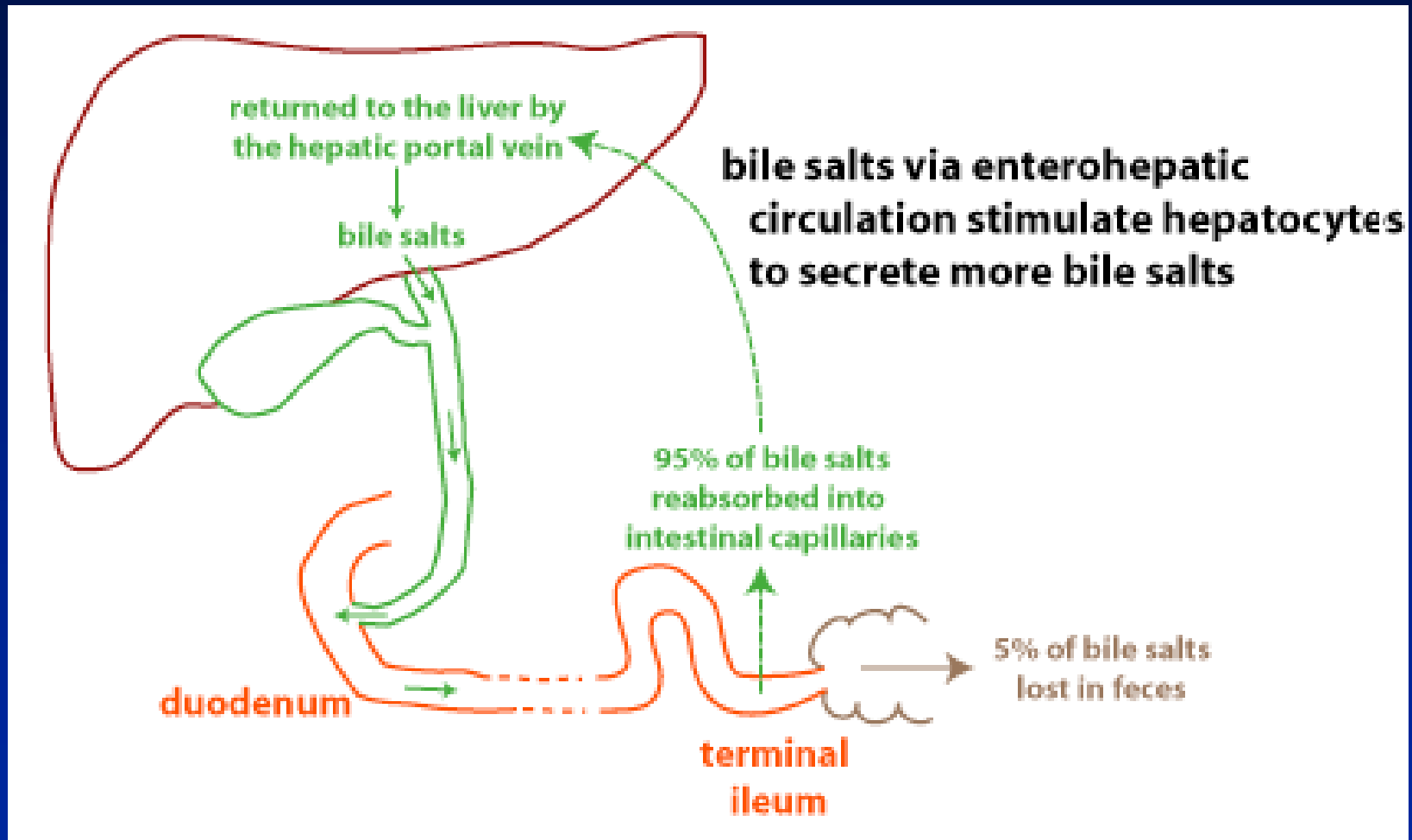
- Rationale:
  - Pancreatic enzymes critical to fat digestion
  - Loss of function post resection
    - Acid hypersecretion inactivates enzymes
    - Loss of intestinal cells which produce hormones that trigger pancreatic enzyme release

# Pancreatic Enzymes

- Dosing
  - Need at least 30,000 IU of pancreatic lipase per meal
  - Avoid delayed release, encapsulated formulations
  - Use non-encapsulated forms with acid suppressive therapy (e.g., Viokase 16)



# Bile Acid Therapy



# Bile Acid Therapy

## Bile Acid Resin

- Loss of <100 cm of ileum
  - Malabsorb bile acids
  - Bile acids in colon trigger secretory diarrhea
  - Treatment =  
Cholestyramine

## Bile Acid Replacement

- Loss of >100 cm of ileum
  - Malabsorb bile acids to greater extent
  - Liver synthesis of bile acids can't keep up
  - Develop bile acid deficiency
  - Treatment =  
Cholylsarcosine

# Bacterial Overgrowth Rx

- Overgrowth of bacteria common
  - Post surgical anatomic hold ups
  - Loss of ICV
  - Adaptive bowel dilation
- Treatment:
  - Antibiotics +/- probiotics
  - Cyclical use encouraged
    - Use first 7-10 days each month
    - Rotate antibiotic used

# Intestinal Rehab: Trophic factors

- Trophic Factors
  - Promote structural changes in the intestine that enhance absorption
  - Available agents
    - Growth Hormone
    - GLP 2 Analog (Teduglitide)

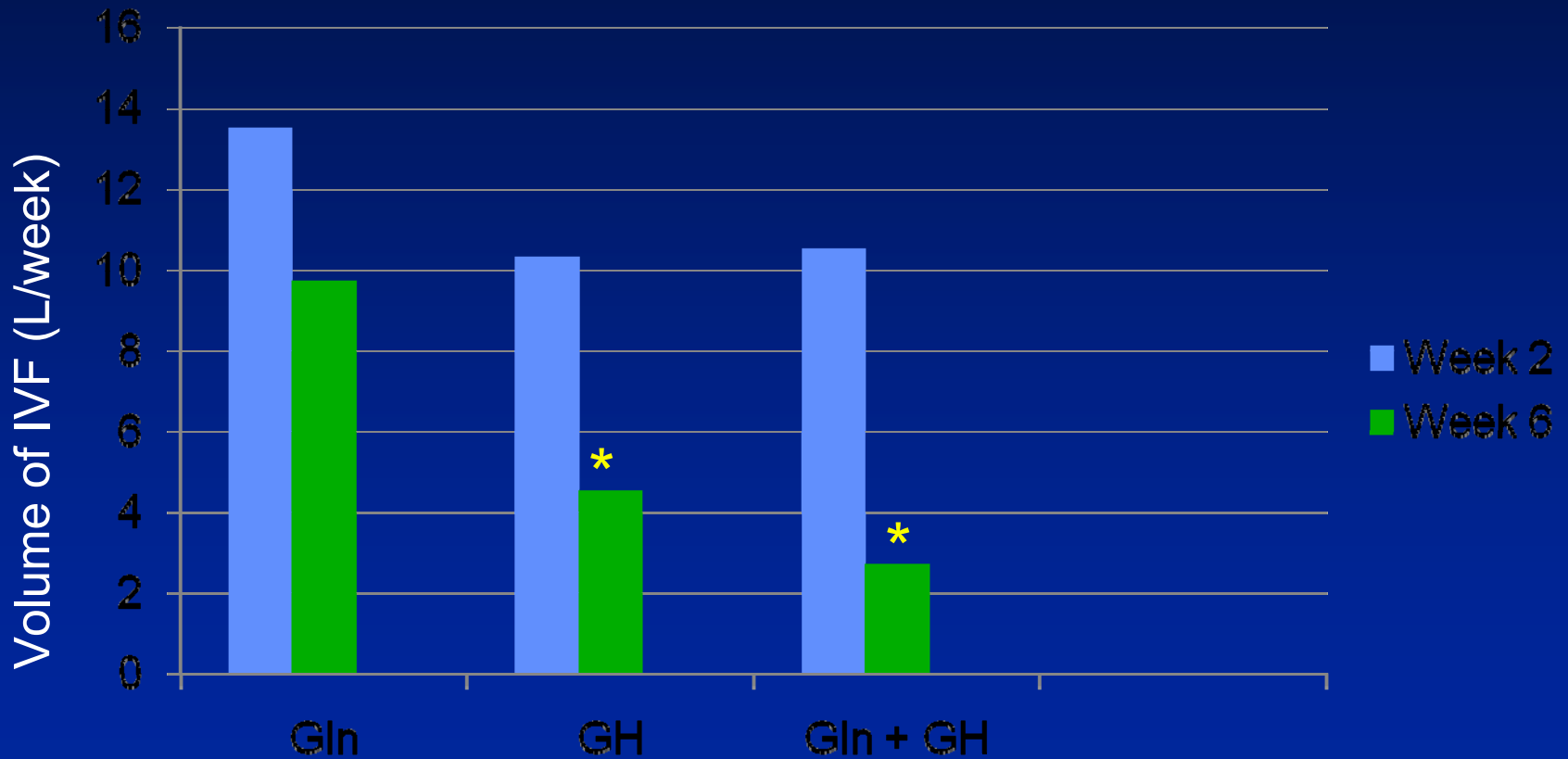
# Growth Hormone

- Evaluated in a number of small open label and randomized trials with mixed methodology and mixed results
- Randomized control trial in 2005 established efficacy and resulted in FDA approval for use in SBS

# Growth Hormone

- Phase 3 clinical trial
  - Randomized 41 patients
  - 3 groups
    - Modified diet plus glutamine
    - Modified diet plus GH (0.1 mg/kg/d)
    - Modified diet plus both glutamine and GH
  - Treated for 28 days total
  - Primary endpoint: Reduction in PN/IVF

# Growth Hormone



# GLP-2 Analog: Teduglutide

- GLP-2 is a hormone produced by L cells in the ileum and colon
- Functions
  - Decreases acid secretion
  - Delays gastric emptying
  - Increases intestinal blood flow
  - Increases villus length



# GLP-2 Analog: Teduglutide

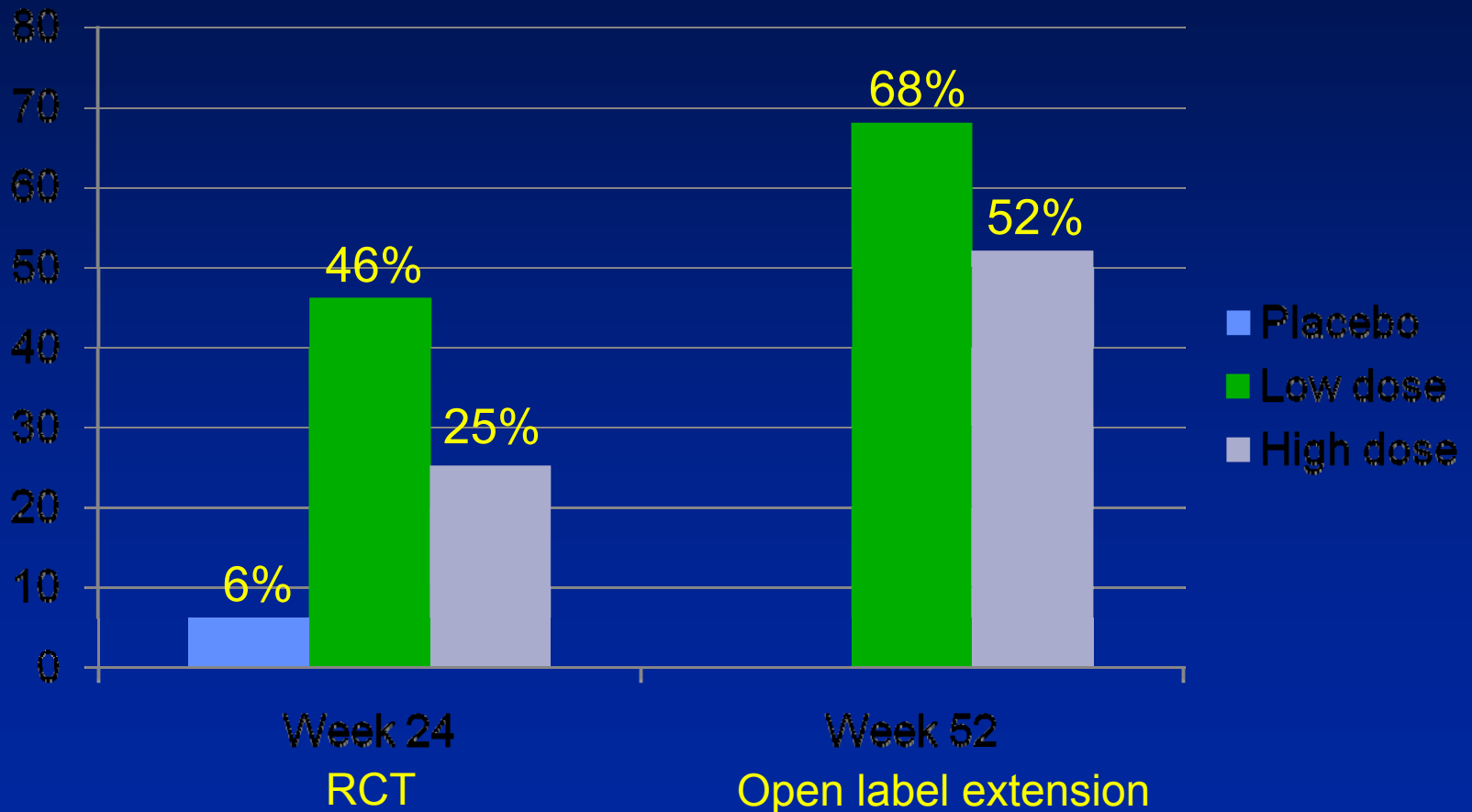
- Open label pilot study
  - 16 patients (10 no colon, 6 portion colon)
  - Treated for 21 days with varying doses
  - Results:
    - Increased wet weight absorption
    - Increased urine output
    - Decreased fecal weight and energy excretion
    - Increased villus height

# GLP-2 Analog: Teduglutide

- Multicenter RCT completed
  - Included 83 patients
  - Randomized to Placebo vs. Teduglutide (Doses 0.05 mg/kg/d or 0.1 mg/kg/d)
  - Primary Endpoint: Reduction of PN volume  $\geq 20\%$

# GLP-2 Analog: Teduglitide

Percent of patients achieving 20% PN reduction



# GLP-2 Analog: Teduglutide

- Repeat multicenter RCT in progress
  - Validation study
  - Mount Sinai Hospital actively enrolling
- Inclusion criteria
  - Adults
  - $\geq 12$  mos PN/IVF dependent SBS
  - PN/IVF  $\geq 3x$  per week
  - Serum cr, BUN  $< 1.5x$  ULN
  - LFTs  $< 2x$  ULN

# Intestinal Rehab: Weaning

- Consider weaning TPN if
  - Stable at optimal weight
  - Adequate fluid and calorie intake
  - Stable BUN and creatinine
  - Vitamin and mineral status normal
- Tube feed transition may be necessary

# Intestinal Rehab: Expectations

- Transition from TPN to enteral nutrition is a gradual process that requires close follow up with an experienced team of providers
- Medical therapy is not always enough and surgery to augment intestinal length and function may be necessary

# Summary

- Intestinal rehabilitation is aimed at reducing TPN dependence and increasing enteral autonomy
- Medical rehab options focus on symptom control, maximizing absorptive capacity, and optimizing nutritional status

# Summary

- Modalities of medical therapy include
  - Nutrition support (TPN, tube feeds) and dietary modification
  - Medications to reduce diarrhea and enhance digestion
  - Trophic agents aimed at augmenting bowel adaptation



# Summary

- A multidisciplinary team is most effective at guiding the rehab process
  - Gastroenterologists
  - Surgeons
  - Dieticians
  - Nurse coordinators