

## Short Bowel Syndrome & Intestinal Transplantation

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## Stages of Therapy

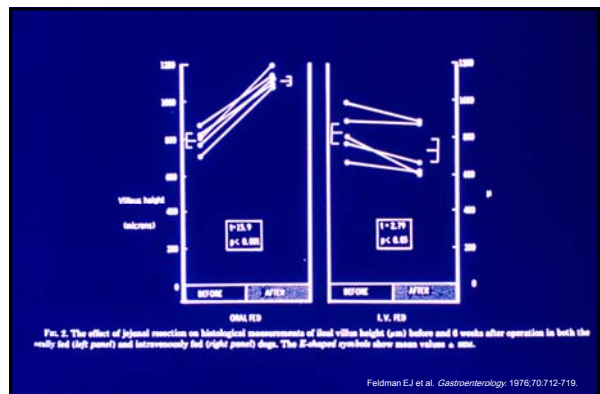
- Total parenteral nutrition
- Combination enteral/IV nutrition
- Continuous enteral feeding only
- Weaning to bolus feeding and solid foods
- Dietary modification alone

## Parenteral Nutrition Management Stage 1

- Baseline parenteral nutrition
- Separate infusion to replace excess losses
- Measure electrolyte output to determine replacement fluids

## Stage 2 Intraluminal Nutrition

- Enteral-hyperplasia
- Parenteral-no hyperplasia



## Benefits of Continuous Enteral Nutrition

- Provides constant mucosal stimulation
- Permits optimal absorption
- Reduces need for parenteral calories
- Decreases risk of TPN liver disease

## Predigested Formulas in SBS

- Rapid absorption
- Full use of absorptive surface
- May not be ideal for adaptation
- Adaptation can be maximized by increased rate of infusion
- Osmolality not an issue when given continuously
- Human milk may be an option

## Short Bowel Syndrome

Nutritional and other postoperative management of neonates with short bowel syndrome correlates with clinical outcomes

Andorsky DJ et al. J Pediatr. 2001;139:27-33.

## Enteral Nutrition Management Protein

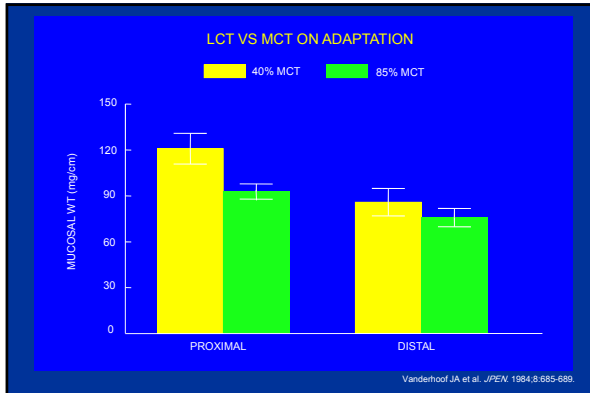
- Complex proteins are best at inducing adaptation
- Amino acid based formula may avoid allergy in younger infants
- Mixture of amino acids & dipeptides best absorbed

## Enteral Nutrition Management Carbohydrates

- Tend to be osmotic in small children-best to avoid high percentage CHO formulas
- SCFA better absorbed by colon in adults  
→fiber benefit later in childhood
- Lactose often not a problem except with extensive jejunal resection
- May contribute to D-lactic acidosis in patients with small bowel bacterial overgrowth

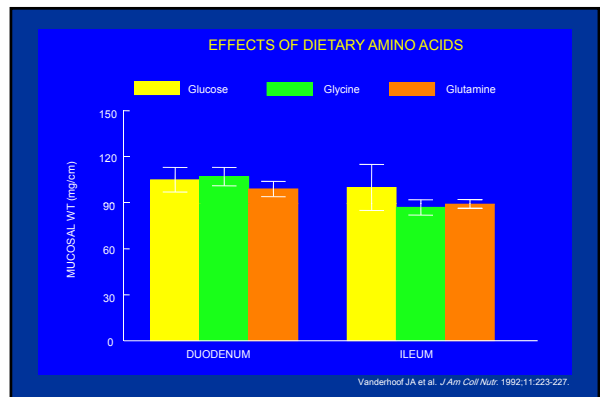
## Enteral Nutrition Management Fat

- LCT most trophic to the gut
- MCT - better absorbed in bile & pancreatic deficiencies, however  
→fewer calories than LCT  
→higher osmotic load than LCT  
→less effective in inducing adaptation
- Mixture MCT & LCT may be beneficial

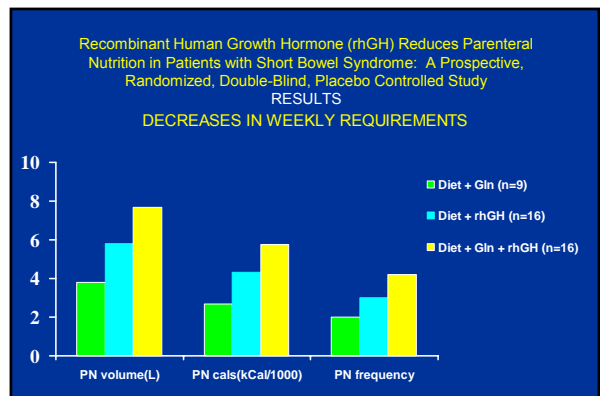


- ### Potential Trophic Factors
- Enteroglucagon
  - Gastrin
  - Neurotensin
  - EGF (epidermal growth factor)
  - IGF-1 (insulin-like growth factor-1)
  - Growth Hormone/Glutamine
  - PYY (peptide YY)
  - Prostaglandins
  - Polyamines
  - GLP-II
  - Bombesin

- ### Glutamine and Growth Hormone
- First attempt at pharmacologic stimulation of adaptation in humans
  - Inconclusive benefits in adult studies
  - Placebo-controlled pediatric trial showed no clear benefit

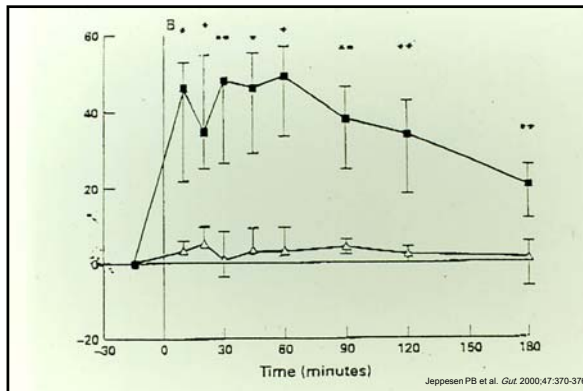


- ### Pediatric Growth Hormone Study
- 4 / 12 children had improved oral/enteral nutrition tolerance
    - One patient receiving 37 kcal·kg<sup>-1</sup>·d<sup>-1</sup> parenterally weaned from parenteral nutrition
    - Three patients on enteral nutrition not growing at baseline were doing so by study end
  - The other 8 had no improvement in oral/enteral nutrition tolerance
  - Nutrient tolerance was not enhanced by GLN supplementation for 3 mo.

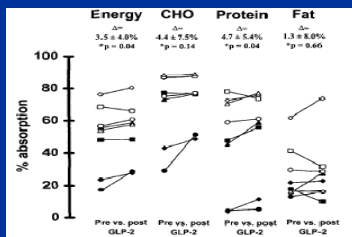


## GLP-II

- Elevated after bowel resection
- Capable of stimulating adaptation
- Produced predominantly in the distal small bowel and colon
- Potentially therapeutically useful in a selected group of patients
  - distal resection
  - no colon



## GLP2 in SBS



Relative absorption of energy and macronutrients before and after 5 weeks of GLP-2 treatment in 8 patients with the short bowel syndrome. Closed symbols represent patients receiving HPN.  
\*Paired Student t test. Δ, Mean ± SD effect of treatment with GLP-2 compared with baseline.

Jeppesen PB et al. Gastroenterology. 2001;120:806-815.

## WEANING FROM PARENTERAL NUTRITION IN SHORT BOWEL SYNDROME: ALL ADAPTATION IS NOT INTESTINAL

- We have observed successful parenteral weaning of several patients with extreme short bowel syndrome despite continued malabsorption. However, cold and exercise intolerance is often a problem in such patients
- *This observation has led us to believe that metabolic adaptation, i.e. depressed metabolic rate, may be a key adaptive factor that is allowing these patients to maintain their growth.*

## WEANING FROM PARENTERAL NUTRITION IN SHORT BOWEL SYNDROME: ALL ADAPTATION IS NOT INTESTINAL

	Patient A	Patient B
Age (yrs)	14	17
BMI (kg/m <sup>2</sup> )	19.1	21.1
Small Bowel Length (cms)	7	19
Mean VO <sub>2</sub> (ml/kg/min)	3.82	3.07
Mean Kcal/min	0.83	0.73
Calculated REE % of Normal	1195 79	1051 67

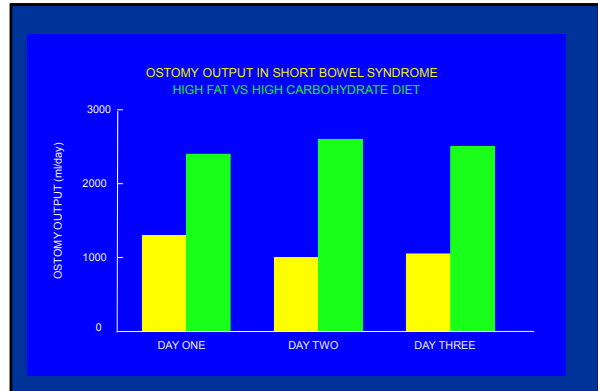
Vanderhoof et al. NASPGHAN, 2004.

## Progressing Enteral Feedings Stages 2 and 3

- Enteral feedings 24 h/day
- Feed solids around NG tube
- Intermittent TPN
- Gradually decrease TPN duration
- May give TPN q.o.d. as needs decrease
- Nighttime enteral infusion helpful

## SBS Solid Foods

- Feed high fat, high protein (meats) in small children
- Avoid carbohydrates (osmotic & ↑bacterial load) in small children
- Use small frequent **balanced** meals in adults



## Chronic Complications Stage 4

- Nutritional deficiency
- Poor bone mineralization
- PN liver disease
- Loss of venous access
- Bacterial overgrowth

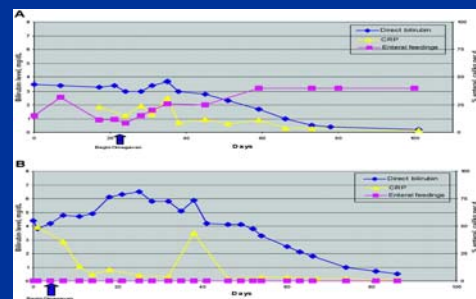
## Nutritional Deficiency States

- Vitamin B12
- Fat-soluble vitamins  
-A,D,E,K
- Trace metals  
-zinc
- Certain minerals  
-calcium, magnesium
- Monitor when PN discontinued

## Prevention of PN Liver Disease

- Aggressive use of enteral feedings
- Prevention of catheter sepsis
- Prevention of bacterial overgrowth
- Cycle TPN
- Correct use of Lipid

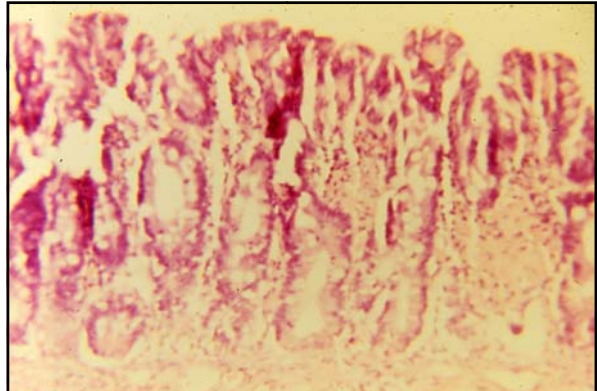
Baseline and follow-up values for direct bilirubin and CRP versus enteral intake (1 cal = 4.184 J) from the start of parenteral fish oil therapy



Gura KM et al. Pediatrics. 2006;118:e197-e201.

### Small Bowel Bacterial Overgrowth Major Factor in Many Cases

- Increased bacterial content in small bowel
- Bile salt deconjugation
- Mucosal inflammation
- All exacerbate malabsorption



### Complications of Bacterial Overgrowth

- D-lactic acidosis
- Colitis or ileitis
- Arthritis

### Possible Pathophysiology of Bacterial Overgrowth

- Increased numbers of organisms
- Predominance of invasive strains
- Immunologic reaction to absorbed bacterial antigens

### Bacterial Overgrowth

- Not always bad – SCFA production, etc
- Problem arises from inflammation
- Mucosal injury impairs absorption and adaptation
- Depends on strains present and individual reactions to these strains

### Treatment Strategies of Bacterial Overgrowth

- Antibiotics: (intermittent, rotating, continuous, *cultures may not help*)
  - Goal: change, not eliminate flora
- Gut lavage (PEG with electrolytes)
  - Goal: Reduce number of invasive bugs
- Immune modulation
  - Goal: Reduce inflammation
- Dietary change
  - Goal: Reduce fermentation

## Probiotic Potential Strain Selection

- Non-invasive strain
- Anti-inflammatory properties
- Produce anti-inflammatory SCFA's
- Down-regulate allergic response
- Clinical experience disappointing

## Functions of Ileocecal Valve

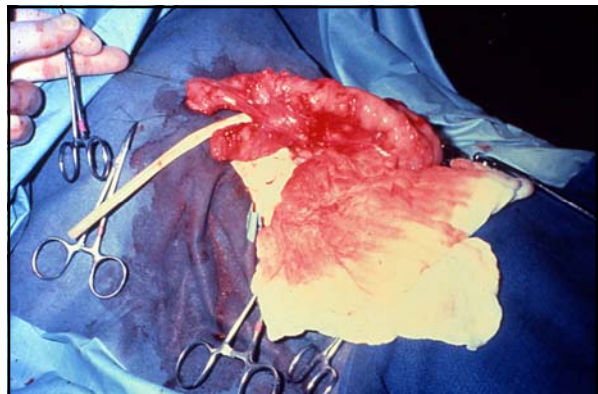
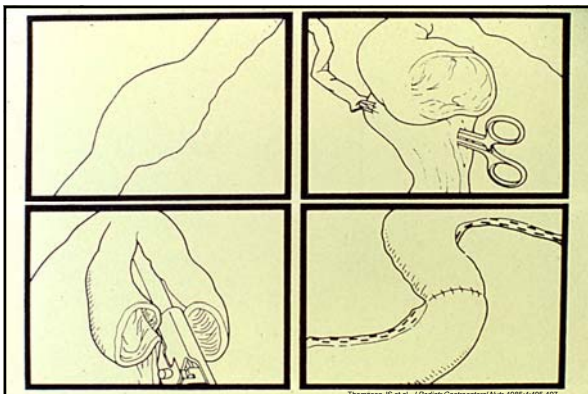
- Loss associated with poor prognosis
- Prevents small bowel bacterial overgrowth
- Increases small intestinal transit time
- Multiple attempts have been made to duplicate its function

## Effect of Anti-motility Agents Loperamide, etc.

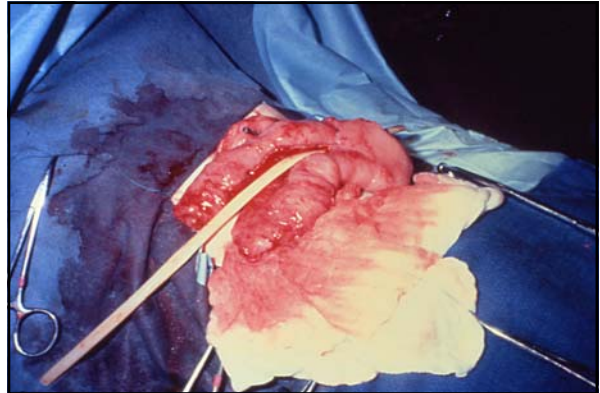
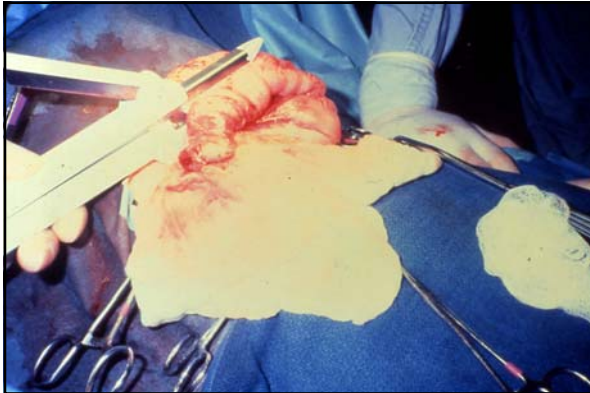
- Positive :increased absorption
  - greater nutrient contact with mucosa
- Negative :increased transit time
  - bacterial overgrowth

## Surgical Options in SBS

- Reduce bacterial overgrowth **YES**
  - taper or narrow bowel
  - resect tight anastomosis
- Increase length of bowel **MAYBE**
  - lengthening procedure (Bianchi)
  - serial transverse enteroplasty (STEP)







### Bianchi Procedure Results UNMC

- 12 patients, age 3.5 months - 19 years
- 7 -- reduction in TPN by 30-80%
- 4 -- permanently off TPN
- 1 -- TPN requirements increased

### Limitations of Bianchi

- Location ( Not duodenum)
- Blood vessel distribution
- Learning curve
- Late dilatation, dysmotility

### STEP Procedure Serial Transverse Enteroplasty

Kim HB et al. J Pediatr Surg. 2003;38:861-865.

### Small Bowel Length Before and After STEP

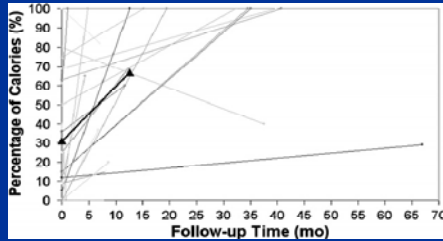
Patient	Pre-STEP (cm)	Post-STEP (cm)
1	~140	~320
2	~130	~240
3	~120	~200
4	~100	~110
5	~80	~90
6	~70	~80

\* $p < 0.0001$

Modi BP et al. J Am Coll Surg. 2007;204:365-371.



## Percent Enteral Calories Before and After STEP



Modi BP et al. *J Am Coll Surg*. 2007;204:365-371.

- The second STEP: the feasibility of repeat serial transverse enteroplasty

- Hannah Piper, Biren P. Modi, Heung Bae Kim, Dario Fauza, John Glickman and Tom Jaksic

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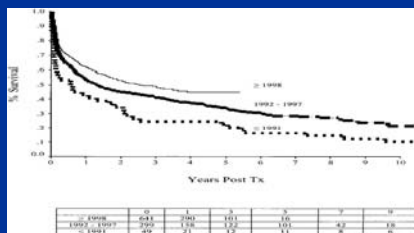
## Factors Influencing Prognosis

- Diagnosis of intestinal atresia
- Small bowel length
- Absence of ileocecal valve
- Loss of colon
- Recurrent sepsis

## Intestinal Transplantation-Stage 5 Indications

- Liver/small bowel - intestinal failure with:
  - end stage liver disease
- Isolated - intestinal failure with:
  - venous access limitations ?????
  - early hepatic dysfunction
  - recurrent sepsis

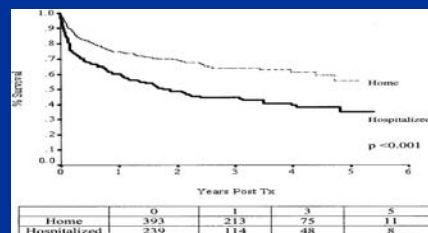
## Survival by Era



Graft-survival rates after intestine transplantation have significantly improved over time ( $P < 0.001$ ).

Grant D et al. *Ann Surg*. 2005;24:607-613.

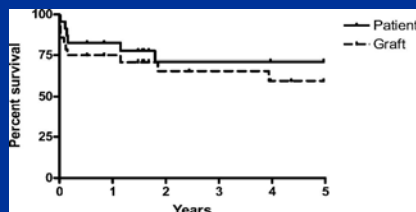
## Healthier Patients Do Better



Patient survival rates plotted by status at the time of transplantation show significantly higher survival rates in patients who are waiting at home.

Grant D et al. *Ann Surg*. 2005;24:607-613.

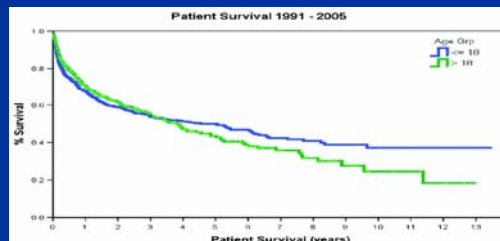
## Isolated Liver Transplantation in Short Bowel Syndrome



Kaplan-Meier probability of patient and graft survival

Botha JF et al. *Liver Transpl* 2006;12:1062-1066.

## Miami Survival 2006



## Long-term Outcome, Growth And Digestive Function In Children 2 To 18 Years After Intestinal Transplantation

Table 5 Balance studies

	Time post-transplantation (years)				
	2	5	7	10	18
n	8	7	3	3	1
Daily energy intake (% recommendation for age)*	138 (24) (112-171)	130 (45) (99-162)	149 (24) (108-150)	119 (32) (63-121)	108
Daily protein intake (g/kg) <sup>†</sup>	4.5	3.15	3.05	2.07	2
Total energy absorption (%)*	88 (1.2) (64-95)	89 (4.2) (83-95)	84 (7) (82-95)	86 (6) (82-91)	86
Fat absorption (%) <sup>†</sup>	86 (5) (73-93)	84 (11) (61-92)	88 (16) (60-91)	84 (13) (62-85)	82

\*Values are medians (SD) with ranges shown in parentheses.

<sup>†</sup>Normal >92%.

Lacaille P et al. *Gut* 2008;57:455-461.

## Ten Year Review Of Short Bowel Syndrome Data From Pittsburgh

- 389 pediatric patients referred for SBS
- Factors predicted weaning from TPN
  - Small Bowel length
  - Total bilirubin
- 95% survival if weaned by 2 ½ years after referral, 52% for those not weaned
- 25 had lengthening procedures-8 weaned without transplant

Nucci, et al. *J Gastrointest surg* 2008 Mar;(3) 429-25

## Decision To Perform Liver/small Bowel Transplant

- What is likelihood of 2 year survival without transplant
  - bilirubin
  - prothrombin time
  - liver biopsy
  - rate of progression
- What is prognosis with transplant?

## Decision To Perform Isolated Bowel Transplant

- Prognosis without transplant
  - is long-term TPN viable?
- Prognosis with transplant
- Lifestyle considerations **No!**
- Cost considerations **Difficult to assess**

### Decision To Perform Isolated Liver Transplant

- Prognosis without transplant
- Gut length and anatomy
- Underlying intestinal disease
- History of adequate trial of aggressive enteral nutrition and appropriate therapy

### Intestinal Transplantation Requirements to Become Standard Therapy

- When compared to home PN
  - better quality of life
  - fewer risks
  - lower costs
- Despite claims otherwise we still are not there