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Nutrition Treatment in Children with Intestinal Failure (IF) with a Special Emphasis on Short Bowel Syndrome

Module 4.3

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DECLARATION OF CONFLICT OF INTEREST

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- **Received honorrarium as a lecturer / invited speaker / consultant from:**

Abbott, BioGaia, Danone,

Fresenius, Nestle, Shire

NUTRITION IN IF /SBS
Lecture objectives

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- Definition & aetiopathogenesis
- Clinical presentation
- Enteral / oral nutrition support (EN)
- Parenteral nutrition support (PN) & complications
- Role of surgery
- Role of team approach

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CHRONIC INTESTINAL FAILURE

Reduction of gut mass/function below minimum for absorption & digestion to support life & growth

Causes:

- Short Bowel Syndrome (60%-70%)
- Intractable diarrhoea – congenital enteropathies (30-41%)
- Intestinal motility disorders (9%)**

D'Antiga L & Goulet O. JPGN 2013; ** Diamanti A, et al. JPGN 2009

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SHORT BOWEL SYNDROME -SBS

Reduction of gut mass & function below minimum for absorption & digestion to support life and growth

AFTER MASSIVE SURGICAL RESECTION

NASPGHAN DEFINITION

need for PN > 60 days after intestinal resection or a bowel length of <25% of expected

Merritt RJ et al. JPGN 2017

SBS causes

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Conditions leading to extensive intestinal resection

PRENATAL	NEONATAL	CHILDREN & ADULTS
Defects of abd. wall (gastroschisis)	**Necrotising enterocolitis**	**Vascular accidents**
Apple peel syndrome	**Midgut volvulus**	**Invagination**
Midgut volvulus	**Meconium ileus**	**Polyposis syndrome**
Multiple atresias	**Vascular accidents**	**Multiple hemangioma**
Extensive aganglionosis	**Primary motility disorders**	**Trauma, Tumours**
		Bypass surgery in obesity

IF: how common

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IF prevalence in children
(per 1000,000 <19y)

- 13.7 in UK — *Beath S et al. Clin Nutr 2011*
- 9.5 in the Netherland — *Neelis EG et al. Clin Nutr 2016*
- 14.1 in Italy — *Diamanti A et al. Nutrients 2017*
- 10.0 estimates for Croatia — *Kolaček S. Report for HZZO 2017*

SBS: factors relevant for pathophysiology

AGE

At birth ► **220-250 cm of small intestine**

In adults ► **400-500 cm of small intestine**

SEGMENT OF THE BOWEL

Jejunum
- leaky tight junctions ► rapid absorption, fast loss of water & Na
- low ability for adaptation

Ileum:
- specific transport for bile acids & vit B12
- huge capacity for adaptation

Ileocoecal valve:
- prevents small bowel bacterial overgrowth

Colon:
- conservation of water & electrolytes + extra starch digestion

INTEGRITY OF THE RESIDUAL INTESTINE

Prognostic determinants of IF caused by SBS

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POSITIVE	NEGATIVE
Ileum as residual segment	Jejunum as residual segment
Ileocecal valve present	High jejunostomy
Colon in continuity	Resection > 1-2 y of age
Early age at resection	Dysfunctional residual segment
„Healthy" residual GUT	

SBS: pathogenesis

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MAJOR DETERMINANTS

- extent of resection
- age at resection
- type & integrity of bowel left

HOW SHORT IS STILL ENOUGH?

- **<40 cm or <20%** ► **full blown SBS**
- **Life possible:**
  - >15-20 cm of small intestine with ileocoecal valve
  - >30-40 cm of small intestine without the valve
- **After adaptation:**
  - 100-120 cm enough for life on peroral intake (+ colon in continuity)

INTESTINAL ADAPTATION

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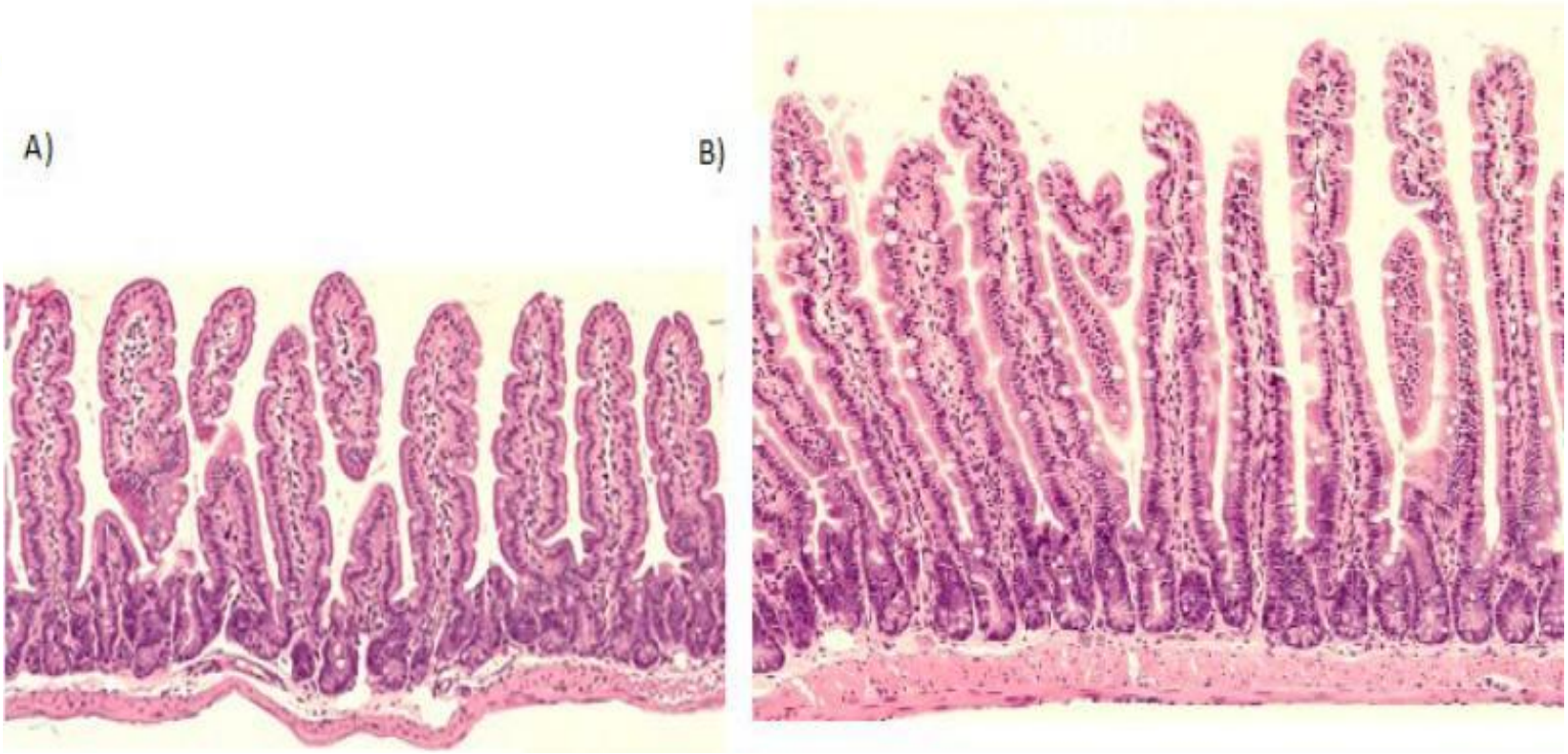

Warner et al. J Pediatr Surg. 2013; 48: 20–26.

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INTESTINAL ADAPTATION

Hypertrophy

- villus elongated
- crypts deeper
- mucosa ticker

Increase in absorptive surface

Functional adjustments

- more transport proteins
- more enzymes
- slower motility

Faster, more efficient metabolism

Control of adaptation

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Luminal nutrients!!!

Saliva, bile, pancreatic secretion...

Blood irrigation & Motility

Trophic factors/hormons

glucagon like peptide 2 – GLP2, IGF, epidermal GF, GH, insulin, polyamines...

SBS: Clinical presentation

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Early phase	Intermediate phase	Late phase
(weeks after resection)	(months after resection)	(steady state after adaptation)
Huge loss of water and electrolytes *(jejunum vs .ileum vs. ileum + colon)*	**Malabsorption of nutrients & loss of nutrients requiring specific transport**	**Dependence on PN complete / partial and / or special nutr. requirments and / or development of complications** *IFALD, loss of venous access, lithiasis, bone mineralization, D-lactacidosis...*

Wales PW et al. Seminars in Pediatric Surgery 2010

MANAGEMENT OF SBS

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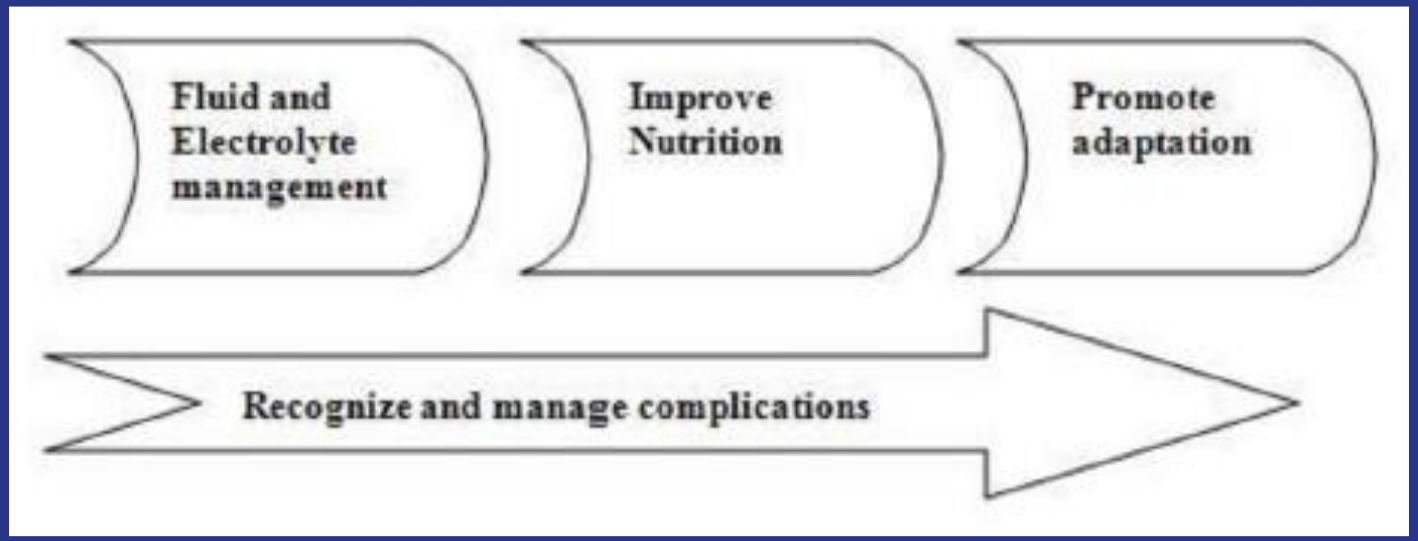

Batra A et al. Arch Dis Child Fetal Neonatol Ed 2017

IF/SBS: major determinants of treatment

1. Provide nutrition to sustain life and support growth: PN+EN

2. Maximize intestinal adaptation

3. Prevent major complications of PN

- CVC related sepsis / loss of venous access
- IFALD *(Intestinal Failure Associated Liver Disease)*

SBS: Enteral nutrition

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ROLE

- promotion of intestinal adaptation
- prevention of IFALD

RECOMMENDATION

- GUT to be used to a maximum extent but without worsening diarrhoea ▸ avoid overfeeding!!

OPTIONS ???

- breast feeding; standard formula extensivelly hydrolyzed (eHF), amino acid based (AA)

MODE ???

- bolus *versus* continuous???

Lacaile F et al JPGN 2015
Diamanti A et al. Expert Rev Gastroenterol Hepatol 2017

EN in SBS: type of formula

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What to recommend ??

- Only expert opinions!!
- Breast milk best option
- At start use eHF or AA, particularly in infants with dilated short segment ► prone to cow's milk protein allergy
- In older infants / children switch to polymeric
- Start with weaning as age appropriate

Lacaile F et al JPGN 2015
Diamanti A et al. Expert Rev Gastroenterol Hepatol 2017

EN in SBS: mode?

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Benefits of continuous

Better utilization of reduced surface & transport proteins

Osmotic load better tolerate

Improved growth & intestinal adaptation

Benefits of boluses

Physiologic hormonal surge & gallblader emptying

Improved mobility & QL

Promote normal feeding, habits & skills

Recommendations

- Combine small boluses over day & night continuous
- Switch to boluses when appropriate

Lacaile F et al JPGN 2015
Hojsak I, Kolacek S. Liječ Vjesn 2013

Intestinal failure: PN

1. Provide balanced *iv* intake

2. Save central veins
   (prevent CVC related infections)

3. Prevent other major complications

- **IFALD (Intestinal Failure Associated Liver Disease)**

Balanced PN

Energy, amino acid solutions

- balanced energy intake , avoid excess energy
- age adjusted composition with semi-essential amino acids
  arginine, cystein, taurin, proline, tyrosine

Carbohydrate

- only glucose
- provide 70%-75% of non-protein energy
- introduce stepwise

Lipids

- source of essential amino-aids
- provide 25% - 30% of non-protein energy
- pathogenic role of quantity and quality in IFALD??

Fewtrell M et al. ESPGHAN/ESPEN/ESPR Guidelines on pediatric PN. JPGN 2018

PATHOGENESIS OF IFALD

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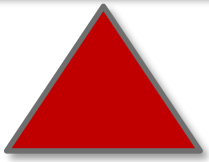
- Empty GUT
- Imature liver (prematurity)
- Early & recurrent sepsis
- Intestinal stasis & bacterial overgrowth
- Lipids: quantity & quality
- Phytosterols (from soya)

- Enteral feeding
- Balanced macro&micro-nutrient i.v. supply
- Cyclic PN & Home PN & Team approach
- Balanced omega 3/ omega 6 (fish oil)
- High alpha-tocopherol

Liver injury  **Liver protection**

Adapted from: D'Antiga L, Goulet O. JPGN 2013

Lipid emulsion – short term use

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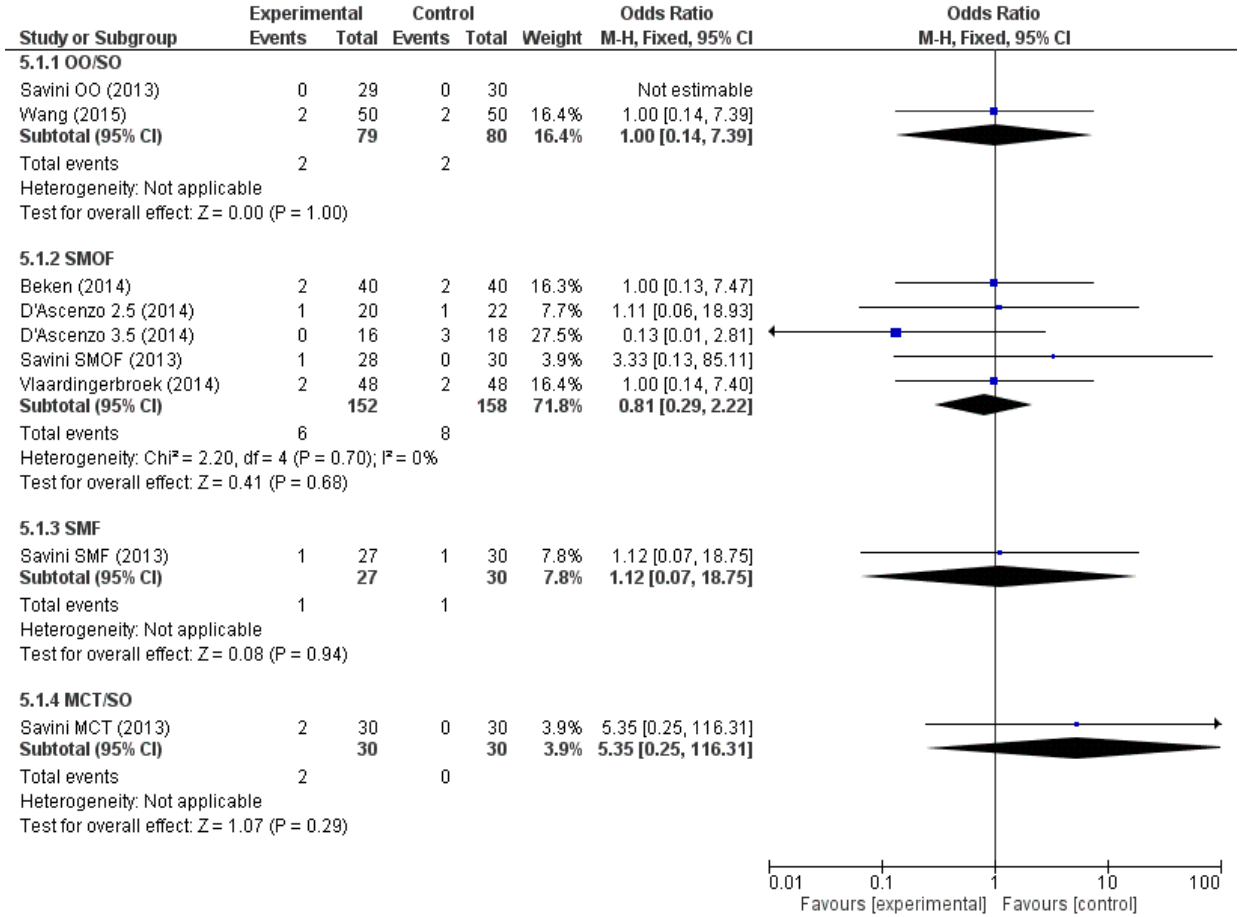
The use of any specific ILE for short term use in infants and children for the prevention and treatment of PNALD cannot be recommended

Hojsak I et al. ESPGHAN Committee on Nutrition Comment. JPGN 2016



PN: Pure fish oil *vs* fish oil in combination

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- Pure fish oil is effective, but as a sole source may not meet EFAs requirements on long-term basis

- Emulsion with fish oil as 1 component:
  - useful & safe
  - possible benefit for long-term PN

ESPGHAN Commitee on Nutrition JPGN 2016
Fewtrell M et al. ESPGHAN/ESPEN/ESPR Guidelines on pediatric PN. JPGN 2018

Type of Paediatric PN

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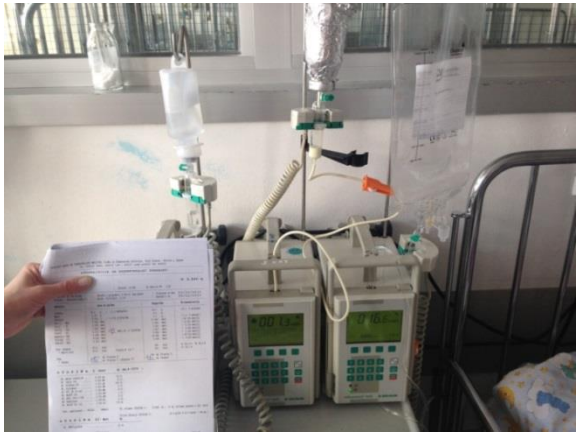
- **Ready made**
  - cheaper, available
  - not suitable for small children & changing requirements

Tailor-made

- adapted to requirements of the individual child
- more appropriate for changing requirements of children with intestinal failure



Paediatric PN in IF: prevention of common complications

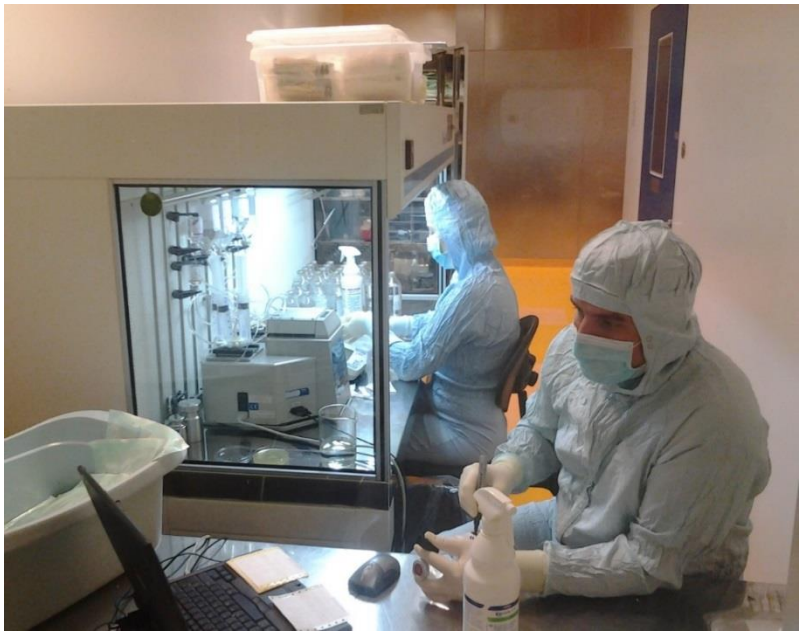
- Strict aseptic procedures on insertion & during CVC maintenance !!!

- Home parenteral nutrition

- Team approach

Fewtrell M et al. ESPGHAN/ESPEN/ESPR Guidelines on Pediatric PN. JPGN 2018

Paediatric PN: compounding



Aseptic approach: how we do it?

HOME PARENTERAL NUTRITION

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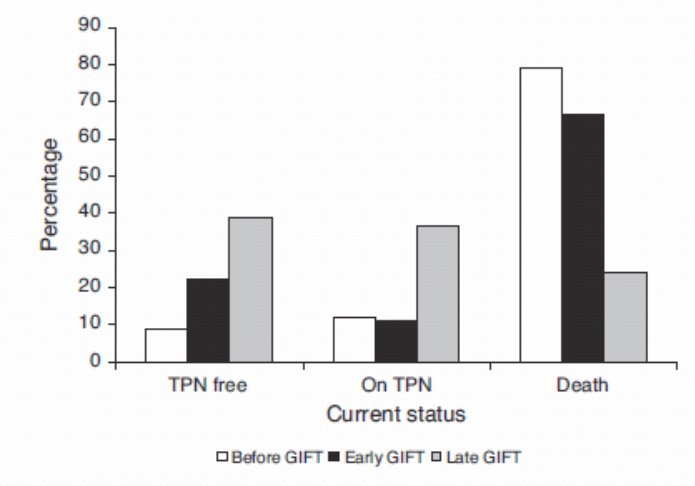
The best option for long-term PN !!

- better quality of life
- lower rate of CVK-related infections
- lower costs (40% - 50%)

For Home PN the following is required

- stable patient on cyclic PN
- structured training of caregivers
- back-up of experienced centre & nutrition support team
- availability of care 7 days/week for 24 h

Results of intestinal rehabilitation programs & TEAM APPROACH

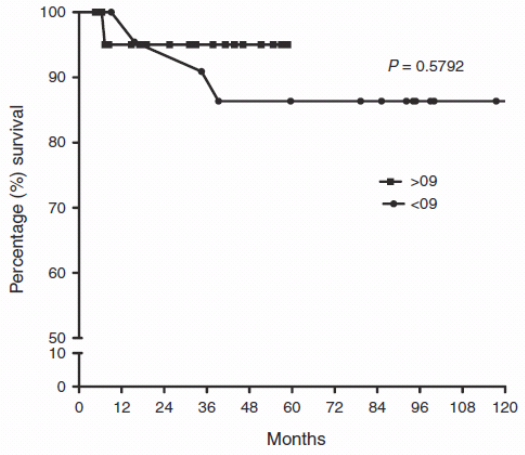


Avizur Y et al. JPGN, 2015.
Single center 10y cohort from Toronto, N = 84
Data compared before intruduction of intestinal rehabilitation program, first 3y with program and last 4 y.

Figure presents patient status at last follow-up

Merras-Salmio, Pakarinen. JPGN, 2015
Single center 25y experience from Finnland
on management of SBS, N=48
At 2009 implementation of detailed protocol

Figure presents survival before and after structured team approach



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TREATMENT OF IF / SBS
Role of intest. rehabilitation program

„... Management of IF by Intestinal Rehabilitation Programs is current state of art, with limited, but highly encouraging, supporting data on their medical efficacy"

Merrit RJ et al. JPGN 2017

Multimodal, multidisciplinary evidence –based approach involving:

- gastroenterologist, nutritionist, pharmacist, specialist nurse
- psychologist, speech therapist, physiotherapist
- surgeons

Drug therapy

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Dehmer JJ, et al. Advances in Pediarics 2011;58

To slow transit time	loperamid
To bind bile acids	cholestiramin
To lower secretion	somatostatin
To lower acid secretion	PPI, H2 blockers
To prevent bacterial overgrowth	Trimetoprim, rifaximin metronidazol gentamycin per os.....
To stimulate intestinal adaptation	GH, insulin, glutamin pectins GLP-2 !!

SBS: Current status on GLP-2

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Jeppesen PB. Curr Opin Gastroenterol 2014;30:182-8
Brubarker PL et al. Expert Opinion on Therapeutic Targets 2018 (epub)

1. Increases villus height and crypt depth → higher absorption
2. Tends to slow-down gastric emptying & intestinal transit
3. In SBS patients facilitate weaning from PN

APPROVED BY FDA & EMA FOR PATIENTS WITH SBS-IF

HOWEVE

R

1. In some studies effect was transient
2. Potential to cause hyperplastic /neoplastic changes ???
3. Announced pricing in USA → US$ 295 000 / patient year

SBS: nontransplant surgery

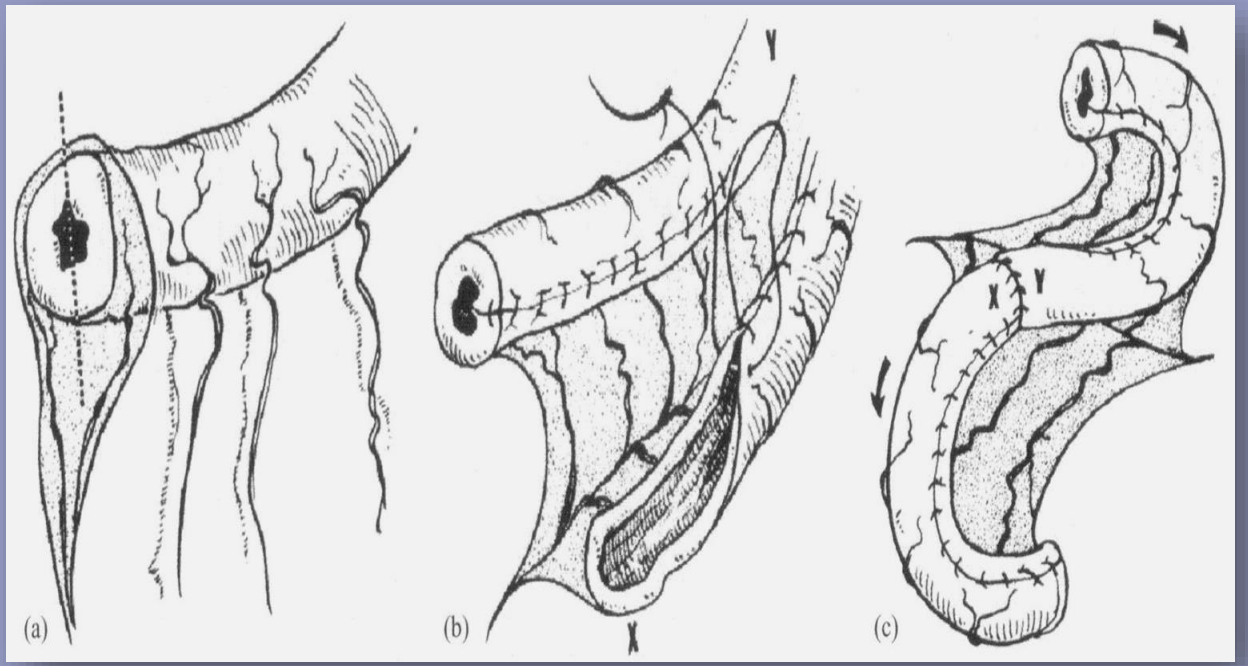
Rege AS, et al. Nutr Clin Pract 2013, Weih S et al. Langenbecks Arch Surg 2012

- bowel lengthening (Biancchi, STEP)
- promotion of motility in dilated segment (tailoring, plication)
- slowing motility (antiperistaltic segment, valves...)

- PN-dependent patient
- time for adaptation lapsed
- deterioration of intestinal function due to dilatation & SBBO

- dilatated intestine >3 cm
- >20 cm of small intestine
- >40 cm of total bowel

LILT – Bianchi procedure



Taken from: ***Sudan D. Autologous reconstruction of the GI tract. In: Langnas AN et al (eds). Intestinal failure: Diagnosis, Management and Transplantation. Malden. Blackwell Publishing 2008; 231-41.***

Serial transverse enteroplasty - STEP

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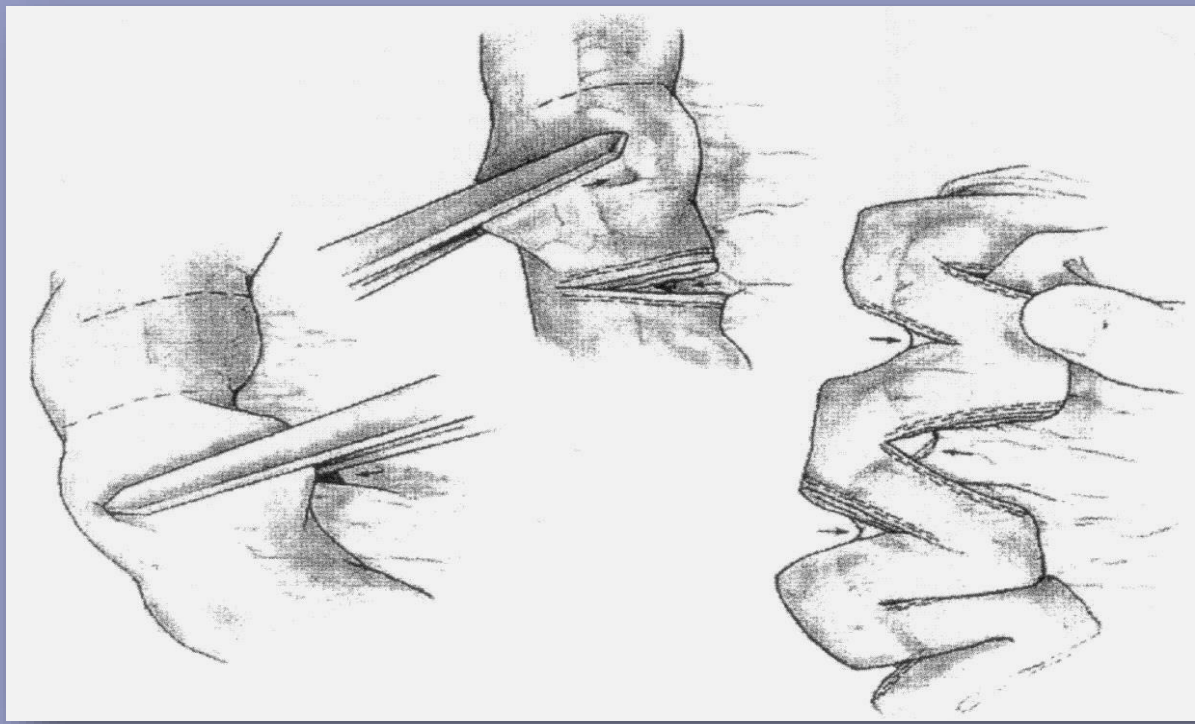

Taken from: ***Sudan D. Autologous reconstruction of the GI tract. In: Langnas AN et al (eds). Intestinal failure: Diagnosis, Management and Transplantation. Malden. Blackwell Publishing 2008; 231-41.***

Intestinal transplantation
When to do it?

D'Antiga L, Goulet O. JPGN 2013

Prolonged PN *versus* Early transplantation (ITx)

- Prognosis after 5y, 10y: 85% , 75% for PN *versus* 50%, 30% for ITx
- Morbidity & mortality significantly improved in centres with multidisciplinary intestinal rehabilitation programs

CURRENT RECOMMENDATIONS

- Long-term PN is the treatment of choice for children with IF including irreversible Intestinal Failure
- IF should be treated in centres with multidisciplinary teams & intestinal rehabilitation programs
- ITx is reserved for irreversible IF with life-treatening complications:
  - loss of venous access
  - severe recurrent sepsis
  - end stage IFALD...

MANAGEMENT OF SBS IN PAEDIATRIC PATIENTS

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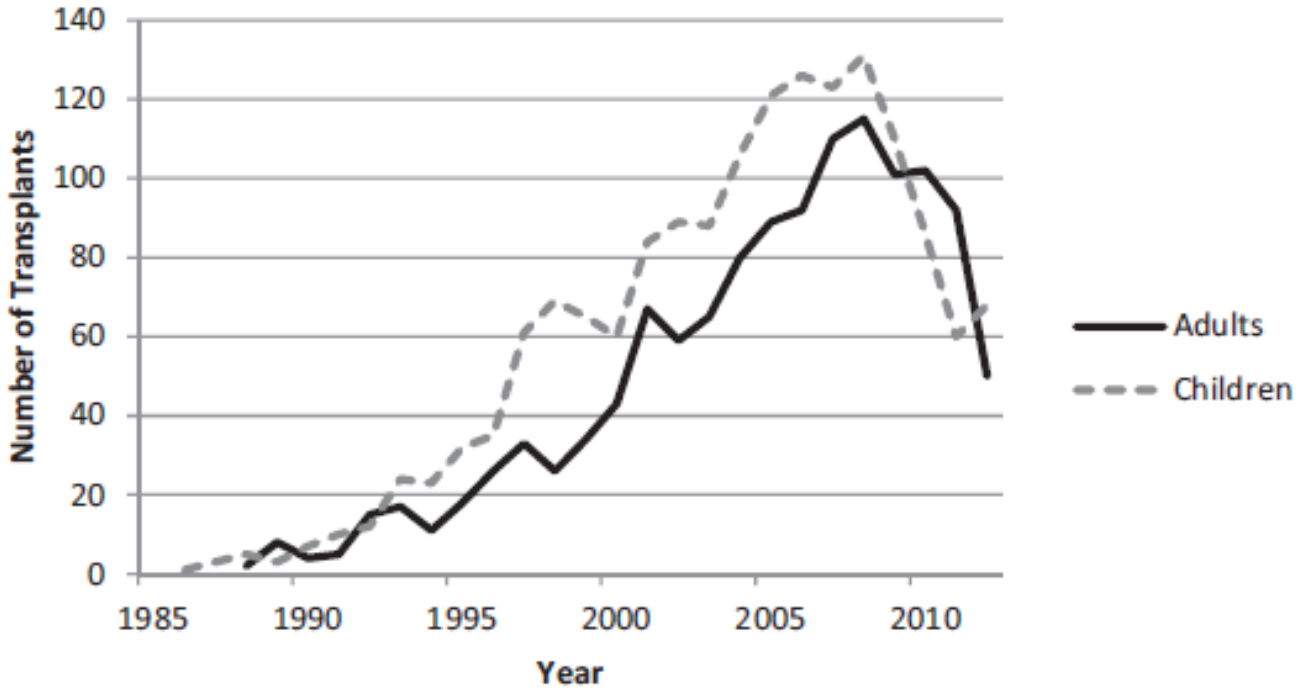

Number of intestinal transplantations – registry

Grant et al. Am J Transplant. 2015 Jan;15(1):210-9.

Nutrition Treatment of IF in children

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Conclusions

1. **Promote appropriate nutrition**
   - **Enteral nutrition to the maximal extent tolerat**
   - **Parenteral nutrition – prevent complications**
     (age adjusted, cyclical PN, at home, aseptic approach……)
2. **Support intestinal adaptation**
   - use GUT as early as possible & to maximum tolerated extent
   - promising role of GLP-2
   - role of surgical intestinal lengthening procedures
3. **Treat in centres with multidisciplinary intestinal rehabilitation teams & programs**
4. **ITx is life saving procedure, not a routine**