

Parenteral Nutrition Associated Liver Disease: Yes or No ?

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Parenteral Nutrition

A truly revolutionary, life saving development in medicine to provide complete nutritional support for patients with acute or chronic intestinal failure.

Parenteral Nutrition

- 1960 first successful PN by Wilmore & Dudrick at CHOP
- 1975 first report of cholestasis by Rager & Finegold

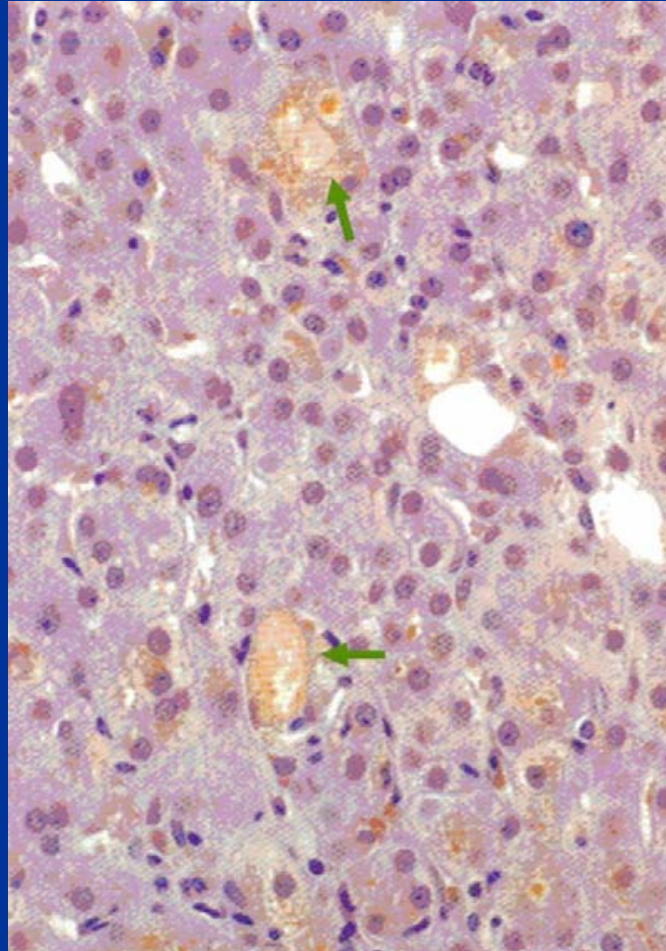
Parenteral Nutrition-Associated Liver Disease

Serum direct bilirubin > 2 mg/dL

↑ Alk P, transaminases, GGT

- Cholestasis
- Steatosis, steatohepatitis
- Fibrosis, cirrhosis
- Liver failure
- Biliary sludge, gallstones
- Cholecystitis

Cholestasis



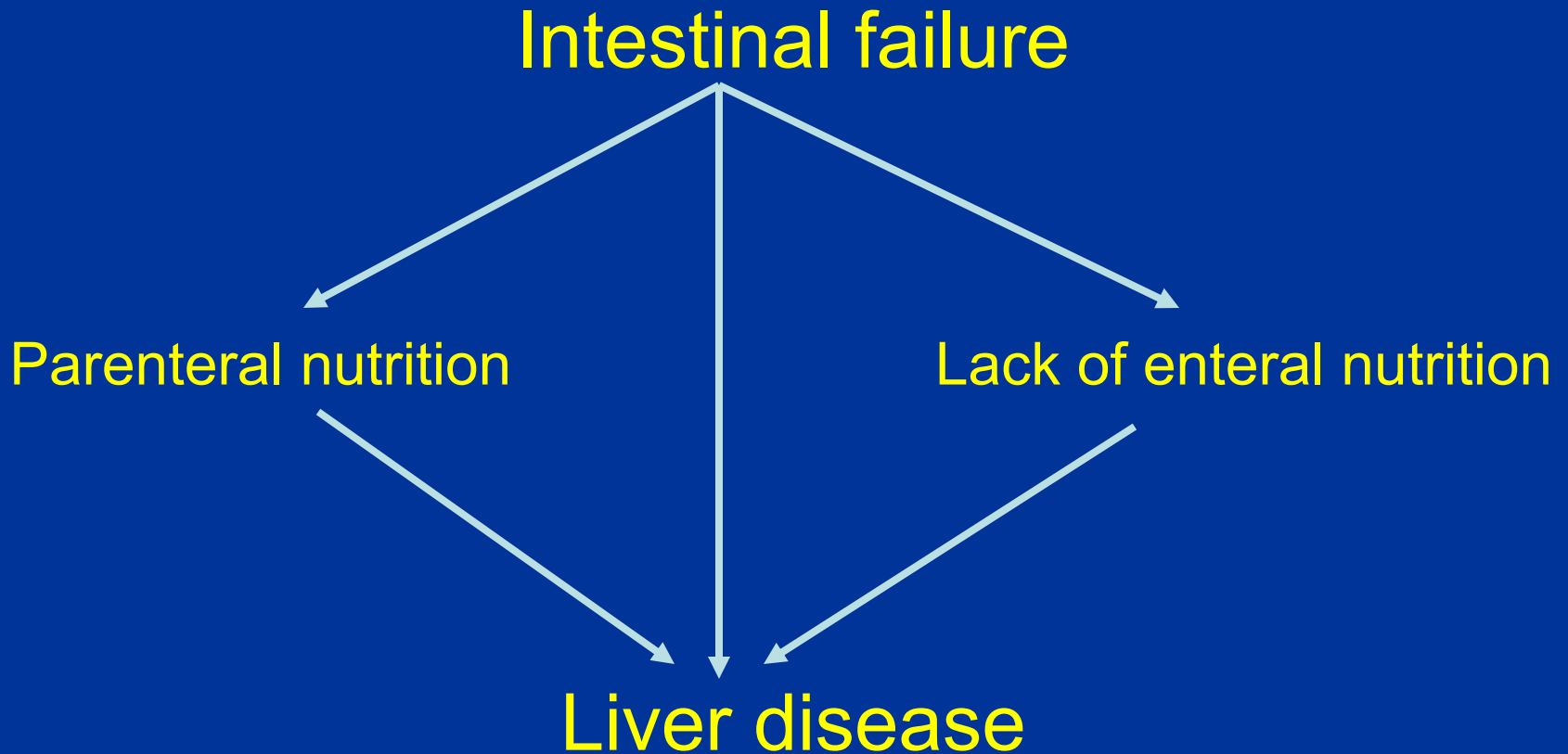
Parenteral Nutrition-Associated Liver Disease

Children > adults
(40-60% in infants, 15-40% adults)

Risk Factors:

- Prematurity and low birth weight
- Residual bowel length
- Duration of PN
- Duration of enteral fasting
- Lack of ileocecal valve
- Recurrent sepsis
- Multiple abdominal surgeries

Parenteral Nutrition-Associated Liver Disease



Parenteral Nutrition Associated
Liver Disease



Intestinal Failure Associated Liver
Disease

Pathogenesis

Multifactorial

- Lack of enteral nutrition
- ↓ ↓ gastrointestinal hormones
 - ↓ gallbladder contractility → biliary sludge
 - Intestinal stasis → SBBO → translocation → sepsis →
- Sepsis: line infection + SBBO + ↓ gut immunity
- Multiple surgeries
- Composition of PN
- Immature neonatal hepatobiliary functions

Components of PN

- Excess non-protein calories
- ↓ taurine and cysteine: essential in neonate
- Choline deficiency
- Manganese toxicity
- Lipid emulsions
 - soybean or soybean/safflower based (omega 6)
 - Soybean oil: phytosterols, inflammatory cytokines

Soybean vs fish oil

Omega-6

Linoleic acid



Arachidonic acid



PGE2, PGI2, LTB4
LTC4, TXA2, LTE4



Pro-inflammatory

Omega-3

Alpha-linoleic acid



EPA → DHA



PGE3, LTB5, PGI3, LTC5
TXA3, LTE5



Anti-inflammatory

Lee et al. Hepatology 2007

Prognosis

- Duration of enteral fasting:
Better, even reversable with early enteral feeds.
- Duration of PN
100% mortality rate within a year if unable to be off PN or w/o transplantation
Wales et al. J Pediatr Surg 2005
- Bilirubin level
poor prognosis if persistent ↑ bilirubin level (>12 mg/dL)

Prevention and Medical Management

- Enteral Nutrition related
- Parenteral Nutrition related
- Prevention of sepsis
- Avoid multiple resections, surgeries
- Avoid hepatotoxic drugs
- Ursodeoxycholic acid (15-45 mg/kg/d)

Enteral nutrition in IFALD

- Start enteral feeds as soon as possible

Likelihood of weaning off PN

- 75% enteral at 12 wk-90% wean off
- 50% enteral at 12 wk-75% wean off
- 25% enteral at 12 wk-50% wean off

Sondheimer et al. J Pediatr 2001; 132:80-84

- Breast milk, amino acid based formulas
- Avoid hyper-osmolar feedings
- Prefer continuous feeds

Parenteral Nutrition

- Prefer cyclic PN
- Avoid excess non-protein calories
 - Min. 2-4% of cal. as linoleic acid
- Amino acids: ↓ methionine, ↑ taurine and cysteine
- Lipid emulsions:
 - MCT, omega 3 not available in US

Soybean vs Fish oil

Omega-6 fatty acid vs Omega-3 fatty acid

Parenteral Fish Oil

Gura et al. Pediatrics 2006

- 2 patients: >50% and 100% PN dependent
- Parenteral fish oil: 1 g/kg/d
- Resolution of cholestasis in 8 weeks
- No evidence for essential fatty acid deficiency

Catheter Related Sepsis: Prevention

Strict antisepsis

- Hand hygiene

- Barrier precautions

- Catheter site antisepsis

Change catheter only if infected or malfunctioning

Remove catheter promptly when no longer necessary

Hadaway LC. Nursing 2006

Bacterial overgrowth

Risk factors:

- absence of ileocecal valve
- dysmotility
- post surgical

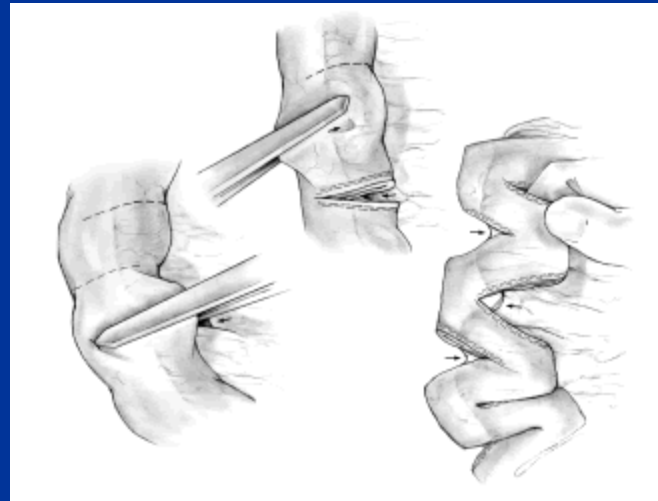
Sx: diarrhea, abdominal pain, distention, FTT

Dx: Duodenal fluid analysis, breath test

Rx: cycled oral abx
probiotics: no data to support routine use.
glutamine in PN: no effect

Surgical treatment

Serial Transverse Enteroplasty (STEP)



International STEP Registry (2004-2006)

38 pts, median f/u 12.6 mo

29/38 doubled enteral caloric intake after STEP

Modi et al. J Am Coll Surg 2007

Surgical treatment

- Isolated liver transplantation
 - Bowel adaptation and improved enteral feeding tolerance is reported.

Horslen et al. Ann Surg 2002

Botha et al. Liver Transpl 2006

- Liver-small bowel transplantation

Thank you