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N2U Table of Contents

Click the titles above to jump to a specific presentation

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NORTH AMERICAN SOCIETY FOR PEDIATRIC GASTROENTEROLOGY, HEPATOLOGY AND NUTRITION

NASPGHAN FOUNDATION
For Children's Digestive Health & Nutrition

NASPGHAN Nutrition University

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Nutrition and the Gastroenterologist: Improving Patient Outcomes with Nutritional Assessment and Therapy in IBD

Inflammatory Bowel Disease

- 25% of cases are diagnosed in childhood or adolescence
  - Crohn's Disease
  - Ulcerative Colitis
    - Pan-colitis is a common presentation
- Presentations
  - Abdominal pain, diarrhea, rectal bleeding, weight loss
  - Pediatric population-growth failure

[1]Shikhare and Kugathasan. *J Gastroenterol.* 2010;45:673-682.
[2]Sandhu et al. *J Pediatr Gastroenterol Nutr.* 2010;50(Suppl.1):S14–34.

Nutritional Complications

- Growth Failure
- Delayed Puberty
- Osteopenia and Osteoporosis
- Anemia
- Micronutrient Deficiencies
  - Iron, folate, B12, vitamin A, vitamin E, beta-carotene, magnesium, selenium, and zinc

[3]Kappelman & Bousvaros. *Mol Nutr Food Res*. 2008:52:867-874.

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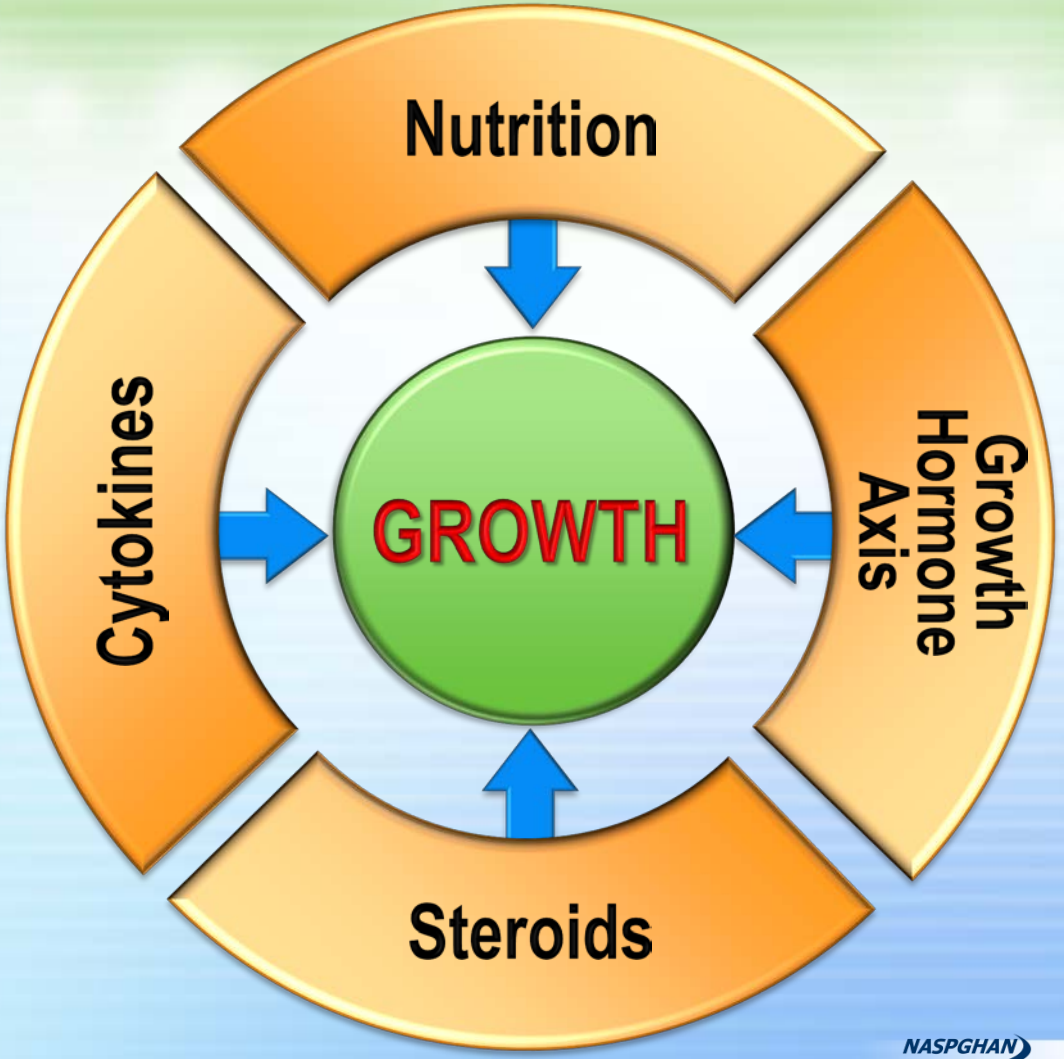
Growth Failure

- Definition
  - Height< 5th percentile
  - Decrease in height velocity below 5th percentile
  - Fall off the child's growth curve
  - Much higher incidence at diagnosis in CD vs UC.
- Inadequate caloric intake
  - Gastritis, esophagitis, fear of worsening symptoms
- Malabsorption
- Increased energy expenditure from chronic inflammation
  - Pro-inflammatory cytokines, decreased IGF-1, exogenous steroids

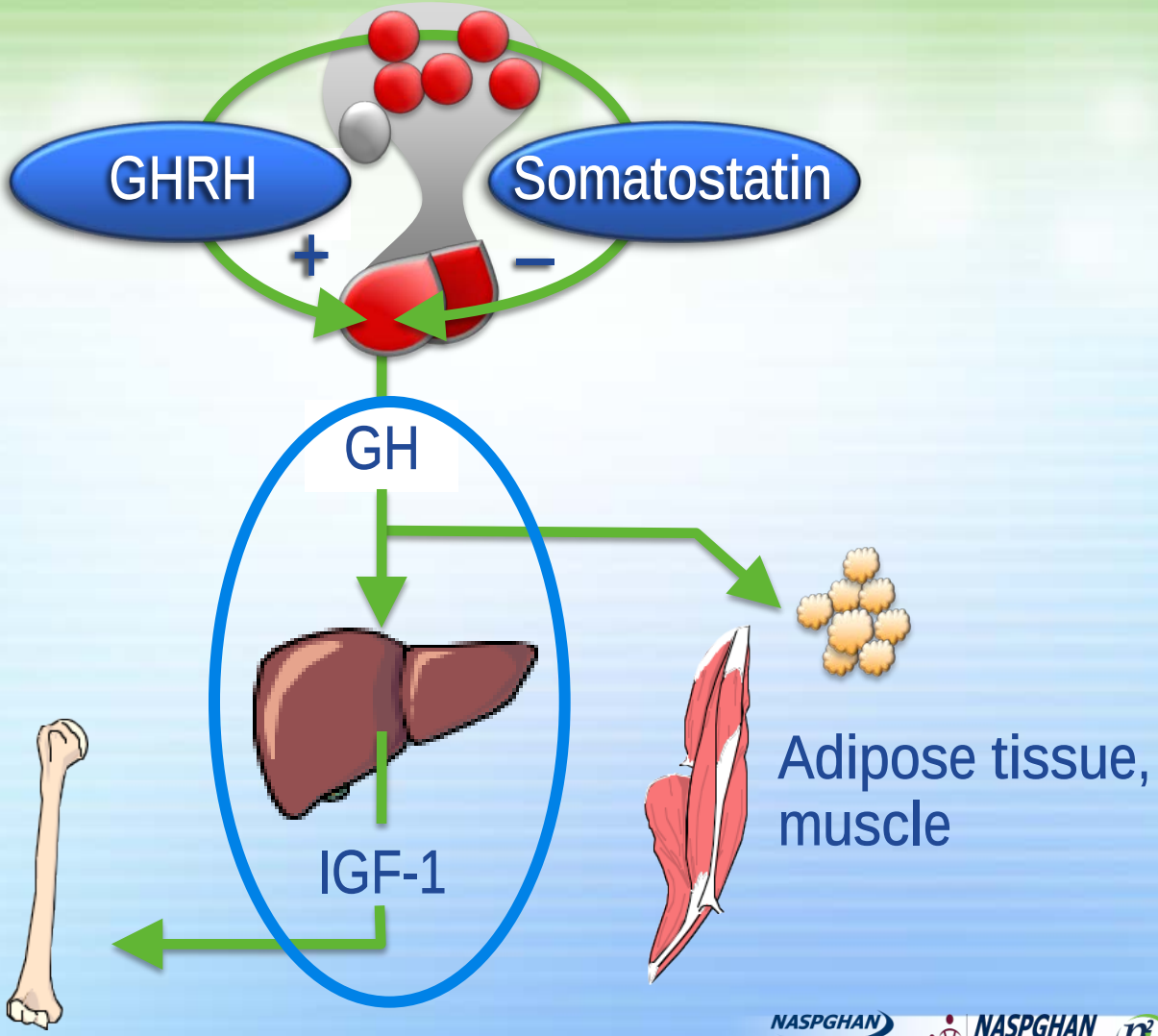
[4]Sawczenko et al. *Pediatrics.*2006;118:124-129.
[5]Tigas et al.*J Pediatr Gastroenterol Nutr.*1993;16:373-380.

Growth in IBD



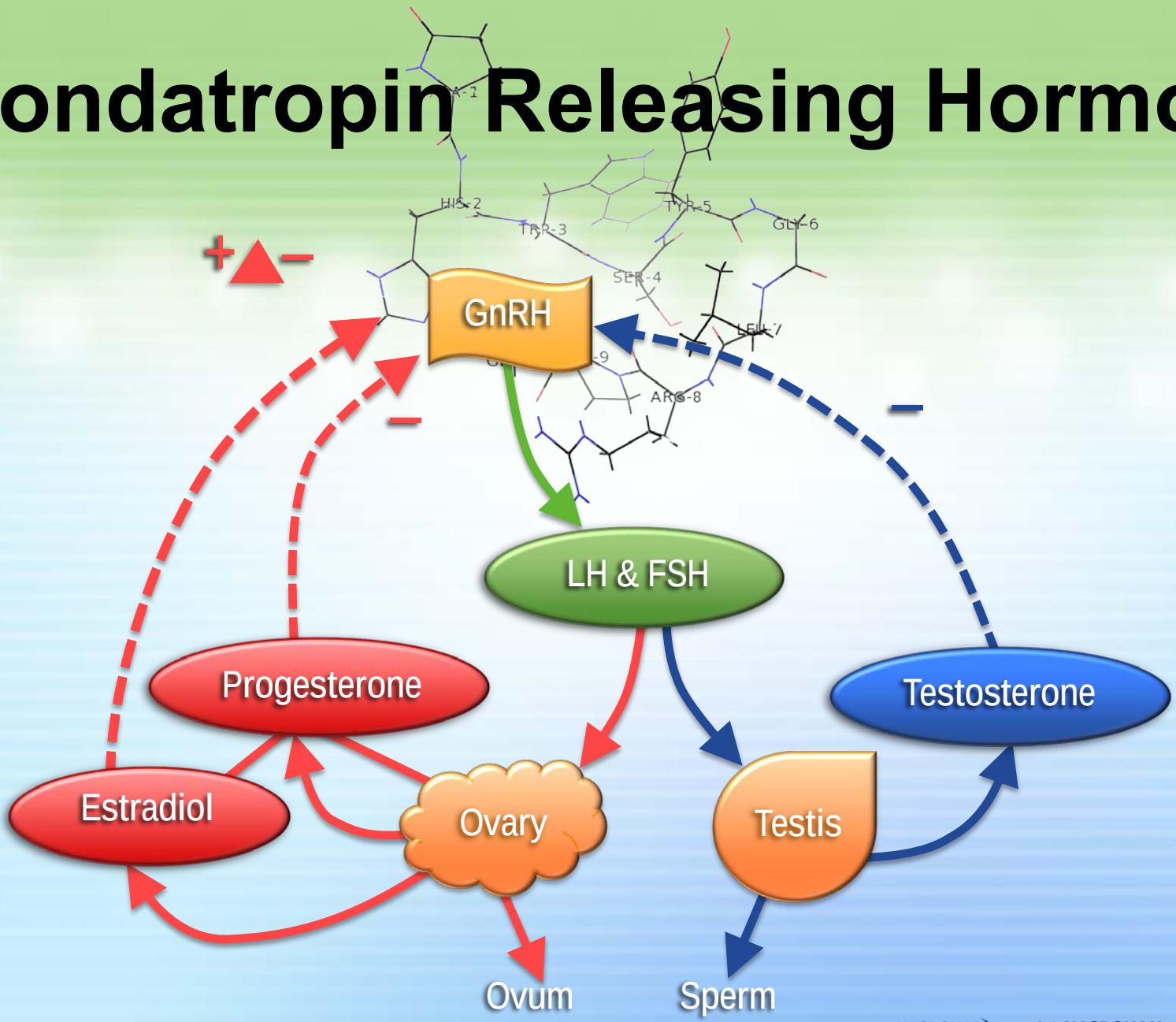
[6]Adapted from Kleinman et al. *J Pediatr Gastroenterol Nutr.* 2004;39:15-2.

Growth Hormone Axis



Adapted From MD Consult and Google Images.

Gondatropin Releasing Hormone



Adapted from www.aphis.usda.gov.

Risk Factors with Growth Failure

- Boys are more at risk
  - Approximately 10% cumulative incidence at 10 year from the time of diagnosis
  - Males with CD were significantly shorter than control subjects regardless of pubertal stage.
  - Adjusted HAZ-score using mid-parental height was below predicted
- Patients with poor growth were twice a likely to undergo surgery

[7]Gupta et al. *Pediatrics.*2007;120:1418-25.
[8]Sentongo et al. *J Pediatr Gastroenterol Nutr.* 2000:31-33-40.
[9]Gupta et al. *Gastro.* 2006:130:1069-1077.

Final Adult Height

- Lee et al 295 patients with IBD
- Parents of growth impaired group had lower mean height Z-scores vs. non-growth impaired
- 108 patients with adult heights
  - Growth impaired group had lower adult height Z-scores (-1.38 vs. 0.05;p<0.001)
  - 11.3% persistently growth impaired as adults
- Lower parental height and minimum patient height Z-score were significant predictors of lower final adult height
- Children < 3rd percentile
  - 59% failed to reach the 3rd% for adult height

[10]Lee et al. *Inflamm Bowel Dis.* 2010;16:1669-1677.
[11]Griffiths et al. *Gut.*1993;34:939-43.

Growth Assessment

- Height and weight measurements by trained staff
- Obtain premorbid height and weight at baseline
- Obtain accurate parental heights and calculate mid-parental height and percentiles
- Evaluate height velocity at 4-6 month intervals

[12]Heuschkel et al. *Inflammatory Bowel Dis.* 2010;14:839-849.

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Delayed Puberty

- Mean age of onset of puberty:
  - Girls: 11.1 years, Boys: 12.4 years
- Delayed Puberty :
  - Girls: 13 years, Boys: 14.5 years
- More likely in patients with CD than UC
- Delay in puberty by 0.7 years in Dutch children with IBD
- 1.5 years in CD children in the US

[13]Boot et al. *Gut.*1998 42:188-194.
[14]Burnham et al. *J Bone Miner Res.*2004;19:1961-68.
[15]Gerasimidis et al. *J Hum Nut Diet.* 2011;24:313-26.

Delayed Puberty

- Retrospective cohort of children with IBD
  - CD patients were more likely to have delay
  - Boys were more commonly affected
- Testosterone has been used effectively to treat pubertal delay in boys
  - 8 boys with IBD median age of 14
  - 7 boys advanced in pubertal stage
  - 6 had >50% increase in height velocity

[16]Mason et al *Horm Res Paediatr*. 2011;76(5):293-9.
[17]Mason et al *Horm Res Paediatr.* 2011;75(1):8-13.

Cytokines & Pubertal Delay

- TNF-α, IL-6, IL-1
  - Induce anorexia
  - Results in decreased sex hormone function
    - Decreased synthesis of testosterone in Leydig cells in testes
    - Decreased synthesis of sex steroids in the ovary

[6]Kleinman et al. *J Pediatr Gastroenterol Nutr.* 2004;39:15-27.

IGF-1

- Sex hormones influence pubertal growth via the GH axis and IGF-1
- Important for statural growth
- Gupta et al
  - Females > 15 yrs and males > 17 years
  - IGF-1 levels reduced in males and similar along all Tanner Stages
    - Inflammatory markers remaining a significant predictor
    - Markers correlated with testosterone levels in males, but not estradiol in females
    - Inflammation on hormone levels may differ in each sex

[18]Gupta et al. *Inflammatory Bowel Dis.* 2011;11:2318-25.

Corticosteroids

- Decreases effects of GH/IGF-1 at target tissue
  - Inhibits bone growth
  - Inhibits collagen synthesis
    - ↓ Type I procollagen levels
- Decreases sex steroid secretion

[6]Kleinman et al. *J Pediatr Gastroenterol Nutr.* 2004;39:15-27.
[12]Heuschkel et al *Inflamm Bowel Dis.* 2008;14:839-49.

Cytokines & Anorexia

- Increased cytokine levels in malnourished patients
- Cytokines induce specific metabolic changes
  - Stimulating muscle breakdown
- Repeated injections of cytokines causes anorexia in animal models
- Metabolic changes can be counteracted by blocking cytokines
- TNF-α, IL-1, and IL-6

[6]Kleinman et al. *J Pediatr Gastroenterol Nutr.* 2004;39:15-27.
[19]Shamir. *J Pediatr Gastroenterol Nutr.* 2009; 48:S86–S88.
[12]Heuschkel et al. *Inflamm Bowel Dis.* 2008;14:839-49.

Medical Management

- Control Inflammation
  - Limit steroid exposure
  - 6-MP or azathioprine
  - Infliximab
- Aggressive nutritional therapy
  - Oral/NG/G-tube nutritional supplementation
    - elemental vs. polymeric
  - Parental nutrition

[6]Kleinman et al. *J Pediatr Gastroenterol Nutr.* 2004;39:15-27.
[2]Sandhu et al. *J Pediatr Gastroenterol Nutr.* 2010;50(Suppl.1):S14–34.

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Bone Mineral Density (BMD)

- Osteopenia
  - Z-scores < -1
- Osteoporosis
  - Z-scores < -2
- Peak Bone Mass
  - 18-20 yrs boys (13-17)
  - 16 yrs girls (11-14)
- Age at diagnosis of IBD = 10 + 4 yrs

[20]Heyman et al. *J Pediatr.* 2005:146:35-40.

Osteopenia & Osteoporosis

- Multi-factorial
  - Decreased calcium intake
  - Calcium malabsorption
  - Steroids
    - Reduce calcium absorption
    - Down-regulate gene expression of calcium binding protein
    - Inhibit osteoblast proliferation
    - Stimulate osteoclast
  - Cytokine mediated bone absorption
  - Hypovitaminosis D

[20]Heyman et al. *J Pediatr.* 2005:146:35-40.

Bone Mineral Density

- Heavily influenced by growth and puberty
  - Correct for age, bone age, or BMI
- Dual x-ray absorptiometry (DXA)
  - 2-Dimensional
  - Measures a ratio of bone mineral content over the area measured and may lead to an underestimation of BMD
- Peripheral quantitative computer tomography (pQCT)
  - 3-D assessment of the structural and geometric properties of the appendicular skeleton
  - Measures muscle cross sectional area- surrogate for total muscle mass

[21]Bechtold et al. *Inflamm Bowel Dis.* 2010;16(2):216-25.

Osteopenia & Osteoporosis

- Osteopenia prevalence
  - Sylvester et al
    - 43% CD (n=58), 39% UC (n= 18), and 29% Controls (n= 49)
  - Gokhale et al
    - 35% of CD vs 22% of UC
- Osteoporosis
  - Sylvester et al
    - 12% vs 6% vs 2%
  - Gokhale et al
    - 18% vs 3%

[22]Sylvester et al. *Inflamm Bowel Dis.* 2007;13:42–50.
[23]Gokhale et al.*Gastroenterology.* 1998;114:902-911.

BMD & IBD

- Prospective cohort assessed over 2 year time period
- Total body BMD Z-score
  - (mean SD) was -0.78 ± 1.02 for Crohn's disease (CD, *n* 58),
  - -0.46 ± 1.14 for ulcerative colitis (UC, *n* 18), and
  - -0.17 ± 0.95 for controls (p<0.001 CD vs Control)
- In CD, a BMD Z-score <1.0 was associated with lower BMI and higher serum IL-6
- Activation of bone formation paralleled clinical improvement, but BMC gain was less than expected over the 2-year study period, especially in CD
- Prednisone use did not correlate with low BMD

[22]Sylvester et al. *Inflamm Bowel Dis*. 2007;13:42–50.

BMD

- Cross-sectional study using pQCT of forearm in 143 IBD patients CD = 98, 29% newly diagnosed
- Height, weight, and muscle mass were lower as compared to age and sex matched controls
- Serum albumin was a good marker for muscle wasting and abnormal bone development
- Decreased mechanical stress may relate to reduced bone health
- Suggest improving lean tissue mass via nuturtional support and weight bearing

[21]Bechtold et al. *Inflamm Bowel Dis.* 2010;16:216–24.
[15]Gerasimidis et al. *J Hum Nutr and Diet 2011;24:313-326*

Vitamin D

- Produced by the skin when exposed to UV radiation
- Serum 25, OH-D is the most abundant metabolite and indicative of overall vitamin D status
- Pappa et al n=488 IBD pediatric patients
  - 58.3% had suboptimal < (25OHD 32 ng/mL),
  - 14.3% had ≤ 20 ng/mL
  - 5.8% had serum ≤15 ng/mL

[24]Pappa et al. *J Pediatr Gastroenterol Nutr.* 2011;53:361-364.

Vitamin D

- Risk factors included darker skin, winter season, lack of vitamin D supplementation
- ESR, a marker of intestinal inflammation, was associated with lower vitamin D levels
  - Malabsorption
  - Losses of protein bound 25, OHD
- Children with CD and UC should be screened for vitamin D deficiency
- Calcium 1300 mg daily
- Vitamin D 400-800 IU

[24]Pappa et al. *J Pediatr Gastroenterol Nutr.* 2011;53:361-364.

Fractures

- 2 year prospective fracture study
  - 2-fold increase in fracture risk with each SD decrease in areal BMD
- No prospective studies between fractures and BMD in pediatric IBD patients
  - Vertebral fractures reported in 5 CD patients with LS BMD -2 to -5

[25]Clark et al. *J Bone Miner Res.* 2006;21:1489-95.
[26]Semeao et al. *Gastroenterology.*1997;112(5):1710-3.

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Anemia

- Blood loss
- Chronic inflammation
- Micronutrient deficiency
  - B12-ileal disease
  - Folate- sulfasalazine
  - Iron-impaired utilization
- Myelosuppression – 6-MP
- Hemolysis

[3]Kappelman & Bousvaros. *Mol Nutr Food Res.* 2008:52:867-874.
[27]Gerasimidis et al. *J Hum Nut Diet.* 2011;24:313-26.
[28]Turner et al. *Inflamm Bowel Dis.* 2011;17(1):336-45.

Diagnosis of Anemia

- Microcytosis vs macrocytosis
- Low serum iron
- Lower ferritin
- Serum transferrin receptor levels
- Serum folate
- Serum B_{12}
- Urine methylmalonic acid

[3]Kappelman & Bousvaros. *Mol Nutr Food Res.* 2008:52:867-874.
[27]Gerasimidis et al. *J Hum Nut Diet.* 2011;24:313-26.
[28]Turner et al. *Inflamm Bowel Dis.* 2011;17(1):336-45.

Vitamin & Micronutrient Deficiencies

- Zinc
- Copper
- Iron
- Folic Acid
- Vitamin C
- Vitamin D

Vitamin & Micronutrient Deficiencies

- Zinc
- Copper
- Iron
- Folic Acid
- Vitamin C
- Vitamin D

Zinc

- Co-factor in more than 300 metalloenzymes
  - RNA and DNA synthesis
  - Lymphocyte proliferation
  - Cytokine production
  - Free radical activity
  - Wound Healing
  - Serum levels don't reflect total body zinc depletion
    - Serum levels depend on albumin binding
    - >95% intracellular
- No controlled studies to determine value

[3]Kappelman and Bousvaros. *Mol Nutr Food Res.* 2008:52:867-874.
[6]Kleinman et al. *J Pediatr Gastroenterol Nutr.* 2004;39:15-27.

Vitamin & Micronutrient Deficiencies

- Zinc
- Copper
- Iron
- Folic Acid
- Vitamin C
- Vitamin D

Folate

- Synthesis, methylation and repair of DNA synthesis
- At the time of diagnosis, higher folate levels in newly diagnosed patients compared to controls
  - Medications over time interfere with metabolism
  - Sulfasalazine and methotrexate
- Recommended dose of 1mg daily is empiric
  - Risk of colorectal cancer and other tumors with folate

[29]Heyman et al. *Am J Clin Nutr.* 2009;89:545–50.

Fish Oil: Omega-3 Fatty Acids

Omega-3 : Polyunsaturated Fatty Acids (PUFA)

- Shown to have positive effects in a variety of diseases
  - Cardiovascular, immunologic and inflammatory conditions
- Benefits secondary to anti-inflammatory, vasodilatory, and hypolipidemic properties
- Regulatory effects on cell growth and death
  - Anti cancer effects

[28]Turner et al. *Inflamm Bowel Dis.* 2011;17(1):336-45.
[6]Kleinman et al. *J Pediatr Gastroenterol Nutr.* 2004;39:15-27.

Omega-3 PUFA: Mechanism of Action

- Omega-3 incorporate into wall of cells involved in inflammation
- Results in decreased production of inflammatory proteins
  - Halts inflammatory cascade
- Sources—vegetables, fish oil (largest source)

[6]Kleinman et al. *J Pediatr Gastroenterol Nutr.* 2004;39:15-27.

Fish Oil & IBD

- Biologic rationale for use
  - Animal models of IBD and tissue samples from patients with IBD demonstrate strong anti-inflammatory benefits of omega-3
- However, clinical trials show limited or absent clinical benefit
  - Limitations: inadequate delivery system (poor absorption) or inadequate dosing

[28]Turner et al. *Inflamm Bowel Dis.* 2011;17(1):336-45.

Fish Oil & IBD

- No data to support their usage!
  - Routine therapies
  - Remission of CD
  - Remission of UC
  - Maintainence of CD
  - Maintainence of UC

Pitfalls of Fish Oil

- FDA does not regulate
  - Mercury and other toxin contamination
  - Reliable supplier
- Side effects
  - Nausea, vomiting, diarrhea, unpleasant taste, bad breath
    - Less common with timed release (enteric coated) preparations
- Compliance
  - May need to take 6-12 capsules daily

Enteral Nutrition

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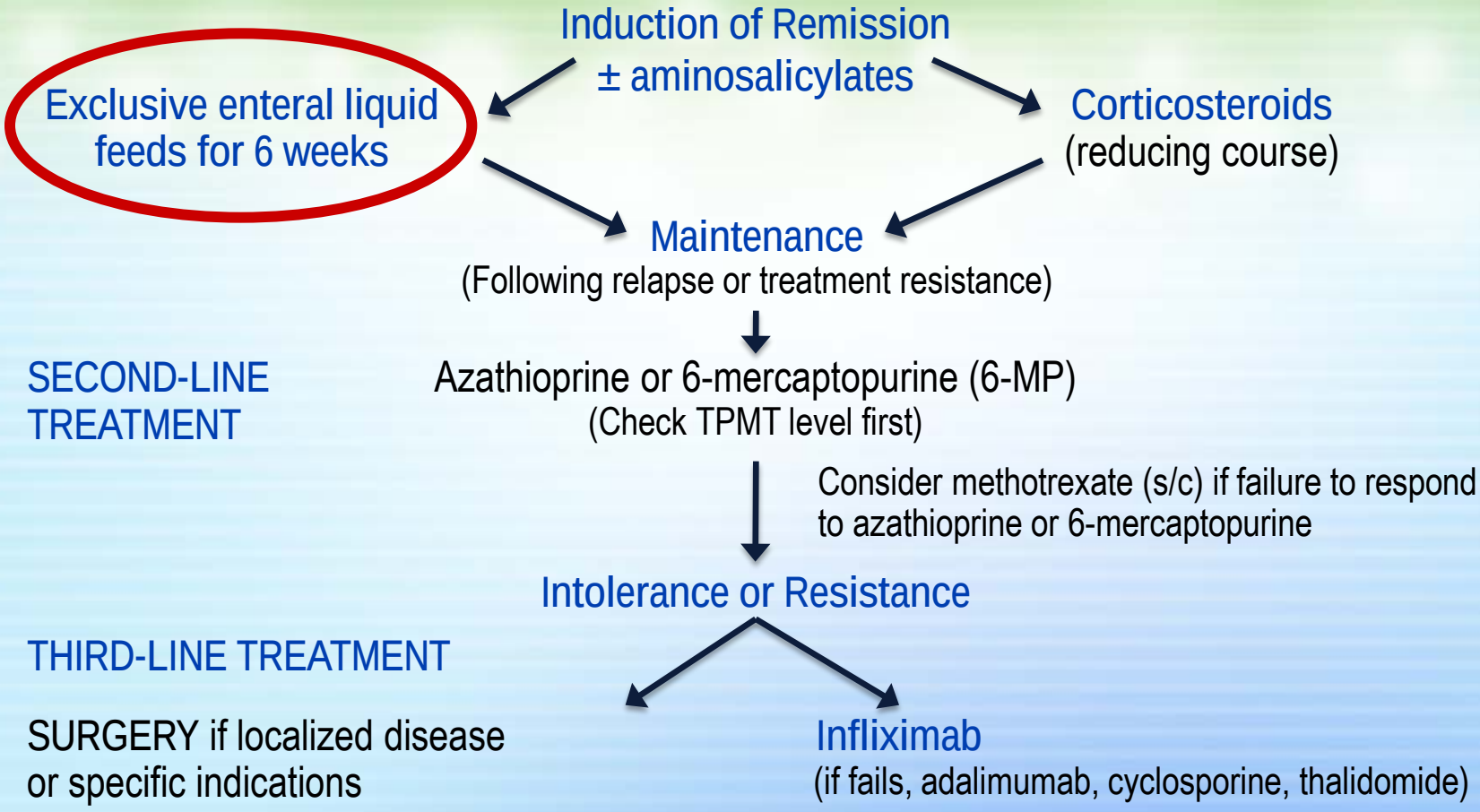
Crohn's Treatment Algorithm



[2]Sandhu et al. *J Pediatr Gastroenterol Nutr.* 2010;50(Suppl.1):S14–34.

Enteral Nutrition

- 4% of N American peds GI use regularly vs 62% of European practitioners
- Exact mechanism of action is actually not clear
  - Elimination of dietary antigen uptake
  - Overall nutritional repletion
  - Correction of intestinal permeability
  - Dimunition of intestinal synthesis of inflammatory mediators via reduction of dietary fat
  - Provision of important micronutrients to the diseased intestine
- Evidence that it affect gut microbiota and anti-inflammatory in nature

[30]Critch et al. *J Pediatr Gastroenterol Nutr.* 2012:54: 298-305.

Evidence for Enteral Nutrition

- Studies have shown up to 20-85% remission in newly diagnosed CD
- Meta analyses showed with 144 subjects found no significant difference in remission rates at 8-10 weeks of therapy with EN vs steroids RR 0.97
- Cochrane review showed an OR of 0.33 favoring steroids
  - Adult and pediatric patients
  - Pediatric studies excluded because of methodology
  - Partial EN vs Full EN
    - Full EN group had remission of 42% vs 15% of partial

[31]Zachos et al.*Cochrane Database Syst Rev*. 2007;(1):CD000542.
[32]Dziechciarz et al *Aliment Pharmacol Ther.* 2007:26:795-806.
[30]Critch et al. *J Pediatr Gastroenterol Nutr.* 2012:54: 298-305.

Candidates for Therapy

- More successful in treatment in patients with small bowel disease
- Afzal et al showed colonic disease not as amenable to EN
  - 11/12 ileal
  - 32/39 with ileocolonic
  - 7/14 isolated colonic
  - Zachos et al
    - No significant difference
- Acceptable to trial in any Crohn's disease patients

[33]Afzal et al Dig Dis Sci 2005;30:501-7.
[31]Zachos et al. *Cochrane Database Syst Rev*. 2007;(1):CD000542.

Formula Composition

- Elemental
- Semi-elemental
- Polymeric formula
  - More palatable
  - Less expensive
  - Perhaps avoid an NG tube
  - ? More weight gain than elemental
- NG vs PO

[3]Kappelman & Bousvaros. *Mol Nutr Food Res.* 2008:52:867-874.
[6]Kleinman et al. *J Pediatr Gastroenterol Nutr.* 2004;39:15-27.
[39]Critch et al. *J Pediatr Gastroenterol Nutr.* 2012:54: 298-305.

Growth & Mucosal Healing

- Variable depending on the study
- Height velocity standard deviation scores were significantly increased over steroids at 6 months
- Mucosal healing
  - Fell et al 79% remission in children reaching a polymeric diet with supplemental TGFβ-2 (n=29)
  - Histologic improvement with 8 cases in volving small bowel and 2 in the colon.

[34]Fell et al. *J Pediatr Gastroenterol Nutr* . 2005;29:S126-133.

Protocol

- Duration of therapy
  - 3-12 weeks
  - Mean 8.5 ± 1.7 weeks
  - 81% 6-8 week period of EEN
- Inflammatory markers improve within a week
- Time to remission 11 to 2.5 days
- At least 3-4 weeks are the current recommendation

[30]Critch et al. *J Pediatr Gastroenterol Nutr.* 2012:54: 298-305.
[2]Sandhu et al. *J Pediatr Gastroenterol Nutr.* 2010;50(Suppl.1):S14–34

Re-feeding Syndrome

- Fluid shifts and electrolyte abnormalities including hypophosphatemia and hypokalemia when patient is started on enteral nutrition after being malnourished.
- BMI < -1.5 should be hospitalized and monitored for re-feeding
- Daily electrolytes
- Phosphate and or potassium supplementation
- Gradual re-feeding

[35]Byrnes et al. *Curr Opin Clin Nutr Metab Care.* 2011;14(2):186-92.

Reintroduction of Diet

- Subject of much debate
- UK guidelines
  - Reintroduce food cautiously during the course off 1-3 weeks
- US guidelines
    - Introducing a meal every 2-3 days appears a reasonable strategy.

[30]Critch et al. *J Pediatr Gastroenterol Nutr.* 2012:54: 298-305.
[2]Sandhu et al. *J Pediatr Gastroenterol Nutr.* 2010:50(Suppl.1):S14–34.

Success Rates

- Enteral nutrition has been used as monotherapy or in combination with other standard medicines
  - 6-MP, infliximab, and mesalamine
- Hospital for Sick children
  - 28 children NG overnight with regular diet during day
  - 19 patients who discontinued drip feedings
    - 43% vs 79% relapse rate at 1 year

[36]Wilschanski et al. *Gut.*1996;38(4):543-8.

Enteral Therapy

- Enteral therapy offers an alternative to steroids in patients with CD
- Has potential to improve growth and height velocity
- Avoids the side effects of steroids
- Need further research to determine the mechanism and the best regimen

[30]Critch et al. *J Pediatr Gastroenterol Nutr.* 2012:54: 298-305.
[2]Sandhu et al. *J Pediatr Gastroenterol Nutr.* 2010;50(Suppl.1):S14–34

Conclusion

- Growth failure and pubertal delay are multi-factorial in etiology
- Close monitoring of vitamin levels, growth, and height velocity are necessary
- Osteopenia and osteoporosis can occur in IBD patients
- Enteral nutrition is a potential therapy in treatment of Crohn's disease

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Energy and Protein Metabolism

Components of Energy Needs[1-3]

- Basal metabolic rate (BMR)
- Diet-induced thermogenesis
- Physical activity (PA)
- Growth
- Energy needs may be affected by
  - *Nutritional status, underlying diseases, energy intake, energy losses, age, and gender*

[1]Grund, et al. *Int J Obes Relat Metab Disord*. 2000;24:299-305.
[2]Goran, et al. *J Pediatr*. 1994;125:362-367.
[3]Bitar, et al. *Am J Clin Nutr*. 1999;69:1209-1216.

Basal Metabolic Rate[4]

- Amount of energy needed for maintaining vital processes of the body, not including activity and food processing

BMR	Resting Energy Expenditure (REE)
Not usually measured	Measured instead of BMR
Measured • In a recumbent position • Thermoneutral environment • After a 12- to 18-hour fast • Just when the individual has awakened before starting daily activities	Measured • At rest • Thermoneutral environment • After an 8- to 12-hour fast • Not immediately after awakening
	REE does not differ by more than 10% from BMR

[4]Shulman and Phillips. *J Pediatr Gastroenterol Nutr*. 2003;36:587-607.

Diet-Induced Thermogenesis[5-7]

- Reflects the amount of energy needed for food digestion and absorption
  - *Can be affected by the route of food administration*
  - *~ 10% of daily energy needs*

[5]Romon, et al. *Am J Clin Nutr*. 1993;57:476-480.
[6]Lerebours, et al. *JPEN J Parenter Enteral Nutr*. 1988;12:360-364.
[7]Putet, et al. *Arch Fr Pediatr*. 1984;41:111-115.

Activity[8]

- Activity is the amount of energy spent for daily movements and PA
- In older children, activity accounts for a large proportion of total energy expenditure
- Estimated energy requirements (boys 3-18 years) =

(88.5 – (61.9 × age)) + PA × ((26.7 × Wt) + (903 × Ht)

Activity Level	Boys Aged 3-18 Years
Sedentary	1
Moderately active	1.13
Active	1.26
Very active	1.42

[8]The National Academies Press Web site. http://www.nap.edu/catalog.php?record_id=10490. Accessed March 26, 2012.

Growth[9]

- The energy needed to maintain accelerated growth represents 30-35% of the energy requirements in term neonates and is greater in preterm infants
- Energy cost for 1 g of tissue deposition ranges between 4.9 kcal/g in premature infants and 6.4 kcal/g in adults recovering from anorexia nervosa

[9]World Health Organization. *World Health Organ Tech Rep Ser*. 1985;724:1-206.

Catch-Up Growth[10]

- Children recovering from malnutrition need extra calories to correct their growth deficits
  - *Energy needs may be calculated based on the 50th percentile of weight and height for the actual age, rather than the present weight*
  - *Or calculation may be based on the actual weight multiplied by 1.2-1.5*
- Further caloric needs should be adjusted according to weight and height gain

[10]Koletzko, et al. *J Pediatr Gastroenterol Nutr*. 2005;41(Suppl 2):S1-S87.

Estimating Energy Needs[11]

- Energy needs can be either measured or calculated based on acceptable equations

[11]Torun, et al. *Eur J Clin Nutr*. 1996;50(Suppl 1):S37-S80.

Energy Estimates (10-18 Years)

- World Health Organization[9]
  - ♂ *REE = 17.5 × Wt + 651*
  - ♀ *BMR = 12.2 × Wt + 746*
- Schofield[12]
  - ♂ *BMR = 17.7 × Wt + 657*
  - ♀ *BMR = 13.4 × Wt + 692*
- Harris-Benedict[13]
  - ♂ *REE = 66.47 + (13.75 × Wt) + (5.0 × Ht) – (6.76 × age)*
  - ♀ *REE = 655.1 + (9.56 × Wt) + (1.85 × Ht) – (4.68 × age)*

[9]World Health Organization. *World Health Organ Tech Rep Ser*. 1985;724:1-206.
[12]Schofield. *Hum Nutr Clin Nutr*. 1985;39(Suppl 1):5-41.
[13]Pop and Miu. *Nutr Ther Metab*. 2010;28:117-128.

Estimating Energy Needs (cont'd)[11]

- The best way to assess energy needs in children is to measure total energy expenditure or, alternatively, REE
- All of these equations have been established in normal children and should be used with caution

[11]Torun, et al. *Eur J Clin Nutr*. 1996;50(Suppl 1):S37-S80.

REE: Indirect Calorimetry[14]

- When carbohydrate, protein, and fat are oxidized, oxygen is consumed and carbon dioxide is produced
  - *The amount of oxygen consumed and carbon dioxide produced per gram of carbohydrate, protein, and fat is constant*
  - *The amount of calories generated during the consumption of a liter of oxygen (modified by the amount of carbon dioxide produced) is also constant*
- If oxygen consumption and carbon dioxide production can be measured, the energy released in the course of the utilization of these gases (or the energy expenditure) can be determined
- All oxygen consumed and all carbon dioxide produced during metabolism is exchanged across the lungs, and these gases can be measured by indirect calorimetry
  - *The technique is referred to as indirect, because gas exchange does not actually measure heat production*

[14]Ferrannini. *Metabolism*. 1988;37:287-301.

Protein Metabolism

Protein Content[15]

- In an adult
  - *Skeletal muscle – nearly 50%*
  - *Other structural tissues (skin and blood) each – ~ 15%*
  - *Metabolically active visceral tissues (eg, liver and kidney) – total 10%*
  - *Brain, lung, heart, and bone – ~ 10%*
- This distribution varies with age
  - *Newborn infant has proportionately less muscle and much more brain and visceral tissue*

[15]Lentner. In: *Units of Measurement, Body Fluids, Composition of the Body, Nutrition.* Geigy Scientific Tables. 8th ed. Vol. 1. West Caldwell, NJ: Ciba-Geigy Corporation; 1981.

Protein Reserve[16]

- "Labile protein reserve," which can be gained or lost from the body, as a short-term store for use in emergencies or to take account of day-to-day variations in dietary intake (1% of total body protein)
- This reserve is unlike the fat and glycogen stores, whose primary roles are for energy use
  - *The protein lost during fasting is functional body protein*

[16]Waterlow. In: *Mammalian Protein Metabolism*. Vol. 3. Munro, ed. New York, NY: Academic Press; 1969; 347-348.

"Basal" Protein Losses[17,18]

- Even in the absence of protein consumption, nitrogen continues to be lost
  - *Provided that the energy intake is adequate, these "basal" losses are closely related to body weight and BMR*
- When the diet is devoid of protein, the efficiency of amino acid recycling is > 90% for both indispensable and dispensable amino acids

[17]Castaneda, et al. *Am J Clin Nutr.* 1995;62:40-48.
[18]Neale and Waterlow. *Br J Nutr.* 1974;32:11-25.

Protein Synthesis[19]

	Protein Synthesis (g/kg Per Day)
Preterm infant	17.4
Infant	6.9
Adult	3.0
Elderly	1.9

[19]Adapted from Young, et al. *Nature.* 1975;253:192-194.

Classification of Amino Acids[8]

Indispensable	Conditionally Indispensable	Precursors of Conditionally Indispensable
Histidine	Arginine	Glutamine/glutamate, aspartate
Isoleucine	Cysteine	Methionine, serine
Leucine	Glutamine	Glutamic acid, ammonia
Lysine	Glycine	Serine, choline
Methionine	Proline	Glutamate
Phenylalanine	Tyrosine	Phenylalanine
Tryptophan		
Threonine		
Valine		

Conditionally indispensable is defined as requiring a dietary source when endogenous synthesis cannot meet metabolic need.

[8]Adapted from The National Academies Press Web site. http://www.nap.edu/catalog.php?record_id=10490. Accessed March 26, 2012.

Protein Deficiency[20-22]

- Protein deficiency adversely affects all organs
- In infants and young children
  - *Have harmful effects on the brain and may have longer-term effects on brain function*
- Adverse effects on the immune system, resulting in a higher risk of infections
- Affects gut mucosal function and permeability → possible bacterial translocation → septicemia
- Total starvation will result in death
  - *In adults in 60-70 days*
  - *1000-g neonates in 5 days*

[20]Pollitt. *J Nutr.* 2000;130(Suppl):350S-353S.
[21]Bistrian. *JPEN J Parenteral Enteral Nutr.* 1990;14:329-334.
[22]Heird, et al. *J Pediatr.* 1972;80:351-372.

Assessment of Protein Status[23]

- Midarm muscle circumference
  - *Protein status (unless a myopathy or neuropathy is present)*[24]
- Triceps skinfold
  - *Energy nutritional status*
- Serum albumin is a poor indicator of protein status
  - *Useful prognostically as an indicator of inflammation*

[23]Young, et al. *J Nutr.* 1990;120(Suppl 11):1496-1502.
[24]Canadian Paediatric Society. *CMAJ*. 1994;151:753-759.

Starvation

Pathophysiology[25-27]

- Carbohydrate metabolism → fat and protein catabolism → glucose and ketones for energy
- Loss of lean body mass
  - *Heart – myocardial atrophy → diminished cardiac output*
  - *Liver wasting → decreased protein synthesis and further alteration in metabolism*
  - *Gastrointestinal → causes malabsorption and dysmotility → worsens malnourished state and increases risk for infection*
  - *Kidneys → lose ability to concentrate urine → diuresis*

[25]Kerner and Hattner. In: *Medical Nutrition and Disease: A Case-Based Approach*. Hark and Harrison, eds. 4th ed. Philadelphia, PA: Wiley-Blackwell; 2009; 182-187.
[26]Lauts. *J Infus Nurs*. 2005;28:337-342.
[27]McCray, et al. *Pract Gastroenterol*. 2005;29:26-44.

Pathophysiology (cont'd)[25,27]

- Intracellular loss of electrolytes
  - *Potassium, magnesium, and phosphate*
- Insulin secretion decreases and the BMR slows down to 20-25% to conserve energy
  - *Body becomes bradycardic, hypothermic, and hypotensive*

[25]Kerner and Hattner. In: *Medical Nutrition and Disease: A Case-Based Approach*. Hark and Harrison, eds. 4th ed. Philadelphia, PA: Wiley-Blackwell; 2009; 182-187.
[27]McCray, et al. *Pract Gastroenterol*. 2005;29:26-44.

Classification of Malnutrition[39]

	Moderate Malnutrition	Severe Malnutrition
Symmetrical Edema	No	Yes (edematous Malnutrition)
Weight-for-Height	**-3 ≤** z-score < -2 (70%-79% of median weight-for-height)	z-score < -3 (70% of median weight-for-height) (severe wasting)
Height-for-Age	**-3 ≤** z-score < -2 85%-89% of median height-for-age)	z-score < -3 85% of median weight-for-age) (severe stunting)

[39]*Adapted from Management of Severe Malnutrition: A Manual for Physicians and Other Senior Health Workers*. Geneva, Switzerland: World Health Organization;1999.

Kwashiorkor Versus Marasmus[40-42]

- Kwashiorkor should be correctly termed edematous malnutrition
- The precise reason why some children develop one condition versus the other is unclear

[40]Jahoor, et al. *Am J Clin Nutr*. 2005;82:792-800.
[41]Rossouw. *Am J Clin Nutr*. 1989;49:588-592.
[42]Golden. *Br Med Bull*. 1998;54:433-444.

Refeeding Syndrome

Refeeding Syndrome

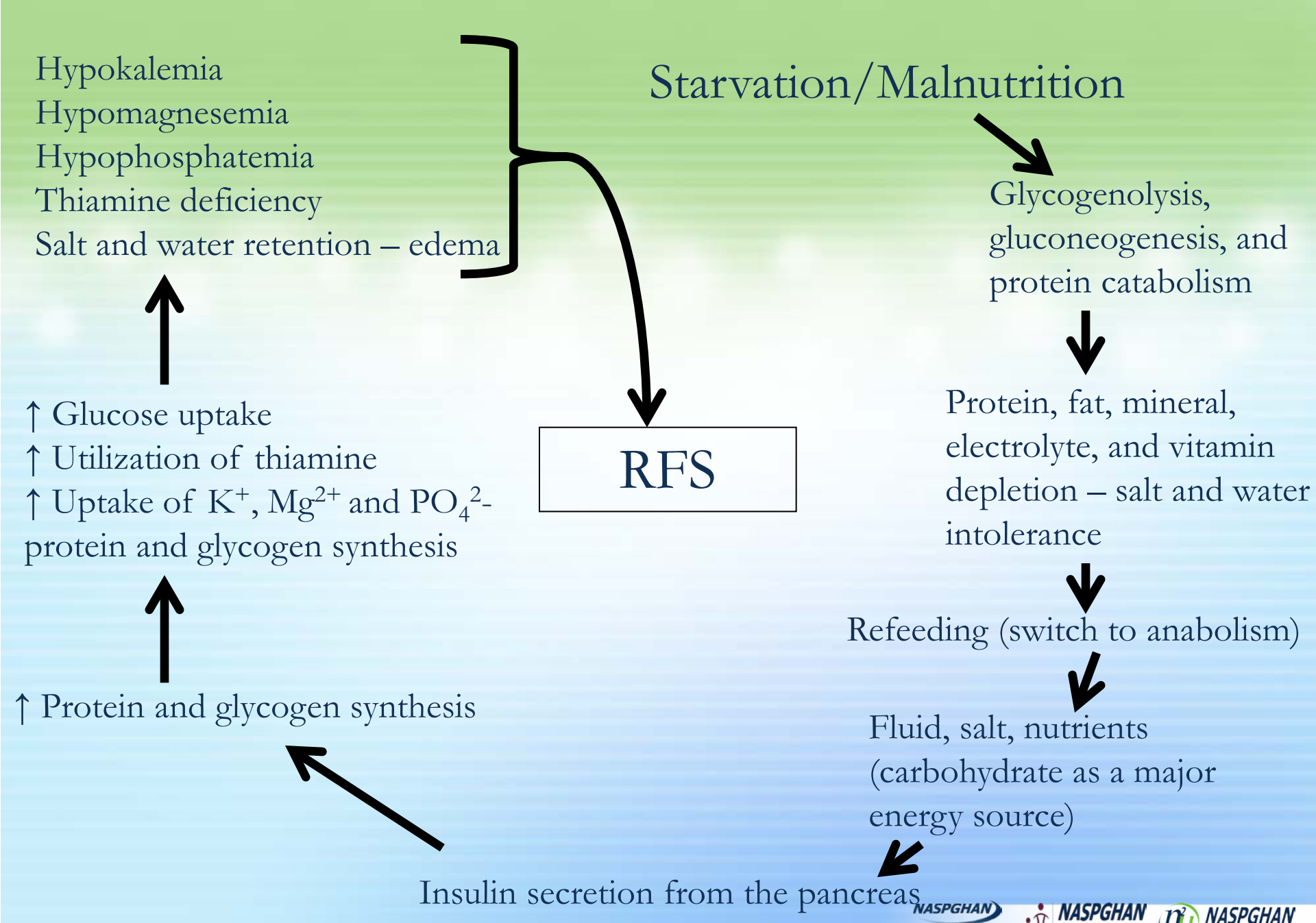
- Refeeding syndrome (RFS) is a term that describes the metabolic and clinical changes that occur upon aggressive nutritional rehabilitation of a malnourished patient

Background[28,29]

- First described after World War II in prisoners of war
  - *Cardiac and neurologic abnormalities upon refeeding after long periods of starvation*
- Normally occurs within 3-4 days after initiating feeds
- Signs/symptoms include weakness, muscle pain, ataxia, paresthesia, confusion, arrhythmia, seizures
- Phosphate depletion is the hallmark and cause of the majority of symptoms associated with RFS

[28]Schnitker, et al. *Ann Intern Med*. 1951;35:69-96.
[29]Solomon and Kirby. *JPEN J Parenter Enteral Nutr*. 1990;14:90-97.

Pathophysiology



[30]Adapted from Stanga, et al. *Eur J Clin Nutr.* 2008;62:687-694.

Patients at Risk of RFS[31]

- Severe malnutrition
- Anorexia nervosa
- Significant weight loss, including massive weight loss in obese patients
- Prolonged intravenous (IV) therapy/fasting

Most frequent identifier for a pediatric patient at risk for RFS was a calculated body weight < 80% of ideal body weight.

[31]Dunn, et al. *Nutr Clin Pract*. 2003;18:327-332.

Serum Abnormalities During Refeeding[32,33]

- Hypophosphatemia
- Hypokalemia
- Hypomagnesemia
- Glucose abnormalities
- Thiamine deficiency
- Derangements of sodium, nitrogen, and fluid balance

[32]Crook, et al. *Nutrition.* 2001;17:632-637.
[33]Brooks and Melnik. *Pharmacotherapy.* 1995;15:713-726.

Phosphorus[29,34]

- Important roles of phosphorus
  - *Adenosine triphosphate (ATP) and 2,3-diphosphoglycerate (2,3-DPG) generation*
- During refeeding
  - *Glucose intake leads to insulin surge, pulling phosphorus intracellularly, leading to deficits in both intra/extracellular phosphorus levels*
  - *Increased demand for and utilization of 2,3 DPG and ATP*
- In malnutrition, baseline cardiac muscle atrophy
  - *More vulnerable to the deleterious effects of phosphate depletion → ventricular dysrhythmias and sudden death*

[29]Solomon and Kirby. *JPEN J Parenter Enteral Nutr*. 1990;14:90-97.
[34]Heymsfield, et al. *Am Heart J*. 1978;95:584-594.

Potassium and Magnesium[31,35,36]

- Role of potassium
  - *Potassium is driven intracellularly by insulin in response to glucose intake*
  - *Significant potassium depletion*
    - Cardiac arrhythmias (QTc prolongation and torsades de pointes) and cardiac arrest
- Role of magnesium
  - *Hypomagnesemia can result in cardiac and neuromuscular dysfunction*

[31]Dunn, et al. *Nutr Clin Pract*. 2003;18:327-332.
[35]Kraft, et al. *Nutr Clin Pract*. 2005;20:625-633.
[36]Mehanna, et al. *BMJ*. 2008;336:1495-1498.

Glucose Dysregulation[36]

- After periods of starvation, glucose must be replaced at a slow and intentional rate
  - *Replacement of large quantities of glucose quickly can result in hyperglycemia → osmotic diuresis, dehydration, metabolic acidosis, and ketoacidosis*
- Other complications
  - *Fatty liver disease due to lipogenesis*
  - *Increased CO_2 production, leading to hypercapnia and eventually respiratory failure*

[36]Mehanna, et al. *BMJ*. 2008;336:1495-1498.

Fluid Balance[37]

- Carbohydrate intake leads to a rapid decrease in renal excretion of sodium and water
- If extra fluids are given to maintain "normal" urine output → fluid overload → cardiac failure

[37]Palesty and Dudrick. *Nutr Clin Pract*. 2006;21:147-154.

Guidelines for Management[38]

- IDENTIFY PATIENTS AT RISK OF RFS
- Before initiation of feeds, check electrolytes, including potassium, calcium, phosphorus, magnesium, blood urea nitrogen, and creatinine
- Start refeeding at 50-75% of goal calories and increase to goal over 3-5 days
- Protein does not need to be restricted
- Rehydrate carefully, being careful not to fluid overload
- Monitor potassium, calcium, phosphorus, and magnesium levels frequently during first 4 days and replace appropriately

[38]Afzal, et al. *Clin Nutr*. 2002;21:515-520.

Baseline Replacements[38]

Potassium	2-4 mmol/kg daily
Phosphorus	0.3-0.6 mmol/kg daily
Magnesium	0.2 mmol/kg daily IV OR 0.4 mmol/kg daily orally

- Multivitamin and mineral supplementation
  - To supplement thiamine, zinc, and selenium
  - Iron usually not given during initial phase, as increased risk of infection and oxidative stress

[38]Adapted from Afzal, et al. *Clin Nutr*. 2002;21:515-520.

Summary: Principles of RFS

- Malnourished patients have altered metabolism
- Patients are severely intracellularly deficient in several electrolytes that are important in basic cell functions, including phosphorus, potassium, and magnesium
- Aggressive refeeding in the initial phase and rehydration can prove deadly if deficiencies are not anticipated, corrected, and monitored carefully
  - *Initial management should focus on correction of metabolic mechanisms and electrolyte repletion prior to initiating aggressive nutritional support*

Questions?

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Nutrition Assessment & Growth Charts: What do we Really Need to Know

Nutritional Goals

- Well-nourished children with adequate fat, muscle and organ development
- Normal body composition not limited by food intake
- Growth at genetic potential
- Normal pubertal development

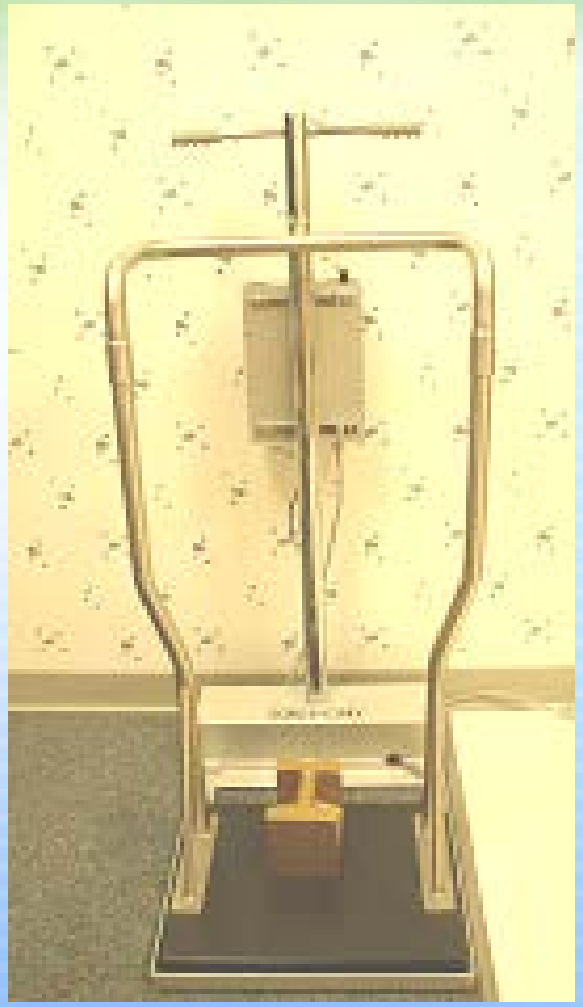
Overview

- Nutrition Assessment
  - History and physical examination including physical examination
  - Diet assessment: 24 hr food recall; 3 day diet record
  - Growth measurements
    - Traditional: weight, length/height, head circumference, arm anthropometry (UAC, TSF)
    - Alternative measures: lower leg length, arm span, etc
  - Laboratory tests
  - Bone age
  - DXA : bone health and body composition
  - Resting Energy Expenditure measurements
  - Subjective Global Assessment
- Calculations:
  - Body mass index: Preferred measure of weight for length/height; % Ideal body weight not recommended
  - Upper arm fat area, upper arm muscle area
  - Mid arm circumference/head circumference ratio
- Growth charts
  - NCHS, WHO, CDC, Neonatal (Olsen), disease specific

[1] Kanawati et al. *Nature.* 1970: 228:573-575.

Proper Anthropometric Techniques

- Use safe, reliable, accurate equipment
- Calibrate equipment regularly
  - daily for stadiometer with a calibration bar
  - weekly for electronic scales with calibration weights
  - weekly for calipers with a calibration bar
  - inspect tape measures for wear
- Reproducible measurements take time and sometimes require two people



Infant Weight

- Infants should be nude (without diapers) to the nearest 0.01 kg
- Children should be in light clothing and without shoes to the nearest 0.1 kg
- Wheelchair accessible scales are available - measure with and without the child in the wheelchair

Height

- Length - to the nearest 0.1 cm in children less than 2 years or in older children who can not stand
- Stature - to the nearest 0.1 cm in children (age $\geq$ 2 yr) who can distribute weight evenly on both feet and support their weight
- Measure without footwear
- Remove hair ornaments
- Heels, buttocks, shoulders and back of head should be against the stadiometer
- Position head in the Frankfurt plane
- Feet flat and heels together
- Legs straight and knees together

The Frankfurt Plane

- When measuring height, the head is in the Frankfurt plane when the horizontal line from the lower border of the orbit to the auditory meatus (ear canal) is parallel to the floor and perpendicular to the vertical backboard of the stadiometer
- When measuring recumbent length, the horizontal line is parallel to the fixed head piece and perpendicular to the backboard of the infantometer

Length

- Position head in the Frankfurt plane and against headboard
- Straighten and stretch legs so that knees are flat and foot is at a 90 degree angle with foot board
- Take three readings and average them

Head Circumference

- Remove hair ornaments
- Secure tape measure above supra-orbital ridge with one hand
- Slide the tape measure evenly around the back of the skull
- Adjust position until the maximum circumference is obtained
- Compress hair and skin to obtain the reading to the nearest 0.1 cm

Mid-Parental Height

- An indicator of genetic potential, so important for identification of growth failure
- Method 1
  - Falkner and Tanner 1986
  - For girls, subtract 13 cm from father's height
  - For boys, add 13 cm to mother's height
  - Average parental heights
  - Target height range: ± 10 cm for boys, ± 9 cm for girls
- Method 2
  - Tanner and Whitehead 1970
  - Boys: ([father's height (cm)+mother's height (cm)+13])/2 ±8.5
  - Girls: ([father's height (cm)+mother's height (cm)-13])/2 ±8.5

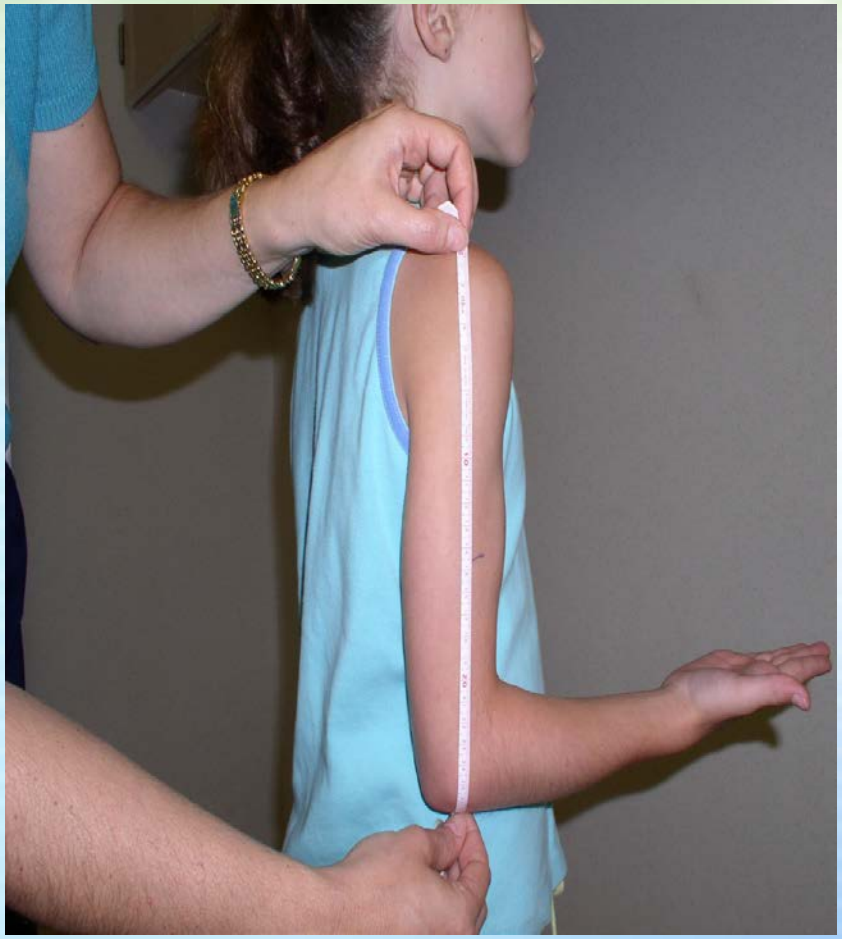
[2]Tanner & Whitehead. *Arch Dis Child.*1970;45:755-762.
[3]Falkner & Tanner eds.*Human Growth*.Vol 2;Plenum;1-22.

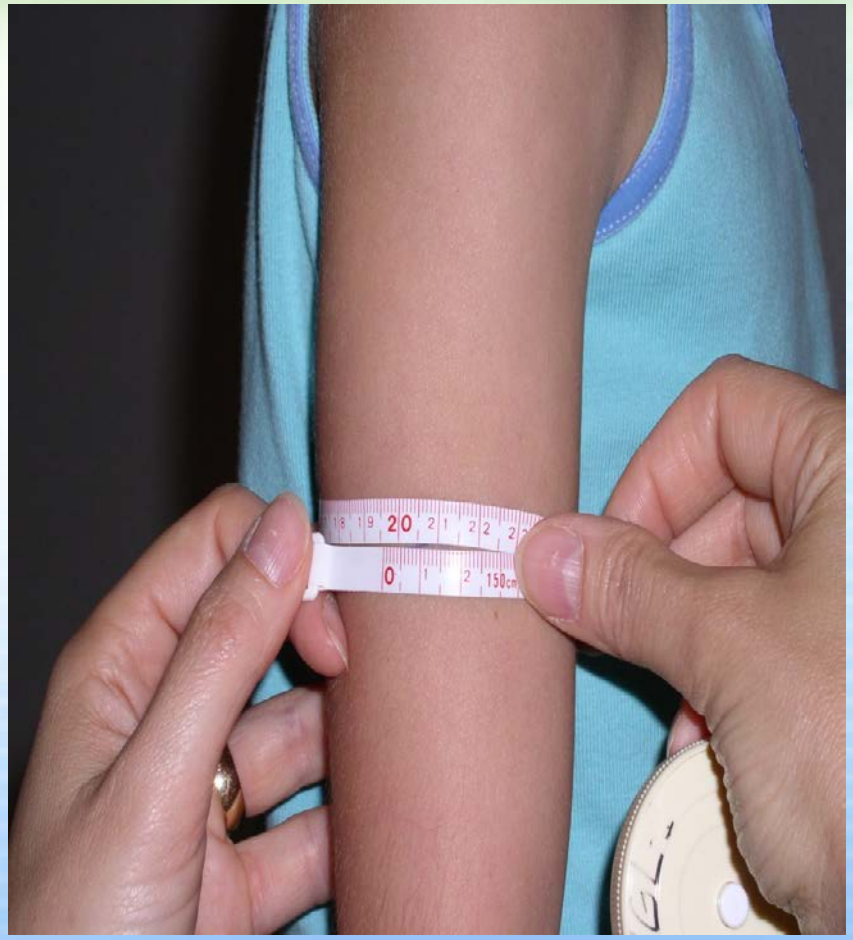
Upper Arm Anthropometry

- Good indicator of nutritional status
- Can calculate UAMA and UAFA which muscle mass and fat stores
- Good reference data
- Normal ranges based on NCHS reference data
- Correlate well with whole body measures

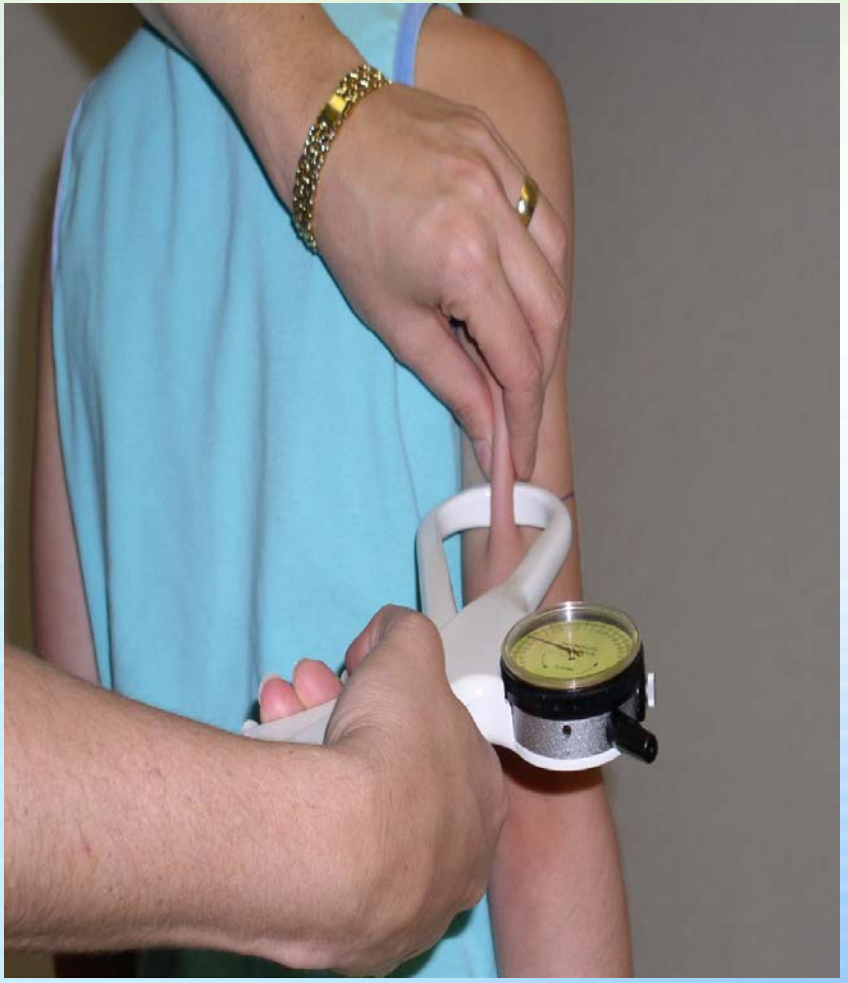
[4]Frisancho. *Am J Clin Nutr.* 1981;34:2540.

Mid-upper Arm Circumference





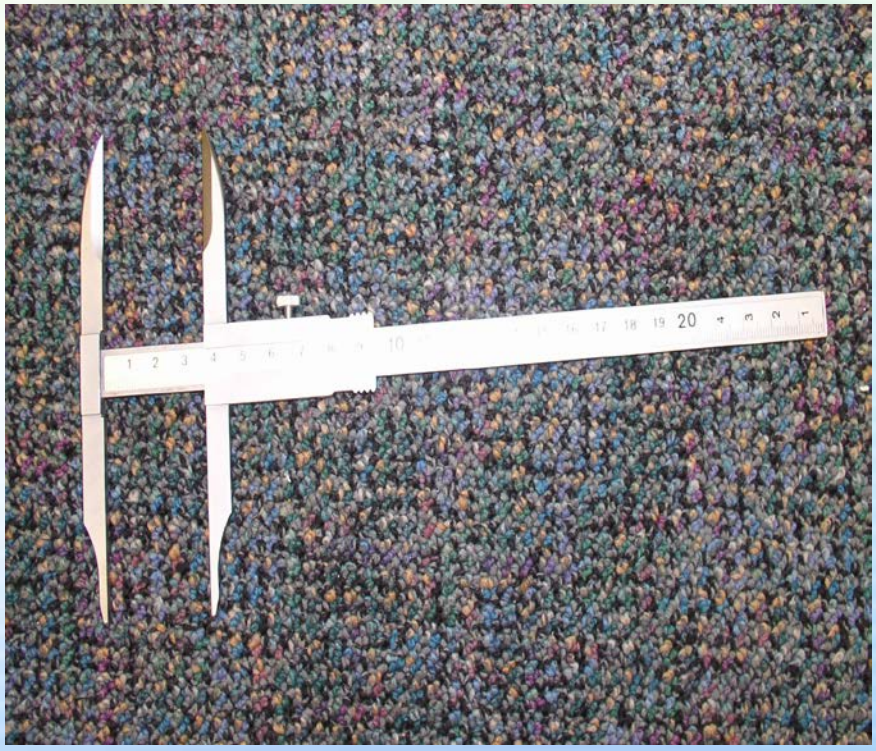
Triceps Skinfold



- Subject upright with the arm dangling and relaxed
- Measure at the midpoint of the upper arm at the level of the mark, centered over the posterior portion of the arm over the triceps muscle
- Count to 3 and take reading to the nearest 0.1 to 0.5 mm, depending on the calipers

Alternative Measures of Growth

- Upper limb
- Ulnar length
- Knee height
- Arm span
- Sitting height

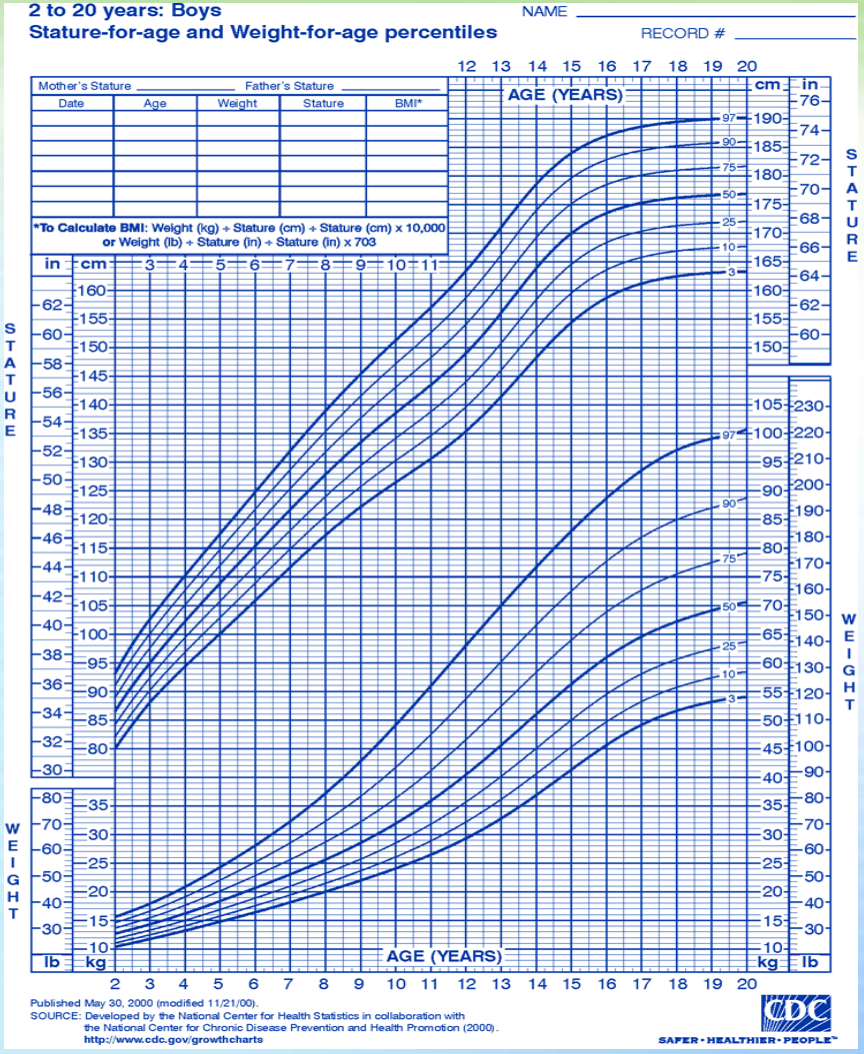


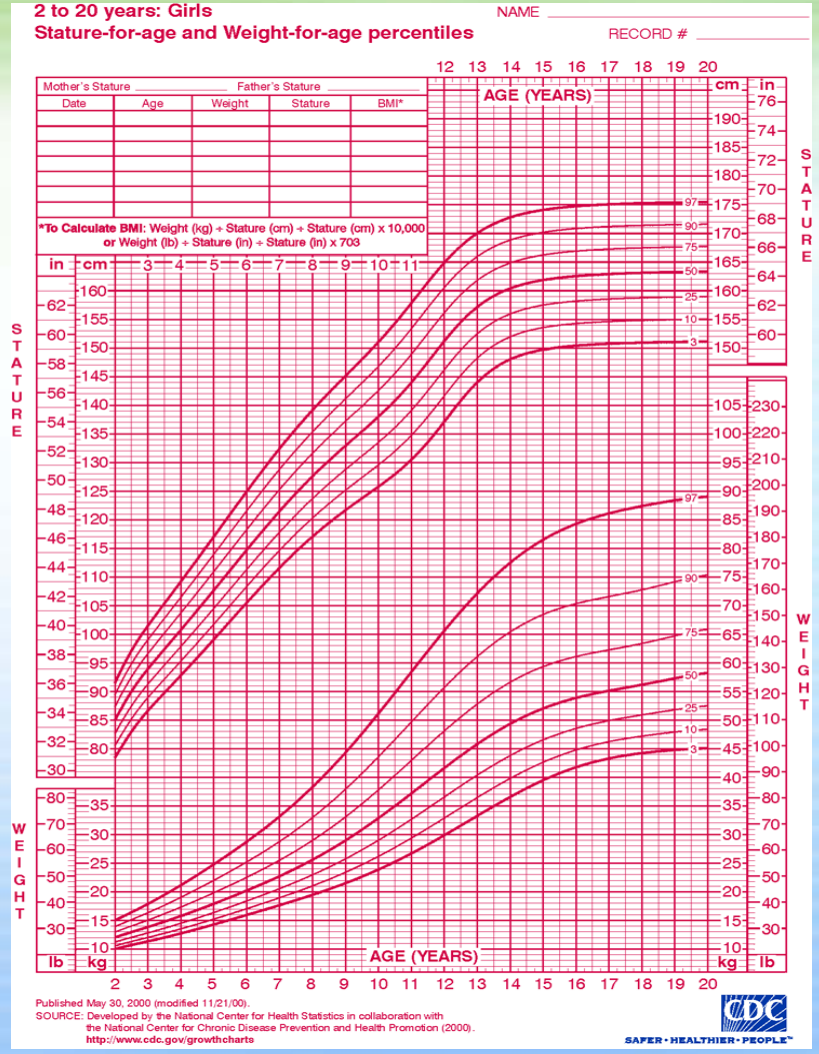
[5]Hibbert et al.*Thorax* 1988;43: 657–659. [6]Jarzem &Gledhill. *J Pediatr Orthop.1993;*13:761–765. [7]Cheng et al. *Clin Orthop.*1996;323: 22–30. [8]Parker et al. *Am J Respir Crit Care Med. 1996;*154:533–536. [9]Linderholm et al. *Acta Orthop Scand*. 1978;49:469–474. [10]Johnson et al. *J Am Diet Assoc* 1991;1283–1284. [11]Gauld et al. *Dev Med Child Neurol.* 2004;46(7)475-480. [12]Spender et al. *Dev Med Child Neurol* 1989; 31:206-214.

Growth Charts

- NCHS growth charts; late 70's; did not adequately represent early childhood growth
  - Longitudinal sample from birth to 3 years
  - Children of European ancestry only from a single community in the US.
  - Statistical approach was too limited to reflect the pattern and variability of growth
- CDC growth charts: 1970 to early 1990s from USA children; cross-sectional data
  - No data from birth to 2 mo,
  - Mixed feeding: 1/3 breastfed for 3 mo; Includes breastfed and formula fed infants, with representative birth weights
    - Multi-ethnic, multi-regional (74% Non-hispanic whiles, 14% Non-hispanic blacks, 9% Hispanics, 2% Asian, 1% Native American)
    - LBW infants included, VLBW excluded
    - Added 3rd and 97th percentiles
    - Extended age to 20 years
    - Created BMI charts for assessment of underweight and overweight
    - 85th percentile added to BMI charts to identify "at-risk" of overweight (85^{th} - 95^{th}%)

CDC Growth Charts





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For Children's Digestive Health & Nutrition

NASPGHAN Nutrition University

WHO Multicenter Growth Reference Study (MGRS)

- Breast feeding as norm; Complementary feeding choices
- Non-smoking mothers
- Single term birth, LBW infants not excluded
- Environmental conditions to support unconstrained growth, favoring growth at child's full genetic potential . SES, <1500 m altitude, medical care
- International sampling (1997-2003): Brazil, Norway, Ghana, Oman, India, United States
- ~ 8500 children
- With and height velocity curves
- Birth to 5 years
  - Longitudinal Sample: 21 visits on weeks 1, 2, 4, & 6, monthly from 2 to 12 months, bimonthly to 24 months
  - Cross-sectional sample: children aged 18-71 months

[13]de onis et al. *Food Nutr Bull*. 2004 Mar;25(1 Suppl):S15-26.
www.cdc.gov/growthcharts/WHO_charts.htm.

WHO: Length and Weight Velocity for Boys

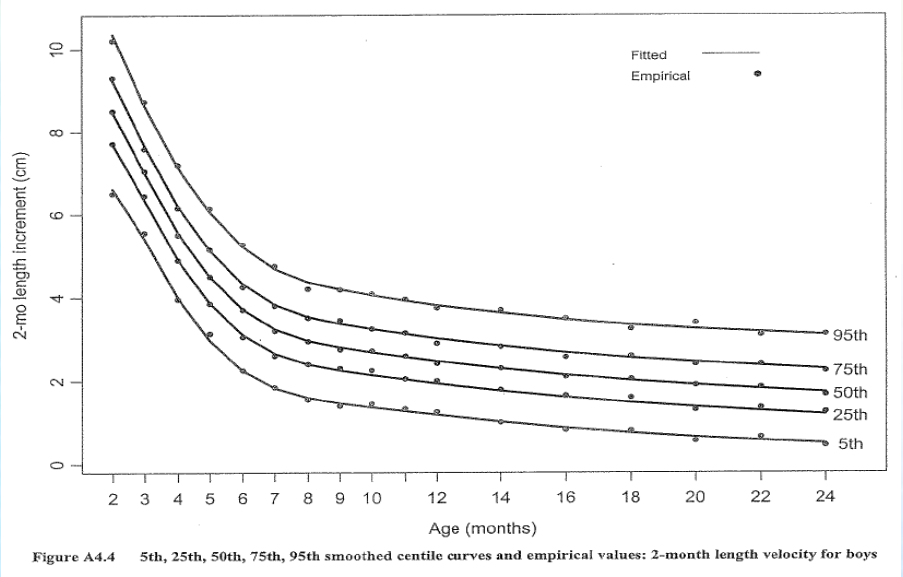


Figure A4.4 5th, 25th, 50th, 75th, 95th smoothed centile curves and empirical values: 2-month length velocity for boys

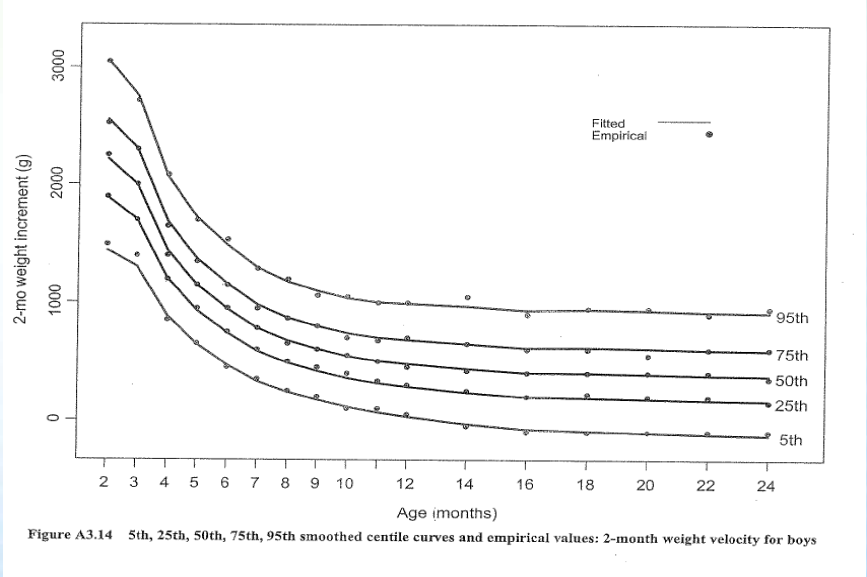


Figure A3.14 5th, 25th, 50th, 75th, 95th smoothed centile curves and empirical values: 2-month weight velocity for boys

Comparison of Growth Charts

Length not significantly different

WHO 2006	CDC 2000
Optimal growth	Conditions not optimal
Faster gain 1st 3 mo	Slower gain 1st 3 mo
Slower gain after	Faster gain after
If cross % risk obesity intervene PRN	BF infants fall off curves
BF infants follow curves	Over Dx underwt/age
Lower Dx underwt/age	Higher Dx overwt/length
Lower Dx overwt/length	

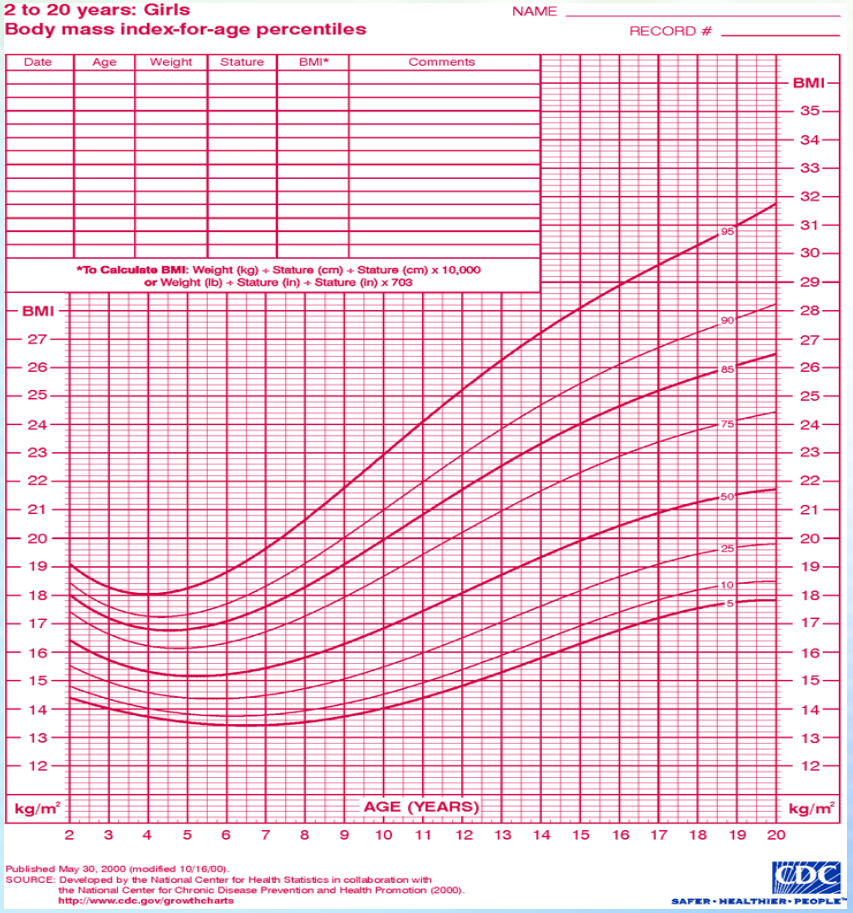
How to Calculate Body Mass Index

$$BMI = \left(\frac{\text{Weight in Pounds}}{(\text{Height in inches}) \times (\text{Height in inches})} \right) \times 703$$

$$BMI = \left(\frac{\text{Weight in Kilograms}}{(\text{Height in meters}) \times (\text{Height in meters})} \right)$$

Or use the BMI calculator:
www.cdc.gov/nccdphp/dnpa/bmi/calc-bmi.htm
Or tables:
www.cdc.gov/nccdphp/dnpa/growthcharts/bmi_tools.htm

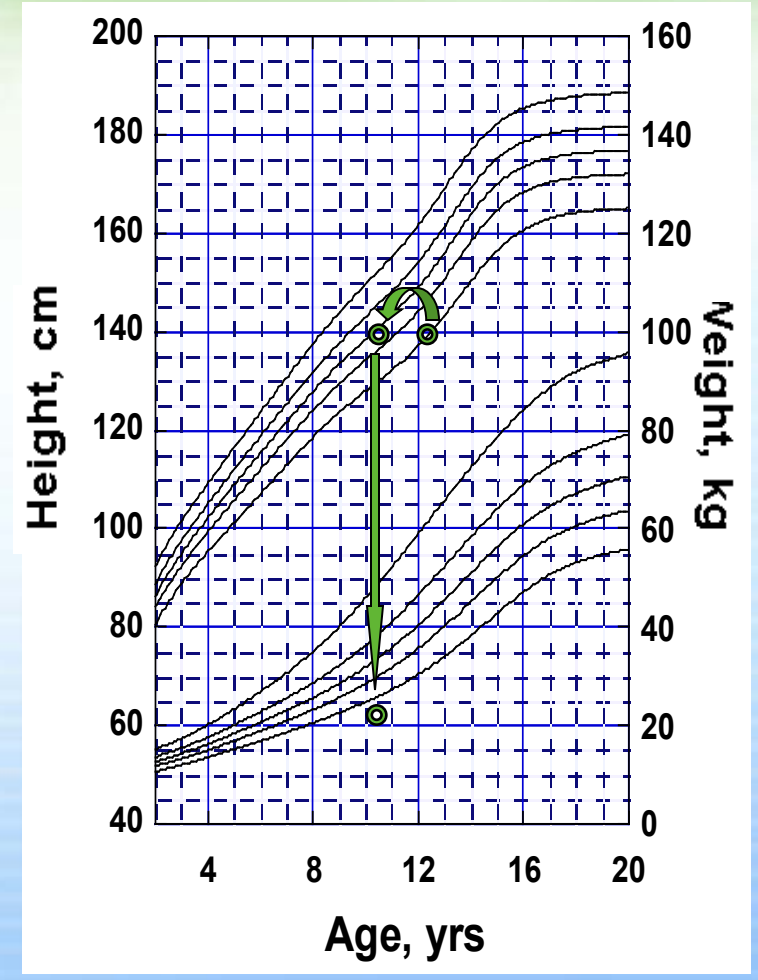
CDC 2000 Growth Chart: Body Mass Index (Girls for-age)



- Median BMI changes with age
- Distribution changes with age
- Use for monitoring over time

Percent Ideal Body Weight: Height Age

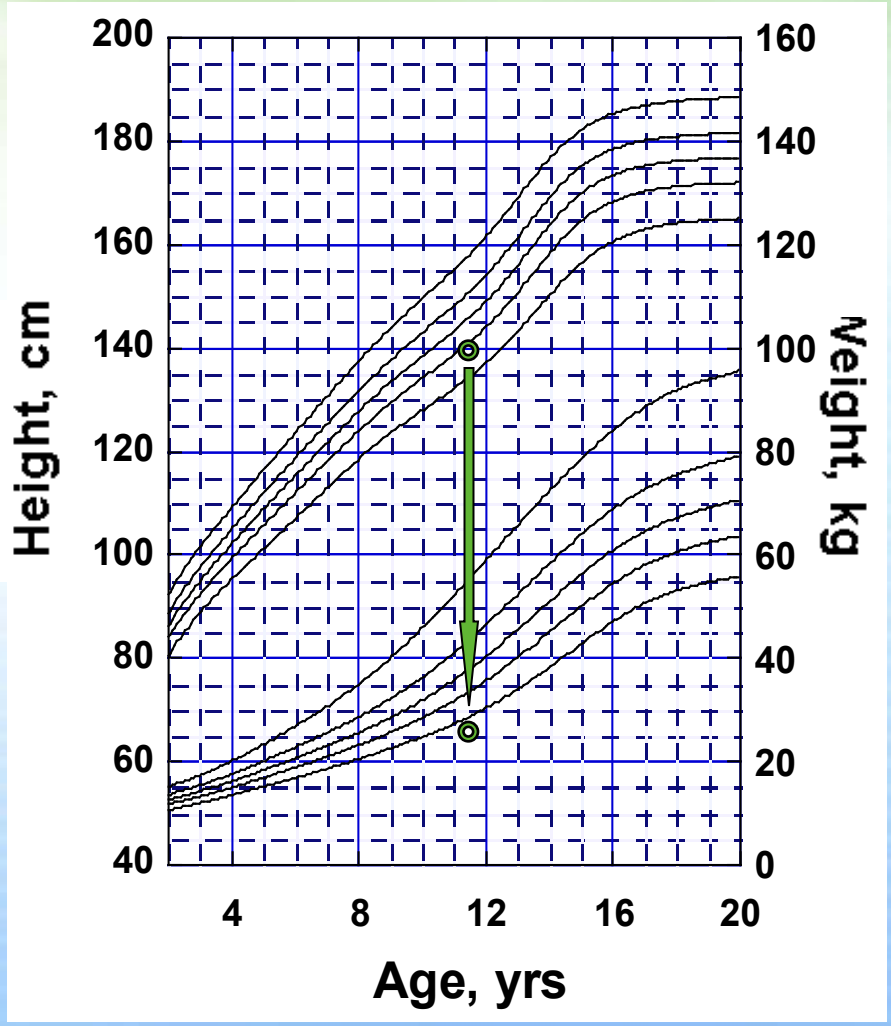
- Limitations:
  - Crosses age and puberty groups to find height age
  - Weight-height relationship is dependent on development
  - Assumes that children at the 50th %tile for height have a mean weight at the 50th %tile for weight



[14]Mclaren et al; *Lancet.* 1975;2:219-20.

Percent Ideal Body Weight: Height Percentile

- Limitations:
  - Assumes that percentile distributions for height correspond to the percentile distributions for weight
  - Doesn't reflect real height-weight combinations in children



[15]Moore et al. *Nutr Res.* 1985;5:797-9.

Discussion

- The two weight-for-height indexes, %IBW and BMI % show good agreement for children of average stature, and particularly for children < 10 years of age
- %IBW underestimates the severity of malnutrition in short children and overestimates in tall children
- %IBW assumes that the weight value corresponds to the same percentile ranking as the child's height-for-age
  - This assumption does not hold for children with short or tall stature
  - BMI % better represents the actual weight and height relationships found for children in the reference population - also reflects the actual SD scores

Growth Charts: Premature Infants

Intrauterine:

- Lubcheno 1966: classify AGA, SGA, LGA
- Olsen 2010: classify AGA, SGA, LGA; 23-41 wk PMA

Postnatal:

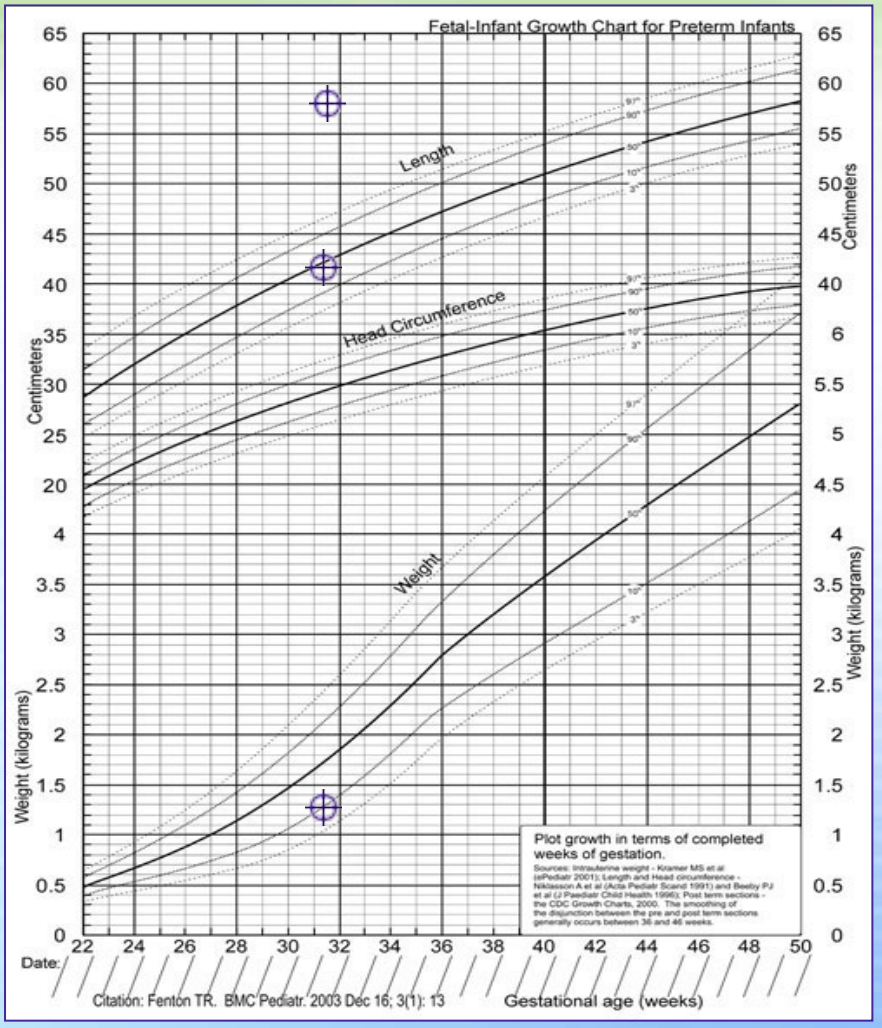
- Ehrenkranz 1999: individualized
- IHOP 1999: 2-38 months corrected age, LBW, VLBW M/F

Intrauterine & Postnatal:

- Babseon/Benda 1976: 26 week PMA-12 mo corr
- Fenton 2003: 22wk to 50 wk PMA

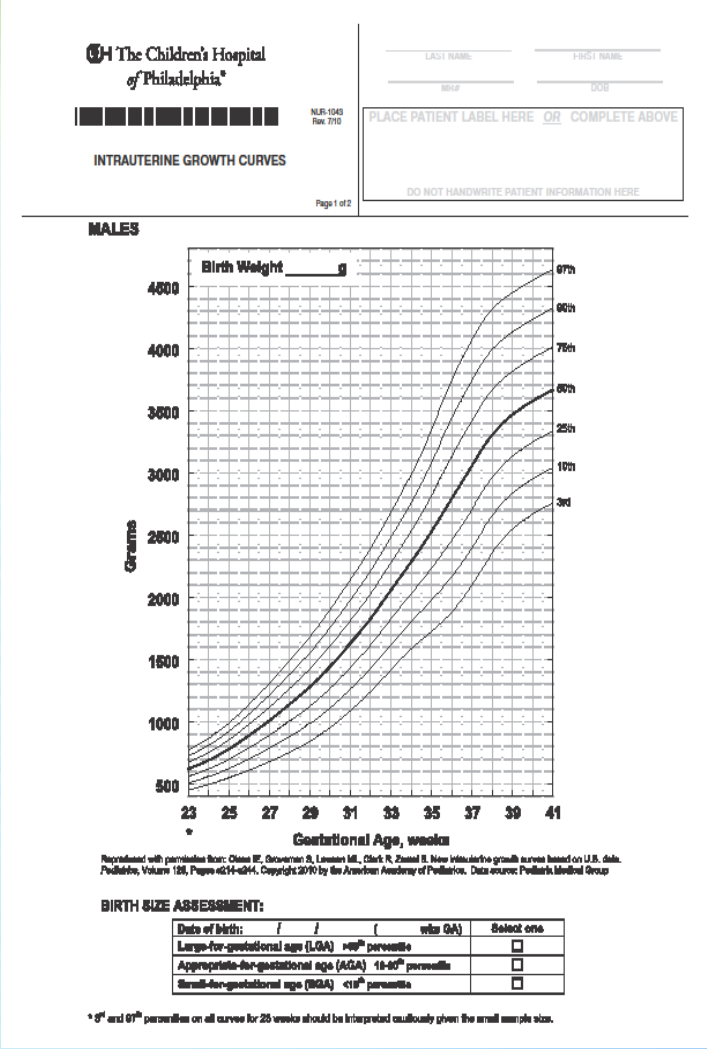
[16]Lubcheno et al, *Pediatrics.* 1966; 37:403-408. [17]Ehrenkranz et al. *Pediatrics.*1999; 104:280-289. [18]Weaver. *Eur J Clin Nutr.* 2011;65:3-9. [19]Olsen et al. *Pediatrics.* 2010;125:214-224. [20]Stettler et al. *Curr Opin Clin Nutr Metab Care.* 2010;13:294–299. [21]Centers for Disease Control and Prevention. *Morb Mortal Wkly Rep.* 2010;59:1-13. [22]Bertino et al. *Ped Endocrinol Rev. 2*008 ;6(1):9-13. [23]Babson et al. *J Pediatr.*1976,89:814-820. [24]Fenton. *BMC Pediatrics.* 2003, 3:13.

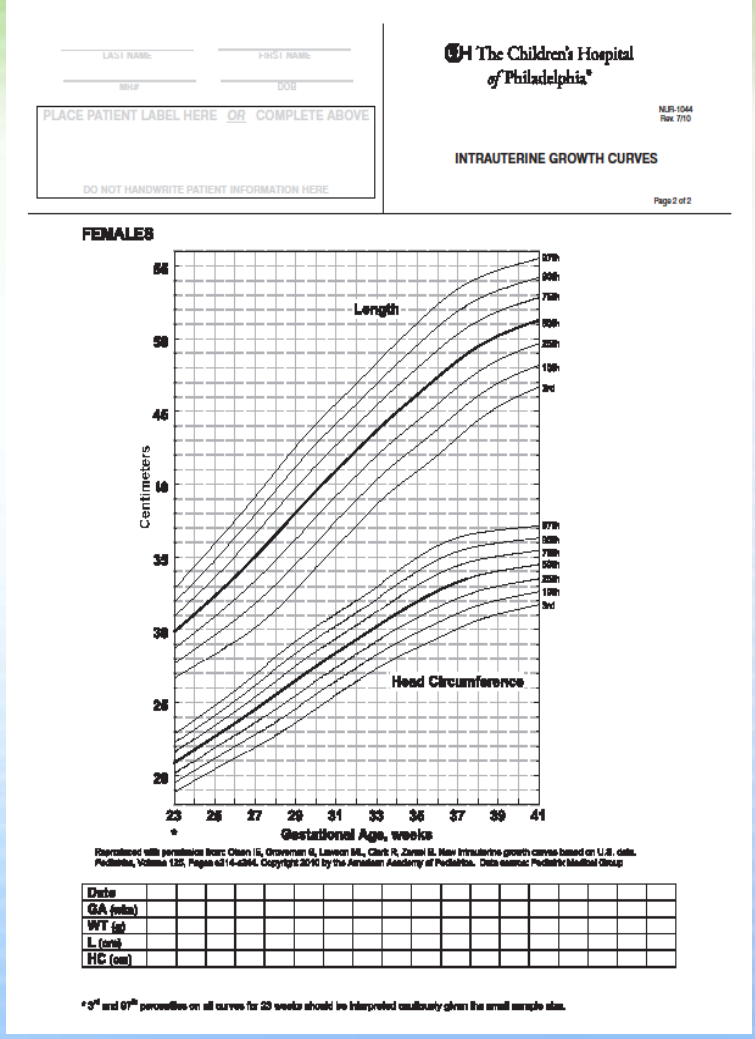
Fenton Growth Chart



[24]Fenton. *BMC Pediatrics.* 2003;3:13

Olson Growth Chart





[19]Olsen et al. *Pediatrics.* 2010;125:214-224.

Comparison of Premature Growth Charts

Fenton 2003

- Data set : Canada, Sweden, Australia
- 1982-1996
- Unisex
- n= ~4300
- Historical data
- Post term data CDC
- 22→50 wk PMA
- Primarily Caucasian
- NOT used to classify AGA/SGA/LGA

Olsen 2010

- Data set: USA
- 1998-2006
- Sex specific
- n= ~250,000
- Actual measurements
- Ends at term (41 wks)
- 23-41 wk PMA
- Racially diverse
- Used to classify AGA/LGA/SGA
- Follow growth to term

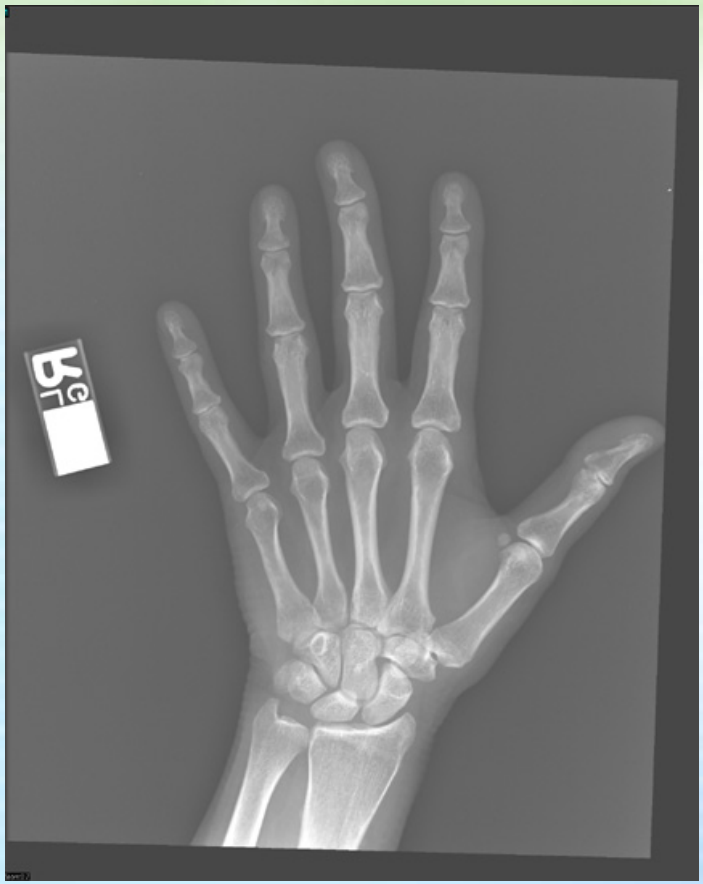
[24]Fenton. *BMC Pediatrics.* 2003;3:13. [19]Olsen et al. *Pediatrics.* 2010;125:214-224.

Disease Specific Growth Charts

- Down syndrome
- Turner's syndrome
- Noonan's syndrome
- Cerebral palsy
- Myleomeningocele
- Prader-Willi syndrome
- Neurofibromatosis type 1
- Achondroplasia
- Klinefelter syndrome
- William's syndrome
- Duschene's Muscular Dystrophy

[25]Cronk et al. *Pediatr* 1988;81(1):102-110. [26]Greenswag et al. *Management of Prader Wili Syndrome*, Springer Verlag.1988. [27]Ekvall. *Pediatric Nutrition in Chronic Diseases and Developmental Disorders*. Oxford University Press;1993; [28]Horton et al.*J Pediatr*.1978; 93(3): 435-438. [29]Lyon et al. *Arch Dis Child.* 1985;60:932-935. [30]Witt D et al. *Clin Genet.*1986;30:150-153,:[31]Morris et al. *J Pediatr* 1988; 113-318-26. [32]Krick et al. *J Am Diet Assoc.*1996;96:680-685. [33]Willig et al. *Dev Med Child Neurol.*1993;35:1074-1082. [34]Clementi et al. *Am J Med Genêt*. 1999;87(4):317-323 28.

Bone Age



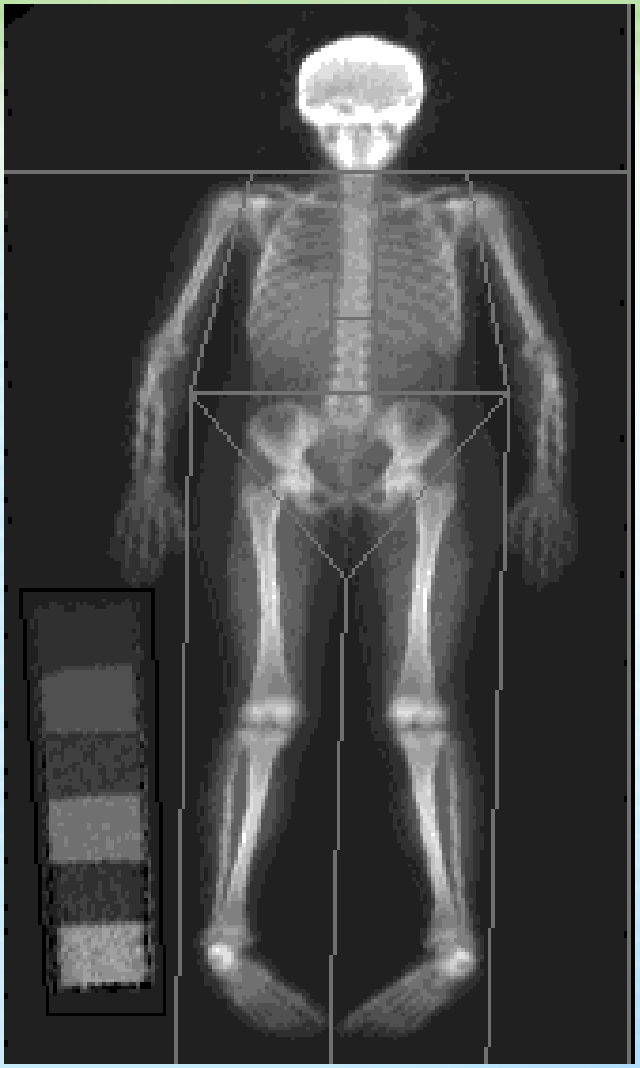
- Gruelich and Pyle 1950
-Tanner and Whitehouse 1983-
- Read by radiologist and endocrinologist
- drawbacks

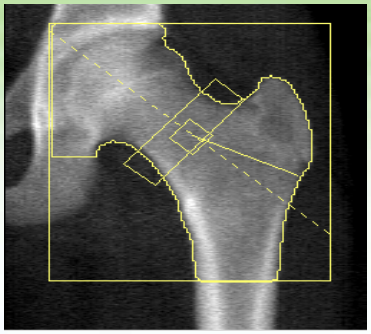
[35]Greulich & Pyle. *Radiographic Atlas of Skeletal Development of the Hand and Wrist*. Stanford, California: Stanford University Press, 1950. [36]Tanner et al, *Assessment of skeletal maturity and prediction of adult height*, 2nd Ed. Academic Press. [37]Loder et al, *Am J Dis Child 1993*;147:1329-1333. [38]Bull et al. *Arch Dis Child* 1999; 81:172-173.

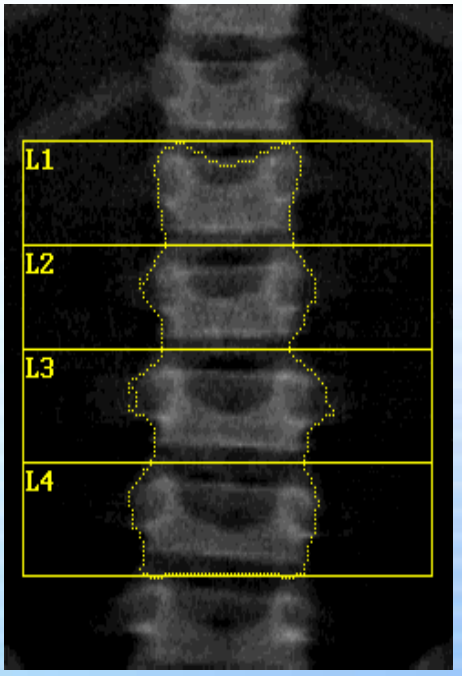
Laboratory Tests

- Blood
  - CBC with differential
  - Electrolytes: BMP; ionized calcium, magnesium, phosphorus
  - Protein status: albumin, prealbumin, BUN
  - Minerals: ferritin, iron, TIBC, transferrin, transferrin saturation, serum zinc
  - Vitamins: retinol, retinyl palmitate, 25 hydroxy vitamin D, serum or RBC folate, PIVKA11, alpha-tocopherol levels, Vitamin C, serum B12, MMA
  - Trace elements
  - Others: carotene, lipid panel, TSH, free T4, IGF BP3, somatomedin C, CRP, PTH, triene to tetraene ratio
- Urine: creatinine/height index, calcium/creatinine ratio, protein
- Stool: coefficient of fat absorption

DXA : Dual Energy X-ray Absorptiometry







- Age 3 years and older
- Z-score vs. T-score
- Body composition
- Other scans: forearm, distal femur
- Follow bone health over time
- PQCT

Classification of Nutritional Status

- Need multiple growth data points
- In general: weight falls off before length; last parameter to suffer is head circumference
- Can have crossing of percentiles between 9 and 18 months
- Overweight: BMI>85th;Obese: BMI>95th.
- Malnourished: ?BMI <5th or <10th
- Use WHO weight velocity charts in infants
- Classifications of malnutrition: Waterlow, WHO, marasmus, kwashiorkor
- Subjective global assessment
- Frequency of growth measurements: AAP Recommendations for preventive pediatric health care

Micronutrients

- Vitamins:
  - Fat Soluble:
    - A, D, E, K
  - Water soluble:
    - thiamine, riboflavin, niacin, pyridoxine, cobalamin, folate, vitamin C, pantothenic acid, biotin
- Minerals:
  - calcium, phosphorus, magnesium, iron
- Trace elements:
  - zinc, copper, manganese, selenium, iodine, chromium, cobalt, molybdenum, arsenic, nickel, silicon, vanadium, aluminum

Fat-Soluble Vitamins

- Intestinal absorption dependent of pancreatic enzymes & bile acids
- Need normal fat digestion, absorption and transport
- Deficiency seen in CF, celiac disease, SBS, ileal disease, cholestatic liver disease or inadequate intake or light exposure (D)

Water-Soluble Vitamins

- Deficiencies rare in formula fed infants & in breast fed infants of mothers on a normal diet
- Limited whole body stores & lack of endogenous synthesis: risk of deficiency
- Inborn errors of metabolism
- Predisposing conditions: celiac disease, Crohn's disease, CF, food refusal, anorexia nervosa, HIV

Trace Elements

- Components of many enzyme systems & integral components of metalloenzymes
- Cofactors for enzymes activated by metal ions
- Effects of deficiency are most severe during periods of rapid growth – important to pediatricians
- Trace element shortage in parenteral nutrition
- 13 trace elements: iron, zinc, copper, fluoride, iodine, selenium, manganese, chromium, cobalt, molybdenum, nickel, silicon, vanadium

Micronutrient Deficiencies: Vitamins

Vitamin	Deficiency
Vitamin A	Night blindness, xerophthalmia, keratomalacia, poor bone growth, impaired immunity, follicular hyperkeratosis
Vitamin D	Rickets, osteomalacia
Vitamin E	Hemolytic anemia, hyporeflexia, spinocerebellar & retinal degeneration
Vitamin K	Bleeding, poor bone health
Thiamine	Beriberi, neuritis, edema, cardiac failure, hoarseness, anorexia, restlessness, aphonia
Riboflavin	Photophobia, cheilosis, glossitis, poor growth, corneal vascularization
Niacin	Pellagra, dermatitis, diarrhea, dementia
Pyridoxine	Depression, fatigue, hypotension, muscle weakness, abdominal pain
Cobalamin	Pernicious anemia, neurologic deterioration
Folate	Megaloblastic anemia, impaired cellular immunity, irritability, paranoid behavior, neural tube defects
Vitamin C	Bleeding gums, perifolicular hemorrhage, scurvy

Micronutrient Deficiencies: Minerals

Mineral	Deficiency
Calcium	Tetany; osteopenia, seizures
Phosphorus	Osteopenia
Magnesium	Seizures
Iron	Anemia, neurological and developmental (cognitive and motor) deficits, increased absorption of Pb and Mn

Micronutrient Deficiencies: Trace Elements

Trace element	Deficiency
Zinc	Anorexia, altered taste, growth retardation, delayed puberty, impaired wound healing, skin lesions
Copper	Anemia, growth retardation, osteoporosis, neutropenia, decreased pigmentation
Manganese	In animals growth retardation, ataxia, bone abnormalities
Selenium	Cardiomyopathy
Chromiun	Impaired glucose utilization
Iodine	Goiter, impaired mental function, developmental delay

Summary

- There is no single direct measure of nutritional status
- Growth chart with multiple data points is very informative
- Need to use multiple measures including subjective global assessment
- Use age appropriate growth charts: WHO, CDC and Olsen
- Look for possible micronutrient deficiencies in at risk patients

Following Slides for Reference Only

Vitamin A

- Sources: fortified milk, liver, egg, cheese, yellow fruits and vegetables
- Deficiency: night blindness, xerophthalmia, keratomalacia, pigmentary retinopathy, poor bone growth, impaired resistance to infection (measles), follicular hyperkeratosis
- Assessment: serum retinol and RBP; retinyl esters for toxicity
- At risk: malnutrition, malabsorption
- Treatment: water soluble preparations in patients with fat malabsorption

Vitamin D

- Sources: fatty fish, liver, eggs, fortified milk, OJ and cereals; best source is the sun
- Deficiency:
  - Usually asymptomatic
  - Hypocalcaemia, hypophosphatemia, tetany
  - Rickets: craniotabes, enlarged costochondral junctions, bowing of legs, enlarged wrists
  - Osteomalacia - vague symptoms, bone pain, achiness, muscular weakness, feeling of heaviness in the legs, chronic musculoskeletal pain, fatigue
  - Associated with cancer, cardiovascular disease, hypertension, stroke, diabetes, Multiple Sclerosis, Rheumatoid Arthritis, IBD, Periodontal disease, macular degeneration, depression, propensity to fall, influenza/other winter-time infections, Aatism
- Assessment:
  - Calcium, phosphorus, intact PTH
  - Vitamin D (25-OH) level depends on: latitude, season, air pollution, atmospheric ozone, cloud cover, sunblock, obesity, melanin content, clothing covering the body
- At risk: limited sun exposure, liver disease, CF, pancreatic disease, IBD
- Treatment: cholecalciferol, ergocalciferol preparations

Vitamin E

- Requirement increased by large amount of PUFA
- Sources: sardines, green leafy vegetables, vegetable oils, wheat germ, whole grains, butter, liver, egg yolk
- Deficiency:
  - hemolytic anemia in preterm infants, hyporeflexia spinocerebellar and retinal degeneration; peripheral neuropathy, proximal muscle weakness, ophthalmoplegia, cognitive and behavioral abnormalities
  - Familial isolated vitamin E deficiency: congenital deficiency of a hepatic transport protein.
  - Neurological effects (ataxia) may be irreversible if untreated
- Assessment: serum alpha-tocopherol, ratio of serum alpha tocopherol to total lipids
- At risk: biliary atresia, chronic cholestatic liver disease, CF, Pancreatic disease
- Treatment: water soluble form best; may improve absorption of other fat soluble vitamins & drugs if given concurrently

Vitamin K

- Synthesized by intestinal bacteria; antagonized by Coumadin, salicylates & some antibiotics
- Sources: cow milk, green leafy vegetables, pork, liver, soybean oil
- Assessment: PT, Factor levels: 2,7,9,10, PIVKA II
- Deficiency:
  - bleeding, low BMD
  - Newborns: bleeding from GIT, umbilicus, circumcision; increased risk of hemorrhagic disease due to vitamin K deficiency (poor placental transport of vitamin K, decreased number of gut bacteria)
- At risk: newborns, fat malabsorption, chronic liver disease, highly restricted diets, after bariatric surgery, CF, cholestatic liver disease
- Treatment:
  - All newborns get prophylactic dose
  - Maternal vitamin K administration may prevent IVH in preterm infants

Thiamine

- Sources: enriched cereals & breads, lean pork, whole grains, legumes, in small amounts in most nutritious foods
- Causes:
  - Inadequate intake, malabsorption, excessive loss, defective transport,
  - Mother at risk for deficiency: poor thiamine intake, alchoholic, GI disease, hyperemesis gravidarum, HIV infection
- Assessment: transketolase activation test, TPP levels
- At risk: infants born to deficient mothers, food fads, anorexia nervosa, gastric bypass surgery, chronic dialysis, congestive heart failure, chronic TPN
- Deficiency
  - Beriberi:
    - Dry: progressive, symmetrical peripheral neuropathy resulting in increasing weakness, muscle wasting, difficulty walking, ataxia, painful paresthesias & loss of DTR
    - Wet: cardiac failure and edema
    - Infantile: breast fed child whose mother has a subclinical thiamine deficiency. Sudden onset of shock in a previously well child between 2-3 months of age & preceding by hoarse, weak cry, poor feeding and vomiting
  - Wernicke encephalopathy: ophathlamoplegia, nystagmus , ataxia in addition to altered consciousness . Can be seen in infants & children
  - Other: hoarseness, anorexia, restlessness, aphonia
- Treatment

Riboflavin

- Sources: meat, dairy products, eggs, green vegetables, whole grains, enriched breads & cereals
- Deficiency:
  - Pure deficiency: rare. Accompanied by other B complex vitamins deficiencies because of riboflavin's role in the metabolism of folate, pyridoxine & niacin
  - Mild: very non specific symptoms.
  - Severe: pharyngitis, angular stomatitis, photophobia, cheilosis, glossitis, or magenta tongue, seborrheic dermatitis in nasolabial folds, flexures of extremities ad genital areas, corneal vascularization, poor growth
  - Thyroid and adrenal insufficiency can impair synthesis of riboflavin cofactors & may precipitate the deficiency
- Assessment: 24 hour urine for riboflavin; RBC glutathione reductase activity coefficient
- At risk: poor socioeconomic status with decreased meat or dairy intake; breast fed infants after weaning, neonates undergoing phototherapy, PEM, celiac disease, SBS, CF
- Treatment

Niacin

- Sources: milk, eggs, poultry, meat, fish, whole grains, enriched cereals & grains
- Assessment: 24 hour urine collection of N1-methylnicotinamide, RBC NAD & NADP concentrations
- At risk: malnourished individuals in developing countries, homeless, Crohn's disease, anorexia nervosa, INH therapy, long term anticonvulsants
- Deficiency: observed only with use of antagonists
  - Pellagra or rough skin in Italian
  - Dermatitis, diarrhea, dementia
  - Skin: painful erythema in sun exposed areas which progress to exudative rash – vesicle and bullae formation. Affected skin becomes rough hard and scaly. Hair and nails are spared
  - GI: glossitis, angular stomatitis, cheilitis, diarrhea 30-50 % of patients
  - Neuro: insomnia., fatigue, nervousness, irritability, depression, mental dullness, apathy, memory impairment & then dementia to death
  - Hartnup disease: disorder of neutral amino acids transport – malabsorption of tryptophan
- Treatment:

Pyridoxine

- Sources: liver, fish, meat, whole grains, legumes, potatoes, banana, eggs
- Deficiency:
  - Isolated deficiency is rare because its metabolism is dependant on adequate levels of riboflavin, niacin and zinc
  - Early 1950s: no pyridoxine in infant formulas – seizures
  - Clinical: irritability, depression, dermatitis, glossitis, angular stomatitis, cheilosis, peripheral neuritis
  - Infants: irritability, convulsions, microcytic anemia
  - Pyridoxine dependant seizures: autosomal recessive disorder intractable seizures due o decreases GABA production
  - Vitamin B6 responsive anemia – microcytic hypochromic
  - Homocystinuria
- Assessment:
  - 24 hour urine for 4-pyridoxic acid
  - Plasma PLP levels
- At risk: malnourished children in developing countries, childhood leukemia & chronic renal failure
- Treatment

Cobalamin and Folate

- Cobalamin
  - Sources: meat, fish, poultry, cheese, milk, eggs, vitamin B12 fortified soy milk
  - Deficiency: Pernicious anemia: macrocytic megaloblastic anemia, Neurological deterioration: ataxia, muscle weakness, spasticity, incontinence, hypotension, vision problems, dementia, psychoses mood disturbances, Methyl-malonic acidemia, Neural tube defects in infants born to deficient mothers, Number of inborn errors of metabolism that are B12 responsive, Imerslung-Rasbeck syndrome: familial selective B12 malabsorption
  - Assessment: elevated homocystine levels, MMA levels, cobalamin levels
  - At risk: breast fed infants of vegan mothers, infants on macrobiotic diets, gastric or ileal resection, PKU
  - Treatment: not always reversed by parenteral B12; use parenteral administration if having malabsorption
  - Interference from OCP, antiepileptic drugs & alcohol
- Folate
  - Sources: meats, liver, leafy green vegetables, oranges, cantaloupe, seeds, fortified breads and cereals
  - Supplemental folate is better absorbed than folate naturally present in food
  - Deficiency: Megaloblastic anemia, Impaired cellular immunity, Irritability, paranoid behavior, Neural tube defects in fetus of pregnant women; Cerebral folate deficiency: auto- antibodies prevent the transfer of folate from the plasma to the CSF
  - Assessment: serum or plasma folate (short term) or RBC folate (long term)
  - At risk: Crohn's disease, HIV infection, chronic dialysis
  - Treatment: oral daily supplements

Vitamin C

- Sources: papaya, citrus fruits, tomatoes, cabbage, potatoes, cantaloupe, strawberries
- Deficiency
  - osmotic diarrhea
  - bleeding gums
  - perifollicular hemorrhage
  - frank scurvy: painful bones, arthropathy
- Assessment: WBC ascorbate levels measures tissue reserves
- At risk: children who eat very few fruit and vegetables; LBW infants are born to deficient moms
- Treatment: oral, IM or IV

Pantothenic Acid and Biotin

- Biotin
  - Deficiency only with large intake of raw egg white (avidin irreversibly binds biotin) or during TPN
  - Action: coenzyme: acetyl-coA carboxylase & other carboxylases
  - Sources: liver, egg yolk, soybeans, milk, meat
  - Deficiency: seen in kids given biotin free TPN. hypotonia & severe exfoliative dermatitis, anorexia, nausea, pallor, alopecia, myalgias, parasthesias
  - Assessment: urine collection
  - At risk: biotin free TPN, children given large amounts of undercooked eggs, chronic anti- convulsants, inborn errors of metabolism

- Pantothenic acid
  - Sources: organ meats, yeast, egg yolk, fresh vegetables, whole grains, legumes
  - WW II prisoners: toes numb and painful burning sensation in their feet relieved by panothenate
  - Deficiency: headache, fatigue, insomnia, Paresthesias of hands & feet, muscle weakness, abdominal pain, Increased sensitivity to insulin
  - Treatment

Zinc Deficiency

- Absorbed in the intestine by active transport
- Acrodermatitis enteropathica: mutation in ZIP4 zinc transporter
- Overdosing of zinc lead to copper deficiency
- Zinc in human milk is more bioavailable than in formula
- Sources: oysters, liver, meat, cheese, legumes, whole grains
- Clinical: anorexia, hypogeusia, retarded growth, delayed sexual maturation, impaired wound healing, skin (acro-orofacial) lesions, affects prenatal growth, increased susceptibility to infections
- Assessment: plasma or serum zinc; hair zinc concentration
- At risk: preterm, CF, Crohn's disease sickle cell disease
- Treatment: supplement with 1 mg/kg/day; improvement in rash in 4-5 days

Copper Deficiency

- Sources: shellfish, meat, legumes, nuts, cheese
- Assessment: serum copper and ceruloplasmin, hair copper, RBC superoxide dismutase; infection raises levels
- At risk: preterm, rapid growth, malabsorption, malnutrition
- Deficiency
  - :Hypochromic anemia: low concentrations of ceruloplasmin or feroxidase needed to incorporate iron into HB
  - Retarded growth, osteoporosis, neutropenia, depigmentation hair and skin, impaired immunity
  - Menke's syndrome: soon after birth, pallor, anemia, steely hair and progressive neurological deterioration; defective protein is a P type adenosine triphosphate ATP7A and copper accumulates in the enterocyte
  - Aceruplasminemia; normal copper status, severe iron deficiency due to decreased release of iron from stores
  - Iron absorption is decreased in copper deficiency due to decreased activity of copper dependant ferroxidase in the intestine which helps with iron uptake
- Treatment

Trace Elements: Manganese and Selenium

- Manganese
  - Sources: nuts, whole grains and tea
  - Deficiency:
    - Humans: none
    - Animals: growth retardation, ataxia of newborn, bone abnormalities, reduced fertility
  - Assessment: blood & serum levels
  - Treatment
- Selenium
  - Sources; seafood meat, whole grains
  - Children with goiter: Se deficiency limits response to iodine supplementation
  - Deficiency: Keshan cardiomyopathy (? low Se in soil); not supplemented chronic TPN; macrocytosis and loss of hair and skin pigmentation
  - Assessment: serum glutathione peroxidase (short term status, RBS glutathione peroxidase (long terms status) serum Se
  - At risk: LBW, HIV infection
  - Treatment

Trace Elements: Chromium and Iodine

- Chromium
  - Sources: meat, cheese, whole grains, brewer's yeast
  - Deficiency:
    - Humans: impairment of glucose utilization; seen in chronic TPN
    - Animals: impaired growth, disturbances protein & lipid metabolism
  - Assessment: only reliable indicator is demonstration of beneficial effect of chromium supplement
  - At risk: PCM
  - Treatment
- Iodine
  - Deficiency: uncommon in USA due to supplementation
  - Children with goiter do not respond to iodine supplementation until given iron
  - Need adequate selenium status to respond to iodine supplementation
  - Treatment

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Parenteral Nutrition

Parenteral Nutrition – History[1,2]

- Late 1930s
  - *Positive nitrogen balance with infusion of protein hydrolysates in children*
- 1944
  - *Glucose, casein, olive oil/lecithin preparation in 5-month-old marasmic infant for 5 days via peripheral vein*
- 1961
  - *Safe intravenous (IV) fat preparation*
- 1966
  - *Administration of hypertonic dextrose/amino acid (AA) solutions via central lines in beagle puppies*
- 1968
  - *First clinical report of successful use of parenteral nutrition (PN) in infant with short bowel syndrome (SBS), resulting in normal growth and development*[3]

[1]Sukarochana K, et al. *Surg Gynec Obstet*. 1965;121:79.
[2]American Society for Parenteral and Enteral Nutrition Web site. www.nutritioncare.org. Accessed March 13, 2012.
[3]Dudrick SJ, et al. *Surgery*. 1968;64:134-142.

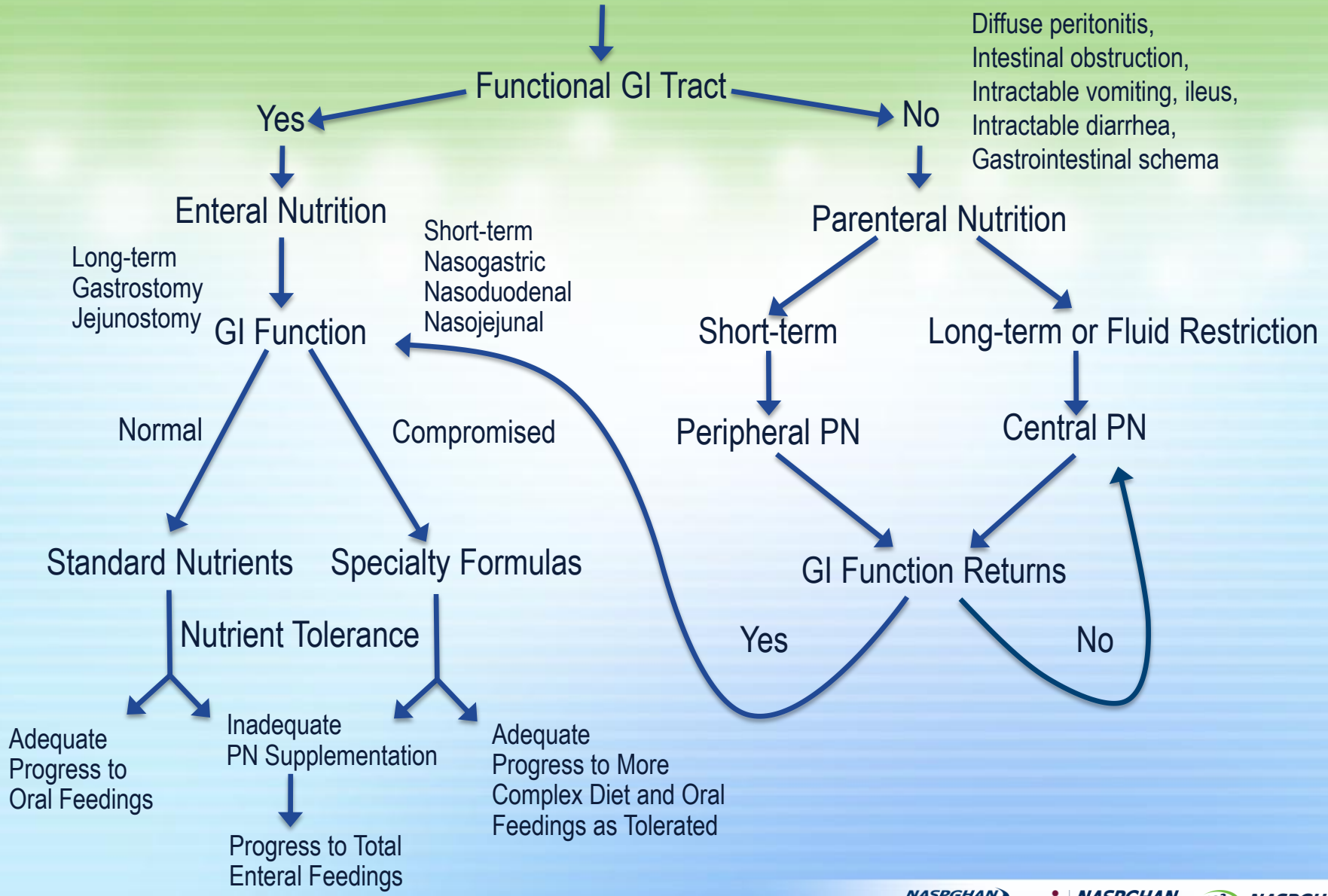
Indications and Route

PN – Indications[3]

- Always use enteral nutrition (EN) whenever possible
- Use PN only when
  - *Unable to meet nutritional requirements via the gastrointestinal (GI) tract*
  - *Bowel dysfunction resulting in inability to tolerate EN for*
    - 1-3 days in infants
    - 4-5 days in children and adolescents
    - 7-10 days in adults
- PN should ONLY be used when there is NO reason to use EN

[3]Braunschweig CL, et al. *Amer J Clin Nutr*. 2001;74:534-542.

Nutrition Assessment



[4]Adapted from ASPEN Board of Directors and the Clinical Guidelines Task Force. *J Parenter Enteral Nutr*. 2002;26(Suppl):1SA-138SA.

PN – Indications (cont'd)

- Very low birth weight infants (birth weight < 1500 g)
- Inability to tolerate enteral feeds (eg, paralytic ileus, chemotherapy, radiation enteritis)
- Small bowel obstruction
- Radiation enteritis
- GI fistula
- Hemodynamic instability with high risk of mesenteric ischemia (eg, necrotizing enterocolitis in preterm infants, extracorporeal membrane oxygenation, shock, acute critical illness)
- Conditions associated with intestinal failure (eg, SBS, diarrhea with irreversible malabsorption, pseudo-obstruction, intestinal epithelial disorders [microvillus inclusion disease, tufting enteropathy])

Inflammatory Bowel Disease – Considerations for Use of PN

- Intolerance to enteral feeds
- Restricted enteral intake/severe perianal disease
- Fistulas, perforation, and intra-abdominal abscesses
- Toxic megacolon
- Intestinal obstruction
- Perioperative nutrition rehabilitation
- SBS
- Unable to sustain growth on enteral feeds

SBS/Intestinal Failure – Nutritional Considerations I[5]

- PN should be used to meet energy needs when EN is insufficient or cannot be tolerated
- Start trophic enteral feeds when possible and advance as tolerated
- Cycle PN regimen when possible
- Energy needs to be provided for treatment of malnutrition and to promote normal growth
  - *Prediction equations may be helpful, but the patient's response is the best guide to adjusting caloric intake*
  - *Avoid overfeeding and provide adequate calorie intake for normal linear growth*

[5]Corkins MR. *Pediatric Nutrition Support Core Curriculum*. Corkins M, ed. Silver Spring, MD: American Society for Parenteral and Enteral Nutrition (ASPEN); 2010.

PN – Route of Administration[4,6,7]

- Central versus peripheral venous access
  - *Defined by where the tip of the catheter is positioned*
- Central
  - *Tip is positioned in the superior or inferior vena cava or right atrium*
  - *Types: peripherally inserted central catheter, tunneled and nontunneled central catheters, umbilical venous catheter, implanted port*
- Peripheral
  - *Tip is not positioned in the superior or inferior vena cava or right atrium*
  - *Type: peripheral IV catheter*
- Intradialytic PN

[4]ASPEN Board of Directors and the Clinical Guidelines Task Force. *JPEN J Parenter Enteral Nutr*. 2002;26(Suppl):1SA-138SA.
[6]Fuhrman MP. *Nutr Clin Pract*. 2009;24:470-480.
[7]Brewer ED. *Am J Kidney Dis*. 1999;33:205-207.

PN – Peripheral Versus Central

Peripheral PN

- Used for < 2 weeks
- Patient has no fluid restriction and nutrient needs can be met
- Osmolality 900-1000 mOsmol/L[8]
  - *Maximum 10-12.5% dextrose*

Central PN

- Used for > 2 weeks
- Patient is fluid-restricted and nutrient needs cannot be met by peripheral PN
- Peripheral access limited
- Can use hypertonic solutions

[8]Mirtallo J, et al. *JPEN J Parenter Enteral Nutr*. 2004;28:S39-S70.

Components

Components of PN

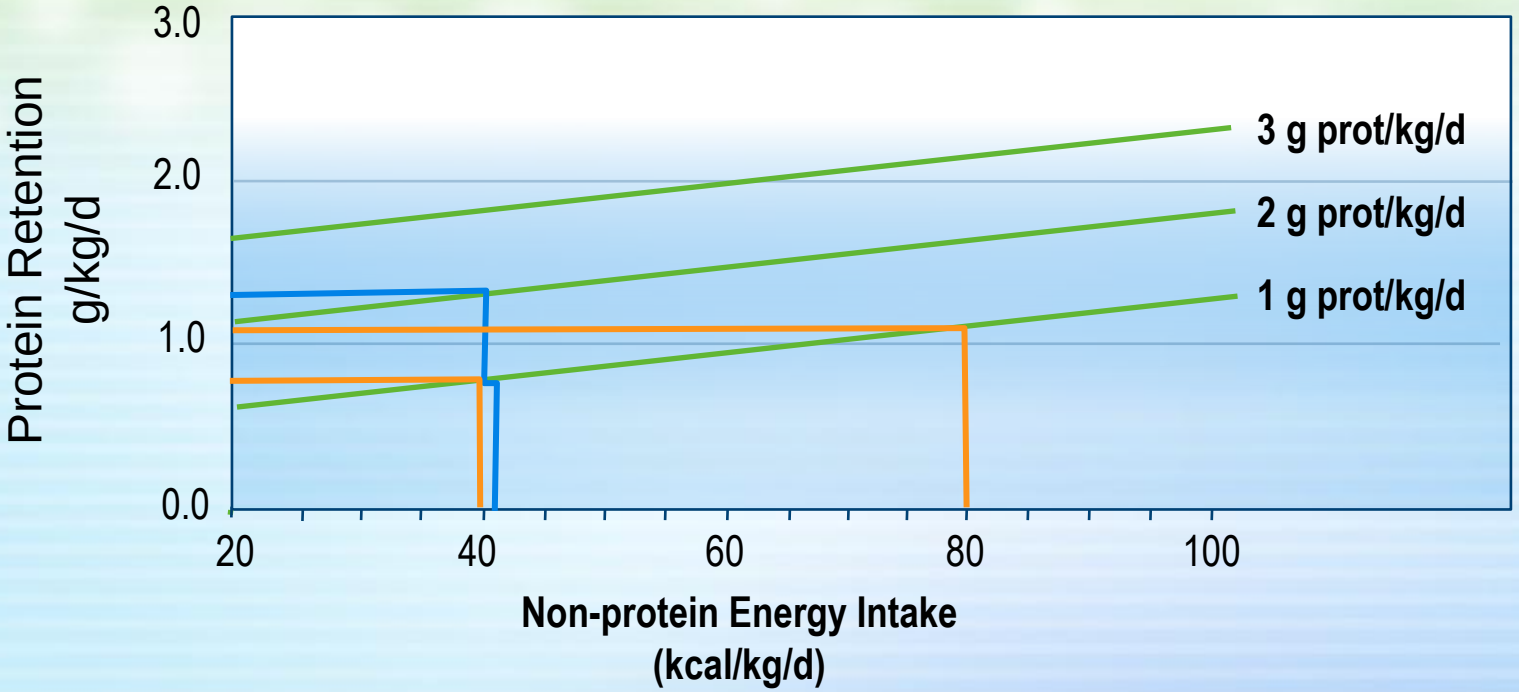
- Nonprotein energy
  - *Carbohydrates (dextrose)*
  - *Fat (lipid)*
- Protein (AAs)
- Electrolytes
- Minerals, vitamins, trace elements
- Water
- Miscellaneous: heparin, medications (i.e., ranitidine)

Components of PN – Macronutrient Guidelines[5,9,10]

American Academy of Pediatrics			American Society for Parenteral and Enteral Nutrition	
	Weight	**Daily Recommendation**	**Weight/Age**	**Daily Recommendation**
Protein	10-20 kg	1-2.5 g/kg	> 10 kg or 1-10 years	1-2 g/kg
	> 20 kg	0.8-2 g/kg	11-17 years	0.8-1.5 g/kg
Energy/Caloric	10-20 kg	60-90 kcal/kg	> 1-7 years	75-90 kcal/kg
	> 20 kg	30-75 kcal/kg	> 7-12 years	50-75 kcal/kg
			> 12-18 years	30-50 kcal/kg
Fluid	> 10-20 kg = 1000 mL + 50 mL/kg > 10 kg			
	> 20 kg = 1500 mL + 20 mL/kg > 20 kg			
Carbohydrates (Dextrose)	10-20 kg	8-28 g/kg	Carbohydrates should comprise 40% to 60% of total caloric intake.	
	> 20 kg	5-20 g/kg		
IV Fat Emulsion	> 10 kg	1-3 g/kg	The minimum fat requirement is determined by essential fatty acid need, and the daily maximum is 50% to 60% of energy.	

[5]Corkins MR. *Pediatric Nutrition Support Core Curriculum*. Corkins M, ed. Silver Spring, MD: American Society for Parenteral and Enteral Nutrition (ASPEN); 2010.
[9]Kleinman RE. *Pediatric Nutrition Handbook*. 6th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2009; 519-540.
[10]Forchielli ML and Miller SJ. *The ASPEN Nutrition Support Practice Manual.* Merritt R, ed. Silver Spring, MD: American Society for Parenteral and Enteral Nutrition; 2005; 38-53.

Protein Balance Versus AA/Energy Intake[11]



AA intake is more important to enhancing protein retention than is energy intake. Doubling AA intake vs. energy intake leads to greater protein retention.

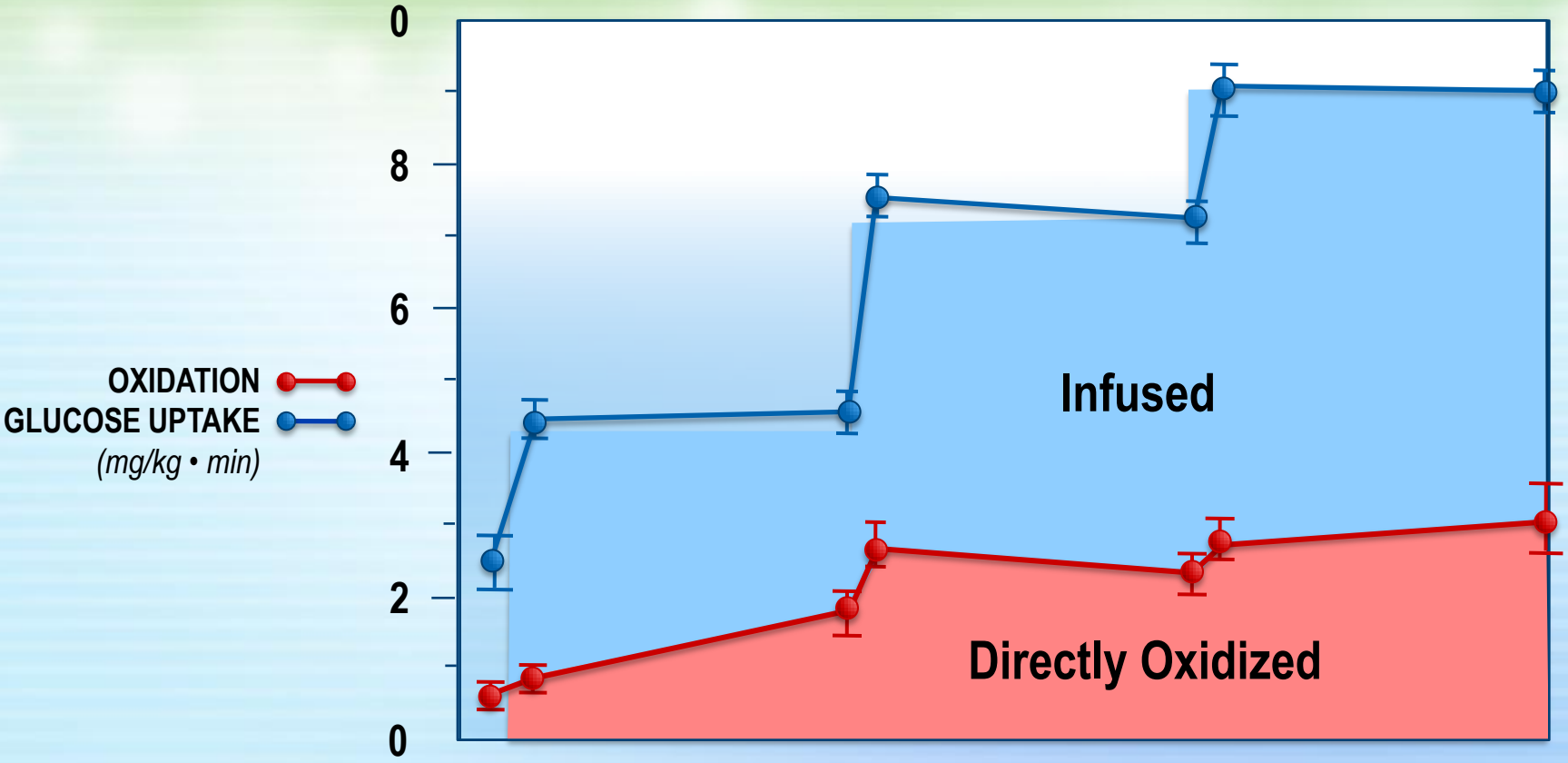
[11]Adapted from Pierro A, et al. *J Pediatr Surg*. 1988;23:538-542.

Components of PN – Dextrose

- Major source of nonprotein calories is D-glucose
- Typically provides 40-55% of caloric intake
- Monohydrate form provides 3.4 kcal/g
- Stepwise increase to allow appropriate response of endogenous insulin, preventing glucosuria and osmotic diuresis
- Glucose increases osmolality (risk of phlebitis)

[14]Shulman RJ. *J Pediatr Gastroenterol Nutr.* 2003;36:587-607.

Glucose Oxidation Is Limited – I[12]



[12]Adapted from Wolfe RR, et al. *Metabolism*. 1980;29:892-900.

Components of PN – Protein[9,10,13]

- Functions of protein
  - *Provides structure (eg, muscle)*
  - *Provides function (eg, enzymes, transport proteins)*
  - *Acts as a nitrogen donor to other compounds (eg, nucleic acids, carnitine, taurine)*
- Protein should not serve as an energy source
- Protein requirements vary by age and disease state
- Infants
  - *Infants need conditional AAs, like histidine, taurine, and cysteine, because of immature synthetic abilities*
  - *Infant AA solutions are based on the serum AA pattern seen in breastfed infants*
- Excess protein intake leads to hyperazotemia

[9]Kleinman RE. *Pediatric Nutrition Handbook*. 6th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2009; 519-540.
[10]Forchielli ML and Miller SJ. *The ASPEN Nutrition Support Practice Manual.* Merritt R, ed. Silver Spring, MD: American Society for Parenteral and Enteral Nutrition; 2005; 38-53.
[13]Shulman RJ and Phillips S. *J Pediatr Gastroenterol Nutr*. 2003;36:587-607.

Components of PN – Fat[5,13,14]

- Fat
  - *Concentrated source of calories*
  - *In children, only use 20% emulsion (provides 2 kcal/mL)*
  - *Currently, in the United States, lipid solutions are composed of triglycerides from soybean oil and safflower and emulsified by egg yolk phospholipid*
- Minimum of 1-2% of calories from a combinations of linoleic and linolenic acid to meet essential fatty acids (EFA) needs (met with 0.5-1.0 g/kg per day fat)
  - *Serum triene:tetraene ratio is reflective of EFA status*
  - *A triene:tetraene ratio < 0.2 is generally considered to reflect EFA sufficiency*
- Infused over 24 hours to maximize tolerance
- Monitor triglycerides to assess tolerance

[5]Corkins MR. *Pediatric Nutrition Support Core Curriculum*. Corkins M, ed. Silver Spring, MD: American Society for Parenteral and Enteral Nutrition (ASPEN); 2010.
[13]Shulman RJ and Phillips S. *J Pediatr Gastroenterol Nutr*. 2003;36:587-607.
[14]Wolfram G, et al. *JPEN J Parenter Enteral Nutr*. 1978;2:634-639.

IV Fat Clearance[15]

Tissue	Fractional Removal Rate (% of Arterial Concentration)	Removal (% Infused)
Myocardium	6	14
Splanchnic	5	25
Liver	0	0
Skeletal Muscle	10	47
Subcutaneous Tissue	6	13

[15]Adapted from Rössner S, et al. *Acta Chir Scand Suppl*. 1976;466:56-57.

Comparison of Lipid Emulsions*[16]

Fatty Acids	Soy	Fish Oil	SMOF†
Linoleic	50	4	37
Linolenic	9	2	5
Oleic	24	15	55
Eicosapentaenoic	0	20	5
Docosahexaenoic	0	12	5
Arachidonic	0.1	2	1

*Approximate % total fatty acids

†Soybean oil, medium chain triglycerides, olive oil, and fish oil

[16]Adapted from Fresenius Kabi Web site. http://www.fresenius-kabi.com/. Accessed March 13, 2012.

Fish Oil Emulsion[17]

- Le HD, et al.
  - *79 infants with PN-associated cholestasis (PNAC) on soy emulsion switched to fish oil emulsion*
  - *Median duration of soy emulsion was 91 days*
  - *After median of 18 weeks, median direct bilirubin 5.4 → 0.2 mg/dL*
  - *Serum triglyceride, total cholesterol, low-density lipoprotein, very low-density lipoprotein fell significantly (52%, 17%, 24%, 48%, respectively)*
  - *Decline in C-reactive protein: 1.3 → 0.2 mg/dL during fish oil emulsion treatment*

[17]Le HD, et al. *Am J Clin Nutr*. 2011;94:749-758.

Suggested Doses for Lipids[4,5]

	Starting Dose (g/kg/day)	Maximum Dose (g/kg/day)
Neonate/Infant	1	3
Children	1	2
Adolescent/Adult	0.5	1

[4]ASPEN Board of Directors and the Clinical Guidelines Task Force. *JPEN J Parenter Enteral Nutr*. 2002;26(Suppl):1SA-138SA.
[5]Corkins MR. *Pediatric Nutrition Support Core Curriculum*. Corkins M, ed. Silver Spring, MD: American Society for Parenteral and Enteral Nutrition (ASPEN); 2010.

Dose of Lipid

- Diamond IR, et al.[18]
  - *152 postoperative (abdominal) infants*
  - *Predictors for development of direct bilirubin 5.9 mg/dL 1 year later*
  - *Days of AA > 2.5 mg·kg^{-1}·d^{-1} and lipid > 2.5 mg·kg^{-1}·d^{-1} and sepsis episodes*
- Cober MP and Teitelbaum DH[19]
  - Reduced lipid intake if direct bilirubin ≥ 2.5 mg/dL
  - Compared with historical cohort
  - Downward trend in bilirubin for reduced lipid group (P = 0.046)

[18]Diamond IR, et al. *JPEN J Parenter Enteral Nutr*. 2011;35:596-602.
[19]Cober MP and Teitelbaum DH. *Curr Opin Organ Transplant*. 2010;15:330-333.

Calcium and Phosphorus[5,20]

- There are limitations to amounts of Ca and P that can be supplied in PN
- Ca and P can precipitate, depending on the amounts added to the PN solution
- Cysteine lowers pH and may be added to neonate/infant PN (by using TrophAmine®) to increase solubility of Ca and P

[5]Corkins MR. *Pediatric Nutrition Support Core Curriculum*. Corkins M, ed. Silver Spring, MD: American Society for Parenteral and Enteral Nutrition (ASPEN); 2010.
[20]Greene HL, et al. *Am J Clin Nutr*. 1988;48:1324-1342.

Components of PN – Trace Elements[21]

Mineral	Multitrace®-4 (per mL)	Multitrace®-4 (per mL)	Multitrace®-5 Concentrate (per mL)
	Neonatal	Pediatric	(Adolescent/Adult)
Zinc (as Sulfate)	1.5 mg	1 mg	5 mg
Chromium (as Chloride	0.85 mcg	1 mcg	10 mcg
Selenium (as Selenious Acid)	None	None	60 mcg
Copper (as Sulfate)	0.1 mg	0.1 mg	1 mg
Manganese (as Sulfate)	25 mcg	25 mcg	0.5 mg

[21]American Regent Web site. http://americanregent.com/MultipleTraceElementAdditives.aspx. Accessed March 13, 2012.

Components of PN – Designing a Regimen[5]

- Estimate energy needs
  - *Based on age of patient, disease state, severity of illness, activity level, and need for catch-up growth*
- Calculate fluid needs
- Estimate protein needs
- Obtain baseline laboratory values of serum electrolytes, minerals, and triglycerides
- Start with 10% dextrose solution
- Can start with IV lipid at lowest end of dose range and make sure triglyceride levels are within acceptable levels when increasing dose
- Advance regimen to goal caloric and fat intake based on laboratory testing and other clinical evidence

[5]Corkins MR. *Pediatric Nutrition Support Core Curriculum*. Corkins M, ed. Silver Spring, MD: American Society for Parenteral and Enteral Nutrition (ASPEN); 2010.

Components of PN – Energy Requirements[13,22]

- Common methods to calculate calorie needs include World Health Organization (WHO) and Dietary Reference Intake (DRI) equations
  - *DRI equations provide guidelines from birth–adulthood with a need to use activity/adjustment factors*
  - *WHO equations provide guidelines from 1 year–adulthood*
  - *Energy prediction equations should be used as starting guidelines and PN caloric intake adjusted based on response to therapy*
- Energy needs
  - *In the first year of life are expressed in kcal/kg per day*
  - *Beyond the first year of life are expressed as kcal/kg per day or kcal per day*
- Measure energy expenditure using indirect calorimetry when possible
- Birth through 1 year: 80-110 kcal/kg per day

[13]Shulman RJ and Phillips S. *J Pediatr Gastroenterol Nutr*. 2003;36:587-607.
[22]Lloyd DA. *Nutrition*. 1998;14:101-104.

TPN Calculator

- Put together by Robert Rothbaum at Washington University
- http://tpn.wustl.edu/calculator.html
- Does not account for catch-up calorie needs

Components of PN – Minerals and Acid-Base Balance[5]

- Determining starting doses
  - *Use accepted guidelines*
  - *Consider baseline electrolyte and mineral levels*
  - *Consider other sources of electrolytes and minerals (IV fluids, other sources of electrolytes and minerals)*
- Check laboratory values within 24 hours of initiation of PN and adjust levels accordingly
  - *Consider other additional electrolyte and mineral supplements patient received and adjust PN dosages accordingly*
- Acid-base abnormalities can be treated by addition or removal of sodium or potassium acetate
  - *Acetate = bicarbonate precursor*
  - *Bicarbonate contraindicated in PN*
    - Ca/P precipitation
    - High Na load

[5]Corkins MR. *Pediatric Nutrition Support Core Curriculum*. Corkins M, ed. Silver Spring, MD: American Society for Parenteral and Enteral Nutrition (ASPEN); 2010.

Inflammatory Bowel Disease – Nutritional Considerations[5,23,24]

- Energy needs vary based on patient's disease and nutritional status
- Prediction equations provide only guidance
- Protein needs
  - *In general, needs are similar to those for healthy children*
  - *Patients with diarrhea, malabsorption, fistulas, and malnutrition may require increased protein*
- Zn
  - *Needs may be increased if there is malnutrition, diarrhea, high output stomas, and SBS*
- Fe
  - *Fe deficiency is more common in inflammatory bowel disease, due to decreased intake and increased losses; more common in Crohn's disease compared to ulcerative colitis*
- Fluid
  - *Needs should be individualized*
- Vitamin D deficiencies can occur
  - *Measure levels, taking into account the time of year and location of the patient*
  - *Supplement as required*

[5]Corkins MR. *Pediatric Nutrition Support Core Curriculum*. Corkins M, ed. Silver Spring, MD: American Society for Parenteral and Enteral Nutrition (ASPEN); 2010.
[23]Wiskin AE, et al. *Clin Nutr*. 2009;28:652-656.
[24]Azcue M, et al. *Gut*. 1997;41:203-208.

SBS/Intestinal Failure – Nutritional Considerations II[5]

- Increased requirements in patients with GI losses
  - *Fluid*
  - *Zn*
  - *Bicarbonate – needs to be replaced as acetate in PN*
  - *NA (especially in ileostomies): patients will not grow until adequately supplemented; urine Na measurements can be used to guide Na replacement*
  - *Fe needs increased due to GI blood loss and malabsorption, especially if patient has loss of proximal small bowel*

[5]Corkins MR. *Pediatric Nutrition Support Core Curriculum*. Corkins M, ed. Silver Spring, MD: American Society for Parenteral and Enteral Nutrition (ASPEN); 2010.

Cycling

PN – Cycling PN[25,26]

- Daily administration of PN over a period of time which is < 24 hours (eg, 8-22 hours cycle); average 10-12 hours
- Prerequisite
  - *Stable regimen*
  - *Ability to handle large volume of fluid and nutrients over a short amount of time*
  - *The smaller the infant, the less tolerant they may be of the cycle*
- Putative benefits
  - *Decreased hepatic steatosis*
  - *Allows for a more normal daytime routine*
  - *Increases mobility of the patient*
- Wean PN rate for the last hour by decreasing the rate by 50%. Consider starting the PN solution at 50% of the goal rate for first hour.
- Check serum glucose 30-45 minutes after stopping PN with every change in length of cycle. Monitor for glucosuria during cycle.

[25]Slicker J and Vermilyea S. *Nutr Clin Pract*. 2009;24:481-486.
[26]Werlin SL, et al. *J Pediatr*. 1994;124:441-444.

Cycling PN

- 2 studies suggest cycling PN beneficial against PNAC
- Hwang TL, et al.[27]
  - *Adults switched to cyclic when bilirubin increased*
  - *Direct bilirubin increased in those on continuous*
  - *If direct bilirubin around 10 mg/dL, there was no benefit*
- Jensen AR, et al.[28]
  - *Retrospective review of 107 infants with gastroschisis*

[27]Hwang TL, et al. *Hepatogastroenterology*. 2000;47:1347-1350.
[28]Jensen AR, et al. *J Pediatr Surg*. 2009;44:183-189.

Monitoring and Complications

PN – Monitoring

	Initial	With Every Change in PN	Weekly until Stable	Monthly as indicated
Electrolytes	√	√	√	
Glucose	√	√	√	
Calcium	√	√	√	
BUN	√	√	√	
Creatinine	√	√	√	
Magnesium	√	√	√	
Phosphorus	√	√	√	
ALT	√		√	
AST	√		√	
Alkaline phosphatase	√		√	
Total protein	√		√	
Albumin	√		√	
GGT	√		√	
Prealbumin	√		√	
Triglycerides	√	√	√	
Conjugated bilirubin	√		√	
CBC	√		√	√
Iron studies				√
Trace elements				√
Vitamins				√

[5]Adapted from Corkins MR. *Pediatric Nutrition Support Core Curriculum*. Corkins M, ed. Silver Spring, MD: American Society for Parenteral and Enteral Nutrition (ASPEN); 2010

PN – Complications[5]

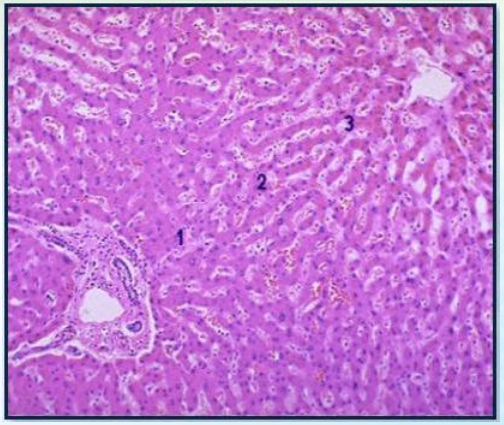
- Infectious
- Mechanical
  - *Infusate-related*
  - *Catheter-related*
  - *Occlusions*
- Metabolic
  - *Electrolyte-, mineral-, trace element-, and vitamin-related*
  - *PN-associated liver disease*
  - *Bone disease*
  - *Overfeeding and underfeeding*
  - *Refeeding syndrome*
  - *Allergy*
  - *Miscellaneous (eg, nephropathy)*

[5]Corkins MR. *Pediatric Nutrition Support Core Curriculum*. Corkins M, ed. Silver Spring, MD: American Society for Parenteral and Enteral Nutrition (ASPEN); 2010.

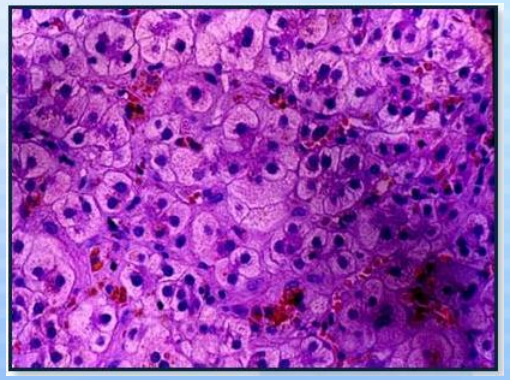
PN – Liver Disease I[29]

- Well-described complication of PN
- Develops in 40-60% of neonates; ~ 15% in children
- Variable degree of injury
  - *Mild: mild cholestasis; gall stones; hepatic steatosis*
  - *Severe: can result in cirrhosis and liver failure*
- Pathogenesis
  - *Multifactorial*
  - *Prolonged duration of PN*
  - *Lack of enteral feeding*
  - *Prematurity and low birth weight*
  - *Early and recurrent sepsis*
  - *Length of bowel remnant*
  - *Reduced enterohepatic circulation*
  - *Deficiency or toxicity of components of PN solutions (excess glucose, excess energy, AA content, Mn, Cu, and fat emulsions)*

Normal Liver



Cholestasis



[29]Ovchinsky N. JPEN. *J Parenter Enteral Nutr*. 2010;34:473-474.

PN – Liver Disease II[30,31]

Treatment

- Provide maximal tolerated EN
- Provide cyclical PN as soon as possible
- Consider and treat small bowel bacterial overgrowth
- Consider reducing IV lipids to 1 g/kg per day if conjugated bilirubin rises with no other explanation
  - *Consider fish oil–based lipids if the above strategy fails*
- If transaminases, alkaline phosphatase, or conjugated bilirubin continue to increase, consider commencing ursodeoxycholic acid

[30]Gura KM, et al. *Pediatrics*. 2008;121:e678-e686.
[31]Koletzko B, et al. *J Pediatr Gastroenterol Nutr*. 2005;41(Suppl 2):S1-S87.

PN – Liver Disease III[31-33]

- Consider early referral to an experienced liver-intestinal transplant or intestinal rehabilitation program for children with a poor prognosis or if on PN > 3 months and ≥ 1 of the following:
  - *Serum-conjugated bilirubin > 3 mg/dL*
  - *Platelet count < 100,000/µL*
  - *Prothrombin time > 15 seconds*
  - *Partial thromboplastin time > 40 seconds*
  - *Hepatic fibrosis*
  - *Concerns about central venous access*

[31]Koletzko B, et al. *J Pediatr Gastroenterol Nutr*. 2005;41(Suppl 2):S1-S87.
[32]Selvaggi G, et al. *Transplantation*. 2005;79:1639-1643.
[33]Mittal NK, et al. *Pediatr Clin North Am*. 2003;50:1419-1433.

Fish Oil and Portal Fibrosis

- Soden JS, et al.[34]
  - *2 infants with PNAC*
  - *Cholestasis resolved or improved (direct bilirubin 1.9 mg/dL)*
  - *Liver biopsy after fish oil emulsion treatment (11 months and 3 months)*
  - *Decreased inflammation, but portal fibrosis in 1 plus bridging fibrosis in the other*

[34]Soden JS, Lovell MA, Brown K, et al. *J Pediatr*. 2010;156:327-331.

Infection[35,36]

- Particular problem in SBS
  - *Small bowel bacterial overgrowth*
  - *Mucosal and systemic inflammation*
    - Elevated fecal calprotectin
    - Elevated serum cytokines
  - *Risk reduced with enteral feedings*
- Increases the risk for cholestasis

[35]Cole CR, et al. *J Pediatr*. 2010;156:941-947.
[36]Kubota A, et al. *JPEN J Parenter Enteral Nutr*. 1988;12:602-606.

Home PN – Infectious Complications I[38]

- Bacterial and fungal causes
- Infection vs. colonization (22% of all hubs)
- Causes
  - *Colonization*
    - Inside catheter or hub
    - Outside of the subcutaneous catheter
    - In fibrin sleeve
    - In subcutaneous tract
  - *Contamination*
    - From blood seeding
    - Skin contamination along the catheter tract
    - Nonsterile entries into the line
    - Contaminated PN solutions
- Risk of sepsis is reported at 1.5 episodes a year in home PN (HPN) patients

[38]Schmidt-Sommerfeld E, et al. *JPEN J Parenter Enteral Nutr*. 1990;14:148-151.

HPN – Infectious Complications II[5]

- Prevention
  - *Hand hygiene*
  - *Sterile technique during placement*
  - *Use line only for PN and not for blood draws*
  - *Dressing changes per protocol*
  - *Tubing changes for dextrose AA solutions and IV lipid*
  - *Avoid multilumen catheters*
  - *Avoid catheters in groin/diaper area*
  - *Inadequate pediatric data on the benefits of antibiotic and ethanol locks and antibiotic-impregnated catheters*

[5]Corkins MR. *Pediatric Nutrition Support Core Curriculum*. Corkins M, ed. Silver Spring, MD: American Society for Parenteral and Enteral Nutrition (ASPEN); 2010.

HPN

HPN – Background[31]

- In the United States, children account for 14% of patients on HPN
- All children dependent on long-term PN should be discharged on HPN if and when
  - *They are stable*
    - Includes stability of the underlying disease, fluid, and electrolyte requirements and reliable central venous access
  - *Familial and social criteria are fulfilled*
- Should be followed by a team with experience taking care of HPN patients
- Resource for patients and parents
  - *The Oley Foundation: http://www.oley.org*

[31]Koletzko B, et al. *J Pediatr Gastroenterol Nutr*. 2005;41(Suppl 2):S1-S87.

HPN – 5-Year Prospective Study[39]

- The primary cause of death on HPN
  - *Underlying disease–related in patients with HPN duration ≤ 2 years*
  - *HPN-related in those on HPN duration > 2 years*
- For children, survival rate was
  - *90.9% for those not transplant eligible (n = 44)*
  - *90.7% for those eligible for transplant, but not transplanted (n = 43)*
  - *75.0% for those actually transplanted (n = 12)*
    - Follow-up period for those transplanted not clear

[39]Pironi L, et al. *Gut*. 2011;60:17-25.

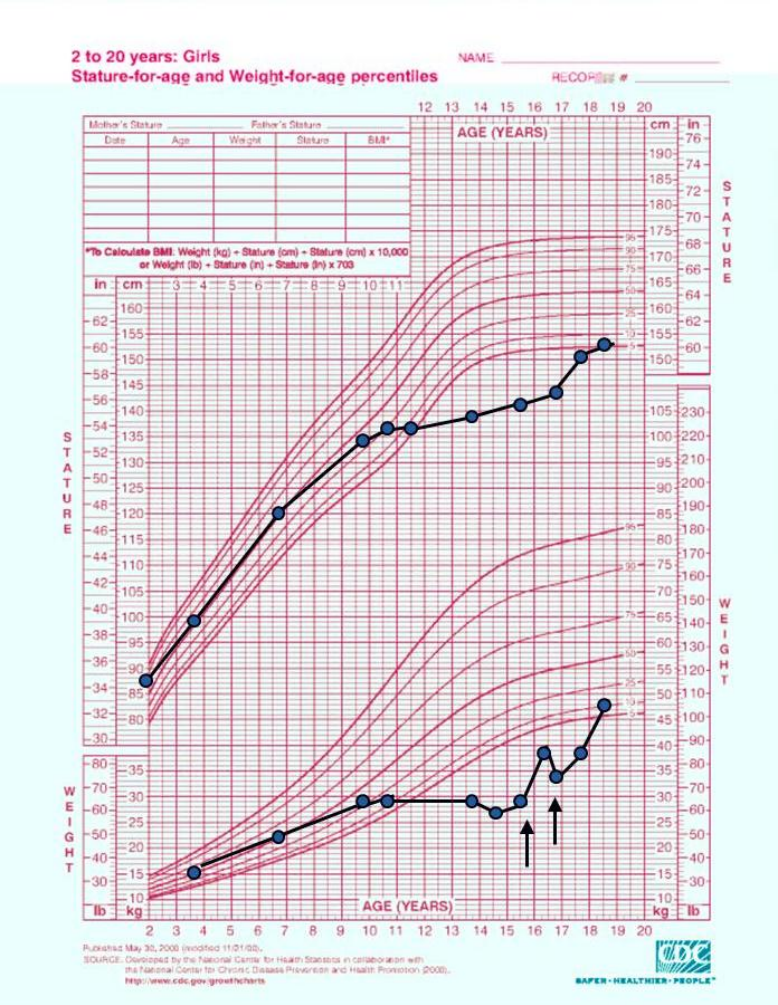
HPN – Economics[40-43]

- HPN is approximately 50-75% more “economical” than in-patient hospital care
- The longer a patient survives on HPN, the more cost-effective home treatment becomes
- HPN in children in the United Kingdom led to cost savings of about 2 million Euros in a single year by decreasing the incidence of septic episodes (1/142 days in hospital to 1/567 days at home)

[40]Colomb V. *Curr Opin Clin Nutr Metab Care*. 2000;3:237-239.
[41]Puntis JW. *Nutrition*. 1998;14:809-812.
[42]Richards DM and Irving MH. *Br J Surg*. 1996;83:1226-1229.
[43]Melville CA, et al. *J Hosp Infect*. 1997;35:197-205.

HPN – Growth in Children[44]

- HPN is successful in maintaining adequate nutritional status
- Most children with SBS will grow along their own percentiles, and some children will exhibit some degree of catch-up growth



[44]Torres C, et al. *J Pediatr Gastroenterol Nutr*. 2007;45:204-212.

Summary

- PN can be life-saving
- PN can be life-taking
- Many problems are iatrogenic
  - *Misuse*
  - *Inattention to detail*
- Very few are just bad luck

Questions?

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Enteral and Parenteral Access: Lines, Locks, and Tubes

Central Lines

- Peripheral lines/intravenous (IV): limited osmolarity; depends on guideline; 900-1200 mOsm maximum[1]
  - *Increases risk of infiltration and phlebetis*
  - *Limits nutrition; risks of problems*
  - *Infant dextrose maximums: term 10%, preterm 12.5%*
- Central lines
  - *Temporary: short-term use; not for home*
  - *Permanent: designed for home use*
  - *Tip needs to be central, usually SVC or junction with right atrium[2]*

[1]Isaacs JW, et al. *Am J Clin Nutr.* 1977;30:552-559.
[2] ASPEN Board of Directors et al. J Parenter Enteral Nutr. 2002;26(suppl1):1SA-138SA.

Permanent Central Lines

- Tunneled, lumens, ports
- Risk of infection: 1.5 infections per year[2]
- Substances of manufacture vary
- Usually heparin lock to prevent thrombosis
  - *Repeated infections suggest ethanol lock*
  - *Meta-analysis supported ethanol lock use in pediatric intestinal failure patients*[3]
  - *Silicone lines only*

[2]Schmidt-Sommerfeld E, et al. *J Parenter Enteral Nutr*. 1990;14:148-151.
[3]Oliveira C, et al. *Pediatrics.* 2012;129:318-329.

Access: Nasal Enteric Tubes

- Placement safety—usually done at bedside
- Checking placement
  - *Inaccurate methods*[4,5]
    - Auscultation
    - Aspiration and pH
    - Capnography (esophagus versus stomach)
  - *Others*
    - Biochemical (bilirubin or enzymes—delay by laboratory)

[4]Metheny N, et al. *Heart Lung.* 1990;19:631-638.
[5]Metheny N, et al. *Nurs Res.* 1990;39:262-267.

Access: Nasal Enteric Tubes (cont'd)

- Only verified method to confirm placement is x-ray
- Radiation concerns in children
- Also similar literature on gastric versus small bowel[6]

[6]American Association of Critical-Care Nurses Web site. http://www.aacn.org/WD/Practice/Docs/PracticeAlerts/Verification_of_Feeding_Tube_Placement_05-2005.pdf. Accessed March 6, 2012.

Nasal Enteric Tubes: Maintaining Placement

- NG surveillance
  - *Mark insertion point*[7]
  - *Recheck x-ray if change in tube length*
- Nasal enteric surveillance
  - *As above*
  - *Small intestinal tube in stomach has increased residual volume*

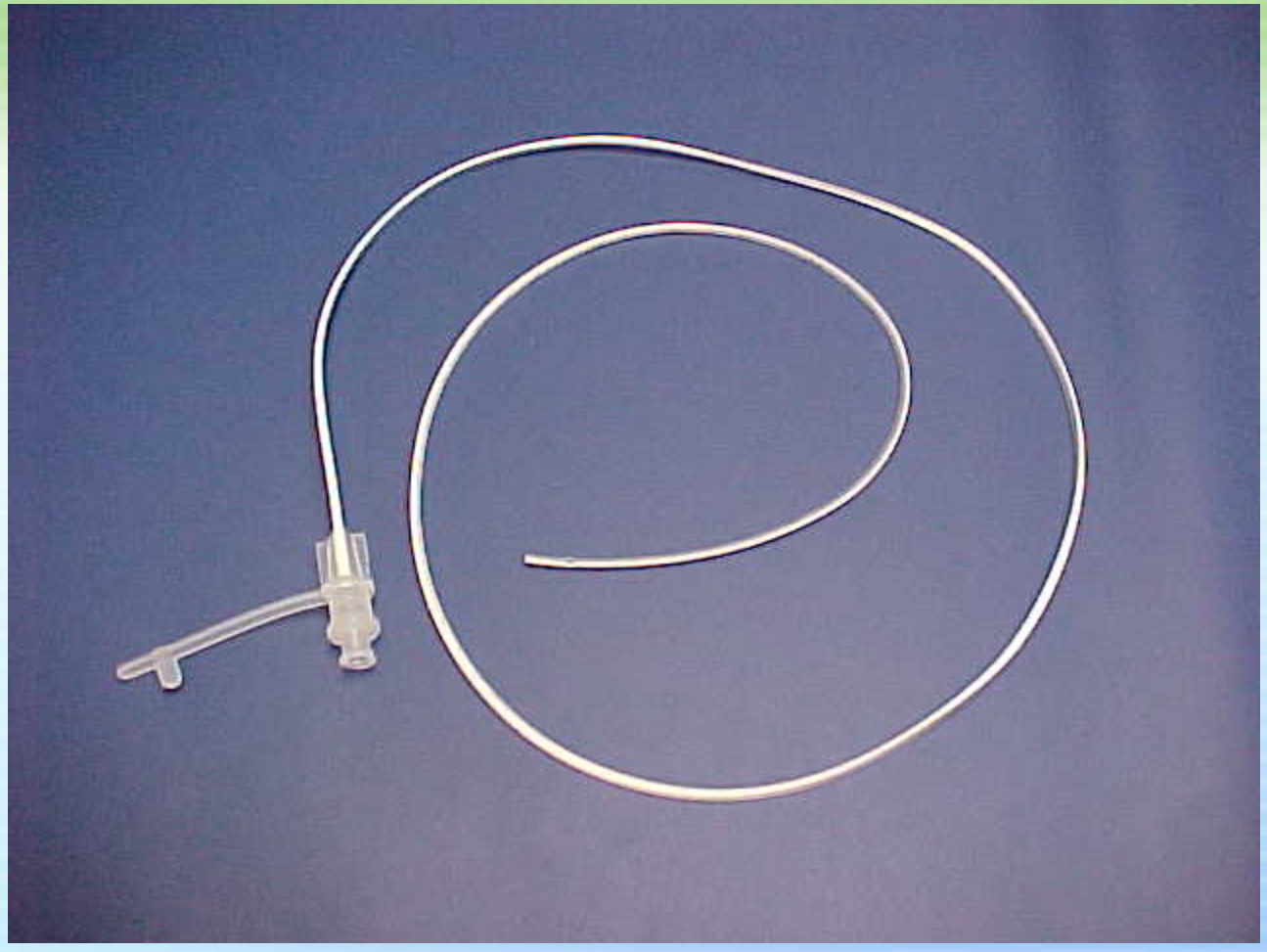
[7]Metheny NA, et al. *J Neurosc Nurs*. 2005;37:320-325.

Enteral Access Case

- Jaycee is a 6-month-old referred to the gastrointestinal (GI) clinic for poor weight gain. She does not spit up or have diarrhea. The parents state that she seems satisfied with a few ounces at each feeding and then refuses further intake. Workup?
- A NG tube is placed, and with increased calories, she gains weight. Any further workup?
- At clinic a month later, her weight gain is good, but the oral intake is still inadequate. Next steps?

NG Tubes

- First choice is NG tube in most situations
- Placement teaching
  - *Anatomy is designed to swallow*
  - *Cannot always get an x-ray*
- Securing the tube is crucial
- Once in, left in for a month



"Tube" Basics

- Do you need an upper GI series first?
  - *Usually do as part of workup for disease process*
  - *Ensure anatomy is as expected*
- Do you need a gastric emptying study?
  - *If suspect motility issues*
  - *Usually part of appropriate workup*
- Do you need a pH probe study?

Selection of Enteral Device

- Persistent dysphagia indicates need for a permanent feeding device[8,9]
- NG feeds for short-term use
  - *Literature indicates that, if over 4 weeks, need to consider permanent device*[10]
  - *Neonates have opportunity for developmental improvement*

[8]Norton B, et al. *BMJ.* 1996;312:13-16.
[9]Park RH, et al. *BMJ.* 1992;304:1406-1409.
[10]Bankhead R, et al. *JPEN J Parenter Enteral Nutr*. 2009;33:143-149.

"Permanent" Tubes

- Nutrition challenge successful to gain weight
  - *Attempt to wean off unsuccessful*
  - *Inadequate nutrition without it*
- Problems with NG
  - *Otitis and sinusitis*
  - *Repeated placements*

Gastrostomy

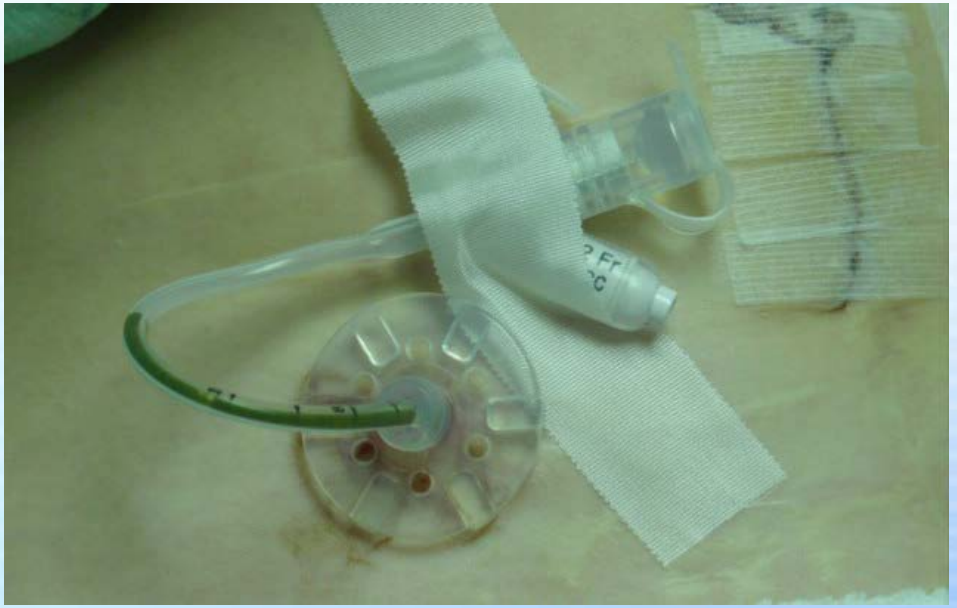
- Open versus PEG
- Open with other procedures: fundoplication, pyloromyotomy
- PEG quick with rapid recovery

PEG

- Scope used to pick site
- Hollow needle pushed into stomach
- Guide wire into the stomach; grasp with snare
- Endoscope used to pull guide wire out of mouth
- Gastrostomy introducer attached and pulled through mouth, down esophagus, and into stomach
- Scope follows gastrostomy and visualizes placement in the stomach

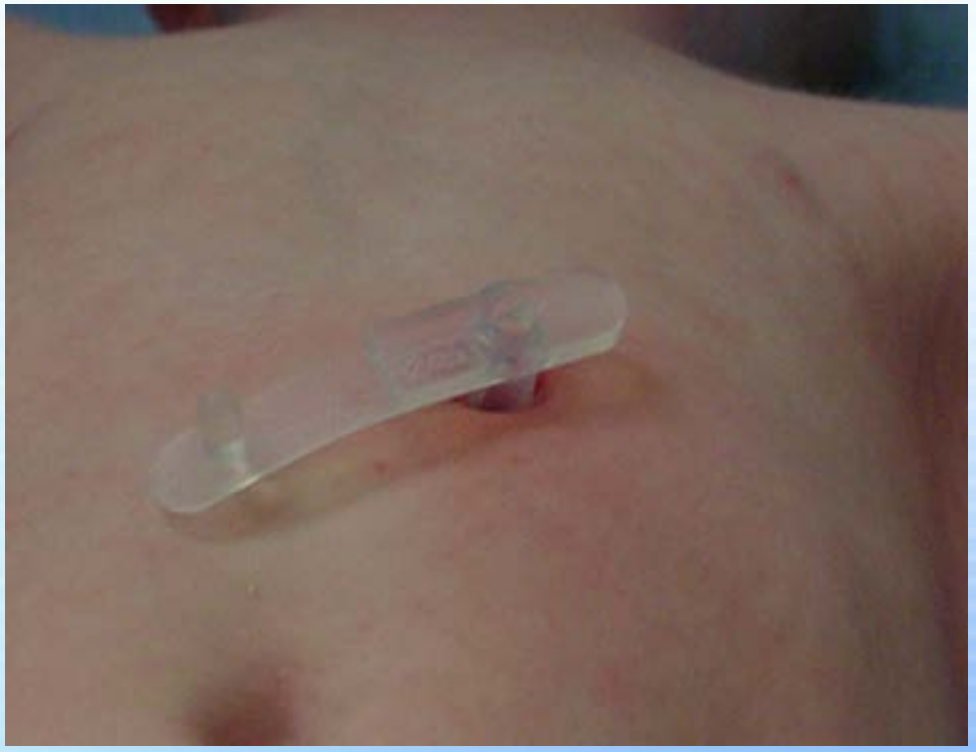
Gastrostomies

- Old fashioned type was a tube



Gastrostomies

- Currently primary “button” placement

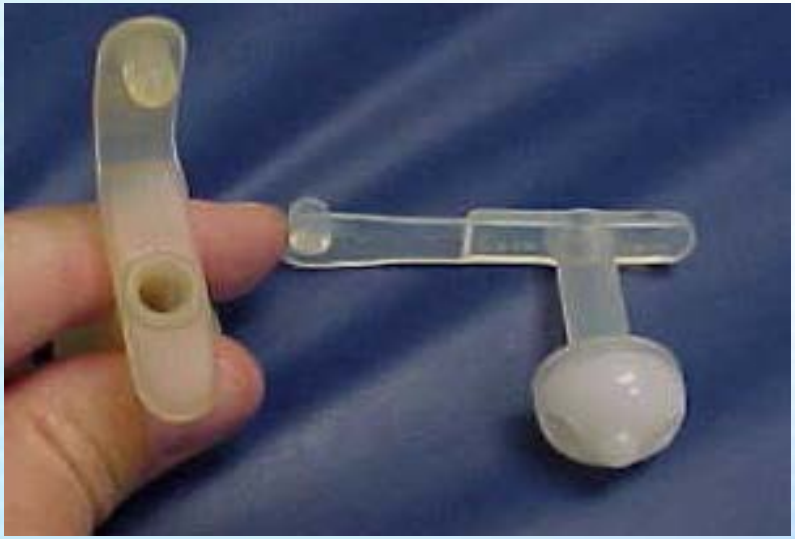


Button Replacement

- Flap or valve broken in button
  - *Prevent reflux back through button*
- Bigger size needed
- Rigid dome tip requires an obturator
- Balloon tip replaced by parents

Buttons

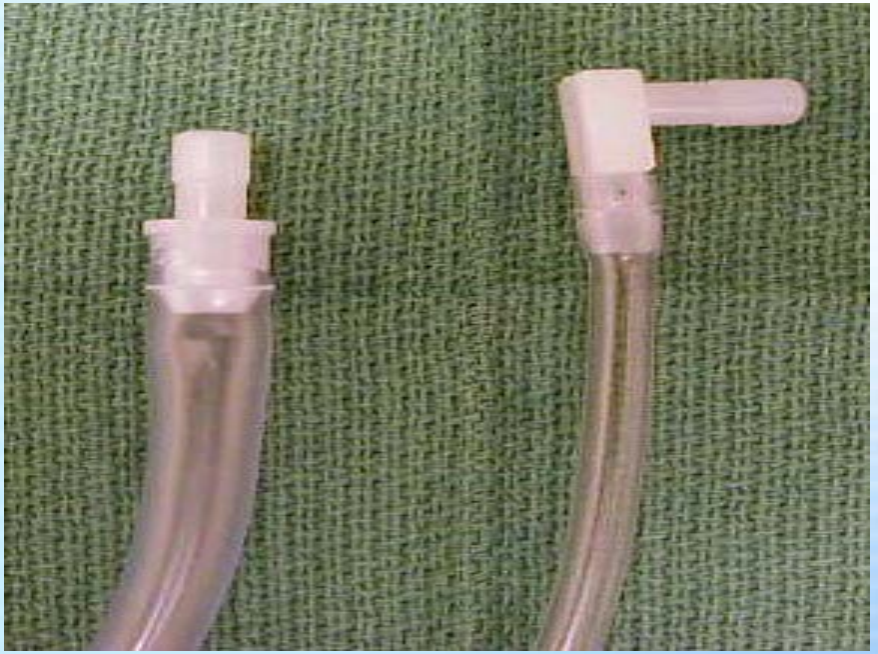
- Domed buttons



- Balloon buttons

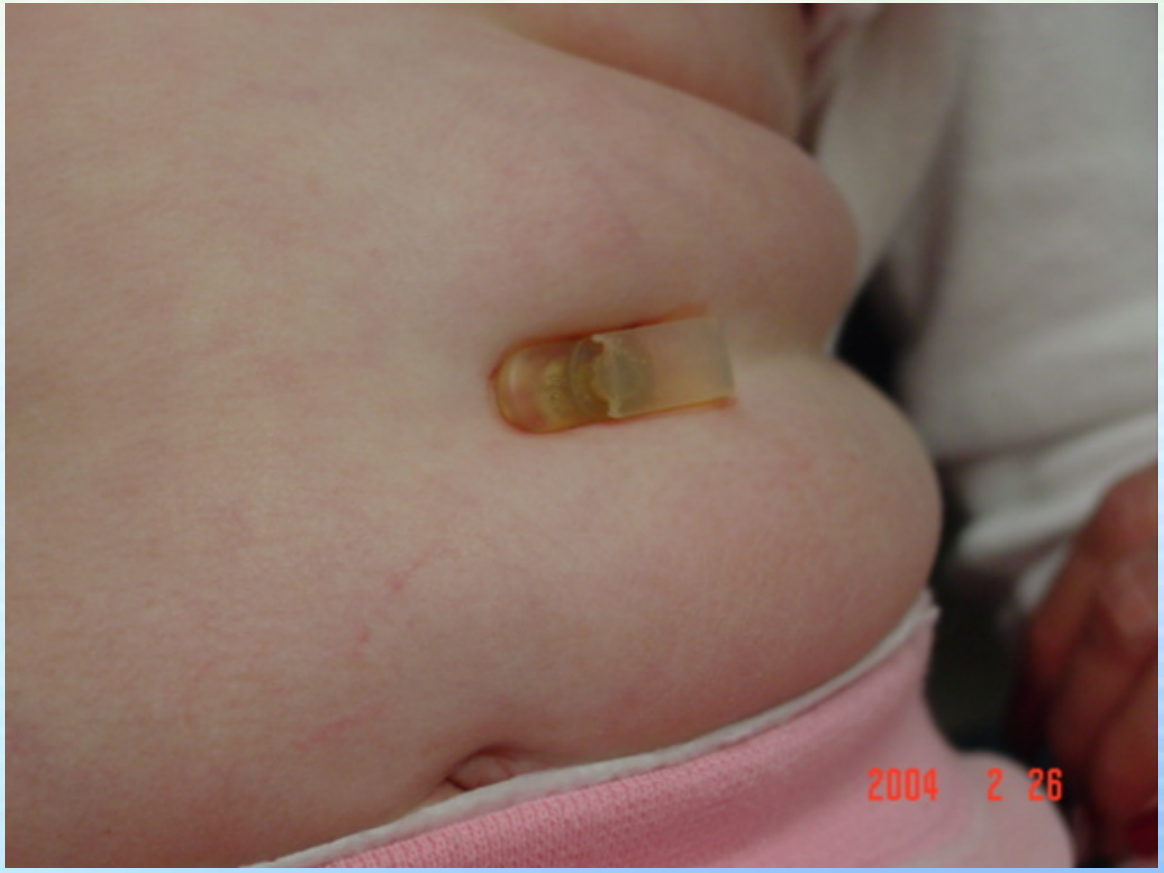
Button Connections

Domed

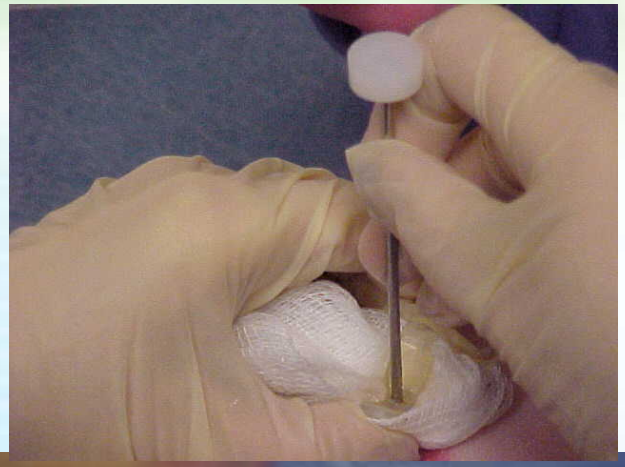


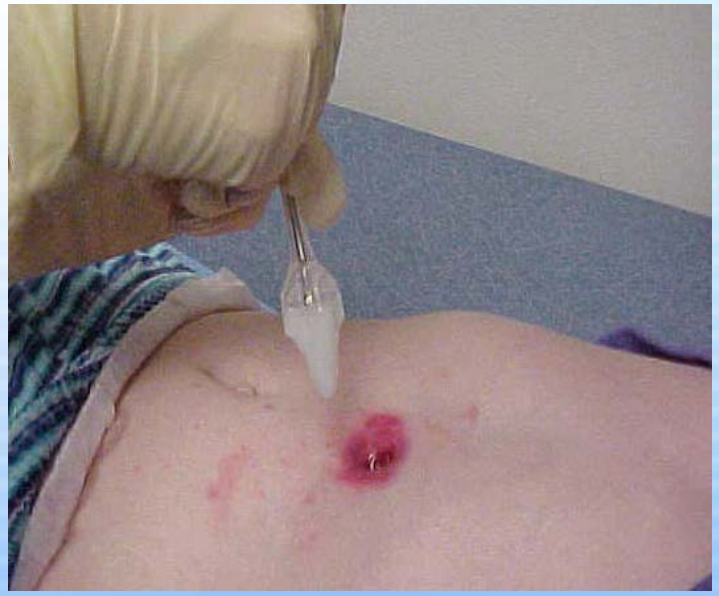
Balloon

Button Too Tight



Changing a Dome Button





Access: PEG

- Feeding after placement: literature indicates immediately to several hours
  - *Recommendation is 2 hours in adults, 6 hours in children*[11]
  - *Study of feeding at 3 hours in children*[12]

[11]Werlin S, et al. *Gastrointest Endosc.* 1994;40:692-693.
[12]Corkins MR, et al. *J Pediatr Gastroenterol Nutr*. 2010;50:625-627.

Gastrostomy

- Need for fundoplication?

- Reflux potential minimal, except neurologically impaired with abnormal pH probe preplacement[13]

[13]Sulaeman E, et al. *J Pediatr Gastroenterol Nutr.* 1998;26:269-273.

Jejunal Feeds Through Gastrostomy

- Can place a jejunal tube through a gastrostomy site
- Literature indicates a direct jejunostomy requires much less intervention[14]

[14]Raval MV and Phillips JD. *J Pediatr Surg.* 2006;41:1679-1682.

Tube Clogging[10]

- Prevention best
  - Flush after every bolus or every 4 hours of continuous
  - Lowest volume necessary to clear tube
- Mechanical devices sold and used in adults, none made for pediatric sized tubes
- Lots of substances described to dissolve a clog
  - Warm water with instill/withdraw protocol recommended
  - Safe and low cost

[10]Bankhead, R et al. *J Parenter Enteral Nutr*. 2009;33:122-167.

Preventing Misconnections

- Train family members and visitors not to reconnect lines
- Avoid modifying or adapting IV devices for enteral use
- When reconnecting lines, trace it back to the origin on the body
- Retrace all lines to the origin when doing a handoff or shift change

Questions?

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Critical Care Nutrition Pearls

Malnutrition in the Pediatric Intensive Care Unit[1-3]

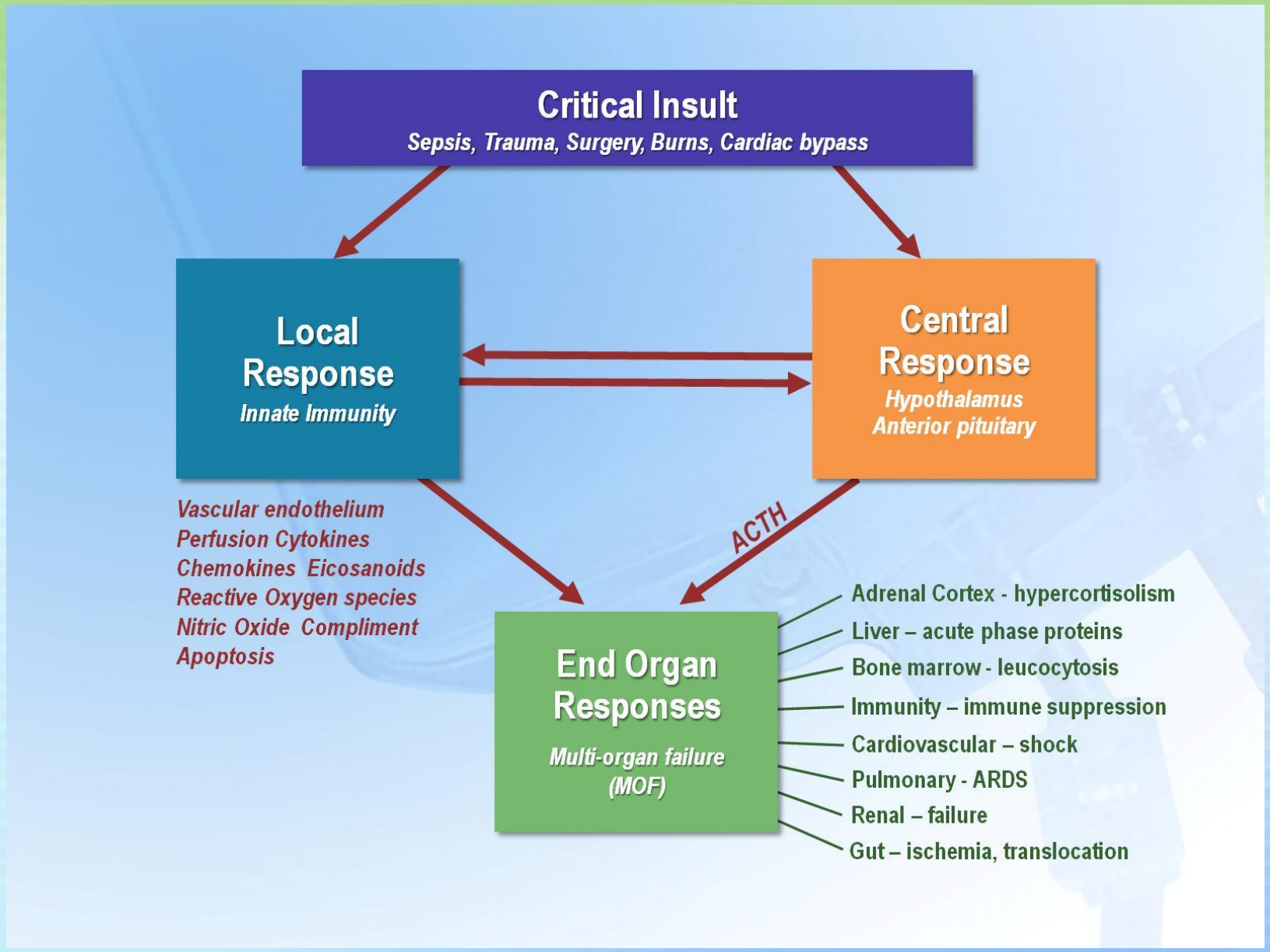
- 24% of patients in Netherlands
- Up to 53% of Brazilian children
- Has deleterious effects on patient outcomes
  - *Higher rate of infections and non-infection complications*
  - *Increased mortality*
  - *Longer hospital stay*
  - *Increased costs*

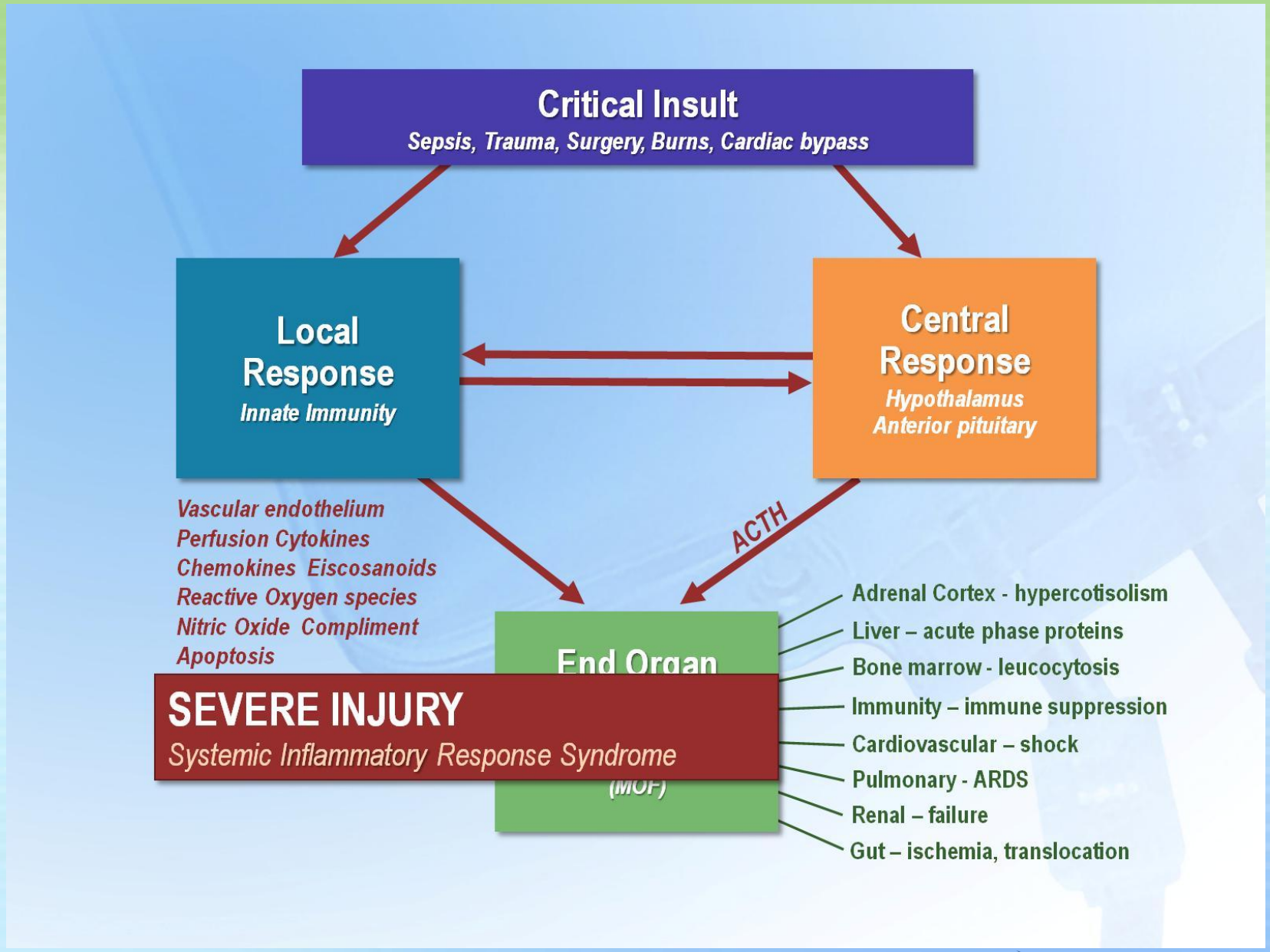
[1]Bistrian, et al. *JAMA*. 1976;235:1567-1570.
[2]Correia and Waitzberg. *Clin Nutr*. 2003:22:235-239.
[3]Mehta and Duggan. *Pediatr Clin North Am*. 2009:56:1143-1160.

Etiology of Malnutrition[3]

- Pediatric malnutrition
  - *Protein-energy malnutrition*
- Multifactorial
  - *Increased demands secondary to the metabolic stress response*
  - *Failure to estimate energy expenditure accurately*
  - *Inadequate substrate delivery at the bedside*

[3]Mehta and Duggan. *Pediatr Clin North Am*. 2009:56:1143-1160.





Critical Illness: Systemic Inflammatory Response Syndrome[4]

- Preresuscitative ebb phase (hours)
  - *Hypometabolic phase*
- Hypermetabolic flow phase (days)
  - *But resting energy expenditure (REE) is often reduced*
    - Patients are typically ventilated and sedated
    - Children cannot grow during this phase
- Recovery phase (weeks)
  - *Hypermetabolism can persist for a month (eg, the "chronic" pediatric intensive care unit [ICU] patients with progressive malnutrition)*
  - *Children can grow during this phase*

[4]Chwals. *Curr Opin Pediatr*. 1994;6:334-340.

Nutritional Assessment[5]

- Z-scores from World Health Organization
  - *Weight for age*
  - *Length or height for age < 2 years*
  - *Body mass index (BMI) > 2 years*
- Malnourished
  - *Z-scores ≤ –2*
- Overweight
  - *BMI ≥ +2*

[5]World Health Organization. *World Health Organ Tech Rep Ser*. 1985:724:1-206.

Nutritional Assessment (cont'd)[3,6]

- Weights
  - *American Society for Parenteral and Enteral Nutrition (ASPEN) guidelines recommend screening of all patients*
  - *Infrequently obtained due to patient status in ICU*
- Anthropometrics
  - *Mid-upper arm circumference and triceps skin fold, length, BMI*
    - Not reliable measurements, with interuser variability
- Laboratory
  - *Albumin, prealbumin, transferrin, and retinol-binding protein tend to be less accurate during acute illness*

[3]Mehta and Duggan. *Pediatr Clin North Am*. 2009:56:1143-1160.
[6]Mehta, et al. *J Parenter Enteral Nutr*. 2009:33:336-344.

Nutritional Assessment (cont'd)[3,7]

- Prealbumin concentration is lower in patients with liver disease
- C-reactive protein and prealbumin are inversely related
- Infants after surgery
  - *Decrease in C-reactive protein < 2 mg/dL has been associated with return of anabolism and subsequent increase in serum prealbumin*
  - *?Interleukin-6, hallmark of systemic inflammatory response syndrome, may suggest patients at risk for nutritional deterioriation*

[3]Mehta and Duggan. *Pediatr Clin North Am*. 2009:56:1143-1160.
[7]Letton, et al. *J Pediatr Surg*. 1995;30:988-992.

Overfeeding[3]

- Risk factors
  - *Low activity*
  - *Decreased insensible fluid losses*
  - *Absence of growth*
- Increases ventilatory effort because of increased CO_2 production
- Impairs liver function by inducing steatosis and cholestasis
- Increases risk for infection secondary to hyperglycemia

[3]Mehta and Duggan. *Pediatr Clin North Am*. 2009:56:1143-1160.

Energy Requirements[6]

- Indirect calorimetry
  - *Volume of oxygen consumed and the volume of carbon dioxide produced*
  - *Underfeeding promotes use of endogenous fat stores*
    - Decrease in respiratory quotient (RQ); low sensitivity: 63%; high negative positive-pressure ventilation (PPV): 90%
  - *Overfeeding*
    - Increase in RQ > 1.0; low sensitivity: 21%; PPV: 93%

[6]Mehta, et al. *J Parenter Enteral Nutr*. 2009:33:336-344.

PICU Criteria for IC Testing[6]

- Underweight (body mass index [BMI] <5th percentile for age), risk of overweight (BMI >85th percentile for age), or overweight (BMI >95th percentile for age)
- >10% weight gain or loss during medical-surgical intensive care unit stay
- Failure to wean or escalation in respiratory support
- PICU stay >4 weeks
- Suspicion of persistent inflammatory state (oncologic diagnoses including stem cell and bone marrow transplant, systemic inflammatory response syndrome)
- Condition associated with notable altered metabolic rate (status epilepticus, hyperthermia, dysautonomia)
- Clinical suspicion for underfeeding or overfeeding

.

.

[6]Adapted from Mehta, et al. *J Parenter Enteral Nutr*. 2009:33:336-344.

Energy requirements[6,15]

- ASPEN recommends the use of resting energy expenditure (REE) using indirect calorimetry in patients with metabolic alterations or malnutrition
- Boston Children's PICU
  - Prospective cohort
  - 62% of MDs failed to predict true metabolic state
  - 83% of children were overfeed with a cumulative excess of 8000 kcal/week in kids<1 year of age

[6]Mehta, et al. *J Parenter Enteral Nutr*. 2009:33:336-344.
[15]Mehta et al. *Pediatr Crit Care Med.* 2011;12(4):398-405.

Enteral Nutrition[9-11]

- n = 688 randomized controlled trial (RCT) – enteral nutrition at 48 hours vs 3-6 hours has decrease in length of hospital stay 16 vs 13 days and mortality (12% vs 8.5%) in pediatric burn patients
- Early institution of enteral nutrition has been shown to improve outcomes
  - *Interrupted for procedures*
  - *Intolerance of feedings*
- Canadian clinical guidelines
  - *Decrease in length of stay and improved survival*
- Route is still debatable
  - *Gastric vs postpyloric*

[9]Martin, et al. *CMAJ*. 2004;170:197-204.
[10]Mehta, et al. *J Parenter Enteral Nutr*. 2010:34:38-45.
[11]Khorasani and Mansouri. *Burns*. 2010;36:1067-1071.

Total Parenteral Nutrition[6]

- Total parenteral nutrition initiation
  - *At least 5 days prior to reaching goal nutrition*
- Fluid requirements
- Fluid losses
  - *Na, Cl, HCO_3*
  - *Urine electrolytes or measurement in drained fluid*
- Hypophosphatemia
- Hypomagnesemia
- Acidosis or alkalemia

[6]Mehta, et al. *J Parenter Enteral Nutr*. 2009:33:336-344.

Pediatric Gastrointestinal Electrolyte Losses[12]

	Sodium (mEq/L)	Potassium (mEq/L)	Chloride (mEq/L)	Bicarbonate (mEq/L)
Gastric	140	15	155	–
Ileostomy	80-140	15	115	40
Colostomy	50-80	10-30	40	20-25
Secretory	60-120			
Diarrhea	30-40	10-80	10-110	30
Normal stool	5	10	10	0

[12]Wessel and Kocoshis. *Semin Perinatol.* 2007;31:104-111.

Micronutrients[13]

- Zinc
- Copper
- Vitamins B, C, and E
- Selenium
- Vitamin D
- Antioxidants, including trace elements and vitamins, such as high-dose selenium, may lead to improved outcomes

[13]Heyland, et al. *Intensive Care Med*. 2005;31:327-337.

Refeeding Syndrome[14]

- Signs and symptoms that occur after providing adequate nutrition to previously starved patients
- Eating disorders
- Chronic liver disease
- Congenital heart disease
- Malabsorption
  - *Short gut syndrome*
  - *Inflammatory bowel disease*
  - *Cystic fibrosis*
  - *Pancreatic insufficiency*

[14]Byrnes and Stangenes. *Curr Opin Clin Nutr Metab Care*. 2011:14:186-192.

Symptoms Associated With Refeeding Syndrome[14]

- Unintentional weight loss > 10% within 1-3 months
- < 70-80% of ideal body weight
- Prolonged nothing-by-mouth status > 7-10 days
- Muscle wasting
- Chronic dysphagia
- Inadequate nutrition > 10 days

[14]Byrnes and Stangenes. *Curr Opin Clin Nutr Metab Care*. 2011:14:186-192.

Pathophysiology of Refeeding[14]

- Dramatic shift in macronutrient metabolism
  - *Increase in insulin secretion*
  - *Glucagon release is inhibited*
  - *Activation of previously slowed anabolic pathways*
  - *Shift from lipolysis to lipogenesis*
- Depletion of adenosine triphosphate (ATP)
- Reduced electrolytes and vitamins
- Migration of electrolytes to intracellular locations

[14]Byrnes and Stangenes. *Curr Opin Clin Nutr Metab Care*. 2011:14:186-192.

Electrolyte Imbalance[14]

- Hypophosphatemia
  - *Increased insulin leads to intracellular migration of phosphorus*
  - *Required for phospholipids, nucleic acids, and ATP*
- Hypokalemia
  - *Carbohydrate reintroduction leads to increased insulin, which shifts potassium intracellularly*
- Hypomagnesemia
  - *Cofactor for a number of processes*
- Hyperglycemia
- Sodium retention and fluid imbalance
  - *Fluid retention, pulmonary edema, and congestive heart failure*

[14]Byrnes and Stangenes. *Curr Opin Clin Nutr Metab Care*. 2011:14:186-192.

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Nutrition in Liver Disease

Malnutrition and Growth Failure Are Common Among Pediatric Patients With Liver Disease

- This is an observed phenomenon
- Most studies showing disordered metabolism in liver disease have been performed on adults
- Because pediatric studies are lacking, disordered metabolism in children with liver disease must be inferred

Causes of Malnutrition Among Patients With Liver Disease

- Poor dietary intake
  - *Iatrogenic*
    - Unpalatable salt and protein restricted diets
  - *Anorexia*
    - Inadequate leptin catabolism[1]

[1]Ben-Ari Z, et al. *Dig Dis Sci*. 2002;47:183-189.

Causes of Malnutrition Among Patients With Liver Disease (cont'd)

- Poor dietary intake (cont'd)
  - *Zinc deficiency*
    - Ginès and Arroyo[2]
  - *Diabetes/prediabetes*
    - Insulin resistance[3]
  - *Cytokine excess*
    - Tilg[4]

[2]Ginès P and Arroyo V. *Gut*. 2000;46:588-590.
[3]Selberg O, et al. *J Clin Invest*. 1993;91:1897-1902.
[4]Tilg H. *Can J Gastroenterol*. 2001;15:661-668.

Causes of Malnutrition Among Patients With Liver Disease (cont'd)

- Iatrogenic
  - *Dietary sodium and protein restriction*
  - *Large volume paracentesis*
  - *Fluid restriction*
  - *Medication*
    - Neomycin
    - Lactulose
    - Antibiotics
    - Diuretics
    - Cholestyramine

Causes of Malnutrition Among Liver Transplant Candidates

- Nutrient malabsorption or maldigestion
  - *Cholestasis*
  - *Protein-losing enteropathy related to portal hypertension*
  - *Exocrine pancreatic insufficiency*

Pancreatic Insufficiency in End Stage Liver Disease

- Patients with progressive familial cholestasis (type I rather than types II or III)
  - *Knisely*[5]
- Patients with Alagille syndrome
  - *Piccoli and Spinner*[6]
- Patients with recurrent pancreatitis
- Patients with chronic portal hypertension
  - *Lee and Lai*[7]

[5]Knisely AS. *Pediatr Dev Pathol*. 2000;3:113-125.
[6]Piccoli DA and Spinner NB. *Semin Liver Dis*. 2001;21:525-534.
[7]Lee SP and Lai KS. *Am J Gastroenterol*. 1976;65:244-248.

Effect of Elevated Serum Bile Acids Upon Intestinal Function

- Thiry-Vella loop was created
- Successive superior mesenteric artery perfusion of saline cholate, deoxycholate, taurocholate, and taurodeoxycholate at 5, 8 ,12, and 22 µm
- At 8 µm, free bile acid (BA) disturbed transport of H_20, Na, and amino acids (AA) and produced reduction in Na-K adenosine triphosphatase associated with mitochondrial abnormalities
- At 22 µm, conjugated BA disturbed Na and H_20 transport, but not other function
  - *Berant M, et al.*[8]

[8]Berant M, et al. *J Pediatr Gastroenterol Nutr*. 1988;7:588-593.

Disordered Glucose Homeostasis in Liver Disease

- In portal hypertension: insulin resistance
  - *Hyperinsulinemia and hyperglucagonemia both occur*
    - Selberg, et al.[9]

[9]Selberg O, et al. *J Clin Invest*. 1993;91:1897-1902.

When Liver Disease Becomes End-Stage, an Accelerated Starvation Pattern Occurs

- Glycogen stores become depleted when liver disease becomes advanced
  - Gluconeogenesis is increased
- Lipid peroxidation takes place
- Protein catabolism is accelerated
  - *Yamanaka, et al.*[10]

[10]Yamanaka H, et al. Nutrition. 1999;15:749.

Disordered Protein Metabolism in Liver Disease

- Even patients with early cirrhosis (Child's A) have reduced protein stores
  - *Prijatmoko, et al.*[12]
- Adult patients have increased proteolysis that cannot be suppressed by feeding
  - *Tessari*[13]
- Data regarding the value of branched chain AAs in enhancing nitrogen balance and protein accretion are conflicting
  - *Sokal, et al.*[14]
  - *Marchesini, et al.*[15]

[12]Prijatmoko D, et al. *Gastroenterology*. 1993;105:1839-1845.
[13]Tessari P. *Curr Opin Clin Nutr Metab Care*. 2003;6:79-85.
[14]Sokal EM, et al. *Pediatr Res*. 1996;40:66-71.
[15]Marchesini G, et al. *J Nutr*. 2005;135(Suppl):1596S-1601S.

Measurement of Energy Expenditure[16]

- Harris-Benedict equation
  - *Male = 66.1 + [13.8 × wt(kg)] + [5 × ht(cm)] – 6.8 × age = kcal*
  - *Female = 655 + [9.6 × wt(kg)] + [1.8 × ht(cm)] – 4.7 × age = kcal*
- Indirect calorimetry (metabolic cart)
  - *O_2 consumption and $C0_2$ production measured*
  - *Respiratory quotient (RQ) calculated*
    - 0.7 for fat
    - 0.8 for protein
    - 1.0 for carbohydrate (CHO)

[16]University of Virginia School of Medicine Web site. http://www.med-ed.virginia.edu/pda/refcards/criticalcare/Cal.htm. Accessed March 15, 2012.

Hypermetabolism in Liver Disease[17]

- High risk (62% 1-year and 54% 5-year survival)
  - *Measured resting energy expenditure (REE)/calculated REE = 120%*
  - *Measured REE/calculated REE = 100-120% and body cell mass/body wt = < 35%*
- Low risk (88% 1-year and 88% 5-year survival)
  - *Rest of patients*

[17]Selberg O, et al. *Hepatology.* 1997;25:652-657.

Obesity and Liver Disease

- For adults, obesity is defined as a body mass index (BMI) of > 30[17]
- For children, obesity is a BMI of > 85th %tile for age[18]
- Nonalcoholic steatohepatitis and nonalcoholic fatty liver disease are common in these patients (50-70%)[19]
- Those with BMI > 35 have increased incidence of wound dehiscence and multiple organ failure
  - *Sawyer, et al.*[20]

[18]Centers for Disease Control and Prevention Web site. http://www.cdc.gov/nccdphp/dnpa/growthcharts/training/modules/module1/text/module1print.pdf. Accessed March 15, 2012.
[19]Gill HK and Wu GY. *World J Gastroenterol*. 2006;12:345-353.
[20]Sawyer RG, et al. *Clin Transplant*. 1999;13(Pt 2):126-130.

Nutritional Evaluation of Children With Liver Disease

NASPGHAN
NORTH AMERICAN SOCIETY FOR PEDIATRIC GASTROENTEROLOGY, HEPATOLOGY AND NUTRITION

NASPGHAN FOUNDATION
For Children's Digestive Health & Nutrition

NASPGHAN Nutrition University

Techniques of Nutritional Evaluation

- Indirect calorimetry (metabolic cart)
- Anthropometry/BMI
- Biochemical evaluation
  - *Blood*
  - *Urine*
  - *Gut effluent*
- Histology
- Radiology

Indirect Calorimetry in Infants

Photograph courtesy of Dr. Conrad Cole.

Whole Body Calorimetry

Photograph courtesy of Dr. Conrad Cole.

What Can We Learn From Calorimetry?[16]

- Can determine REE
- Can determine RQ
  - *CO_2 eliminated/O_2 consumed*
  - *Among anabolic individuals receiving a balanced diet, the normal quotient is approximately 0.8*
    - If the patient is primarily metabolizing CHOs, the quotient is ~ 1.0
    - If the patient is primarily metabolizing fats, the quotient is ~ 0.7

[16]University of Virginia School of Medicine Web site. http://www.med-ed.virginia.edu/pda/refcards/criticalcare/Cal.htm. Accessed March 15, 2012.

Estimation of Body Composition[21]

- Body fluid volume
  - *Dilution of an isotope, a dye*
- Body element content
  - *K, Na, etc. are proportionate to fat-free mass*
- Body density
  - *Weight on land/weight submerged*

[21]Woodrow G. *Perit Dial Int*. 2007;27(Suppl 2):S245-S249.

Anthropometry

- Mid arm muscle area
- Triceps skin fold
- Biceps skin fold
- Abdomen: hip circumference
- BMI

Nutritional Assessment – *Caveats*

- BMI
  - *Highly unreliable among patients who have overt ascites and/or edema due to hyperaldosteronism*

Imaging Techniques for Body Content Estimation

- Computed tomography scan
- Magnetic resonance imaging
- Dual-energy x-ray absorptiometry (DEXA)
  - 2 x-ray beams of different intensity are focused on the area in question
- Bioelectric impedance
  - AC current applied and resistance measured
  - Impedance is equal to length/cross section area

Tests of Intestinal Function

- Breath hydrogen
- Fecal fat
- D-xylose
- Nitrogen balance
- Fecal elastase

Histology[22]

- Small intestinal histology
  - Are villi long?
  - Is there inflammation?
  - Is the histology consistent with gluten enteropathy?

[22]Rubio-Tapia A and Murray JA. *Hepatology*. 2007;46:1650-1658.

Radiology

- Upper gastrointestinal/small bowel series
  - *Gives a rough idea of gastric capacity and emptying time*
  - *Gives a rough idea of mucosal relief*
  - *Gives an idea of how well roux-limbs (in biliary atresia) empty*
- Gastric emptying scan

Anthropometric Analysis

- Weight, height, weight for height, BMI
- Mid arm circumference
- Triceps skin fold measurement
- Bioelectric impedance
- DEXA

Biochemical Markers

- Hemogram
- Total protein/albumin
- Prealbumin/retinol-binding protein (RBP)
- Ca, Mg, PO_4
- Electrolytes, blood urea nitrogen, creatinine
- Liver panel
- Triene:tetraene ratio
- Trace elements

Use of Various Proteins in Assessing Acuity of Malnutrition Is Dependent Upon Their Half-Lives[23]

Protein	Half-life
Albumin	18 days
Transferrin	8 days
Prealbumin	2-3 days
RBP	2 days
Ferritin	30 hours

[23]Campillo B, et al. *Gastroenterol Clin Biol*. 2006;30:1137-1143.

Trace Element Measurements[24]

- Can be obtained, but serum (or tissue) levels do not necessarily correlate well with clinical deficiency states
  - *For example, zinc, selenium, manganese, molybdenum, etc. are widely distributed in many body compartments*
- Some patients with cholestatic liver disease are hypermanganesemic and hypercupremic, but this may represent an epiphenomenon
  - *Are these oxidants damaging to the liver during cholestasis? Not necessarily.*

[24]Best C and Gourley GR. *Therapy*. 2009;6:75-81.

Carnitine

- Synthesized from lysine and methionine[25]
- Facilitates entry of long-chain fatty acids (FAs) into mitochondrion for β oxidation[25]
- About 20% of ingested carnitine is absorbed[25]
- Very low birth weight prematures are typically carnitine-deficient
  - *MeLegh, et al.*[26]
- Carnitine synthesis may be inhibited during cholestasis
  - *Sekas and Paul*[27]
- Best marker of status is acyl/free ratio (normal = < 0.4)[28]

[25]Rebouche CJ and Chenard CA. *J Nutr*. 1991;121:539-546.
[26]MeLegh B, et al. *Acta Paediatr*. 1996;85:345-350.
[27]Sekas G and Paul HS. *Biochim Biophys Acta*. 1992;1125:196-202.
[28]Campoy C, et al. *Early Hum Dev*. 1998;53(Suppl):S149-S164.

Medium-Chain Triglycerides Versus Long-Chain Triglycerides for Cholestatic Patients?

Medium-Chain Triglycerides Versus Long-Chain Triglycerides as a Nutrient Source

- Medium-chain triglyceride (MCT)
  - *Advantages*
    - Bypasses lymphatics
  - *Disadvantages*
    - Fewer kcals
    - High osmotic load
    - Energy cannot be stored
    - Oxidation produces FAs
- Long-chain triglyceride
  - *Advantages*
    - Excellent in producing adaptation
    - High caloric density
    - Low osmolality
  - *Disadvantages*
    - Less efficient absorption

Excessive medium chain triglycerides at the expense of essential fatty acids can result in essential fatty acid deficiency.[29]

[29]Kaufman SS, et al. *Pediatrics*. 1992;89:151-154.

Triene:Tetraene Ratio[30]

- 20:3ω9/20:4ω6
- Arachidonic and linoleic acids comprise the tetraenes
- The mead acid comprises the trienes
- ω3, ω6, and ω9 FAs all compete for the same desaturases. Only when ω3 and ω6 are deficient, the mead acid (ecosatrienoic acid) is synthesized.
- A triene:tetraene ratio of > 0.2 correlates highly with essential FA (EFA) deficiency

[30]Oregon State University Web site. http://lpi.oregonstate.edu/infocenter/othernuts/omega3fa/. Accessed March 15, 2012.

Water Soluble Vitamins

- Patients getting multivitamin infusions are generally sufficient
- During times of shortage, deficiencies may appear
- Most patients with liver failure do fine if supplemented

Surrogate Markers For Micronutrient Deficiency

- A good surrogate marker for Zn deficiency is reduced alkaline phosphatase level
- A good surrogate marker for pyrodoxine deficiency is reduced alanine aminotransferase level
- A good surrogate marker for copper deficiency is neutropenia

Fat Soluble Vitamin Deficiency Is Common Among Cholestatic Children

How should we monitor for fat soluble vitamin deficiency?

Monitoring Vitamin A Status

- Hepatic Concentration
  - Best marker because >90% of retinol is stored in liver
- Relative Dose Response[31]
  - Measure retinol at time 0, give a test dose of retinyl palmitate and measure retinol 5 hours.
    - RDR $(R5 - R0)/R5$
      - >20% is always associated with reduced stores
      - <10% is never associated with reduced stores
- Seven other tests of vitamin A status in descending order of sensitivity/specificity compared to RDR[32]
  - Serum retinol>retinol binding protein (rbp)>retinol/rbp ratio>corneal touch cytology (cic)>slit lamp>tear film breakup exam>Shirmer test
  - Controversy exists vis a vis relationship between RDR and retinol[33]

[31] Amedee-Manesme O, et al. Am J Clin Nutr 1987;46:286-289.
[32] Feranchek AP, et al. Hepatology 2005; 42:782-792.
[33] Verhoef H and West CE. Am J Clin Nutr 2005;81:835-839.

Monitoring Vitamin D Status

- 25-OH vitamin D
- 1, 25-OH vitamin D
  - Although this is the active form, it tells us nothing about vitamin D stores
- PTH level
- Tubular reabsorption of Phosphate[34]
  - 1-(urine PO4/serum PO4 x serum creatinine/urine creatinine) x 100=% of PO4 reabsorbed.
    - Should be ~100% in the face of low serum PO4 and >80% in the face of normal serum PO4

[34] Payne RB. Ann Clin Biochem 198;35:201-206.

Monitoring Vitamin E Status

- Serum Vitamin E level
- Serum Vitamin E/Total Serum Lipids[35]
  - Slightly more sensitive (when sural nerve biopsy or neurologic symptoms are the gold standard) among cholestatic infants
    - Measuring total serum lipids is preferable to using serum cholesterol or serum triglycerides alone
    - Serum cholesterol is more reliable than serum triglycerides in children because triglycerides vary greatly with feeding[36]

[35] Sokol RJ, et al. N Engl J Med 1984;310:1209-1212.
[36] Thurnham DI, et al. Ann Clin Biochem. 1986;23:514-520.

Monitoring Vitamin K Status

- Vitamin K Level
- PIVKA (prothrombin in vitamin K deficiency)[37]
- Prothrombin Time
- Factor VII level
  - Among the vitamin K dependent factors (II, VII IX, X)

[37] Motohara K et al. Pediatr Res 1985;19:354-357

Nutritional Management of Children With Liver Disease

- Fluids, electrolytes, trace elements
  - Restriction of fluid and salt should not be excessive for fear of "overshooting" and precipitating hepatorenal syndrome [38]
  - Excessive zinc losses may precipitate zinc deficiency so zinc supplementation is prudent[39]

[38] Gines P, Guevara M. Hepatology 2008;48:1002-1010.
[39] Saner G, et al. J Trace Elements in Exp Med. 2000;13:271-276.

Nutritional Management: Energy Requirements in Pediatric Liver Disease [10,40]

- Resting energy expenditure is 127-140% of predicted energy expenditure
- Infants and children should receive 130-150% of recommended daily allowance based upon **ideal** weight rather than **wet** weight
- Nocturnal feedings or a late-night snack is important to minimize gluconeogenic response and protein catabolism.

[10] Yamanaka H, et al. Nutrition. 1999;15:749

[40] Pierro A, et al. J Pediatric Surg. 189;24:534-538.

Nutritional Management: Protein and Carbohydrate

- Under most circumstances, protein should not be restricted in children with chronic liver disease[41]
- Supplying 45-65% of the daily caloric distribution as carbohydrate will have a protein sparing effect and will satisfy the USDA Dietary Reference Intake[42]
- Supplementation with some branched chain amino acids may improve nitrogen balance[15]

[15] Marchesini G, et al. *J Nutr*. 2005;135(Suppl):1596S-1601S

[41] Plauth M, et al.Clin. Nutr. 2006; 25: 285–94

[42] USDA CNPP website. http://www.cnpp.usda.gov/Publications/DietaryGuidelines/2010/PolicyDoc/Appendices.pdf

Nutritional Management:Fat

- No rationale for restricting lipids (even in patients with fat malabsorption)
- MCT supplementation is advisable, but diets should contain adequate quantities of essential fatty acids to prevent deficiency[43]
- Recommendations for fat soluble vitamin supplementation are as follows:[44,45]
  - Vitamin A—10000 u if given with tocopherol polyethylene glycol succinate
  - 25-OH Vitamin D—2-4 mcg/kg/day
  - Vitamin E—25-50 IU/kg/day as tocopherol polyethylene glycol succinate
  - Vitamin K—2.5-5 mg 2-7 x/week.

[43] Pettei MJ et al. Am J Clin Nutr. 1991; 53:1217-1221
[44] Sokol R. Gastroenterol Clin North Am 1994;23: 673-705
[45] Argao EA, Heubi JE. Current Opin Pediatr 1993;5: 562-566

Summary

- Indirect calorimetry is a helpful adjunct in nutrition planning for undernourished patients with liver disease
- The patient with liver disease should not be deprived of calories or protein
- Patients should be monitored for signs of glucose intolerance
- Nitrogen balance seems better if branched chain AAs enhance other AAs rather than replacing them
- End-stage liver patients may benefit from nighttime feedings
- Among cholestatic patients, fat soluble vitamins should be supplemented
- Medium chain fats are important energy sources among cholestatic patients, but adequate EFA must be provided

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Enteral Nutrition

How to Feed[1]

- Oral
  - *Increase calorie density*
- Oral supplements: formulas
- Nasogastric tube: bolus, nipple/gavage approach
  - *Goal set for each feeding, time limit*
  - *Feed as much as possible and gavage remainder*
  - *Works if normal gastrointestinal (GI) tract function*

[1]Bankhead R, et al. *J Parenter Enteral Nutr*. 2009;33:122-167.

How to Feed[1] (cont'd)

- Nighttime drip
  - *Hunger later in the day*
- Continuous drip; gastric, then jejunal[1]
  - *No hunger, best tolerance*
  - *GI tract dysfunction*
    - Motility
    - Short bowel syndrome

[1]Bankhead R, et al. *J Parenter Enteral Nutr*. 2009;33:122-167.

Enteral Nutrition Orders

- Every order should contain 4 standard elements
  1. Patient information
  2. Formula details (name, strength)
  3. Delivery site/device
  4. Administration method and rate

[1]Bankhead R, et al. *J Parenter Enteral Nutr*. 2009;33:122-167.

Enteral Feeding Formulas Used in Pediatrics

- Human breast milk
- Infant and “premie” formulas
- Pediatric formulas
- Blenderized whole food formulas

What to Feed[2]

- Under 1-year-old infant: breast milk/formula
  - *Increase caloric density, if needed*
  - *Special formulas for specific diseases*
- Over 1 year: standard is 30 cal/oz formulas

[2]Stettler N, et al. In: *Nelson Textbook of Pediatrics*. 19th ed. Philadelphia, PA: Saunders Elsevier; 2011: Chapter 42.

Reconstituted Infant and Pediatric Formulas: Hospital Standards[1]

- Use sterile water
- Use a special formula kitchen with trained staff using aseptic technique
- Formula is good for 24 h
- Formula is to be refrigerated within 1 h of preparation
- Amount of formula required for a 4-h interval or bolus feed is warmed in a bottle warmer or in warm water shortly before use

[1]Bankhead R, et al. *J Parenter Enteral Nutr*. 2009;33:122-167.

Formulas[3]

- Polymeric
  - *Standard proteins, fats, and carbohydrates*
  - *Cheapest, most milk-based*
- Semielemental
  - *Predigested, di- and tripeptides*
  - *Some with medium-chain triglycerides (MCTs)*
- Elemental
  - *Amino acid–based*
- Modular

[3]Diamanti A. *Nutritional Therapy and Metabolism*. 2010;28:40-45.

Infant Feeding

Breast Milk[4]

- 2011 Breastfeeding Report Card: Centers for Disease Control and Prevention (CDC)
  - *75% of mothers initiate breastfeeding*
  - *44% are breastfeeding at 6 months*
  - *24% are breastfeeding at 12 months*
  - *35% and 15% are breastfeeding exclusively at 3 and 6 months, respectively*

[4]CDC Web site. http://www.cdc.gov/breastfeeding/data/reportcard2.htm 2011. Accessed March 2, 2012.

Human Milk[5]

- Colloidal dispersions of casein molecules, emulsions of fat globules, fat globule membranes, and live cells
- Ratio of whey to casein: 70-80% whey to 20-30% casein decreases over time to 55% whey and 44% casein in mature milk
- Iron, vitamin K, and vitamin D are low in human milk, and deficiency in the infant can occur

[5]Picciano MF. *Pediatr Clin North Am*. 2001;48:53-67.

Human Milk

- Vitamin D—400 IU/day until infant is weaned[6]
- Iron supplementation should start at 4 months with 1 mg/kg/day oral iron; continue until adequate oral iron from foods[7]

[6]Wagner CL, et al. *Pediatrics*. 2008;122:1142-1152.
[7]Baker RD, et al. Pediatrics. 2010;126:1040-1050.

Human Milk Benefits[8]

- Reduced risk of acute otitis media, nonspecific gastroenteritis, severe lower respiratory tract infections, atopic dermatitis, asthma in young children, obesity, type 1 and 2 diabetes, childhood leukemia, sudden infant death, and necrotizing enterocolitis

[8]Ip S, et al. AHRQ Publication No. 07-E007. Rockville MD: U. S. Department of Health and Human Services, 2007.

Premature: Breast Milk[9]

- Breast milk does not meet calorie and micronutrient needs of premature infants
- Modular or fortifiers added to human breast milk are done in a specially designated area
- Where possible, liquid fortifiers are used and not powdered, but most available are powdered

[9]Groh-Wargo S and Sapsford A. *Nutr Clin Pract*. 2009;24:363-376.

Premature: Breast Milk

- Has a 4-h maximum hang time in hospital
- Usually given via syringe pump that is at a 40°-60° angle
- Requires a new feeding set up with every feeding (new syringe and tubing)

Premie Formulas

- Standard 22 kcal/oz
- Come liquid, ready-to-feed
- Higher protein
- Higher fat proportion of MCTs
- Increased calcium and phosphorus

Premie Discharge Formulas

- Standard is 22 cal/oz
- Either powder or ready-to-feed, since concentrate difficult to make 22 cal/oz
- Higher calcium/phosphorus
- Nutrients between hospital premature formula and term formula
- To postnatal corrected age 9-12 months or weight for length is above 25th percentile

Breast Milk Contraindications[10]

- Infections: HIV, human T-cell lymphotropic virus (HTLV) types 1 and 2, or active pulmonary tuberculosis before 2 weeks of treatment should not breastfeed
- Infants with inborn errors of metabolism, such as galactosemia
- Maternal drug use, check LactMed: http://toxnet.nlm.nih.gov

[10]Schanler RJ, et al. *Breastfeeding Handbook for Physicians*. 1st ed. Elk Grove Vilage, IL: American Academy of Pediatrics; 2006.

Donor Human Milk[11]

- Most nonprofit; one for profit
- Protocols from Human Milk Banking Association of North America
- Follows the recommendations of the US Food and Drug Administration and CDC
- Standards for cleanliness and storage of human milk
- Tested for HIV, HTLV types 1 and 2, hepatitis B and C, and syphilis
- Pasteurized

[11]Human Milk Banking Association of North America Web site. https://www.hmbana.org/donate-milk. Accessed March 2, 2012.

Human Milk Handling and Storage[12]

- Hands washed with soap and water
- Hand-expressed or pump
- Glass or hard plastic container
- Frozen if not used within 72 h
  - *Labeled with date and time collected; single-feed aliquots*
  - *Okay for 3-6 months in conventional freezer*
- Thaw rapidly under lukewarm water
- Never refreeze

[12]CDC Web site. http://www.cdc.gov/breastfeeding/recommendations/handling_breastmilk.htm. Accessed March 2, 2012.

Infant Formulas[13]

- Historically, lots of formulas were available
- Deaths linked to a soy formula that was deficient in chloride
- 1980 Infant Formula Act (revised 1986)
  - *Amendment to the Federal Food, Drug, and Cosmetic Act*
  - *Regulate infant formulas*
  - *Establish nutrient levels*

[13]Martinez JA and Ballew MP. *Pediatr Rev*. 2011;32:179-189.

Choosing an Infant Formula

- Start with a standard formula
- If not tolerated:
  - *Determine the most likely cause of the intolerance*
  - *Change to a formula that will treat that condition*
  - *Assess the response to the formula change*
  - *Decide if another formula change is necessary*

Infant Formulas: Protein Content[14]

- Divided into 4 classes of formulas
  - *Cow's milk–based formulas*
  - *Soy formulas*
  - *Casein hydrolysate formulas*
  - *Amino acid–based formulas*

[14]University of Washington Web site. http://depts.washington.edu/growing/Nourish/Formula.htm. Accessed March 2, 2012.

Infant Cow's Milk–Based[15]

- Widely available
- Cheap starting material
- Constantly tweaked to attempt to simulate breast milk

[15]United States Department of Agriculture Web site. http://www.nal.usda.gov/wicworks/Topics/FG/Chapter4_InfantFormulaFeeding.pdf. Accessed March 2, 2012.

Infant Soy Formulas[16]

- Soy formula for vegans
- Galactosemia and hereditary lactase deficiency (rare)
- No proven benefit in infantile colic or fussiness
- Crossover with cow's milk formula protein allergy is high

[16]State of Wisconsin Department of Health Services Web site. http://www.dhs.wisconsin.gov/publications/P4/P40077A.pdf. Accessed March 2, 2012.

Special Infant Formula Proteins

- Hydrolysate first line for formula protein allergy[17]
  - *Reflux guidelines recommended 2-week trial*[17]
  - *Data about prevention of atopic disease*[18]
- Amino acid–based formula if hydrolysate not tolerated[17]

[17]Carney LN. *Today's Dietitian*. 2009;11:48.
[18]Jung AD. *Am Fam Physician*. 2001;64:1853-1861.

Infant Formulas – Carbohydrate

- Main types of carbohydrates in formulas[19]
  - *Lactose*
  - *Sucrose*
  - *Glucose polymers*
- Galactosemia: soy formulas, because they do not contain lactose[20]
- Which formulas contain sucrose?[19]
  - *Alimentum® and soy formulas, except Prosobee®*

[19]Perlstein D. MedicineNet Web site. http://www.medicinenet.com/infant_formulas/article.htm. Accessed March 2, 2012.
[20]Bhatia J and Greer F. *Pediatrics*. 2008;121:1062-1068.

Infant Formulas – Fat Content

- Main types of fats in formulas
  - *Long-chain triglycerides*
  - *MCTs*
- When are MCTs beneficial?
  - *Impaired fat absorption or lymphatic abnormalities*
  - *Cystic fibrosis, short gut syndrome, and protracted diarrhea*
- Which formulas contain MCTs?
  - *Alimentum® (33%), Pregestimil® (55%)*
  - *Elecare® (33%), Neocate® (33%)*
  - *Portagen® (87%), Vital® HN (45%)*

[21]Green-Corkins K and Sentongo T. In: *The A.S.P.E.N. Pediatric Nutrition Support Core Curriculum*, Corkins M, ed. Silver Spring, MD: American Society for Parenteral and Enteral Nutrition; 2010.

DHA and ARA[21]

- Docosahexaenoic acid (DHA) and arachidonic acid (ARA)
- Long-chain polyunsaturated fatty acids
- Present in breast milk; were not in formulas
- Rat studies showed increased visual acuity and neurologic development; some infant studies agree
- No harmful effects found
- Now in most infant formulas

[22]Groh-Wargo S, et al. *Pediatr Res*. 2005;57:712-718.

Immune Input[22]

- Probiotics
  - *Evidence of decreased infectious illnesses, especially diarrheal illnesses*
  - *Now present in some infant formulas*

[23]Weizman Z, et al. *Pediatrics*. 2005;115:5-9.

Infant Formulas End Thoughts[23]

- Made 20 cal/oz, because like breast milk
  - *Infants need more free water; kidney function immature*
  - *Increased caloric density increases risk of dehydration*
- Some newer studies show that actual caloric content of breast milk is < 20 cal/oz

[24]University of Washington Web site. http://depts.washington.edu/growing/Nourish/Concform.htm. Accessed March 2, 2012.

Infant Formula End Thoughts[23]

- Can underdilute to 24 cal/oz
- Above this, need supplementation
  - *Modulars: protein, fat, carbohydrate*

[24]University of Washington Web site. http://depts.washington.edu/growing/Nourish/Concform.htm. Accessed March 2, 2012.

Infant Formula End Thoughts[24]

- Infection reports
  - Enterobacter sakazakii *now* Cronobacter
  - *Powdered formula not sterile, reports of infections in infants with this bacteria (4-6 per year)*

[25]CDC Web site. http://www.cdc.gov/Features/Cronobacter/. Accessed March 2, 2012.

Metabolic Infant Formulas

- Specific formulas for specific diseases
- Carbohydrate-free formulas
  - *Require addition of a carbohydrate*
- Modified fat formulas
- Reduced mineral formulas

Complementary Foods[25]

- Recommendations fuzzy, because no literature
- Recommend exclusive breast milk or formula to 6 months of age
- Then discuss starting cereal and single ingredient solids at 4-6 months of age

[26]Kleinman RE, et al. In: *Pediatric Nutrition Handbook*. 6th ed. Gainesville, FL: American Academy of Pediatrics; 2009.

Pediatric Formulas

Enteral Nutrition Case

- Kaycee is a 13-year-old that presents with newly diagnosed Crohn's disease and mild malnutrition. What form of nutrition supplementation would you start?
- She develops a stricture and requires surgical resection of her ileum. Postoperation, she has difficulty with tolerating standard feedings. What enteral interventions could you try?

Pediatric Formulas

- Most are 30 kcal/oz, but some are 45 kcal/oz
- Still need to meet free-water needs
- Higher vitamin and mineral levels to meet pediatric dietary reference intakes

Pediatric Oral Supplements

- First line to increase caloric intake
- Sweetened with sucrose to enhance taste
- Some ready-to-feed, others powdered and reconstituted with whole milk

[27] *Dietary Sources in Pediatric Nutrition Support Handbook*, Corkins M, ed. Silver Spring, MD: American Society for Parenteral and Enteral Nutrition; 2011.

Standard Cow Milk–Based

- Widely available
- Cheap
- Unflavored, which lowers osmolarity
- Lactose-free
  - *Potential for lactose intolerance*
- Fat mixture: mixture of long- and medium-chain fats

Di- and Tripeptide Formulas

- Not designed for allergy or malabsorption conditions
- Better emptying
- Better tolerated
  - *Fats contain a percentage of MCT*

[27] *Dietary Sources in Pediatric Nutrition Support Handbook*, Corkins M, ed. Silver Spring, MD: American Society for Parenteral and Enteral Nutrition; 2011.

Elemental Pediatric Formulas

- Amino acid–based
- None with high MCT
- Use for allergic?
- Short bowel
  - *Better emptying*
  - *Absorption immediately*

[27] *Dietary Sources in Pediatric Nutrition Support Handbook*, Corkins M, ed. Silver Spring, MD: American Society for Parenteral and Enteral Nutrition; 2011.

Enteral Feeding Questions

- Fiber? Helps with stooling issues
  - *Soluble versus insoluble*
- Transpyloric feeds—Elemental?
  - *Tolerance okay*
  - *Animal studies: absorption better*
- When is adult okay?
  - *Adolescent? Calcium and phosphorus needs to be higher*
  - *Do contain higher protein content*

Immune Effects by Formulas

- No pediatric immunomodulating formulas
  - *Formula for inflammatory bowel disease with transforming growth factor–β: not used, so gone*
  - *Formulas containing ω-3 fats under study*
- Specialty formulas for specific situations
  - *Ketogenic diet*
  - *Fat transport defects*

Delivery Systems

- Old fashioned was cans (now some bottles) decanted into bag
  - *Ice pocket on the outside for extended drip feeds*
  - *Good for 24 h*
- Closed systems now available (no infant)
  - *Sterile, good for immunocompromised*
  - *Good for 48 h*
  - *No manipulation possible*

Blenderized Formula

- One commercially available
- Parents perceive as better
  - *Potential to be incomplete without guidance*
  - *Resources available with carefully worked out recipes*
  - *Tons of work for family*

Questions?

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Short Bowel Syndrome

Surgical Causes of Intestinal Failure

	436 Patients From 13 Series (1972-2000)
Necrotizing Enterocolitis	29%
Volvulus	27%
Atresia	23%
Gastroschisis	10%
Aganglionosis	4%
Other	7%

Compiled by Dr. Jane Balint.

The Epidemiology of Short Bowel Syndrome Has Changed

- Gastroschisis is now the second leading cause of intestinal failure in many centers[1]
- *In utero* environment seems crucial in producing gastroschisis
  - *Young maternal age*
  - *Exposure of fetus to agents producing vascular compromise*

[1]Vu LT, et al. *J Pediatr*. 2008;152:807-811.

Factors Contributing to Outcome

- Age at time of injury
- Amount and site of remaining bowel
- Function and motility of residual intestine
- Adaptation
- Other complicating factors
  - *Cholestatic liver disease*
  - *Infections*
  - *Further injury to remaining bowel*

Age at Time of Injury[2]

- Intestine will grow as the infant grows
- Potential for growth is greatest in premature infant
  - *Length of normal jejunum and ileum at autopsy*
    - 19-27 weeks gestation: 115 ± 21 cm
    - 27-35 weeks gestation: 172 ± 29 cm
    - > 35 weeks gestation: 248 ± 40 cm

[2]Touloukian RJ and Smith GJ. *J Pediatr Surg*. 1983:18;720-723.

Loss of Any Bowel

- Decreased surface area for absorption
- Shorter transit time
- Hypergastrinemia[3]
  - *Predilection for acid peptic disease*
  - *Decreased pancreatic enzyme activity*
  - *Precipitation of bile acids*
  - *Damage to epithelium of proximal small bowel*
  - *Stimulates intestinal motility*

[3]Hyman PE, et al. *J Pediatr Gastroenterol Nutr*. 1986;5:191-197.

Loss of Ileum

- Loss of glucagon-like peptide (GLP)2
- Large fluid and electrolyte losses
  - *Sodium loss can contribute to poor growth*[4]
- Malabsorption of bile acids, impairing fat and fat soluble vitamin absorption
- Lack of absorption of vitamin B_{12}

[4]Schwarz KB, et al. J Pediatr. 1983;102:509-513.

Loss of Ileocecal Valve[5]

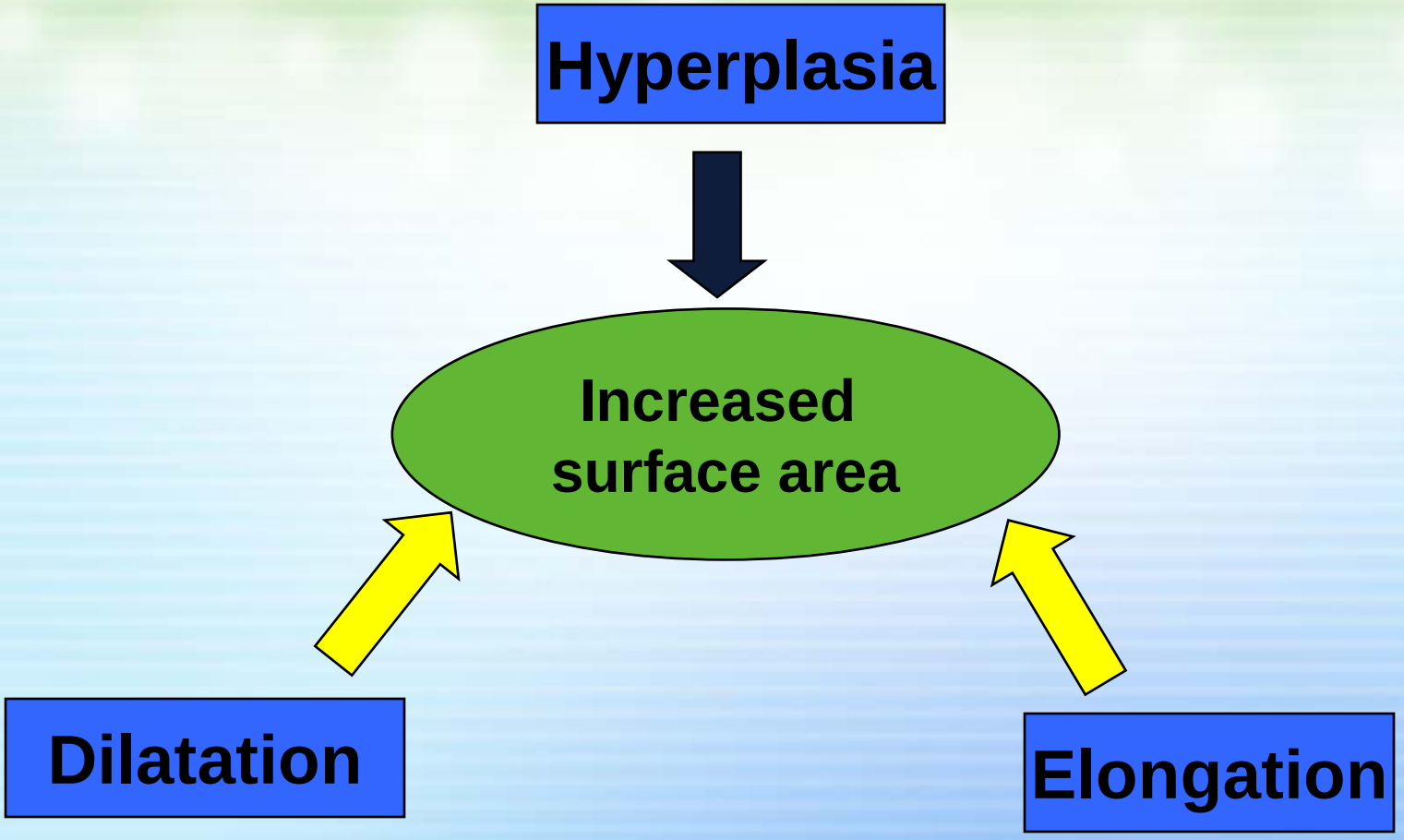
- While the valve is valuable, recent changes in dietary approach have obviated some of the problems associated with its loss
- However, the time to enteral autonomy is increased in patients without an ileocecal valve (ICV)

[5]Spencer AU, et al. *Ann Surg*. 2005:242;403-409.

Loss of Colon

- Loss of colonic brake
- Loss of water and electrolyte resorptive capacity
- Loss of ability to salvage calories from malabsorbed carbohydrates

Components of Adaptation



Adaptation

Promoted by

- **Humoral factors**
- **Luminal nutrients**

Complications of Total Parenteral Nutrition

- Catheter-related
  - *Loss of access*
  - *Sepsis*
- Metabolic
  - *Fluid and electrolyte imbalance*
  - *Abnormal glucose homeostasis*
  - *Cholestasis*

Are These the Culprits?

Strategies to Enhance Adaptation and Maximize Nutritional Status

- Utilize trophic hormones
- Addition of soluble fibers to the feeding
- Acid blockade
- Zinc
- Sodium chloride
- Loperamide

What About Glutamine and Growth Hormone?

- Positive effect upon adaptation among adult subjects[9]
- Less impressive results by others[10,11]
- No controlled pediatric trials

[9]Byrne TA, et al. *Ann Surg*. 2005;242:655-661.
[10]Szkudlarek J, et al. *Gut*. 2000;47:199-205.
[11]Scolapio JS, et al. *Gastroenterology*. 1997;113:1074-1081.

What About GLP2 (and a Dipeptidyl Peptidase Resistant Analog)?

- Enterocyte-specific
- Production is confined to distal small bowel/proximal colon
- Has potent trophic effects[12]
- Adult trials have shown promising results for improved gastrointestinal (GI) function[13]

[12]Jeppesen PB, et al. *Gut*. 1999;45:559-563.
[13]Jeppesen PB, et al. *Gut*. 2011;60:902-914.

What About Soluble Fibers?

Advantages and Disadvantages of Various Fructans[14]

- Short-chain fructooligosaccharide (scFOS)
  - *Rapid hydrolysis, which is advantageous in short gut patients with rapid transit*
- Inulin
  - *Relatively slow hydrolysis, which may render it useless*
- Longer chain oligofructans
  - *Fermentation pattern results in a lower concentration of butyrate*

[14]Kleessen B, et al. *Br. J Nutr*. 2001;86:291-300.

scFOS Fermentation

- Short-chain fatty acids are produced
  - *Enhance water and electrolyte absorption – helpful in management of diarrhea*
  - *Help create an acidic environment unfavorable to growth of some harmful pathogens*
  - *Preferred energy source for colon cells, helping to maintain GI tract integrity and function*

Most Important Strategy: Provide Enteral Nutrition

- Enteral nutrients
  - *Fuel for enterocytes – stimulating hyperplasia*
  - *Promote peristalsis – decreases overgrowth*
  - *Stimulate flow of GI secretions and secretion of humoral factors*

Continuous Versus Bolus

- Very little data on pediatric short bowel syndrome (SBS)
  - *Continuous enteral feeding is beneficial*[15]
  - *Does continuous feeding predispose to translocation?*[16]
- More data are available on intractable diarrhea
  - *Continuous enteral feeding is beneficial*[17]
- An adult study showed improved protein, fat, and energy balance on continuous feedings or mixed feedings versus oral feedings[18]

[15]Parker P, et al. *J Pediatr*. 1981;99:360-364.
[16]Weber TR. *J Pediatr Surg*. 1995;30:1086-1088.
[17]Orenstein SR. *J Pediatr*. 1986;109:277-286.
[18]Joly F, et al. *Gastroenterology*. 2009;136:824-831.

Type of Feeding

- Standard formula
- Breast milk
- Protein hydrolysate formula
- Amino acid formula

Standard Formula

- Increased permeability to intact proteins with mucosal injury
- SBS – dilated intestine, poor motility, bacterial overgrowth
- Allergic reactions to cow's milk or soy protein are common
- Carbohydrate source (lactose)

Breast Milk

- Bolster immune system
- Contain growth factors
  - *Epidermal growth factor and GLP2*
- Induce protective colonic flora
- Shorter duration of parenteral nutrition[19]

[19]Andorsky DJ, et al. *J Pediatr*. 2001;139:27-33.

Protein Hydrolysate Formula

- Lower antigenicity
- Contains some medium-chain triglyceride (MCT) oil – does not require bile acids or micelles for absorption
- Lower peak bilirubin[19]

[19]Andorsky DJ, et al. *J Pediatr*. 2001;139:27-33.

Amino Acid–Based Formula

- 2 infants weaned from TPN using a dilute elemental formula[20]
- 4 patients were able to wean from TPN after change to amino acid–based formula[21]
- Shorter duration of TPN[19]
- Effective in a small series of patients with SBS[22]

[19]Andorsky DJ, et al. *J Pediatr*. 2001;139:27-33.
[20]Christie DL and Ament ME. *J Pediatr*. 1975;87:705-708.
[21]Bines J, et al. J Pediatr Gastroenterol Nutr. 1998;26:123-128.
[22]Saavedra JM, et al. *Pediatr Res*. 2000;47:168A.

Optimal Fat Intake[23]

- 30% MCT: 70% long-chain triglyceride diet increased absorption from:
  - *23-58% preserved colon*
  - *46-58% no colon*

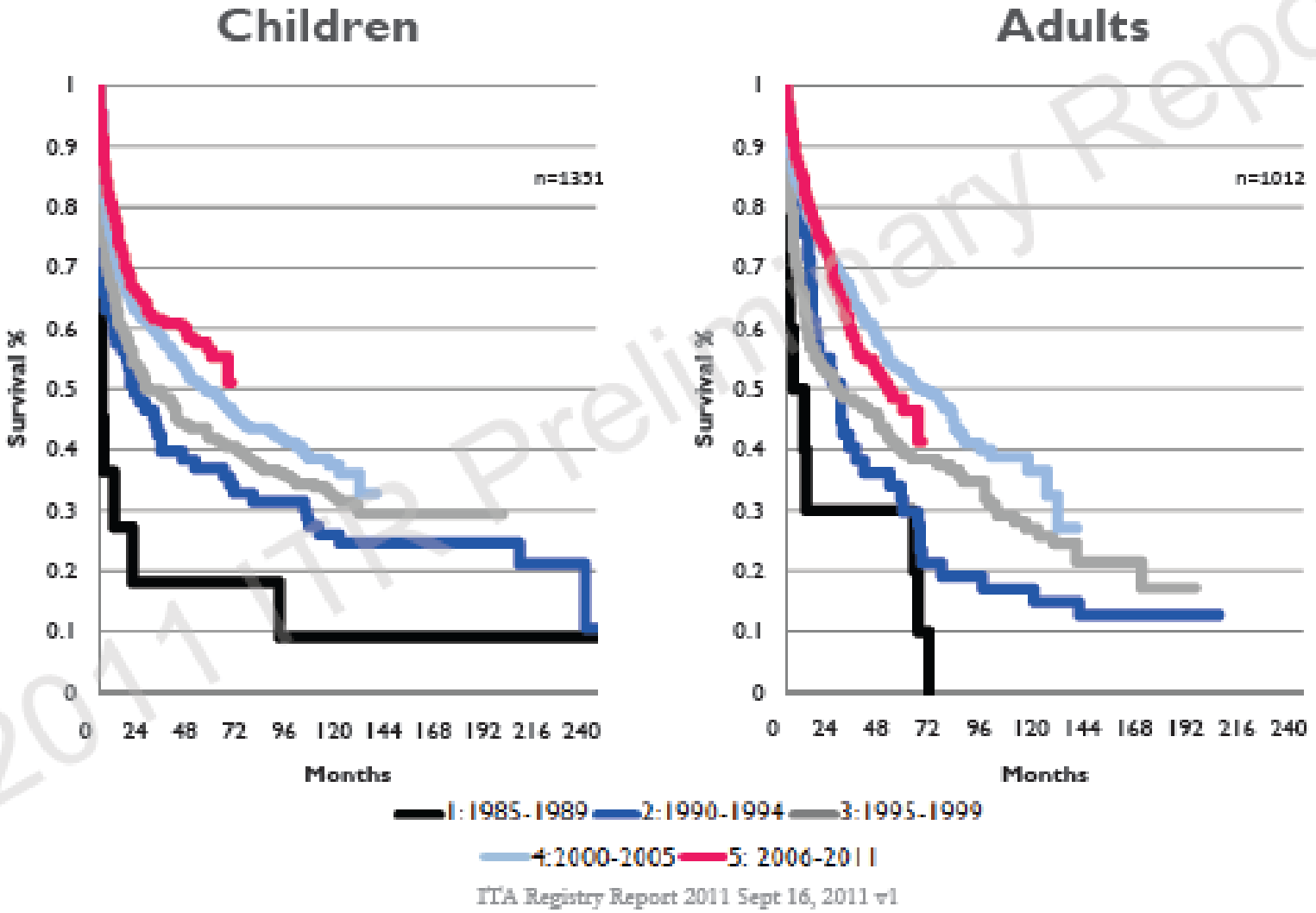
[23]Jeppesen PB and Mortensen PB. *Gut*. 1998;43:478-483.

What If Medical Management Fails?

Autologous Gastrointestinal Reconstruction versus Transplantation

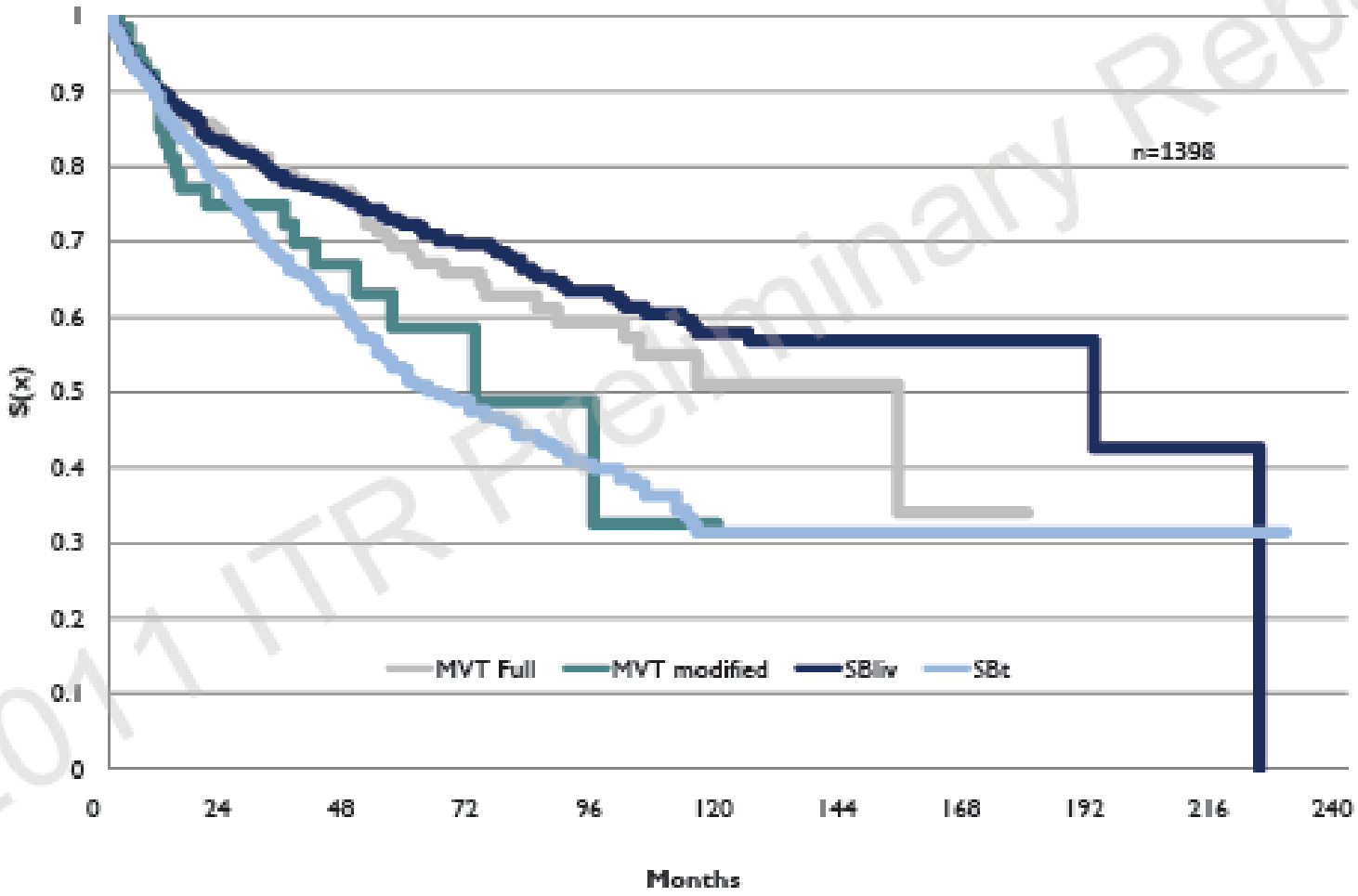
What Sort of Survival Can We Expect From Intestinal Transplantation

Patient Survival by Era



Courtesy of David Grant, MD (presented at the XII International Small Bowel Transplant Symposium, 2011

Conditional Long Term Survival by Transplant Type



ITA Registry Report 2011 Sept 16, 2011 v1

Courtesy of David Grant, MD (presented at the XII International Small Bowel Transplant Symposium, 2011

Summary

- The principles of management
  - *Advance enteral nutrition slowly, but in a determined fashion, providing adequate calories for growth, but not so much enteral nutrition that the child's intestinal function will be compromised*
    - A hydrolysate with structured lipids and scFOS makes physiologic sense
    - A free amino acid formula often works when hydrolysates fail
  - *Minimize risks for life-threatening complications*
    - Protect the liver
    - Protect the line
    - Avoid serious safety events

Case Report

- 7 ½-month-old female
- Born at 37 weeks gestation with *in utero* volvulus
- Presented in the newborn nursery with bilious vomiting in the first day of life
- Abdominal x-rays showed a high small bowel obstruction

Case Report (cont'd)

- At the time of exploratory laparotomy, she was found to have 45 cm of viable proximal intestine, approximately 3 cm of viable terminal ileum, an ICV, and a totally viable colon
- A primary jejunoileal anastomosis was performed

Questions

- What is the potential for adaptation in this near-term child vs. a premature?
- What is in her favor?
- What is the likelihood for adaptation?
- Is the presence of a viable ileum, ICV, and colon common in this disorder?

Questions

- Would most pediatric surgeons do a primary anastomosis?
- What do you predict will happen?

Case Report (cont'd)

- The patient developed a small bowel obstruction and jejunal perforation proximal to the obstruction
- An end ileostomy and Broviac catheter were placed

Case Report (cont'd)

- After recovering from the perforation, was started on parenteral nutrition and on oral feedings with Pregestimil® *ad libitum*

Questions

- What type of formula would you use?
- What laboratory tests would you follow?
- What would you predict would happen if the child gets bolus feedings?

Case Report (cont'd)

- The child required admission to her local hospital twice for hyponatremic dehydration
- She had another "adhesive" obstruction requiring lysis of adhesions
- She grew poorly, gaining an average of 10 g daily
- At 4 months of age, a percutaneous gastrostomy was placed

Questions

- Who among us would do a percutaneous gastrostomy on this infant?
- How would you feed her now?

Case Report (cont'd)

- She was started on Neocate® at a concentration of ½ kcal/mL
- Her enteral caloric intake was 25 kcal/kg daily
- Her TPN provided 62 kcal/kg daily
- She received 2 g/kg daily of lipid
- She received 3 g/kg daily of protein
- She received 2 meq/kg daily of sodium
- She had an episode of gram-negative sepsis and an episode of Candida sepsis

Question

- What do you predict will happen?

Case Report (cont'd)

- She continued to gain less than 10 g daily
- She became progressively more jaundiced
- She developed hepatosplenomegaly
- She developed a gastric ulcer that bled enough to require a blood transfusion
- Her ileostomy output was 300 mL daily

Questions

- How would you treat the ulcer?
- How would you manage the ileostomy output?

Case Report (cont'd)

- She was placed on sucralfate
- She was placed on ursodiol
- She was placed on diphenoxylate/atropine

Case Report (cont'd)

- Physical examination
  - *Wt: 5.6 kg (< 3rd %tile), Ht: 65 cm (15th %tile), occipitofrontal circumference 41.5 cm (< 10th %tile)*
  - *Scleral icterus was present*
  - *She was deeply jaundiced*
  - *Liver was palpable 3 cm below right costal margin; liver was 3+ firm; spleen was palpable 5 cm below left costal margin*
  - *No peripheral edema; no petechiae; no ecchymoses; no palmar erythema; no caput; no telangiectases*

Case Report (cont'd)

- Laboratory tests
  - *Normal Na, K, Cl, CO_2, blood urea nitrogen, creatinine*
  - *Total protein: 4.7 mg/dL*
  - *Albumin: 2.6 mg/dL*
  - *Bilirubin total/direct (T/D): 9.3/6.1 mg/dL*
  - *Alanine transaminase: 322; γ-glutamyl transpeptidase: 183*
  - *International normalized ratio: 1.3*

Questions

- What is her estimated Na requirement?
- Will her liver recover?
- What should be done with her nutrition?
- Does she need surgery? What kind of surgery?

Questions

- What other laboratory tests would you get?

Case Report (cont'd)

- Urine electrolytes and specific gravity (SG)
  - *Na: < 5 meq; K: 38 meq; SG: 1.025*
- Prealbumin: 11 mg/dL
- Triglycerides
  - *322 mg/dL*
- Factor 5 and 7
  - *Factor 5: 63%*
  - *Factor 7: 56%*

Case Report (cont'd)

- We progressively increased enteral caloric intake (full strength formula)
- We "fine tuned" TPN
  - *Increased zinc; decreased copper*
  - *Added carnitine*
  - *Decreased lipid to 1 g/kg daily*
- We asked our surgeon to "take down" the jejunostomy

Denouement

- The patient's nutrition improved
  - *Average wt gain: 35 g daily*
  - *Albumin increased to 3.2 mg/dL and prealbumin to 22 mg/dL*
- Cholestasis improved
  - *Bilirubin T/D was 2.6/1.4 mg/dL by the time she was receiving 75% of her nutrition enterally*
- Patient came completely off TPN

What Do You Predict Will Happen?

Potential "Landmines" That SBS Patients Must Avoid, Even Though TPN Is No Longer Necessary

- Growth failure
- Vitamin B_{12} deficiency
- D-lactic acidosis
- Hyperammonemia
- Gall stones
- Postnecrotic cirrhosis and portal hypertension
- Oxalate renal stones
- Anastomotic ulcers at the jejunocolonic anastomosis

Case Report (cont'd)

- This patient, now 8 years of age, has experienced no sequellae of SBS

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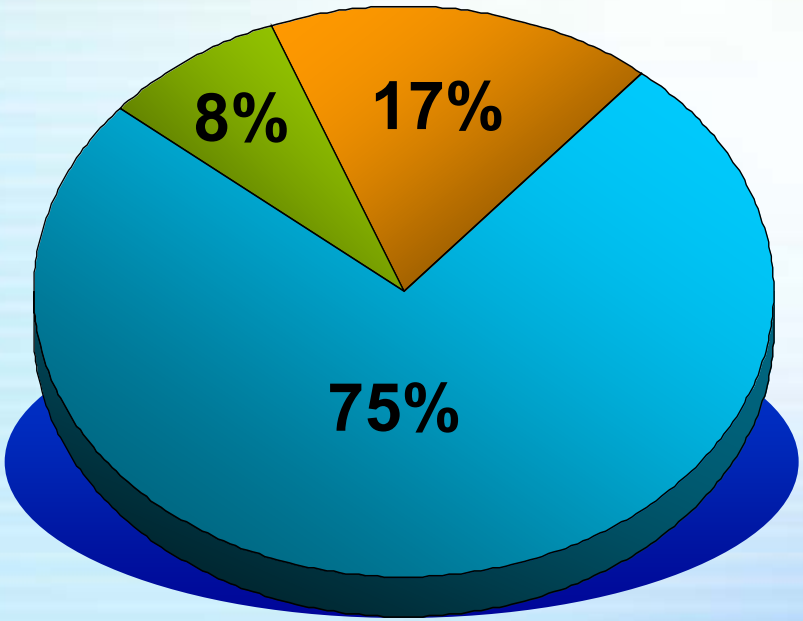
Overview of Obesity and Bariatric Nutrition

Objectives

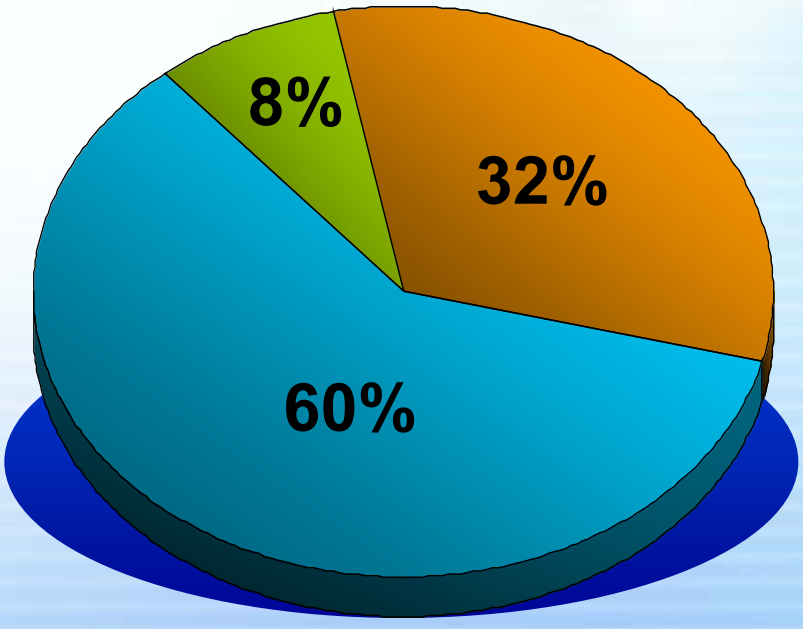
- Provide an overview of the pathophysiology, genetics, and medical complications associated with the development of obesity during childhood
- Outline the major bariatric surgery procedures and general potential nutritional risks
- Provide an overview of the most common micronutrient deficiencies associated with bariatric procedures and review possible treatment strategies

Components of Daily Energy Expenditure[1]

- Thermic effect of feeding
- Energy expenditure of physical activity
- Resting energy expenditure



Sedentary Person
(1800 kcal/d)



Physically Active Person
(2200 kcal/d)

[1]Segal KR, et al. *Am J Clin Nutr*. 1984;40:995-1000.

Obesity Results From Long-Term Positive Energy Balance

Regulation of Food Intake[2]

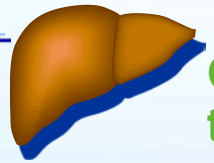
External factors
- Emotions
- Food characteristics
- Lifestyle behaviors
- Environmental cues

Central Signals

Stimulate		Inhibit	
NPY	Orexin-A	α-MSH	CART
AGRP	Dynorphin	CRH/UCN	NE
Galanin	CB1	GLP-I	5-HT

Peripheral signals

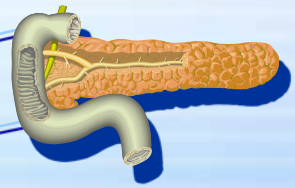
Peripheral organs



Glucose

CCK, GLP-1, Apo-A-IV Vagal

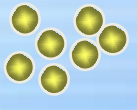
Gastrointestinal tract



Insulin

Ghrelin

Food intake



Leptin

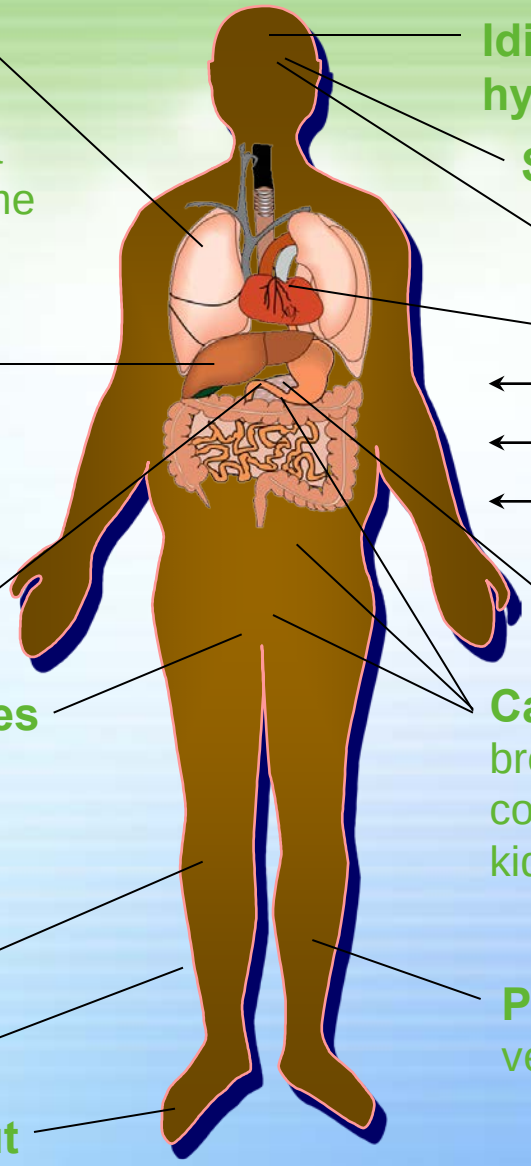
Adipose tissue

Cortisol

Adrenal gland

[2]Schwartz, et al. *Nature*. 2000;404:661-671.

Medical Complications of Obesity



Pulmonary disease
abnormal function
obstructive sleep apnea
hypoventilation syndrome

Idiopathic intracranial hypertension

Stroke

Cataracts

Nonalcoholic fatty liver disease
Steatosis
Steatohepatitis
Cirrhosis

Coronary heart disease

Diabetes

Dyslipidemia

Hypertension

Gall bladder disease

Severe pancreatitis

Gynecologic abnormalities
abnormal menses
infertility
polycystic ovarian syndrome

Cancer
breast, uterus, cervix
colon, esophagus, pancreas
kidney, prostate

Osteoarthritis

Skin

Gout

Phlebitis
venous stasis

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For Children's Digestive Health & Nutrition

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Organic Causes of Obesity

- Somatic dysmorphic syndromes
- Central nervous system insult
- Endocrinopathy

Genetic Disorders and Childhood Obesity[3]

Syndrome	Locus	Select Clinical Features
POMC	2p23.3	Early onset obesity, red hair, adrenocorticotropic hormone deficiency, hyperphagia
Carpenter		Acrocephaly, polydactyly, syndactyly, short stature, high palate, hypogonadism, heart anomaly
Alstrom	2p13	Retinitis pigmentosa, nerve deafness, acanthosis nigricans, male hypogonadism
Laurence-Moon-Bardet-Biedl	11q13 and 16q21	Early onset obesity, retinitis pigmentosa, moderate mental retardation (MR), polydactyly, deafness, hypogonadism, obsessive compulsive disorder
Cohen	8q22	Mild MR, microcephaly, short stature, low hairline, heart anomalies
Albright Hereditary Osteodystrophy Type 2	15q11-13; abnormal PTH adenylase cyclase complex	Pseudohypoparathyroidism, vitiligo, hypothyroidism, precocious puberty, short stature, brachydactyly, polydactyly, hypocalcemic tetany, mild MR
Prader-Willi-Labhart	Paternal 15q11-13	Small hands and feet, short stature, MR, cryptorchidism, hypothalamic hypogonadism

[3]Adapted from Haqq AM. In: *Pediatric Obesity: Etiology, Pathogenesis and Treatment*, Freemark M, ed. New York: Springer; 2010; 47-64.

Principles of Bariatric Procedures

- Creation of microgastria
- Bypass of proximal small bowel
  - *Malabsorption*
  - *? Alteration in bacterial flora*
- Combination of both

Criteria for Adolescent Bariatric Surgery[4]

- Fail more than 6 months of organized weight management
- At or near physiologic maturity
- Severely obese (body mass index (BMI) ≥ 35*-40) with serious obesity comorbidities or BMI ≥ 40*-50 with less serious comorbidities
- Commitment to comprehensive medical and psychological evaluations pre- and postoperation
- Capable and willing to adhere to nutrition requirements
- Avoid pregnancy for at least 1 year postoperation
- Have sufficient capacity to provide informed assent
- Supportive social environment/resources

[4]Inge, et al. *Pediatrics*. 2004;114:217-223.

Contraindications to Consideration of Bariatric Surgery[4]

- Medically correctable cause of obesity
- Substance abuse problem within the past year
- Medical, psychiatric, cognitive inability to comply with required dietary and medication regimen
- Current lactation, pregnancy, or planned pregnancy within 1-2 years of surgery
- Inability of patient/parents to fully comprehend the surgical procedure, medical consequences, and required long-term surveillance

[4]Inge, et al. *Pediatrics*. 2004;114:217-223.

Nutrient Absorption in the Gastrointestinal Tract[5]

Stomach	Duodenum	Jejunum	Ileum
Water	Calcium	Thiamin	Ca	Vitamin C
Copper	Iron	Riboflavin	PO_4	Folate
Iodine	PO_4	Niacin	Mg	B_{12}
Flouride	Mg	Pantothenate	Fe	D
Intrinsic factor	Copper	Biotin	Zn	K
ETOH	Selenium	Folate	Cr	Mg
	Thiamin	B_6	Mn	Bile acids
	Riboflavin	ADEK		
	Niacin	Vitamin C		
	Biotin	Peptides		
	Folate			
	ADEK			

[5]Adapted from Shikora SA, et al. *Nutr Clin Pract.* 2007;22:29-40.

Adjustable Gastric Band

- Adjustable restrictive procedure
- Expected weight loss 30-50% of excess weight
  - *Nibblers/sweet drinkers: less weight loss*
  - *Frequent band adjustment*
- Nutritional deficiencies
  - *Iron most common*
  - *Vitamin D second most likely*

Sleeve Gastrectomy

- Residual gastric structures minimize dumping beyond initial postoperative phase
- Excess weight loss 72% at 4 years; 55% at 6 years (adult)[6]
- Nutritional deficiencies[7]
  - *Anemia (26%)*
    - Iron >> folate > B_{12}
  - ***Vitamin D↓/↑parathyroid hormone (PTH) (39%)***
  - *Hypoalbuminemia (15%)*
  - *B_1 (11%)*

[6]D'hondt M, et al. *Surg Endosc*. 2011;25:2498-2504.
[7]Aarts EO, et al. *Obes Surg*. 2011;21:207-211.

Roux-en-Y Gastric Bypass (RYGBP)[8]

- Expected weight loss 60-70% of excess weight
  - *Nutritional issues*
    - Fe most common deficiency (50% by 2 years)
    - B_{12} 2nd most common deficiency (30% at 1-9 years)
    - Vitamin D deficiency common
- Dumping risk 40-60%

[8]Malinowski SS. *Am J Med Sci*. 2006;331:219-225.

Biliopancreatic Diversion (BPD)

- Rarely done in adolescents
- Excess weight loss 82% at 10 years[9]
- 72% fat and 25% protein malabsorption; no carbohydrate malabsorption[7]
  - *Protein/calcium malnutrition 7-12%*
- Multiple vitamin and mineral deficiencies[8]
  - *ADEK twice daily*
  - *> 2400 mg calcium citrate daily*
  - *Cu, Zn*

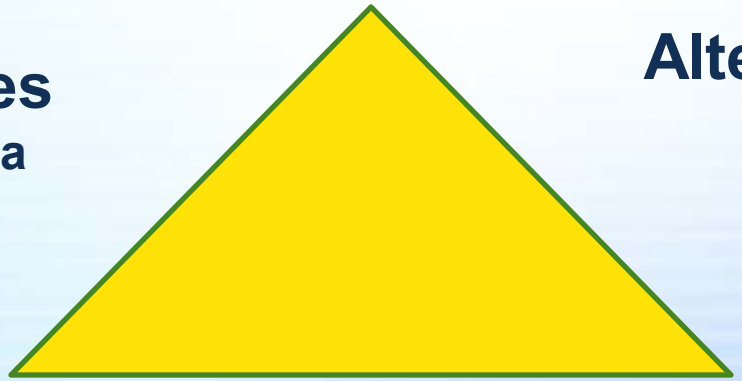
[8]Malinowski SS. *Am J Med Sci*. 2006;331:219-225.
[9]Marceau P, et al. *Obes Surg*. 2010;20:1609-1616.

Hallmarks of Thiamin Deficiency

- Burning feet
- Numbness and tingling starting in the feet and occasionally progressing to hands
- RED FLAG: persistent emesis
- Diabetes: increase thiamin needs 5-fold

Wernicke's Encephalopathy

Visual abnormalities
Opthalmoplegia
Nystagmus
Ptosis
Diplopia



Altered mental status
Disorientation
Apathy
Memory loss

Ataxia
Peripheral neuropathy

Treatment of Thiamin Deficiency

- Give B_1 with intravenous (IV) dextrose if suspect
- B_1 with B-complex, Mg for maximum absorption and neurologic function
- Early symptoms resolve with oral B_1 until symptoms disappear
- 50-100 mg daily IV or intramuscularly for advanced neuropathy or protracted vomiting

Clinical Features of B_{12} Deficiency

- Numbness and tingling of extremities
- Macrocytic anemia
- Pernicious anemia (late stage)
- 1/2 of patients with symptoms of deficiency have normal B_{12} levels
- Methylmalonic acid more accurate for screening

Treatment: 700-2000 mcg weekly for several weeks

Folic Acid

- Etiology of deficiency
  - *Inadequate intake*
    - Stores deplete in a few months postoperation
  - *Noncompliance with supplements*
  - *Malabsorption*
  - *Medications*
- Symptoms
  - *Early: fatigue, weakness, headaches, palpitations, diarrhea, and red painful tongue*
  - *Chronic: smooth, shiny tongue*
- Assessment
  - *Homocysteine with red blood cell folate most sensitive indicator of status*
- Treatment
  - *1 mg daily folic acid*

Calcium and Vitamin D

- Absorption of calcium is facilitated by vitamin D in an acidic environment
- Low acid environment after gastric resection results in poor calcium carbonate absorption
  - *Calcium citrate is absorbed 22-27% better than calcium carbonate, regardless of meal status*[10]
    - Sleeve gastrectomy series – 65 patients on multivitamin infusion and calcium carbonate[11]
      - *1/3 had vitamin D deficiency and increased PTH*
- Treat with vitamin D and calcium citrate

[10]Sakhaee K, et al. *Am J Ther*. 1999;6:313-321.
[11]Fouad RH, et al. *Surg Obes Relat Dis*. 2009;5:S53-S54.

Copper Deficiency

- No reports with sleeve gastrectomy and banding
- Occasionally seen with RYGBP and BPD
  - *9.6% in adult RYGBP series*[12]
  - *50% in adult BPD series*[13]
- Symptoms
  - *Numbness, tingling of hands and fingers*
  - *Gait disturbance*
  - *Anemia*
- Treatment with copper supplement

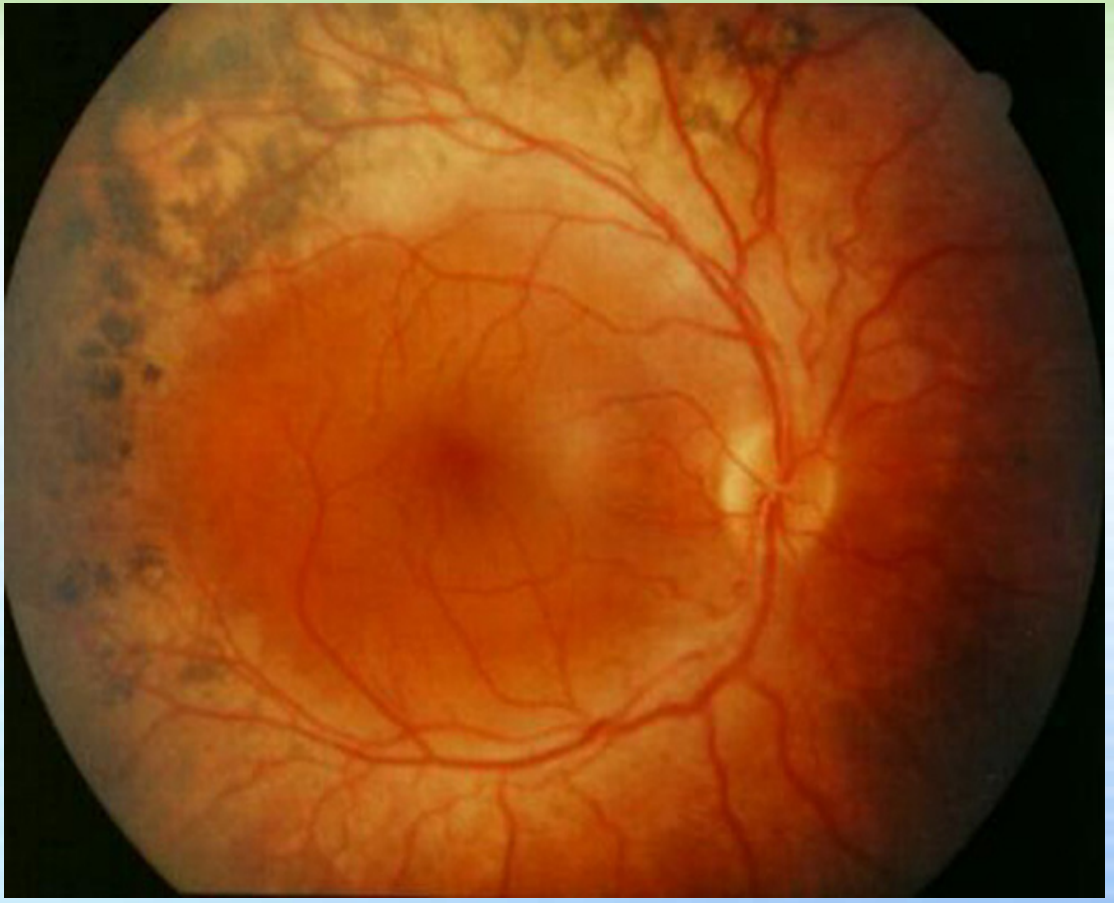
[12]Gletsu-Miller N, et al. *Int J Obes (Lond).* 2011. Epub ahead of print.
[13]Balsa JA, et al. *Obes Surg*. 2011;21:744-750.

Obesity and Bariatric Case Challenges

Case 1

- 4-year-old Latin American male with mild developmental delay referred by primary medical doctor for mildly elevated liver enzymes
  - *Strong family history of diabetes*
  - *Several aunts are legally blind*
  - *Pertinent examination findings: body mass index: 35; moderate acanthosis; hepatomegaly*

Physical Findings



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http://www.eyeatlas.com/box/360.htm.

Case 2

- 17-year-old girl status post RYGBP 2 years ago with symptoms of arm pain, back pain, weakness, and falling
  - *Lost 87% of excess body weight during year 1*
  - *Stomach cramping; nausea with protein rich foods*
  - *Referred by primary care physician to neurologist and recently diagnosed with peripheral neuropathy*
  - *Complete blood count with anemia*
    - Iron studies suggestive of iron deficiency

Copper

Special Thank You

- Margaret Furtado, MSRDLDN
- Cristina Germond, PhD
- Amy Manela
- Margaret Stallings
- Nutrition committee
- NASPGHAN Foundation
- Nutricia
- ATTENDEES!!!

Questions?

Robert J. Shulman, MD
Professor of Pediatrics
Baylor College of Medicine
Children's Nutrition Research Center
Texas Children's Hospital
Houston, TX

Perioperative Nutrition

Does Nutritional Status Matter?

Malnutrition Increases Operative Mortality

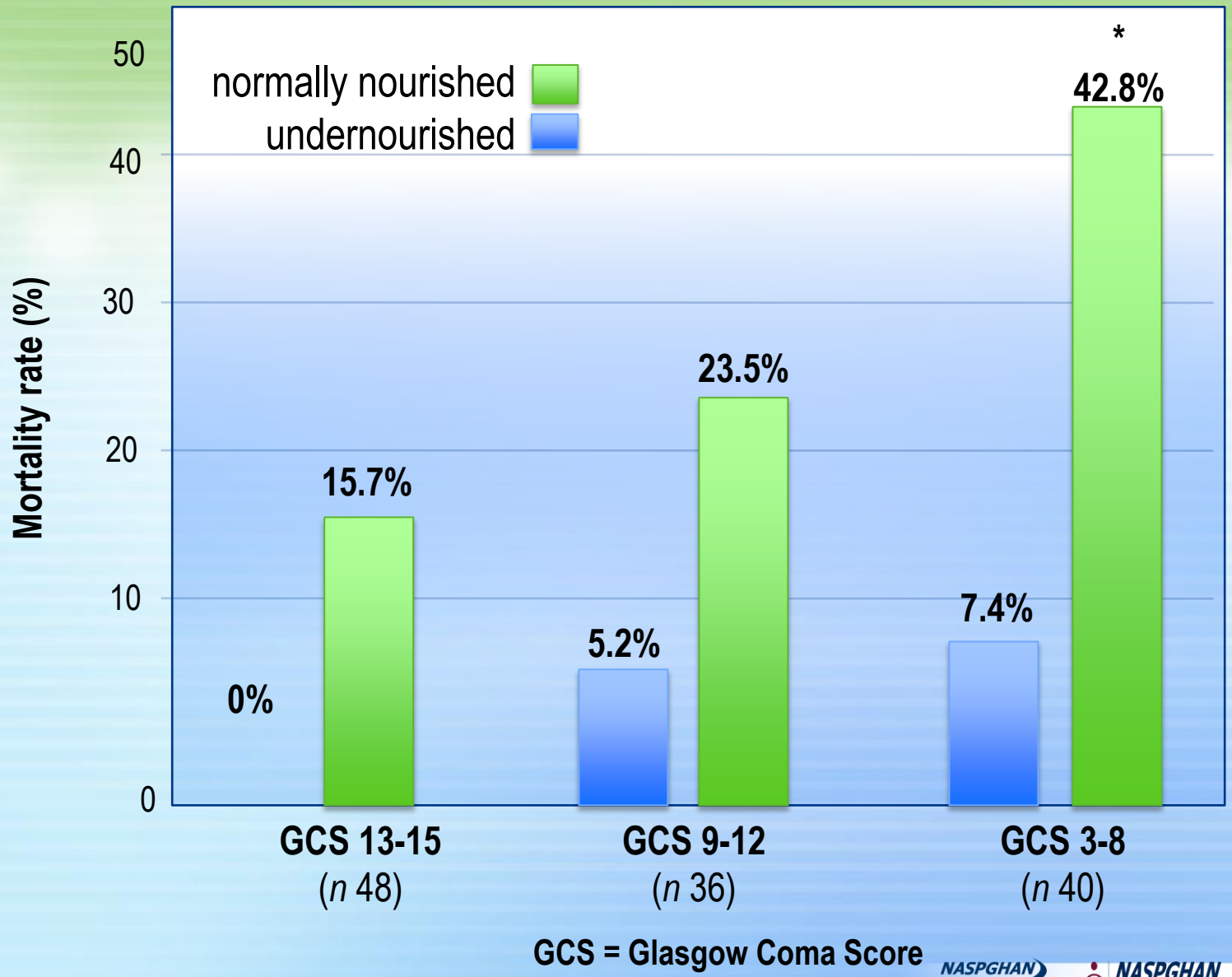
- Studley[1]
  - *Mortality in elective surgery for peptic ulcer*
  - *3.5% if < 20% weight loss*
  - *33% if ≥ 20% weight loss*
- Meguid et al.[2]
  - *Mortality in abdominal surgery for malignant disease*
  - *Well-nourished: 4%*
  - *Malnourished: 23% (includes weight loss > 10%)*

[1]Studley HO. *JAMA*. 1936;106:458-460.
[2]Meguid MM, et al. *Am J Surg*. 1988;156:341-345.

Preoperative Nutritional Status – Kids[3-6]

- 2-year survival after liver transplant related to weight Z score prior to transplant
  - *57% < –1*
  - *95% > –1*
- Hospital stay and infection after cardiac surgery related to weight Z score and serum albumin, respectively
- Neurosurgical shunt surgery complications related to serum albumin

[3]Chin SE, et al. *J Paediatr Child Health*. 1991;27:380-385.
[4]Anderson JB, et al. *J Thorac Cardiovasc Surg*. 2009;138:397-404.
[5]Leite HP, et al. *Nutrition*. 2005;21:553-558.
[6]Jain G, et al. *Br J Nutr*. 2007;98:944-949.



GCS = Glasgow Coma Score

[6]Adapted from Jain G, et al. *Br J Nutr*. 2007;98:944-949.

Does Nutritional Intervention Matter?

Perioperative Enteral Versus No Treatment Meta-Analysis[7]

- Fewer infections with enteral
- Tendency for fewer intra-abdominal and intrathoracic complications
- No differences in mortality
- No differences in total/major/wound complications

[7]Koretz RL, et al. *Am J Gastroenterol*. 2007;102:412-429.

Perioperative Enteral Versus Parenteral Nutrition Meta-Analyses[7,8]

- Fewer infectious complications
- Fewer major complications
- Fewer intra-abdominal and intrathoracic complications
- Shorter hospitalization

[7]Koretz RL, et al. *Am J Gastroenterol*. 2007;102:412-429.
[8]Mazaki T and Ebisawa K. *J Gastrointest Surg*. 2008;12:739-755.

ESPEN Guideline on Enteral Nutrition: Surgery[9,10]

- Indicated if oral intake
  - *Likely inadequate > 14 days (7-10 days postoperation)*
  - *≤ 60% recommended for > 10 days*
- Contraindications
  - *Intestinal obstruction/ileus*
  - *Severe shock*
  - *Intestinal ischemia*

[9]Weimann A, et al. *Clin Nutr*. 2006;25:224-244.
[10]Awad S and Lobo DN. *Curr Opin Anaesthesiol*. 2011;24:339-348.

ESPEN Guideline on Enteral Nutrition: Surgery[9,10]

- Preoperatively indicated
  - *Weight loss > 10-15% within 6 months*
  - *Body mass index (BMI) < 18.5 kg/m²*
  - *Serum albumin < 3 g/dL (not liver/renal)*
- Requires 7-10 days treatment
- Not indicated otherwise

[9]Weimann A, et al. *Clin Nutr*. 2006;25:224-244.
[10]Awad S and Lobo DN. *Curr Opin Anaesthesiol*. 2011;24:339-348.

ESPEN Guideline on Parenteral Nutrition: Surgery[10-12]

- Presumes enteral feeding not tolerated
- Preoperatively indicated if
  - *Weight loss > 10-15% in 6 months*
  - *BMI < 18 kg/m^2*
  - *Serum albumin < 3 g/dL (not liver/renal)*
- Requires 7-10 days treatment
- Improved postoperative outcome

[10]Awad S and Lobo DN. *Curr Opin Anaesthesiol*. 2011;24:339-348.
[11]Braga M, et al. *Clin Nutr*. 2009;28:378-386.
[12]Gustafsson UO and Ljungqvist O. *Curr Opin Clin Nutr Metab Care*. 2011;14:504-509.

ESPEN Guideline on Parenteral Nutrition: Surgery[10,11]

- Postoperative parenteral nutrition (PN) indicated if
  - *Malnourished and unable to receive adequate intake enterally for ≥ 7 days*
- Some enteral intake is preferable

[10]Awad S and Lobo DN. *Curr Opin Anaesthesiol*. 2011;24:339-348.
[11]Braga M, et al. *Clin Nutr*. 2009;28:378-386.

Pediatric Randomized Trial(s)

- Marín[13]
  - *n = 63 with peritonitis due to perforated appendix*
  - *Randomized to PN (24-48 hours postoperation) or control for 5 days*
  - *PN had greater nitrogen balance and serum insulin-like growth factor-1*

[13]Marín VB, et al. *J Pediatr Surg*. 1999;34:1330-1335.

ERAS – Enhanced Recovery After Surgery[14]

- Effort to reduce hospital stay after colonic resection
- n = 60
  - *Preoperation – epidural catheter for pain treatment*
  - *Postoperation*
    - 0-24 hours
      - *No nasogastric tube*
      - *Oral protein drinks; normal food allowed*
      - *Cisapride*
    - 24-48 hours
      - *Normal diet with protein drinks*
    - 48 hours
      - *Removal of epidural catheter*
      - *Discharge*

[14]Basse L, et al. *Ann Surg*. 2000;232:51-57.

Consensus Review of ERAS[15]

- 20 guideline points backed by grade A evidence
- Preoperative nutrition
  - *Limit fasting to 2 hours for liquids and 6 hours for solids*
  - *Patients should receive carbohydrate loading*
    - Reduces postoperative insulin resistance
    - Results in accelerated recovery and shorter hospitalization
    - Mechanism not completely elucidated – ? decreased inflammatory response

[15]Lassen K, et al. *Arch Surg*. 2009;144:961-969.

Randomized Trial of ERAS[16,17]

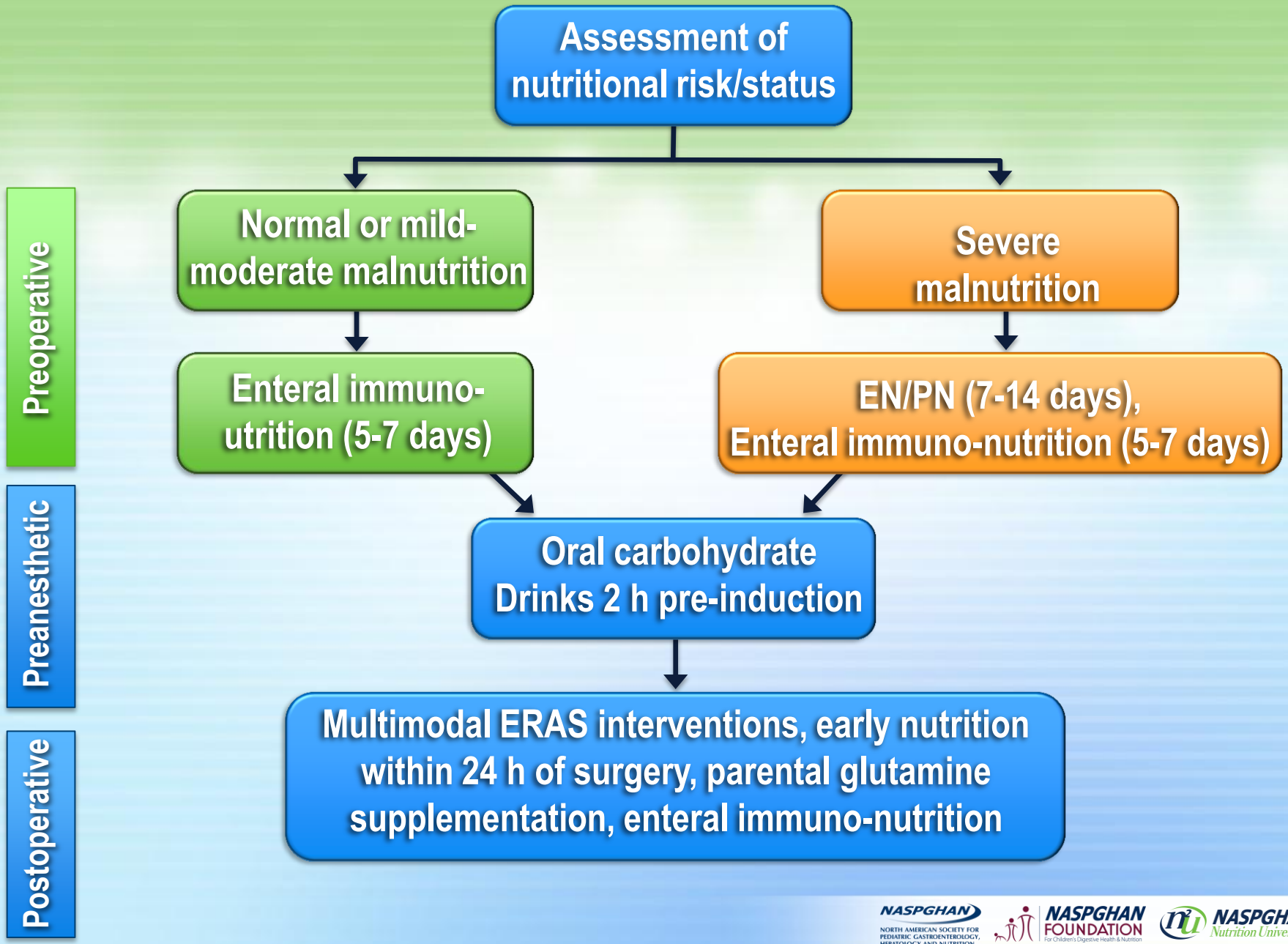
- n = 597 patients undergoing elective colorectal resection
- Control group fasted preoperatively and did not receive postoperative intake until flatus passed
- ERAS group
  - *Less insulin resistance; lower serum cytokines*
  - *Shorter hospital stay (1 day) and 10% reduction in cost*
  - *No differences in complications*
- Matches finding of previous meta-analysis

[16]Ren L, et al. *World J Surg*. 2012;36:407-414.
[17]Varadhan KK, et al. *Clin Nutr*. 2010;29:434-440.

Specialized Nutrition Support Meta-Analyses[10,18-20]

- Fish oil or glutamine dipeptide (given in PN) decreased
  - *Length of stay*
  - *Infection*
- Immunonutrition (arginine and/or glutamine and/or ω-3 fatty acids and/or nucleotides) decreased
  - *Complications*
  - *Infection*
  - *Hospitalization (mean 2.1 days)*

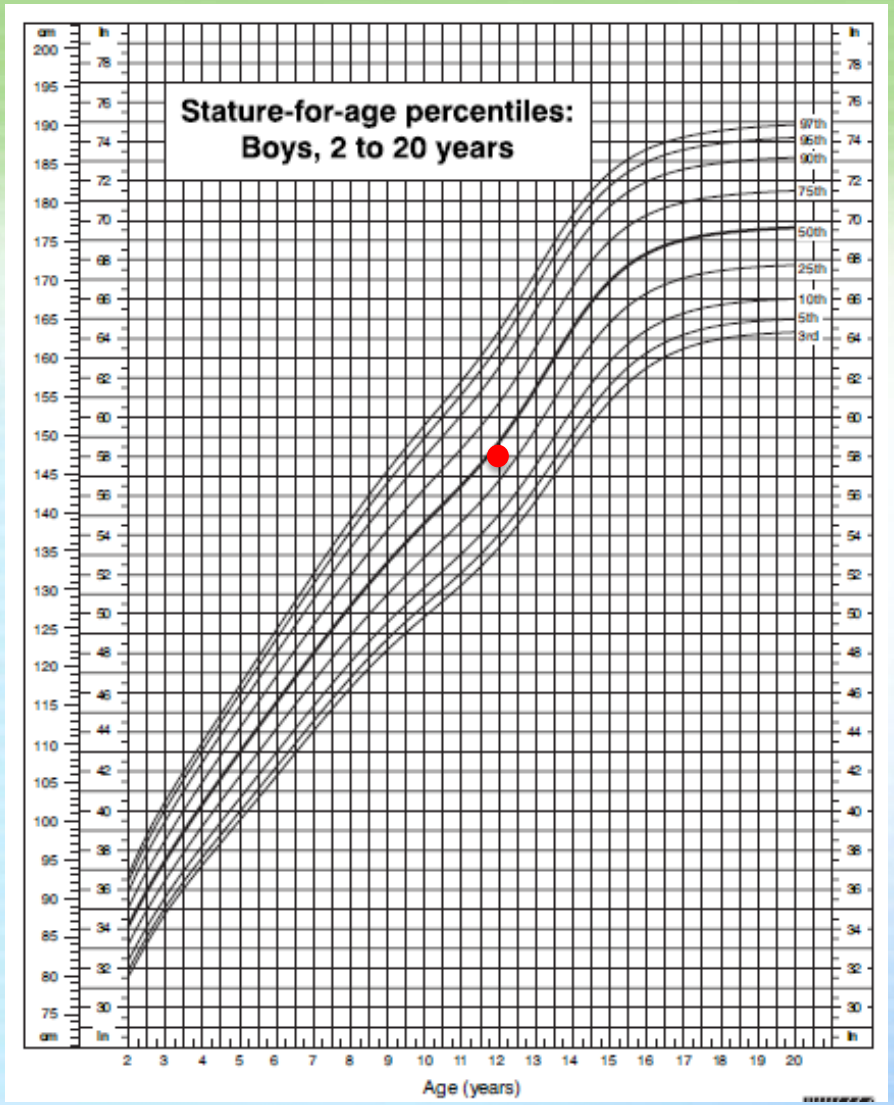
[10]Awad S and Lobo DN. *Curr Opin Anaesthesiol*. 2011;24:339-348.
[18]Chen B, et al. *JPEN J Parenter Enteral Nutr*. 2010;34:387-394.
[19]Zheng YM, et al. *World J Gastroenterol*. 2006;12:7537-7541.
[20]Cerantola Y, et al. *Br J Surg*. 2010;98:37-48.

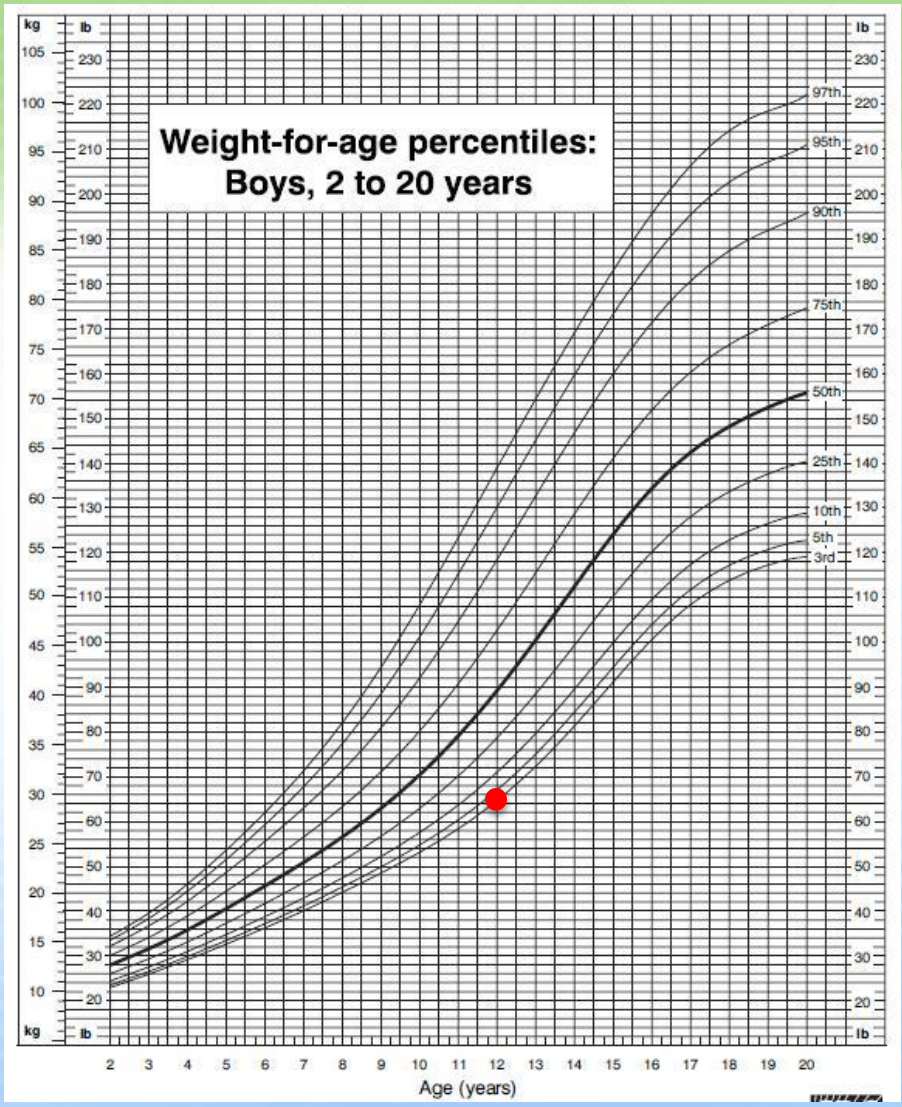


[10] Adapted from Awad S and Lobo DN. *Curr Opin Anaesthesiol*. 2011;24:339-348.

Case Study

- 12-year-old African American male with familial pancreatitis presents with 10 days of increasing abdominal pain and decreased appetite. Physical examination, blood work, and abdominal ultrasound consistent with pancreatitis. His usual hospital stay is 7-10 days.





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For Children's Digestive Health & Nutrition

NASPGHAN Nutrition University

Questions?

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Professor of Pediatrics
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Director, Gastrointestinal Eosinophilic Diseases Program
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Food Allergies and Eosinophilic Gastrointestinal Diseases

Amazing Mucosal Surfaces![1]

- Imagine a sheet of cells
- One side—everything you eat and 2 kg of bacteria (10^{14})
- Other side—sterile

[1]Atkins D and Furuta GT. *J Allergy Clin Immunol*. 2010;125(Suppl 2):S255-S261.

2-Year-Old Boy[2]

- One month history of:
  - *Vomiting*
  - *Irritability with eating*
  - Food aversion
  - *Slow weight gain*
- Comorbid conditions
  - *Eczema*
  - *Anaphylactic food allergy (FA) to peanut*
- Failed treatments
  - *Proton pump inhibitors (PPIs)*
  - *Formula changes*

[2]Newton J, et al. *Gastroenterol Nurs*. 2011;34:147-152.

2-Year-Old Boy (cont'd)[2,3]

- Diagnostic evaluation
  - *Upper endoscopy*
    - Linear furrowing
  - *Pathology*
    - 47 eosinophils(eos)/high-powered field (HPF) in proximal and distal
    - Basal cell hyperplasia
    - Normal gastric and duodenal mucosa
  - *Normal pH impedance study*

[2]Newton J, et al. *Gastroenterol Nurs*. 2011;34:147-152.
[3]Fleischer DM and Atkins D. *Immunol Allergy Clin North Am*. 2009;29:53-63.

17-Year-Old Boy[2]

- 3-year history of:
  - *Dysphagia*
  - *Food sticking, especially pills*
  - *Chewing food thoroughly, especially meat*
  - *Drinking fluids needed to wash food down*
  - *Heartburn*
- Comorbid history of FAs
- Family history of allergies, food sticking

[2]Newton J, et al. *Gastroenterol Nurs*. 2011;34:147-152.

17-Year-Old Boy (cont'd)[2]

- Diagnostic evaluation
  - *Barium esophagram*
    - Proximal esophageal stricture
  - *Upper endoscopy*
    - Proximal web and ring trachealization
- Diagnostic evaluation
  - *Pathology*
    - 48 eos/HPF
    - Degranulation and microabscesses
    - Normal gastric and duodenal mucosa

[2]Newton J, et al. *Gastroenterol Nurs*. 2011;34:147-152.

Eosinophilic Esophagitis: Update on Consensus Recommendations

GASTROENTEROLOGY 2007;133:1342–1363

AGA INSTITUTE

Eosinophilic Esophagitis in Children and Adults: A Systematic Review and Consensus Recommendations for Diagnosis and Treatment

Sponsored by the American Gastroenterological Association (AGA) Institute and North American Society of Pediatric Gastroenterology, Hepatology, and Nutrition

Clinical reviews in allergy and immunology

Series editors: Donald Y. M. Leung, MD, PhD, and Dennis K. Ledford, MD

Eosinophilic esophagitis: Updated consensus recommendations for children and adults

LIACOURAS ET AL

J ALLERGY CLIN IMMUNOL
JULY 2011

2011 Updated Consensus Report[4]

- Eosinophilic esophagitis (EoE) is a clinicopathologic disease
- Clinically characterized by esophageal dysfunction
- Pathologically 1 or more biopsies show eos predominant inflammation (≥ 15 eos in peak HPF)
- Histopathology is isolated to esophagus
- Other causes need to be excluded
- "PPI-responsive esophageal eosinophilia"
- Diagnosis made by clinicians
- Rarely < 15 eos/HPF (if other clinicopathologic features present)

[4]Liacouras CA, et al. *J Allergy Clin Immunol*. 2011;128:3-20.

New Diagnostic Guideline 2011 Conceptual Definition[4]

"Eosinophilic esophagitis represents a chronic, immune/antigen mediated, esophageal disease characterized clinically by symptoms related to esophageal dysfunction and histologically by eosinophil-predominant inflammation."

[4]Liacouras CA, et al. *J Allergy Clin Immunol*. 2011;128:3-20.

Food Allergic Disease

- Immune-mediated reaction to a specific food product (protein), causing symptoms (gastrointestinal tract, skin, nose, eyes, or lungs)
- Reproducible reaction to the food
- Resolves with removal of antigen

Bioavailability of Food Allergens

- Preingestion
  - *Ripening*
  - *Cooking*
  - *Enzyme treatment*
  - *Addition of ingredients (spices, preservatives, etc.)*
  - *Combinations of the above*
- Postingestion
  - *Complex interactions with other ingested foods*
    - Matrix effects
  - *Enzymes*
  - *pH changes*
  - *Other host factors (inflammation, gut motility)*

Allergy Testing

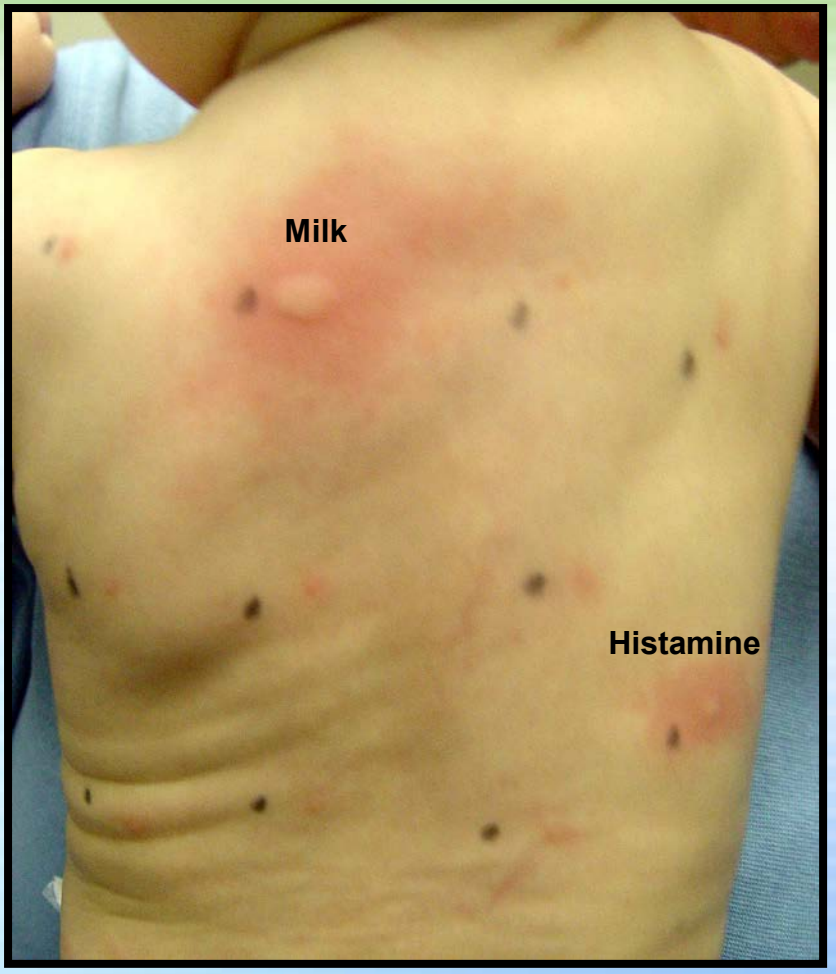
- Food sensitization = food specific immunoglobulin E (IgE) detected by skin or blood testing
- FA = reproducible physical response to IgE-mediated food

Rationale for Prick Skin Testing With Freshly Prepared Extracts

- Instability of selected fruit and vegetable allergens
- Lack of available commercial extract
- Check negative results obtained with a commercial extract in a patient with highly suggestive history
- Detection of unexpected ingredient
- These extracts are not standardized

Courtesy of Dan Atkins, MD.

Skin Testing to Food Allergens



Courtesy of Dan Atkins, MD.

Guidelines for the Diagnosis and Management of Food Allergy in the United States: Report of the NIAID-Sponsored Expert Panel

J ALLERGY CLIN IMMUNOL
VOLUME 126, NUMBER 6

Skin prick testing (SPT)[5]

- Safe and useful for diagnosis of IgE-mediated FA
- Reagents and methods are not standardized
- Positive SPT correlates with the presence of allergen-specific IgE bound to mast cells
- Compared with oral food challenges, they have low specificity and low positive predictive value for making an initial diagnosis of FA

[5]Boyce JA, et al. *J Allergy Clin Immunol*. 2010;126(suppl):S1-S58.

Guidelines for the Diagnosis and Management of Food Allergy in the United States: Report of the NIAID-Sponsored Expert Panel

J ALLERGY CLIN IMMUNOL
VOLUME 126, NUMBER 6

Allergen-specific serum IgE[5]

- Useful for diagnosis of IgE-mediated FA, but not diagnostic
- "Cutoff" levels, defined at 95% predictive values, may be more predictive than SPTs of clinical reactivity in certain populations
- Different assays yield variable results

[5]Boyce JA, et al. *J Allergy Clin Immunol*. 2010;126(suppl):S1-S58.

Guidelines for the Diagnosis and Management of Food Allergy in the United States: Report of the NIAID-Sponsored Expert Panel

J ALLERGY CLIN IMMUNOL
VOLUME 126, NUMBER 6

Allergen-specific serum IgE[5]

- Predictive values vary among studies
  - Patient selection (patients' ages)
  - Clinical disorder studied
- Negative test in face of highly suggestive history—consider medically supervised food challenge
- Quality of evidence: moderate
- Contribution of expert opinion: significant

[5]Boyce JA, et al. *J Allergy Clin Immunol*. 2010;126(suppl):S1-S58.

Variability in Skin Test Results

- Allergen extract
- Device
- Skin test technician
- Difficulty with application
- Sensitivity of skin to pressure
- Changes in level of sensitization
- Medications

Frequency of Allergic Disease in EoE Patients

Author/Year	Patients	AS%	Allergic Rhinitis (AR)%	Atopic Dermatitis %	FA (Ana)%
Spergel 2008[6]	620	50	61	21	5.7
Assa'ad 2007[7]	89	39	30	19	9
Sugnanam 2007[8]	45	66	93	55	24
Guajardo 2002[9]	39	38	64	26	23
Roy-Ghanta 2008[10]	23	26	78	4	N/A

[6]Spergel JM and Shuker M. *Gastrointest Endosc Clin N Am*. 2008;18:179-194.
[7]Assa'ad AH, et al. *J Allergy Clin Immunol*. 2007;119:731-738.
[8]Sugnanam KK, et al. *Allergy*. 2007;62:1257-1260.
[9]Guajardo JR, et al. *J Pediatr*. 2002;141:576-581.
[10]Roy-Ghanta S, et al. *Clin Gastroenterol Hepatol*. 2008;6:531-535.

Rationale for Allergy Evaluation in EoE

- Most patients (~ 80%) have coexistent asthma, eczema, AR, or FA
- Most patients are sensitized
- Seasonal variability of symptoms
- Improvement on elimination diets

1995 Esophageal Eosinophilia Responds to Elemental Diet[11]

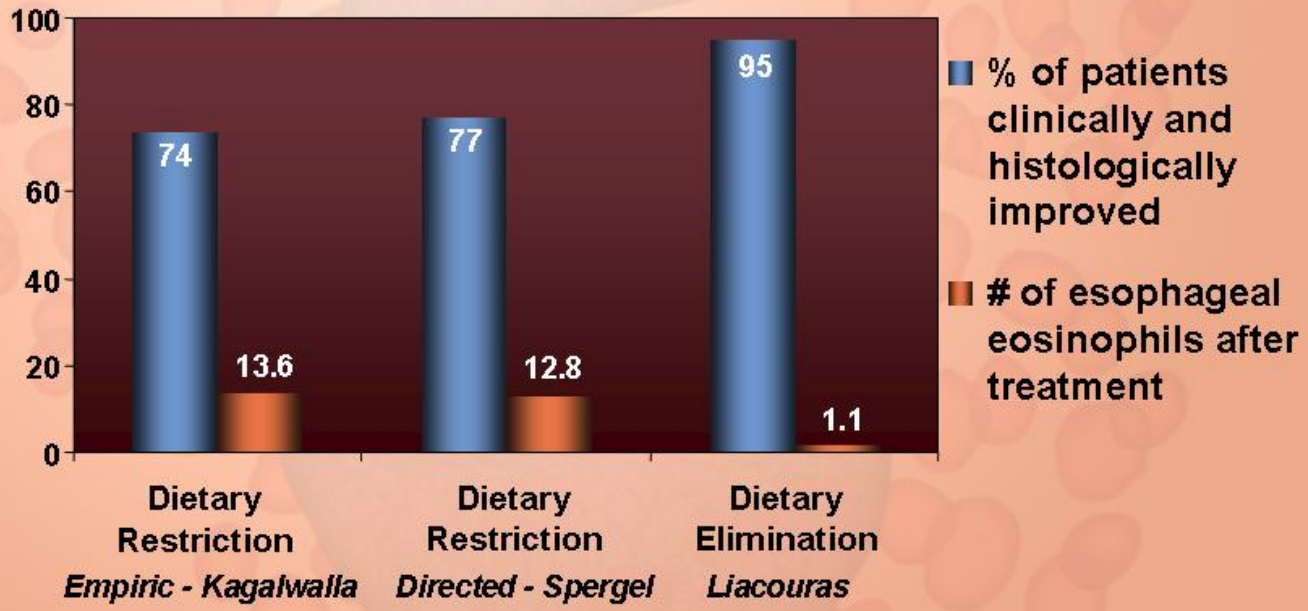
Eosinophilic Esophagitis Attributed to Gastroesophageal Reflux: Improvement With an Amino Acid–Based Formula

KEVIN J. KELLY,*,† AUDREY J. LAZENBY,§ PETER C. ROWE,* JOHN H. YARDLEY,‖
JAY A. PERMAN,*,† and HUGH A. SAMPSON*,¶

Divisions of †Pediatric Gastroenterology/Nutrition and ¶Pediatric Allergy/Immunology and Departments of *Pediatrics and ‖Pathology, The Johns Hopkins University School of Medicine, Baltimore, Maryland; and §Department of Pathology, University of Alabama at Birmingham, Birmingham, Alabama

[11]Kelly KJ, et al. *Gastroenterology*. 1995;109:1503-1512.

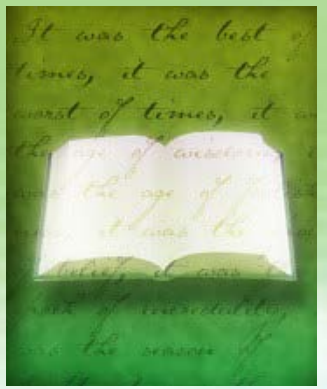
Dietary Restriction vs. Elimination



Kagalwalla, et al; *Clin Gastroenterol Hepatol* 2006; 117(2Suppl):S470.
Liacouras, et al; *Clin Gastroenterol Hepatol* 2005; 3:1198.
Spergel, et al; *Ann Allergy Asthma Immunol* 2005; 95(4):336.

[12]Kagalwalla AF, et al. *Clin Gastroenterol Hepatol*. 2006;4:1097-1102.
[13]Liacouras CA, et al. Clin Gastroenterol Hepatol. 2005;3:1198-1206.
[14]Spergel JM, et al. *Ann Allergy Asthma Immunol*. 2005;95:336-343.

Two Stories



- “Fear of Feeding”
- “Reluctant Carnivore”

2-Year-Old Boy

- Medications
  - *Lansoprazole 7.5 mg twice a day—to be weaned*
  - *Fluticasone propionate 44 mcg 2 puffs swallowed twice a day*
  - *Epinephrine 0.15 mg/delivery*
- Allergy
  - *Positive skin prick and serum IgE testing led to further diet restrictions of milk, soy, egg, pork, and wheat*

2-Year-Old Boy

- Nutrition
  - *Elemental formula supplements*
  - *Addition of extra calories to foods*
  - *Calcium and vitamin D supplements*
- Feeding
  - *Food aversion evaluation*

17-Year-Old Boy

- Medications
  - *Esomeprazole magnesium 40 mg twice a day—to be weaned*
  - *Fluticasone propionate 220 mcg 2 puffs swallowed twice a day*
  - *Epinephrine 0.3 mg/delivery*
- Allergy
  - *Positive SPT led to additional diet restrictions of oats, tree nuts, and potatoes*

17-Year-Old Boy

- Nutrition
  - *FA education*
  - *Increased fruit/vegetable intake*
  - *Multivitamin added*

Questions?

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Failure to Thrive

Objectives

- Definition
- Prevalence
- Normal variants masquerading as failure to thrive (FTT)
- Medical risk factors
- Management

Definition[1,2]

- FTT
  - *More likely (and more accurately) described in developing countries as protein-energy malnutrition*
  - *Not a disease*
  - *Symptom representing the final common pathway of medical, psychosocial, and environmental processes*

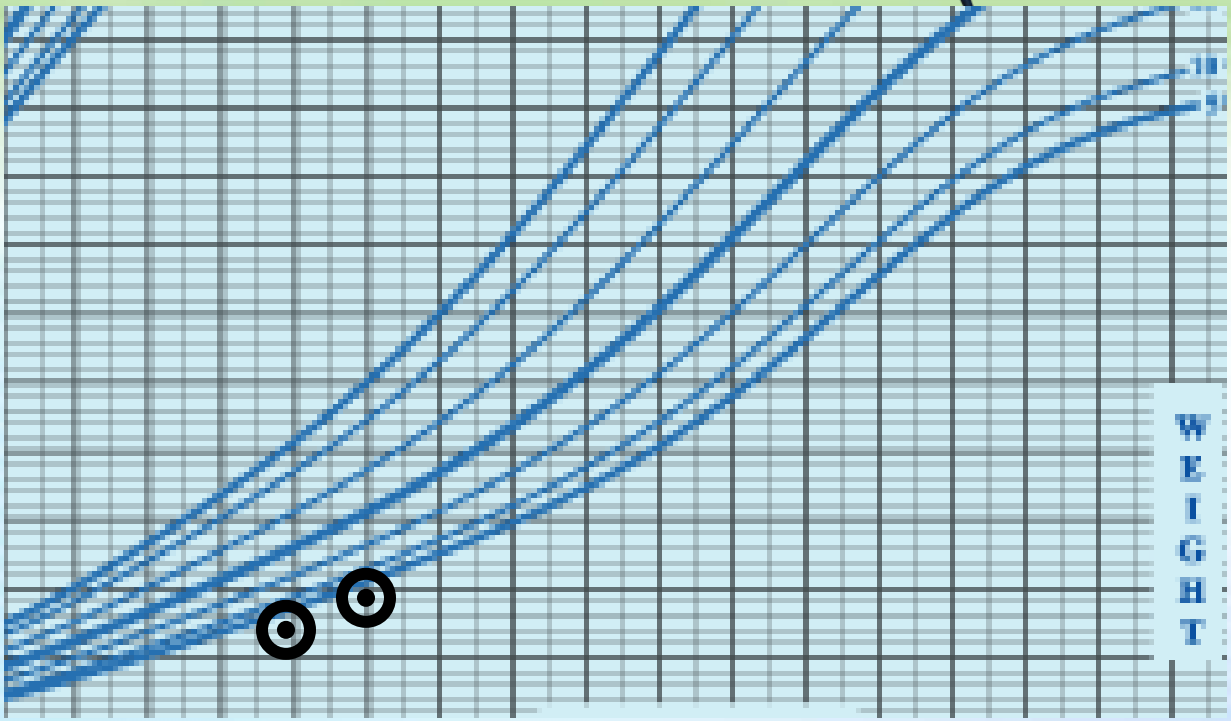
[1]Black M and Dubowitz H. *J Dev Behav Pediatr*. 1991;12:259-267.
[2]Gahagan S. *Pediatr Rev*. 2006;27:e1-e11.

FTT: Definitions[3]

1. Weight < 75% of median weight for chronologic age (Gomez criterion)
2. Weight < 80% of median weight for length (Waterlow criterion)
3. Body mass index for chronologic age < 5th centile
4. Weight for chronologic age < 5th centile
5. Length for chronologic age < 5th centile
6. Weight deceleration crossing more than 2 major centile lines from birth until weight within the given age group
7. Conditional weight gain = lowest 5%, adjusted for regression towards the mean from birth until weight within given age group

[3]Olsen EM, et al. *Arch Dis Child*. 2007;92:109-114.

Definition (cont'd)



- Is 3% of the population below the 3rd percentile?
- Is weight alone enough?
  - *Proportionately small children are often not failing to thrive*
  - *Weight-for-length or body mass index (BMI) < 3rd percentile may be a better marker of FTT*

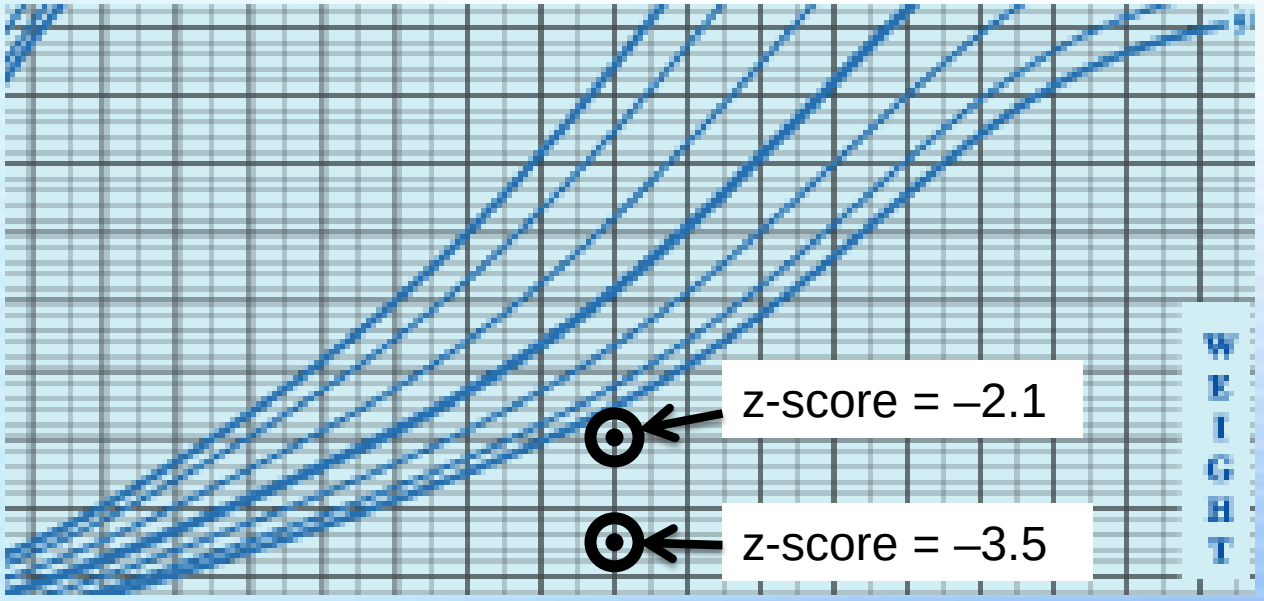
Waterlow Classification[4]

	Acute Malnutrition (% of Ideal Body Weight)	Chronic Malnutrition (Height-for-Age)
Normal	> 90%	> 95%
Mild	80-90%	90-95%
Moderate	70-80%	85-90%
Severe	< 70%	< 85%

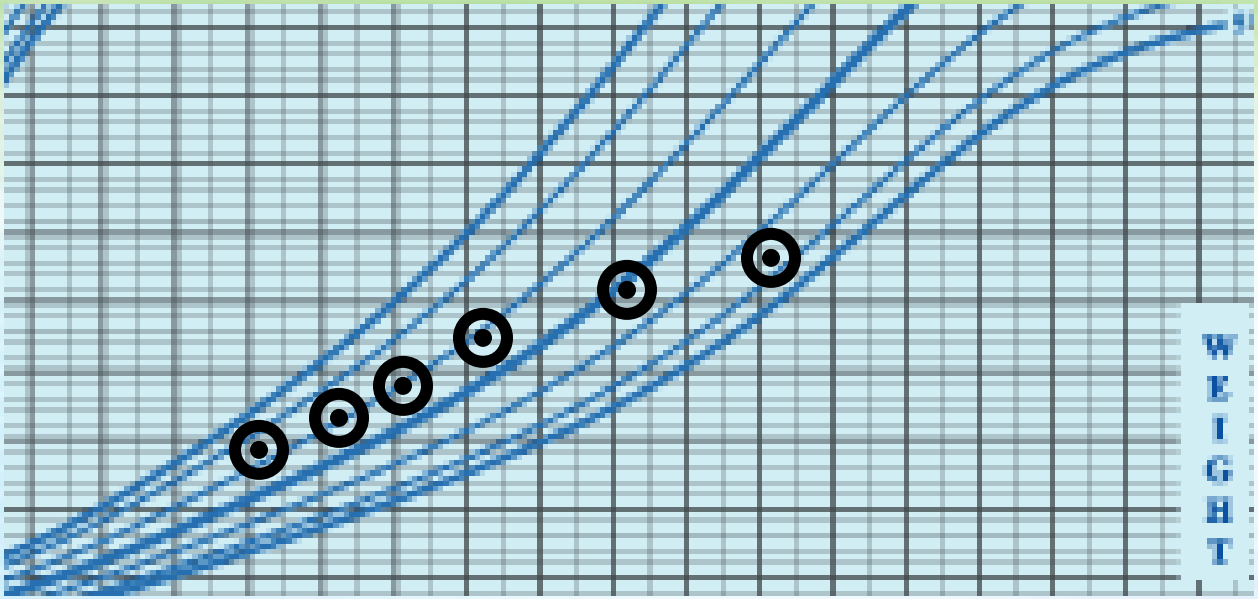
[4]Waterlow JC. *Br Med J.*1972;3:566-569.

The Use of Z-Scores

- Z-scores allow more precision in describing anthropometric status



Definition (cont'd)[5,6]



- What is stable growth during infancy?
  - *30% of full-term infants cross 1 percentile and 23% cross 2 percentiles between birth and 2 years*
  - *Study correlated weight at age 1 year with weight between 4-8 weeks than at birth*
- Growth curves are averages that are mathematically smoothed out

[5]Smith DW, et al. *J Pediatr.* 1976;89:225-230.
[6]Edwards AG, et al. *Arch Dis Child.* 1990;65:1263-1265.

Centers for Disease Control and Prevention Recommendations[7]

- 0-2 years: use World Health Organization (WHO) growth standards
  - *Regardless of type of feeding*
  - *Use the 2.3rd and 97.7th percentiles (labeled as the 2nd and 98th percentiles) to identify children with "abnormal" growth*
- 2 years and older: use Centers for Disease Control and Prevention growth charts
- Fewer US children will be identified as underweight using the WHO charts
- Slower growth among breastfed infants during ages 3-18 months is normal

[7]Grummer-Strawn LM, et al. *MMWR Recomm Rep*. 2010;59:1-15.

Prevalence[3]

- Danish birth cohort
  - *Significant undernutrition = 3% under the age of 1 year*
  - *Poor concurrence among all 7 criteria*
  - *None of the FTT children met all the criteria*
  - *Most met only one criterion*
  - *Most single criteria*
    - Identified less than half of these children
    - Or included too large a proportion of the total cohort

[3]Olsen EM, et al. *Arch Dis Child*. 2007;92:109-114.

Normal Variants Masquerading as FTT

Normal Variants Masquerading as FTT

- Genetic short stature
  - *Short parents*
  - *Low percentiles, but do not cross percentiles*
- Midparental height
  - *To the average of the parents' heights*
    - Add 2.5 inches if male
    - Subtract 2.5 inches if female
  - *This is the median height expected for that child*
    - 8.5 cm on either side of the median will give 2 standard deviations on either side

Normal Variants Masquerading as FTT (cont'd)

- Ex-premature infant
  - *Normal birth weight, if corrected for gestation*
  - *Low percentiles if uncorrected, but may show catch-up growth*
- Catch-down growth
  - *Above expected birth weight*
  - *Initial fall in percentiles, then follow percentiles*

Small for Gestational Age[8,9]

- The most common definition of small for gestational age refers to a weight below the 10th percentile for gestational age
- ~ 90% of infants exhibit spontaneous catch-up growth
- Appropriate weight gain ("Goldilocks" amounts) is associated with the best neurologic outcomes
  - *↑↑ weight gain (> 5000 g in the first 16 weeks of life) associated with ↓ cognition and ↑ BMI at age 7 years*

[8]Karlberg J and Albertsson-Wikland K. *Pediatr Res*. 1995;38:733-739.
[9]Pylipow M, et al. *J Pediatr*. 2009;154:201-206.

Practical "Definition" of FTT

- Weight-for-length or BMI z-score < –2.0
- Poor or no weight gain over a period of time that varies according to the age of the child
  - *In general, the younger the child, the shorter the interval in which there is little or no weight gain*
- Significant downtrend in weight percentiles
- Additional considerations:
  - *Assessment of parental size/growth*
  - *Correction for prematurity (where applicable)*

Medical Risk Factors[10-12]

- < 5% of children who fail to thrive have organic disease
- Does failure to find an organic cause for FTT = neglect?
- Only 5-10% of FTT infants are followed by child protection services

[10]Wright CM, et al. *BMJ.* 1998;317:571-574.
[11]Wright C and Birks E. *Child Care Health Dev.* 2000;26:5-16.
[12]Skuse D, et al. *J Med Screen*. 1995;2:145-149.

A Simple Approach to FTT

- Inadequate intake of calories
- Loss of calories
  - *Vomiting, maldigestion, malabsorption*
- Increased caloric need
  - *Cardiorespiratory disease, liver disease, renal disease, chronic infections*
- Inability to utilize calories consumed
  - *Chromosomal, endocrine, and metabolic disorders*

Inadequate Food Intake

- Failure of food intake underlies most cases of FTT
  - *Lack of available food*
  - *Lack of knowledge about infant feeding*
  - *Maternal depression*
  - *Specific dietary beliefs*
- Parent-child interaction
  - *Parent not offering food*
  - *Child refusing to take food*
- Specific organic issues in the infant

Approach to the Patient With FTT

FTT: History

- Pregnancy and labor
- Birth weight
- Early neonatal history
- Feeding issues in the first year of life
- Immunizations
- Development
- Medical or surgical illnesses
- Frequent infections

FTT: Growth and Nutrition History

- Plot previous points
- Feeding behavior and environment
- Allergies to foods
- Quantitative assessment of intake
  - *24-hour food recall*
  - *3-day diet record*

FTT: Social History

- Who feeds the child?
- Life stresses in the family
- Social and economic supports
- Perception of growth failure as a problem

The Physical Examination

FTT: Measurements

- Vital for accurate assessment of growth
- Length
  - *Length board until age 2 years*
- Weight
  - *< 24 months*
    - Nude or in clean, dry diaper
  - *≥ 24 months*
    - Light clothing

Short Stature[13]

- Causes
  - *Familial/constitutional: 80%*
  - *Medical causes: 10%*
  - *Idiopathic: 5%*
  - *Endocrine: <5%*
- Children with growth hormone deficiency are not usually malnourished
- In malnutrition, serum insulin-like growth factor-1 will be low

[13]Lindsay R, et al. *J Pediatr*. 1994;125:29-35.

Laboratory Evaluations[14]

- Most children with FTT do not need laboratory evaluations
- Laboratory evaluations
  - *Significant FTT*
  - *FTT not due to inadequate calorie intake*
- Common laboratory evaluations
  - *Complete blood count, erythrocyte sedimentation rate*
  - *Metabolic panel, electrolytes*
  - *Anti–tissue transglutaminase (tTG) immunoglobulin A (IgA), serum IgA level*
  - *Fecal elastase*
  - *Urinalysis*

[14]Sills RH. *Am J Dis Child*. 1978;132:967-969.

Assessing Intake

- Have parents describe typical day
- Look for red flags
  - *Excessive juice intake*
  - *Excessive milk intake*
  - *"Grazing"*

Juice Versus Milk[15,16]

- Juice
  - *15 calories per ounce, no protein*
  - *Contributing factor to FTT*
- Promote appropriate milk intake

AAP Recommendations

Age	Limit
< 6 mos.	0
1 – 6 years	4 – 6 ounces
7 – 18 years	8 – 12 ounces

AAP: American Academy of Pediatrics

[15]Smith MM and Lifshitz F. *Pediatrics.* 1994;93:438-443.
[16]Committee on Nutrition. *Pediatrics*. 2001;107:1210-1213.

High Calorie Beverages

- Pediasure®, Boost®, Nutren Jr.®
  - *30 calories/ounce*
  - *Appropriate for children 1-10 years old*
- Carnation Instant Breakfast® with whole milk
  - *30 calories/ounce*
  - *Cheaper than Pediasure ($0.50/packet)*
- Whole milk with heavy whipping cream
  - *30 calories/ounce*
  - *Cheapest*

Mealtime Behaviors

- Meals/snacks
  - *At table or in high chair*
- Structured meals and snacks
  - *No more than 20-30 minutes to eat/drink*
  - *Feed every 3 hours*
- Only water between meals and snacks

Zinc[17]

- Supplementation improves gains in height and weight
- Patients at risk for inadequate zinc intake
  - *Mostly breastfed infant*
  - *Picky eater on cow's milk*
  - *Dose: 0.5-1 mg/kg*
- Most complete multivitamins
  - *½ tablet for 2- and 3-year-olds*
  - *Full tablet for ≥ 4 years old*

[17]Brown KH, et al. *Am J Clin Nutr.* 2002;75:1062-1071.

Management

Management

- Ensure that the child is failing to thrive
- Work out the basic reason for FTT
  - *Inadequate calories*
  - *Loss of calories*
    - Vomiting/diarrhea
    - Malabsorption
  - *Increased caloric needs*
  - *Other*

Inadequate Calories: Initial Steps

- Decrease or eliminate juice intake
- Regular meals and snacks
  - *Feeding every 3 hours*
  - *Preferably in a high chair*
  - *Meals limited to 20 minutes*
  - *No feeding outside mealtimes, except for water*

Inadequate Calories: Next Steps

- Increase calorie content of formula
- Increase caloric values of all foods
- In children with feeding disorders
  - Work with speech-language pathologist
  - Maximize intake by optimize feeds (eg) thickening
  - May need gastrostomy feeds

Inadequate Calories: Pediasure® or Its Equivalents

- In moderate or severe failure to thrive
- Unmotivated families
  - *Risk of child worsening if something is not done*
- Balance between Pediasure® and solid food
- Wean off Pediasure® at the first possible opportunity

Inadequate Calories: Loss of Calories

- Investigate and appropriately treat causes of vomiting and diarrhea
- Investigate for malabsorption if child is consuming sufficient calories

Inadequate Calories: Increased Caloric Needs

- Eliminate juice
- Eliminate grazing
- Maximally concentrate all solids and liquids
- Consider tube-feeding early

What Works?[18]

- Simple dietary advice may be all that is needed – but only rarely
- Long-term treatment and a follow-up plan
  - *Nutritional advice*
  - *Behavioral modification*
  - *Social work intervention*

[18]Bithoney WG, et al. *J Dev Behav Pediatr*. 1991;12:254-258.

Hospitalization

- May be necessary
  - When nothing else works
  - To show that child is not being fed at home
- Usually only of use in children under the age of 2-3 years
- Initially start with what is being done at home
- Change feeds and / or institute other therapy, if necessary

Follow-up

- More frequent follow-up
  - Very young children
  - Significant FTT
- Mode of follow-up
  - Weight check vs pediatrician visit vs dietitian vs pediatric GI
  - Needs to be individualized

Prognosis[19-21]

- Meta-analysis involving FTT children < 2 years of age
  - *3-point reduction in IQ in children at age 3 years*
- Another meta-analysis
  - *Less-exacting inclusion criteria*
  - *FTT in infancy is associated with adverse intellectual outcomes sufficient to be important*
- A study of adolescents who had FTT in infancy failed to show any evidence of emotional deficit in cases compared with controls

[19]Rudolf MC and Logan S. *Arch Dis Child.* 2005;90:925-931.
[20]Corbett SS and Drewett RF. *J Child Psychol Psychiatry.* 2004;45:641-654.
[21]Drewett RF, et al. *J Child Psychol Psychiatry.* 2006;47:524-531.

Conclusions

- The diagnosis of FTT is based on a careful history
- Anthropometric measurements are important
- Cut out juice and grazing
- Work with a multi-disciplinary team

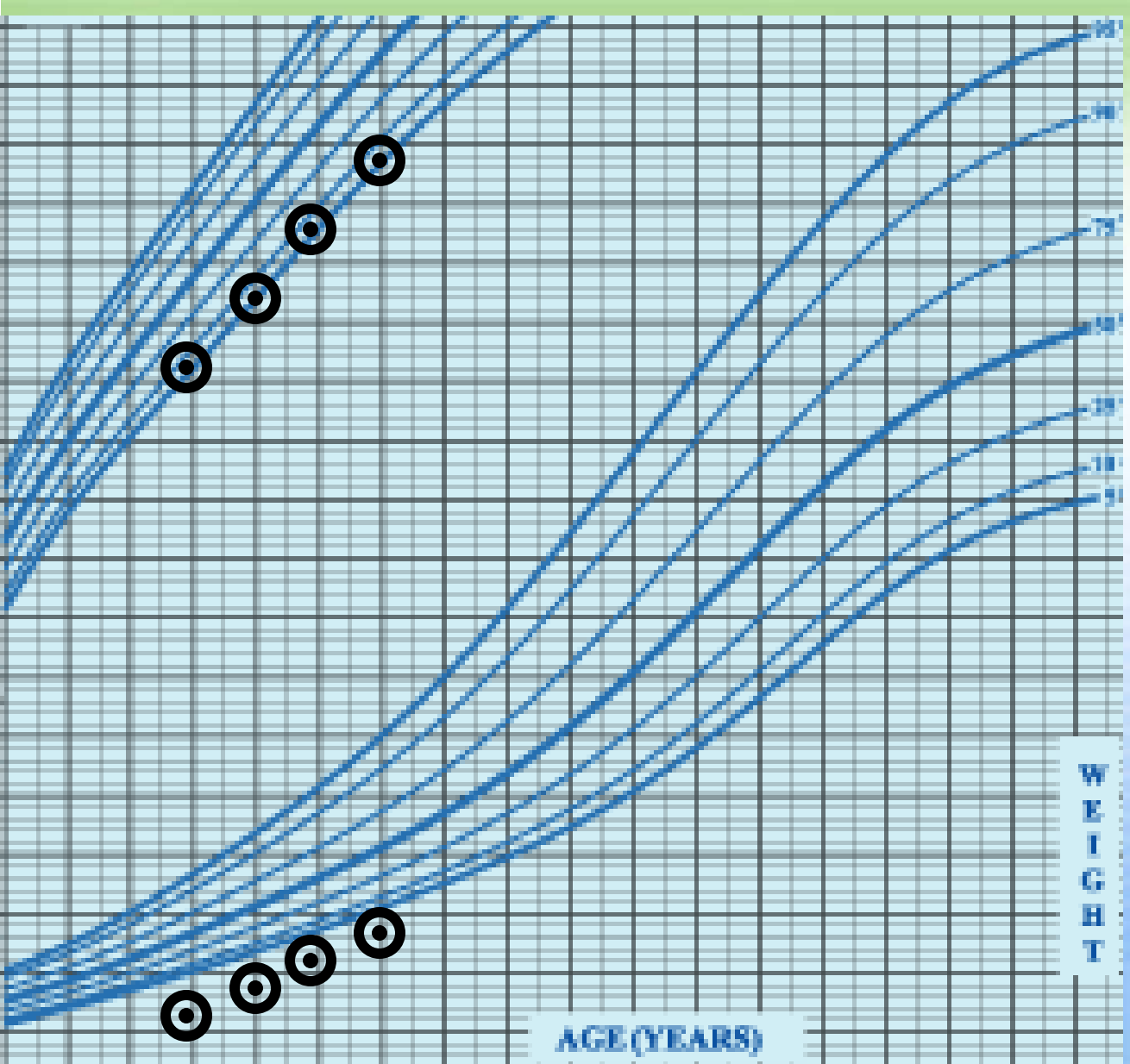
Case Studies

Case 1

- 15-month-old with FTT
- Breastfed through 13 months → then transitioned to whole milk
- Started Poly-vi-sol® as infant and still takes 1 cc daily
- Weight, length, and weight-for-length
  - *Now below 3rd percentile for age*
- Diet history
  - *Never seems hungry*
  - *Loves sippy cup with whole milk – "never puts it down" – drinks 32 ounces whole milk daily*
  - *"Grazes" on crackers, pretzels, and other finger foods throughout the day*
  - *Takes only bites at mealtime*

Case 2

- 8-year-old male
- Born at 32 weeks gestation; birth weight: 1.3 kg
- Otherwise healthy; no dietary concerns
- Poor growth
- No other historical concerns
- Normal physical examination



What should you do?

Case 3

- 15-month-old male with mild asthma
- Developmentally normal
- Takes cow's milk and liquids without difficulty, but refuses solid foods
- No weight gain for 3 months

Questions?

Maria R. Mascarenhas, MBBS
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Philadelphia, PA

Cystic Fibrosis

CF and Nutrition

- Improved survival: nutritional state correlates with outcome
- PI is marker for more severe genetic defect
- Energy imbalance: increased needs versus reduced intake
- Lung disease, airway inflammation & infection result in appetite suppression & increased energy expenditure
- Many descriptive studies looking at correlation of nutritional status & pulmonary function
  - improved survival is associated with changes in dietary management
  - declining FEV1 is strongly associated with increased mortality
- Goal is normal growth which depends on:
  - gastrointestinal , hepatic and pancreatic function
  - lung function
  - genetic potential
  - energy & nutrient intake

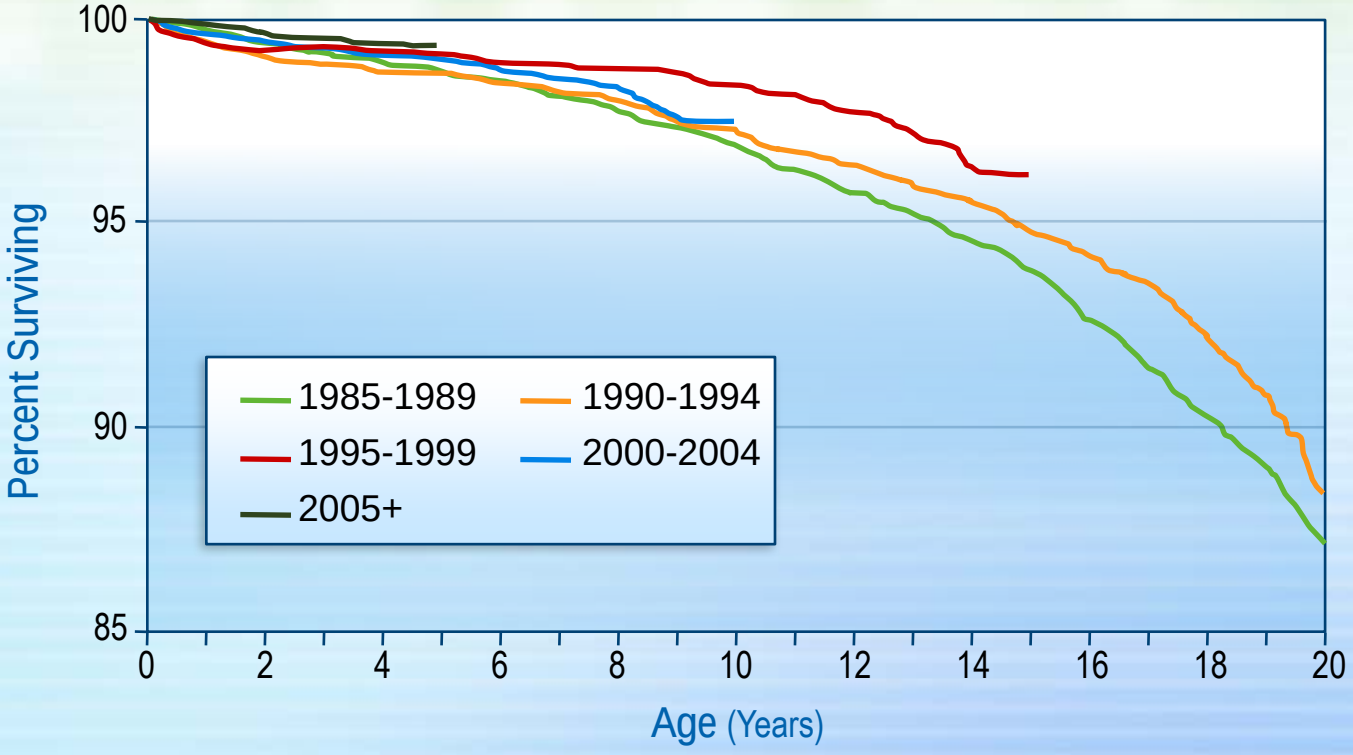
Benefits of Good Nutritional Status & CF

- A comparison of survival, growth and pulmonary function in patients with CF in 2 centers in Boston & Toronto
- Survival 9 years longer in Toronto center
- High fat diet with increased dose of pancreatic supplements
- Good weight and height percentiles
- Improved survival linked to good nutritional status

[1]Corey *et al*. *J Clin Epidemiol 1988*; 41: 583-591.

CF Foundation Center Registry Reports 2009

Survival by Birth Cohort



Of patients born between 1985 and 1989 (the earliest cohort shown here in green), 93.9 percent survived to age 15. For patients born between 1990 and 1994. 95.0 percent survived to age 15. With the exception of the 200-2004 cohort, successive birth cohorts show improved survival.

[2]Cystic Fibrosis Foundation Patient Registry 2010 Annual Data Report Bethesda, Md.

Pathogenesis of Nutritional Abnormalities in CF

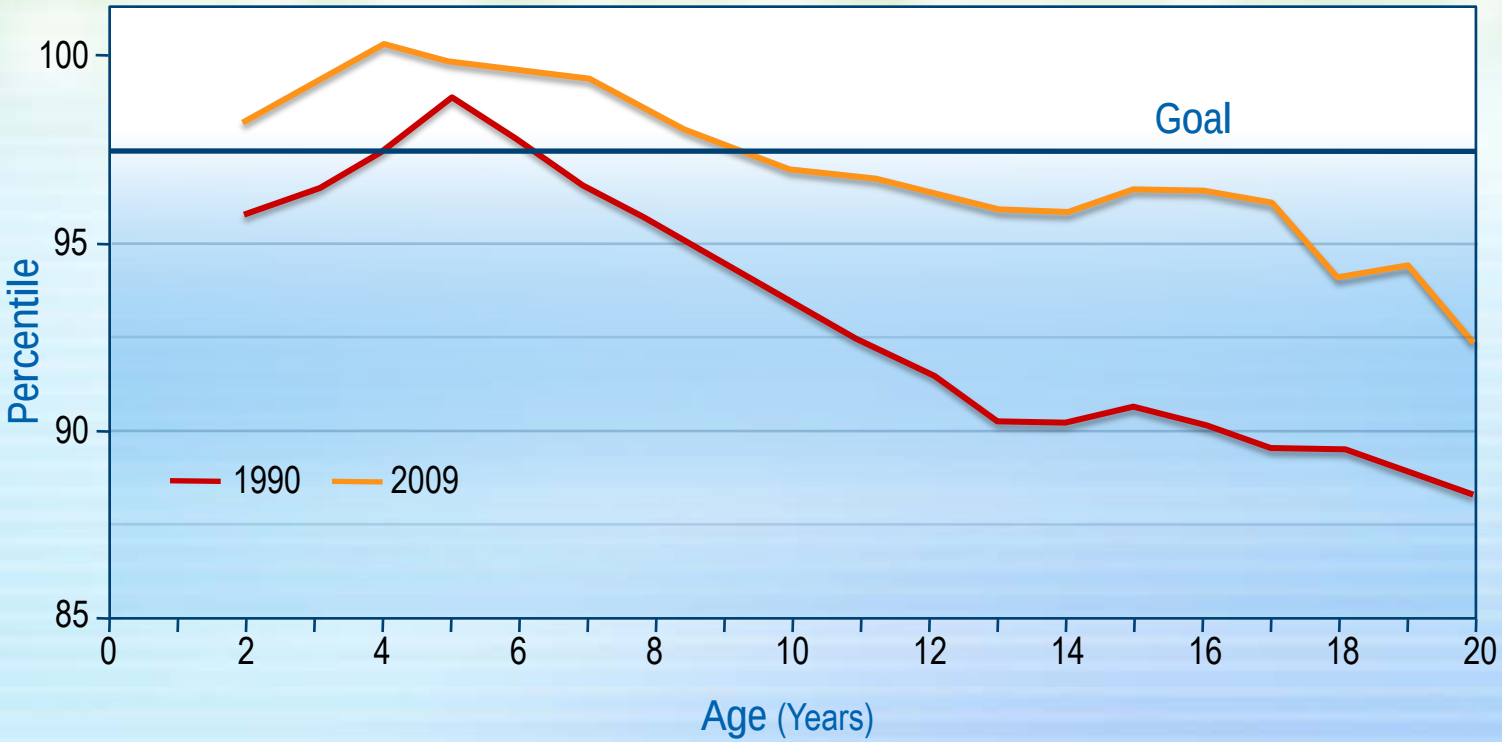
- Energy losses:
  - Malabsorption (pancreatic, liver, intestinal)
  - GER
  - CFRD
  - protein loss in sputum
- Energy intake: iatrogenic fat restriction, esophagitis, anorexia, feeding disorders, depression
- Energy needs: Increased
  - ? Primary defect

Nutritional Abnormalities in CF

- Malnutrition
- Growth failure
- Protein deficiency - infancy
- Micronutrient - vitamins A, E, K, C & D, EFAD, Na, Ca, Fe, Zn, Se, Mg, carotene, glutathione
- Delayed puberty
- Bone disease

CDC BMI Percentile

Median CDC BMI* Percentile vs. Age, 1990 and 2009



Nutritional status as measured by CDC BMI Percentile has improved since 1990, and remains above the CF Foundation goal 7 until age 10. However, the downward trends begins in early childhood.
*BMI percentile are not calculated for patients less than 2 years of age.

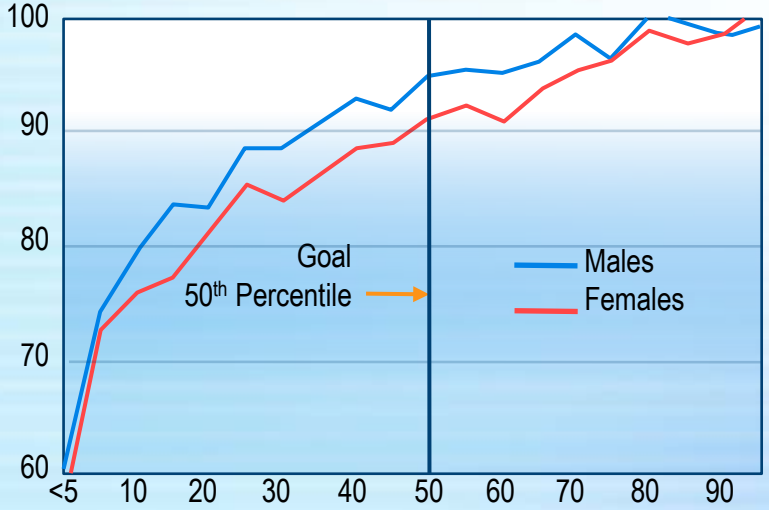
[2]Cystic Fibrosis Foundation Patient Registry 2010 Annual Data Report. Bethesda, Md.

FEV1 and BMI

FEV_1 and BMI Outcomes

The data show that pulmonary function and nutrition status are highly correlated. Some centers are achieving the goals established in the CF Foundation Nutrition Guidelines.

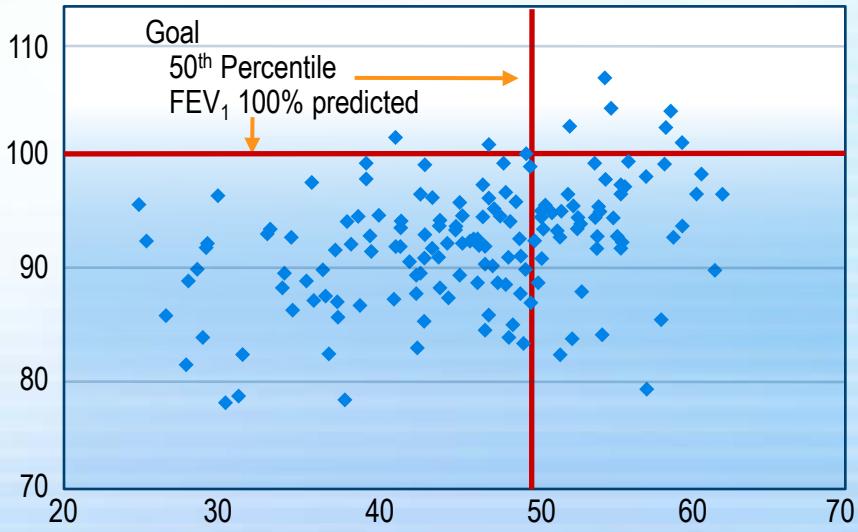
FEV_1 Percent Predicted vs. BMI Percentile in Patients 6 to 20 Years



BMI Percentile

FEV_1 percent predicted is positively correlated with BMI percentile for patients 6 to 20 years of age ($p<0.0001$).

FEV_1 vs. BMI Percentile in Patients 6 to 18 Years, by CF Center



BMI Percentile

Each Dot Represents values from an accredited care center or affiliation program.

[3]Stallings *et al.J Am Diet Assoc.* 2008;108:832-839.

Energy Needs in CF

- Nutritional status (height & weight) is linked to survival
- Association between BMI % ile & FEV1
- Optimal energy intake important for care
- Individual variables: pulmonary exacerbation, maldigestion, malabsorption, pulmonary function, fat-free mass, gender, pubertal status, genetic mutation, age, liver disease, CFRD
- Daily calorie requirements: 110-200% of recommended intakes for normal individuals
- CFF nutrition consensus: equation is a starting point and use gains in weight, height, height velocity and fat stores to assess adequacy

[4]Michel et al. *Pediatr Clin North Am.* 2009;56(5):1123-41.

CF: Protein Needs

- Limited information
- Protein intake correlates with overall caloric intake
- Studies on protein catabolism and protein deposition: varying results which may reflect differences in entry nutritional status and caloric intake during study
- Oral & enteral protein and caloric supplementation studies: conflicting results

[5]White et al. *J Cyst Fibros.* 2004;3:1-7.[6]Vaisman et al *Am J Clin Nutr*. 1992;55(1):63-9. [7]Geukers et al. *Am J Clin Nutr.* 2005;81(3):605-610. [8]Kawchak et al. *J Pediatr.* 1996;129(1):119-29. [9]Poutsie et al. *Br Med J.* 2006;332:632-5.

Vitamin A

- Important for cellular integrity, growth, immune function & vision
- Excessive intake: bone and liver toxicity
- Status: serum retinol, serum retinol-binding protein, functional testing
- Serum retinol decreased in acute inflammatory states; not associated with disease severity
- No trial showing benefits of vit. A supplementation
- 1993: CF specific multivitamins contain vit. A
- Elevated retinol levels in children, adolescents & young adults
- Toxicity: serum retinyl esters

[11]Hakim et al. *J Pediatr Gastroenterol Nutr*. 2007;45(3):347-53. [12]Duggan et al. *Am J Clin Nutr.* 1996;64(4):635-639. [13]Magbool et al. *J Cyst Fibros*. 2008;7(2):137-41. [14]O'Neil et al. *Cochrane Database of Systematic Reviews.* 2008, Issue 1. Art. No.: CD006751.

Vitamin E

- Important for normal development, cell membrane stability, prevention of hemolysis, antioxidant
- Deficient in patients with fat malabsorption
- Oxidative stress & diet high in PUFA may increase needs
  Deficiency in CF before development of CF specific vitamins
  Low level in PS
- Low levels in infants at diagnosis and during childhood
- Varying results effect of vitamin E and lung function
- Status: Vitamin E level; adjust dose based on levels

[14]Wood et al. *J Am Coll Nutr.* 2003;22(4):253-7. [15]Cynamon et al. *J Pediatr.* 113:637-40, 1988. [16]Lancellotti L et al. *Eur J Pediatr*. 1996 ;155(4):281-5. [17]Dorlochter et al. J *Cyst Fibros 2002*; 1: 131-136. [18]Sokol et al. *Am J Clin Nutr.* 50:1064-71. [19]Feranchak et al. *J Pediatr* .1999;135(5):601-610. [10]Hakim et al. *J Pediatr Gastroenterol Nutr.* 2007;45(3):347-53. [20]Bines et al. *J Paediatr Child Health.* 2005 41(12):663-8. [21]Oudshoorn et al. *J Cyst Fibros.* 2007 Jan;6(1):35-40.

Vitamin D

- Important for bone health; other functions being discovered
- Deficiency common: infants at diagnosis, children & young adults
- Factors: season, skin color, sunlight exposure, geographic location, sunscreen use, intake, malabsorption, medications (glucocorticoids antibiotics), reduced fat mass
- New AAP, IOM, CF & Endocrine Society guidelines
- Deficiency: 25-OHy vit. D <30ng/ml or 75nmol/L
- Treatment: hard to raise levels using guidelines; ? cholecalciferol more effective; monitor levels

[19]Feranchak et al. *J Pediatr.* 1999 Nov;135(5):601-10. [22]Neville et al. *J Paediatr Child Health*. 2009;45(1-2):36-41. [23]Rovner et al.*Am J Clin Nutr.* 2007;86:1694 –9. [4]Michel et al. *Pediatr Clin North Am.* 2009;56(5):1123-41. [24]Wagner et al. *J Nutr.* 2008;138:1365–1371. [25]Aris et al *J Clin Endocrinol Metab.* 2005;90:1888–96. [26]Green et al. *J Pediatr.* 2008 153(4):554-9.

Vitamin K

- Important for coagulation and bone metabolism
- Factors: maldigestion/malabsorption, bile salt deficiency, liver disease, bowel resection, bacterial overgrowth, antibiotics, excessive vitamin E supplements, inadequate intake
- Deficiency may decrease bone formation & is associated with low bone mass
- Supplementation improves markers of bone formation
- Prothrombin: delayed marker; PIVKA II: sensitive
- No cases of toxicity

[27]Conway et al. *J R Soc Med.* 2004;97(Suppl 44):48-51. [28]Booth et al. *J Clin Endocrinol Metab.* 2004;89(10):4904-4909. [29]Drury et al. *J Cyst Fibros.* 2008;7(5):457-9. [30]Nicolaidou et al. *Eur J Pediatr.* 2006;165(8):540. [31]Fewtrell et al. *J Cyst Fibros.* 2008;7(4):307-12.

Water-soluble Vitamins

- No recommendations: felt that ingestion of a balanced diet is adequate
- Multivitamins contain water soluble vitamins
- Riboflavin deficiency: angular stomatitis
- Vitamin C levels decreases with age
- Folic acid & vitamin B12 supplements: improved inflammatory responses

[32]McCabe. *J Hum Nutr Diet.* 2001;14:365-370. [33]Scambi et al. *PLoS One.* 2009;4(3):e4782. [34]Winklhofer-Roob et al. *Am J Clin Nutr.* 1997;65:1858-1866. [35]Back et al. *Am J Clin Nutr.* 2004;80(2):374-384.

Minerals: Sodium

- Excessive salt loss through skin: may be influenced by genotype
- Human milk & infant formula does not have enough salt
- Salt depletion can cause anorexia, FTT, metabolic alkalosis with hypoelectrolytemia
- Infants: 2-4 meq/kg; 0.125 tsp till 6 months when it should be increased to 0.25 tsp
- Older patients: high salt diet
- Active in warm environments add 0.25 tsp to 12 oz sports drinks

[36]Leoni et al. *J Pediatr* .1995;127:281-283. [37]Fustik et al *Pediatrics International. 2002;44(3):*289–292. [38]Kriemler et al. *Med Sci Sports Exerc.* 1993;31:774-779. [39]Bar-Or et al. *The Lancet* .1992;3(8795):696-699. [40]Orenstien et al. *Pediatr Res.* 1983. 17(4):267-9.

Trace elements: Zinc

- Important in pulmonary health, immunity & growth
- Lack of appetite, alterations in taste, growth failure & disturbed immune function
- Prior to diagnosis: loss of endogenous zinc & malabsorption
- Can have zinc deficiency with normal levels: RBC zinc level may be better indicator
- Empiric zinc supplementation (1 mg/kg/day elemental zinc) with growth failure for 6 months

[41]Krebs et al. *J Pediatr.* 1998;133(6):761-4. [42]Krebs et al. *Pediatr Res.* 2000:48;256-61. [43]Tinley et al. *J Cyst Fibros.* 2008;7(4):333-5. [44]Borowitz et al.*J Pediatr Gastroenterol Nutr*. 2002;35:246–59. [45]Abdulhamid *Pediatr Pulmonol.* 2008 ;43(3):281-7.[46]Akanli et al. *Acta Paediatr Scand.*1982;71:203–207. [47]Van Biervliet et al. *Arch Dis Child.* 2006;91:771–3.

Trace Elements: Iron

- Anemia frequently seen; associated with poor lung function and vitamin deficiency
- Incidence of iron deficiency: 33% in children; 74% in older patients
- Anemia: true iron deficiency or anemia of chronic disease
- Deficiency: decreased dietary intake, increased loses in sputum & GIT, severity of supurative lung disease
- Iron deficiency not related to PERT
- *P. aeruginosa* actively acquires Fe from proteins in host airway, secrets sideropheres to acquire iron & produces inflammatory cytokines: results in anemia of chronic disease

[48]von Drygalski et al. *Nutr Clin Pract*. 2008; 23(5):557-63. [49]Keevil et al. *Ann Clin Biochem.* 2000;37:662-665. [50]Khalid et al. *Clin Chim Acta.* 2007; 378(1-2):194-200. [51]Fischer et al. *Pediatr Pulmonol*. 2007 ;42(12):1193-7. [52]Weiss et al. *N Engl J Med.* 2005; 352:1011-1023. [53]Reid et al. *Chest*. 2002;121(1):48-54,2002. [54]Reid et al. *Eur Respir J.* 2004;24(2):286-91.

Fatty Acids and CF

- EFA: linoleic acid & alpha linolenic acid
- Deficiency:
  - at diagnosis, alopecia, easy bruisability, skin rashes, suboptimal growth; can have only biochemical deficiency
- Causes:
  - fat malabsorption, abnormal membrane release & metabolism
- Clinical:
  - EFAD associated with ceramide deficiency, CF genotype & pancreatic status
  - Serum linoleic acid status associated with growth & pulmonary status
  - Abnormalities increase with age & presence of CF liver disease
  - Increased arachidonic acid release from membrane phospholipids
  - Decreased linoleic acid, decreased DHA
- Treatment:
  - supplementation with long chain fat & ? Intravenous fat
  - DHA supplementation will raise serum DHA levels in clinical trials, BUT no effects with respect to clinical outcomes safe to use

[55]Guilbault et al. *Am J Respir Cell Mol Biol.*2009;41(1):100-106. [4]Michel et al. *Pediatr Clin North Am*. 2009;56(5):1123-41. [56]Freedman,et al. *N Engl J Med.* 2004;350(6):560–9. [57]Coste et al. *Clin Biochem.* 2007;40(8):511-20.

Bone Health & CF

- Decreased bone density, fractures & kyphosis occur earlier than in healthy controls
- Incidence of osteoporosis & fracture increases with age; > prevalent in adults & those with end stage lung disease
- Risk factors: inflammatory cytokines, vitamin D deficiency, inadequate calcium intake, corticosteroid use, small body size, low weight for height, decreased physical activity, delayed puberty, short bowel syndrome, liver disease, fractures, family history of osteoporosis
- DXA: if > 8 years & have risk factors
- Treatment:
  - Optimize calcium, vitamins D & K, nutritional status; increase physical activity; decrease corticosteroid use if possible; treat hormone deficiencies & bisphosphonate medications

[25]Aris et al. *J Clin Endocrinol Metab* 2005;90:1888–96.
[58]Tangpricha et al. *J Clin Endocrinol Metabo*l 2012. (e pub ahead of print).
[59]Sermet-Gaudelus, et al. *Arch Pediatr.* 2008;15(3):301-12.

Nutritional Management of CF

- All CF patients: different needs at different ages
- Nutritional assessment
- Nutritional education & dietary counseling
- Pancreatic enzyme replacement therapy (PERT)
- Micronutrient supplementation: A, D, E, K, Ca, Fe, Zn, Na (salt), EFA
- Oral (high calorie diet, oral supplements), tube feeds (NG, GT, NJ, GJ, JT), parenteral nutrition

Nutrition and CF: Anticipatory Guidance

- Infants: breast milk, formula, solids, Na
- Toddlers/preschool: calories, feeding behavior, whole milk
- School age: calories, snacks, autonomy, adherence, education
- Adolescence: high-risk period (DM, liver disease, infections, puberty, increased physical activity, adolescent behavior, eating disorders)

[44]Borowitz et al. *J Pediatr Gastroenterol Nutr*. 2002;35(3):246-59.

Nutritional Assessment in Routine CF Center Care

	At diagnosis	Every 3 mo, birth to 24 mo	Every three mo	Annually
Head circumference	x	x		
Weight(to 0.1 kg)	x	x	x	
Length (to 0.1 cm)	x	x		
Height (to 0.1 cm)	x		x	
Mid-arm circumference (to 0.1 cm)	x			x
Triceps skinfold (to 1.0 mm)	x			x
Mid-arm muscle area, mm^2 (calculated from MAC and TSF)	x			x
Mid-arm fat area, mm (calculated from MAC and TSF)	x			x
Biological parents height	x			
Pubertal status, female				x
Pubertal status, male				x
24 hour diet recall				x
Nutrient intake				x
Anticipatory dietary and feeding behavior guidance		x	x	x

[44]Borowitz et al. *J Pediatr Gastroenterol Nutr*. 2002;35(3):246-59.

Lack of Appetite in CF: Common Causes

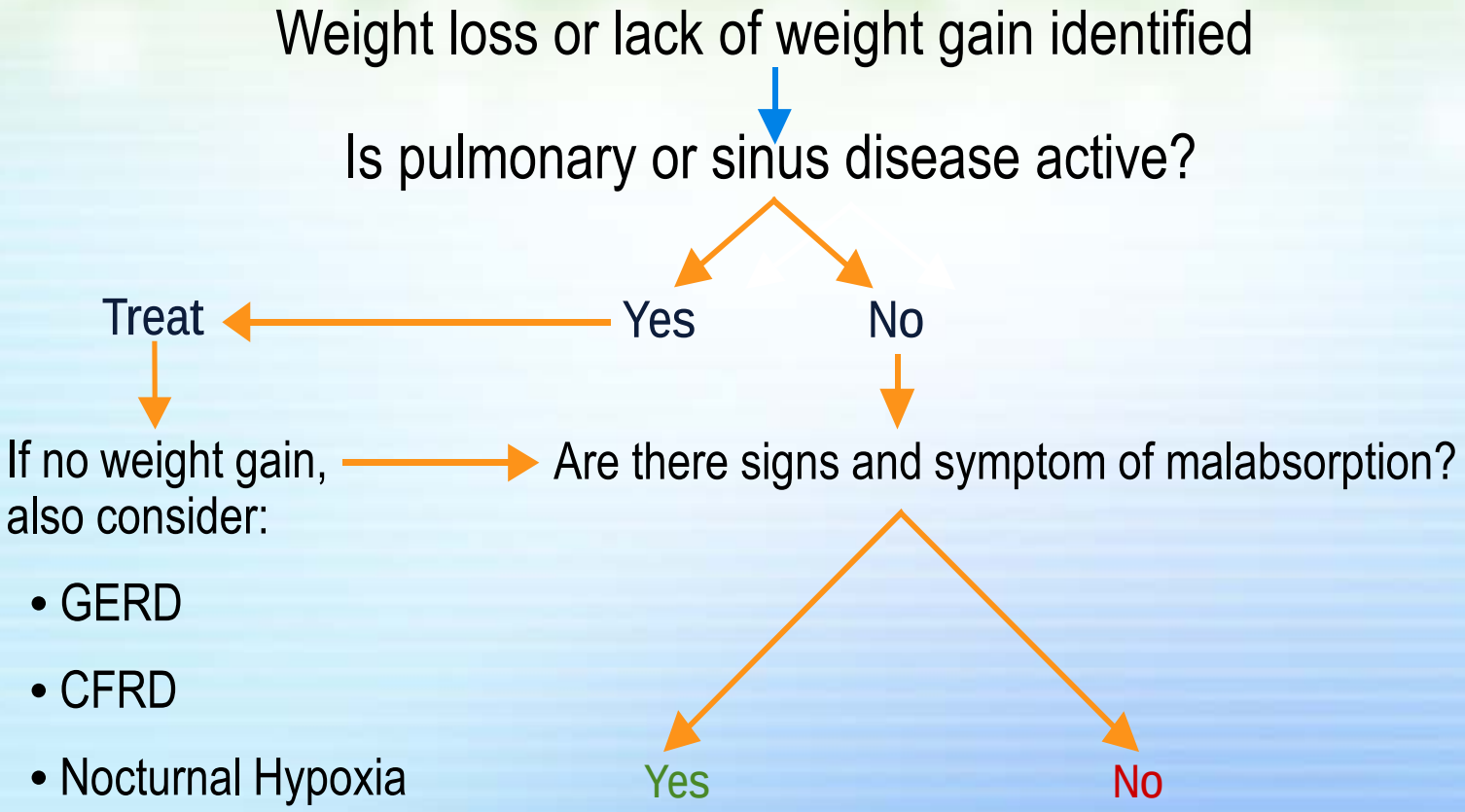
- GERD
- Fullness and bloating from DGE & SBBO
- Abdominal pain from DIOS & SBBO
- Medications: metronidazole
- Poor eating habits
  - lack of mealtime structure
  - behavioral problems
  - ? ADHD
  - eating disorders
- Depression
- Chronic respiratory disease, pulmonary exacerbations (fever, increased cytokines)
- Sinusitis
- Zinc deficiency

What To Do when Poor Growth is Identified in Patients with CF

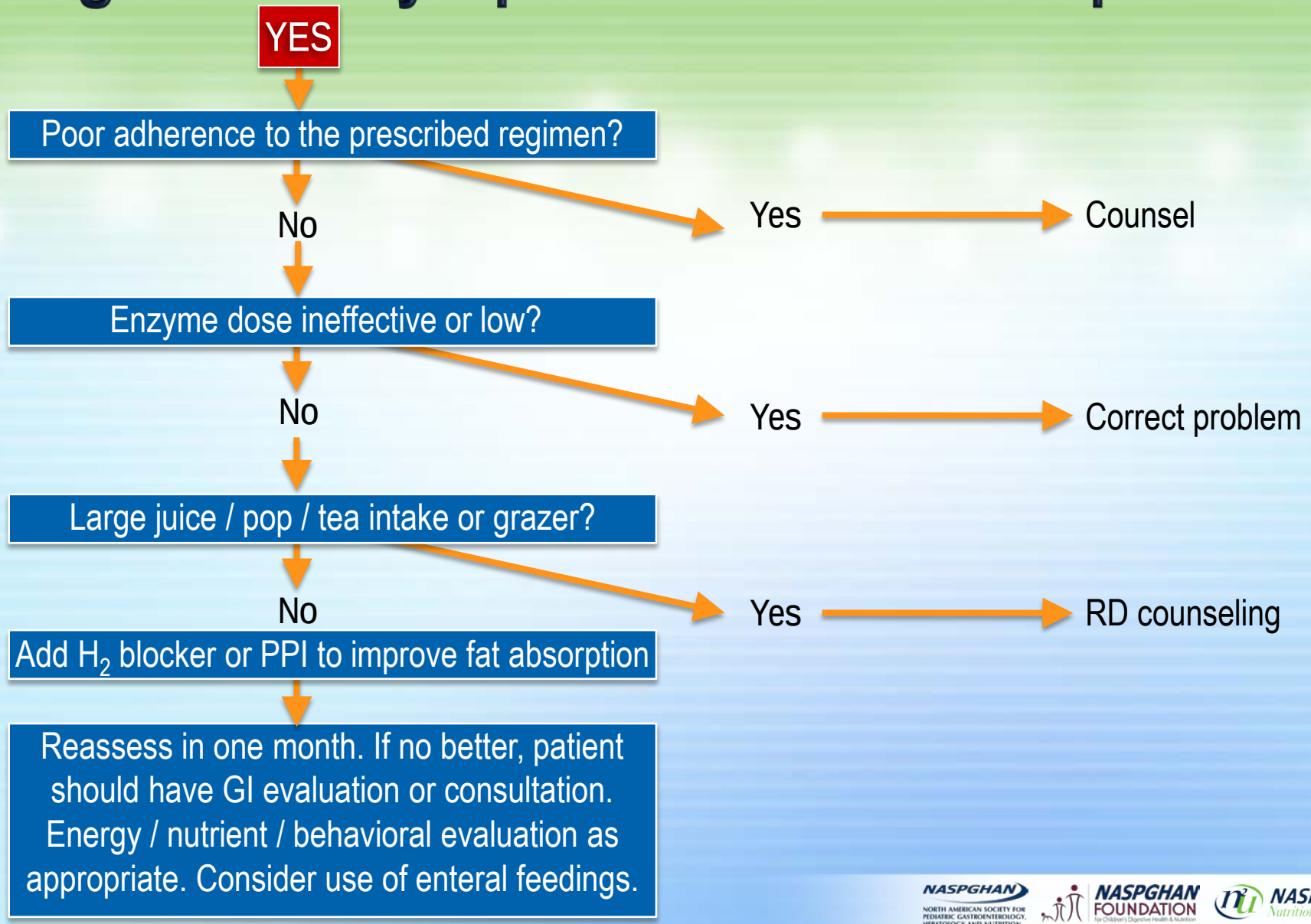
- See patients more frequently with RD:
  - Infants: every 2 - 4 weeks
  - Children 2 years and older: every 4 - 6 weeks
- Include: medical, behavioral, & nutritional assessment, education, interventions
- Diet analysis:
  - Qualitative: where, when, who, which, how much? Patterns: e.g., meal skipping
  - Quantitative: 3-5 day food records to assess kcal and nutrient intake
- Involvement by Registered Dietitian important
- Aim: Achieve patient's target weight for length or BMI percentile taking into account genetic height potential

[44]Borowitz et al. *J Pediatr Gastroenterol Nutr*. 2002;35(3):246-59.

Algorithm for Patients with Weight Loss or Lack of Weight Gain



Signs and Symptoms of Malabsorption?



Signs and Symptoms of Malabsorption?

NO

- RD counseling to maximize energy intake
- Feeding behavior evaluation and intervention
- Psychosocial and economic evaluation and intervention
- R/O CFRD with or without fasting hyperglycemia
- Consider other medical factors:
  - Sino pulmonary disease
  - GERD
  - Bacterial overgrowth
  - Constipation
  - Iron deficiency
  - Other
- Consider use of enteral feedings

Laboratory Monitoring

	At Diagnosis	Yearly
Vitamin A	X	X
Vitamin D	X	X
Vitamin E	X	X
Vitamin K (PIVKA II)	X	X
EFA	*	*
Ca/Bones	*	*
Iron status	X	X
Zinc	*	*
Sodium	X	X
Protein stores	X	X

*** As indicated**

[44]Borowitiz et al. *J Pediatr Gastroenterol Nutr*. 2002;35(3):246-59.

Behavioral Evaluation of CF Patients with Poor Growth

- Assess early
- Check for presence of ineffective feeding behaviors & parenting strategies
- Adolescents with very poor body wt: check for eating disorder eg. anorexia nervosa
- Check for skipping enzymes (30%)
- Encourage being open but discreet about CF

[44]Borowitz et al. *J Pediatr Gastroenterol Nutr*. 2002;35(3):246-59.

Pancreatic Enzyme Replacement Therapy in CF

- Enteric coated (microspheres); vary in pH, source of lipase
- Open capsule in apple sauce; develop a routine
- Check mouth for ulcers, do not crush or add to bottle
- Store enzymes in a cool dry place
- Adequate number required - vary with food amount & composition
- Take with all foods & beverages except simple sugars
- Carry enzymes all the time
- Best if swallowed, check for freshness
- Split if the meal is longer than 20-30 min
- Creon, Zenpep, Pancreaze, Viokace, Ultresa

[44]Borowitz et al. *J Pediatr Gastroenterol Nutr.* 2002;35(3):246-59.

Pancreatic Enzyme Replacement Therapy in CF

- 2008: No data upon which to base dosing recommendations
- 1995: Dose
  - Infants: 2000 - 4000 U lipase/120 ml of formula or per breast feeding
  - Children < 4 yrs: 1000 - 2500 U lipase/kg/meal
  - Children > 4 yrs: 500 - 2500 U lipase/kg/meal
  - Half standard dose with snacks
  - 1000 - 4000 U lipase/gram fat

[44]Borowitz et al. *J Pediatr Gastroenterol Nutr*. 2002;35(3):246-59.
[3]Stallings et *al.J Am Diet Assoc* 2008;108(5):832-9.

Poor Response to Pancreatic Enzyme Therapy

- Symptoms:
  - Bloating, gas, abdominal pain, diarrhea, poor growth
- Causes:
  - Excessive juice intake
  - "Grazing"
  - "Fast food"
  - Enzymes: improper administration or non-compliance, outdated, poor storage, acid intestinal environment
  - GI conditions: lactose intolerance, infections, bacterial overgrowth, liver disease, *C. difficile* colitis, celiac disease, short bowel syndrome, IBD

[44]Borowitz et al. *J Pediatr Gastroenterol Nutr*. 2002;35(3):246-59.

PERT and Gastric Acid Blockage

- Effect of Cimetidine & bicarbonate on PERT
  - N=15 with CF & PI; PERT with cimetidine or bicarb or both
  - Improved fat & nitrogen balance with either cimetidine or bicarb
  - No additive effect when both were used

- Effect of PPI on Absorption in CF
  - Evaluate effect of raising intestinal pH on PERT
  - 1 month cross over study
  - 14/15 patients- improved fat absorption
  - High PERT doses: 13,500 U lipase/kg/day; 3300 U lipase/gm of fat
  - Fat malabsorption decreased from 13% - 6%

[60]Durie et al. *Gut.* 1980;21(9):778-86.

[61]Kalnins et al. *Curr Opin Clin Nutr Metab Care*. 2007;10(3):348-54.

Appetite Stimulants & Anabolic Agents

- Cyproheptadine
- Megesterol acetate: increases appetite & weight, but not sustained; adverse effects
- Insulin:
  - Promotes anabolism & decreases blood sugar
- Growth hormone:
  - Increases height & weight but underweight remains
  - Reverses protein catabolism & decreases inflammatory cytokines
  - Longitudinal studies needed

Should not be routinely used

[62]Nasr et al. *Ped Pul.* 2008;43(3):209-19. [63]Chinuck et al. *J Human Nutr & Dietetics.* 2007;200(6):526-537; [64]Hardin et al. *J Pediatr.* 2005;146:324-328.

Tube Feeds and CF

- Give 30-50% of goal kcals overnight; night time feeds to allow normal day time eating patterns
- Infants: 120-150 kcal/kg/day (catch-up, lung & long term growth
- Titrate calories based on weight gain, fat stores & growth
- Standard (complete protein, long-chain fat) formula well tolerated
- Very low fat elemental formulas: no need for PERT, useful in intubated patients given continuous feeds
- Calorically dense (1.5 - 2 kcal/cc) for adequate calories
- ? MCT containing formulas are beneficial
- Use semi-elemental formulas in patients with excessive anorexia, bloating, nausea

Tube Feeds and CF

- Individualize choice of formula:
  - SBS: high fat, MCT, low simple sugars
  - Malabsorption: partially digested
  - DM: low simple sugars
  - Advanced lung disease: high fat
  - Severe GER: peptide based
  - Food allergies: amino acid based

PERT: Tube Feeds & in the NICU

- Tube feeds
  - Take usual dinner dose orally at start with all feeds except very low fat elemental formulas
  - May give additional doses midway or at end of feeds
  - Check sugar 2-3 hours into feeds and at end of feeds on 2 separate nights
  - Give insulin if blood sugar is > 180mg/dl Repeat blood sugar if pt not gaining weight, is ill, or is on corticosteroids
- NICU
  - Start when formula intake is 60 cc Q3H: 3,000 lipase units PO in applesauce or 1/8 tsp viokace powder
  - With continuous feeds – use 3,000 lipase units or 1/8 tsp viokace powder Q4H
  - Watch for skin breakdown at ostomy & anus
  - Clean mouth after feeds to prevent oral ulcers

[44]Borowitz et al. *J Pediatr Gastroenterol Nutr*. 2002;35(3):246-59.

Case Study

- 5 mo. old with weight loss & diarrhea (6-8/day, loose & foul-smelling)
- Diagnosed by newborn screen and was referred to local CF center
- Father changed jobs; report they are giving all prescribed therapies
- Excellent eater and very hungry, happy, mild developmental delay
- 48 oz/day of standard infant formula & 2 oz rice cereal mixed with water BID
- Medications: standard infant multivitamins; PERT: 6000 units pancrealipase 4 times/day: pour beads down her throat followed by 1 oz water in her bottle
- Exam: weight, length & weight for length <5th percentile; HC 25th percentile, abdominal distension, hepatomegaly, wasting

Nutrition Guidelines for Management of Infants

- Human milk or stand. infant formula; not hydrolyzed prot. formulas
- Calorie dense feeds if wt loss/ inadequate wt gain
- Encourage positive feeding behaviors – educational resources. Growth deficits: intensive treatment with behavioral intervention & nutrition counseling; 1-12 yr
- Start multivitamins with approp. amt for CF shortly after diagnosis ; check fat soluble vitamin levels 2 months later & annually; > freq if values are abnormal
- Trial of elemental Zn 1 mg/kg/d for 6 mo., if not growing well despite adequate caloric intake & PERT
- Salt: 1/8th tsp, diagnosis - 6 mo; ¼ tsp after
- 0.5 - 2 yr: if water has < 0.3ppm, give fluoride 0.25 mg/dl

[65]Cystic Fibrosis Foundation & Borowitz et al. *J Pediatr.* 2009;155(6 Suppl):S73-93.

CF Specific Multivitamins

	CF	Standard
Vitamins A (Beta-carotene), E, D	++	+
Vitamin K (infant formulation)	+	-
Vitamin K	++	+
Zinc, biotin, pantothenic acid	+	-
Vitamins B12 & C, thiamine	++	-
Folate	-	-

[4]Michel et al. *Pediatr Clin North Am.* 2009;56(5):1123-41.

Case Study

- PERT was provided before bottles & cereal
- Salt was added to her diet
- CF specific multivitamin was prescribed.
- Cereal was mixed with formula for increased caloric intake
- Return visit in 2 weeks: weight gain was 45 gms/day. Formula intake decreased but she still gained weight.
- Bms decreased to 2-3 pasty/soft stools daily
- Excellent weight gain & linear growth at monthly visits till she was 1 year of age; after that her visits were every 2-3 months
- Annual study labs including fat soluble vitamin levels & zinc were normal
- Father got a new job & at age 4 she was transferred to another CF center

Case Study

- She returns to your CF Center at age 14 years & says she is doing very well with no problems & “regular” stools
- Pulmonary function tests: FEV1 = 48% predicted
- Examination: weight is <5th percentile, height is 10-25th percentile, BMI is 5th percentile. Bilateral crackles are present & she is admitted for pulmonary & nutritional management
- In the hospital she was noted to have 3-4 foul smelling loose stools/day, excessive gas & poor appetite

Case Study

- Her fat soluble vitamins are all low & she is zinc deficient
- Her baseline breath hydrogen level is high & lactose breath test could not be performed . She is given a course of metronidazole for 10 days
- Celiac panel is negative; normal glucose levels
- She is put on appropriate PERT therapy , CF specific vitamins & zinc supplement. The CF dietitian reviews with her a high calorie diet as well as PERT usage including adjusting her PERT intake depending on the fat content of her meals
- She started oral supplements 1-2/day
- She gains weight by the end of her 14 day admission & is feeling much better at the time of discharge. Her FEV1 improves & is now 80% predicted
- On subsequent visits you notice declining lung function & her inability to keep up with the oral nutritional recommendations by the CF dietitian
- Her BMI drops to the 10th percentile & you are asked to see her

Case Study

- Her PERT administration & dose is optimal
- Psychological assessment is negative for depression or an eating disorder
- You bring up possible tube feeds & she requests that she talk to another adolescent girl who has success with tube feeds
- After much discussion she agrees to tube feeds

Summary

- Nutrition plays an important role in the care of the patient with CF
- Growth assessment should be done at every visit. Goal is BMI at 50th percentile or weight for length at the 50th or above percentile
- Annual monitoring should be part of management
- PERT should be reviewed at every visit (total daily dose) & when the patient is not growing optimally
- The CF center dietitian should evaluate the patient quarterly or more often if there is growth failure

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