Parenteral Nutrition (PN) for the Specialized Patient

NASPGHAN FOUNDATION

NASPGHAN

Outline

- Case
- Parenteral nutrition considerations in
  - Critical illness
  - Extracorporeal membrane oxygenation (ECMO)
  - Chylothorax
  - GI surgery, high ostomies
  - Liver disease
  - Renal disease
  - Inborn errors of metabolism
  - Short bowel syndrome/Intestinal Failure
- Case review

Case

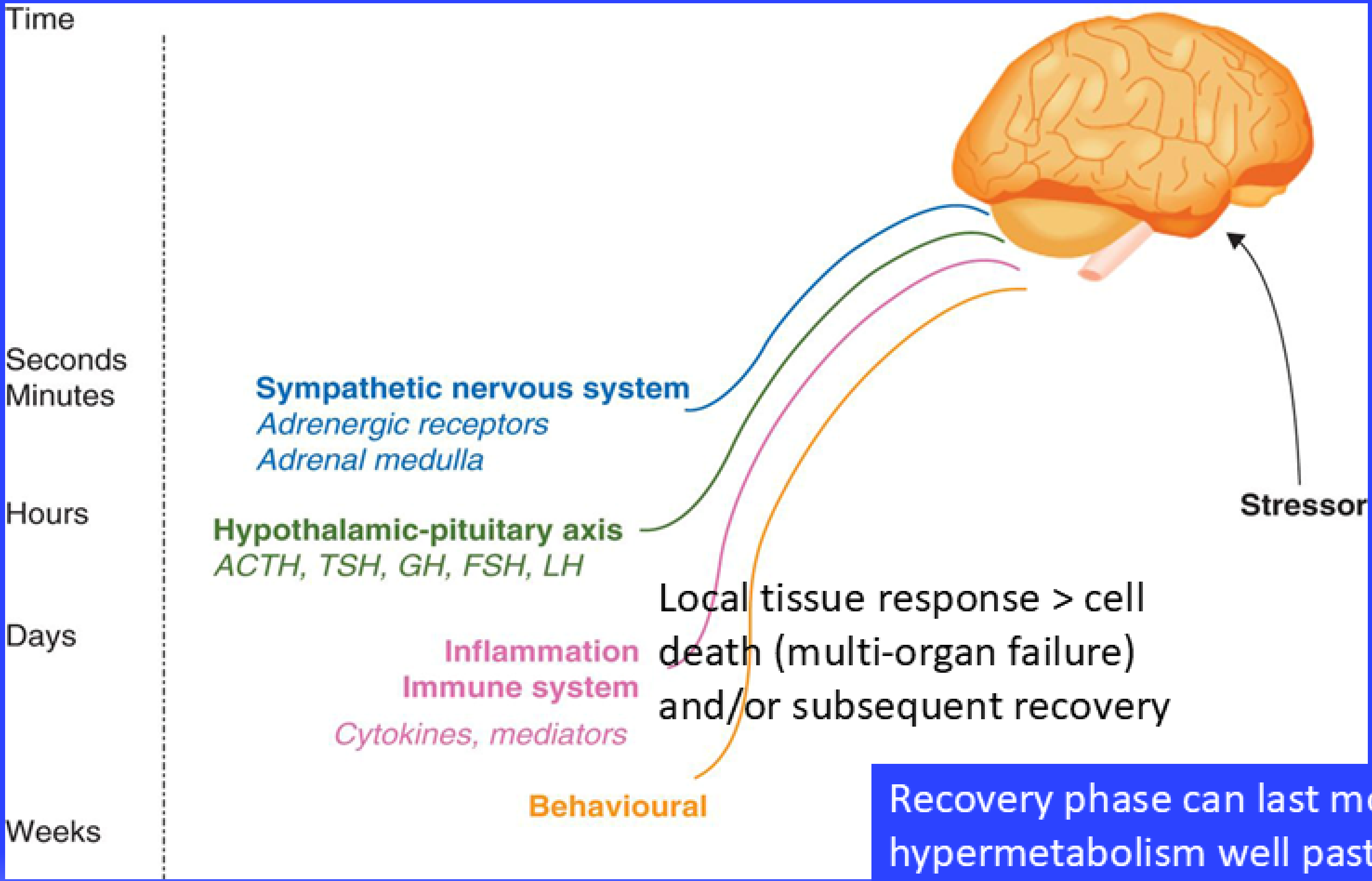
Lucy is a 5-month-old with biliary atresia and progressive end stage liver disease who is listed for transplant. She has been admitted on the GI ward for enteral nutrition to treat worsening malnutrition, however, is now transferred to PICU with fever, tachycardia, poor peripheral perfusion and hypoxia, requiring sedation and mechanical ventilation.

1) What information would you like to assess her nutrition?
2) Would you recommend parenteral nutrition and when?
3) What factors would influence the energy requirements of this patient?

Pathophysiology of Injury in Pediatric Intensive Care (PICU)

Traditionally considered pre-resuscitative ebb phase and ‘often’ hypometabolic

Traditionally considered flow phase and ‘often’ hypermetabolism



Local tissue response > cell death (multi-organ failure) and/or subsequent recovery

Central neuroendocrine response

Sepsis, burns, trauma, cardiac bypass, etc.

Recovery phase can last months with persistent hypermetabolism well past discharge from PICU

Preiser J-C, *et al. Brit J Anaesth.* 2014;113(5):945-54.

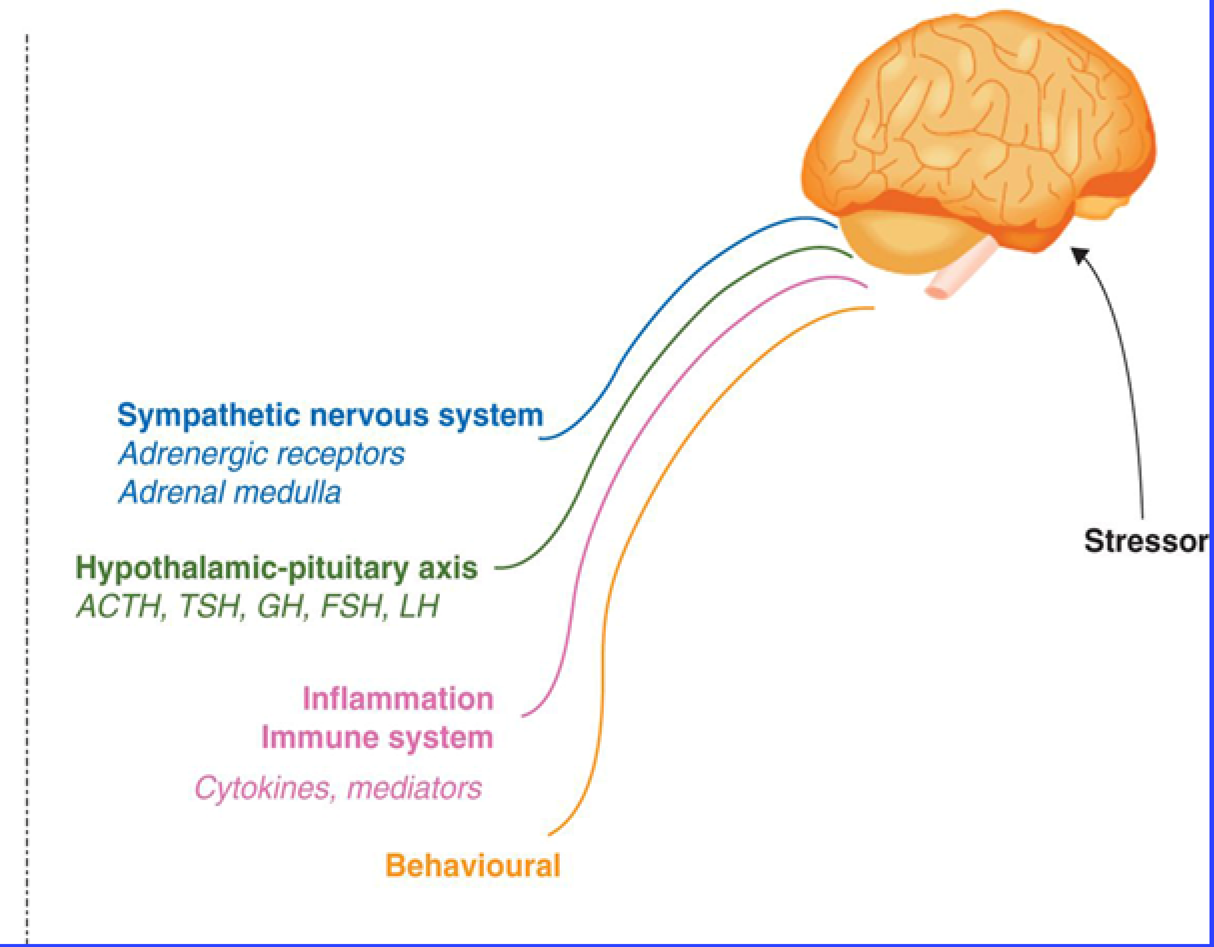
Impact on Intermediary Metabolism

CNS Hormones & Catecholamines

- ↑gluconeogenesis
- ↑glycolysis
- ↑insulin resistance;
- ↑lipolysis & FFA release
- ↑proteolysis & hepatic synthesis acute phase proteins

Cytokines

- ↑proteolysis exceeds synthesis with ↑urinary nitrogen
- ↑lipolysis
- ↑insulin resistance
  ↑demand for and use of oxygen in tissues



Together results in catabolism with resistance to anabolism causing:

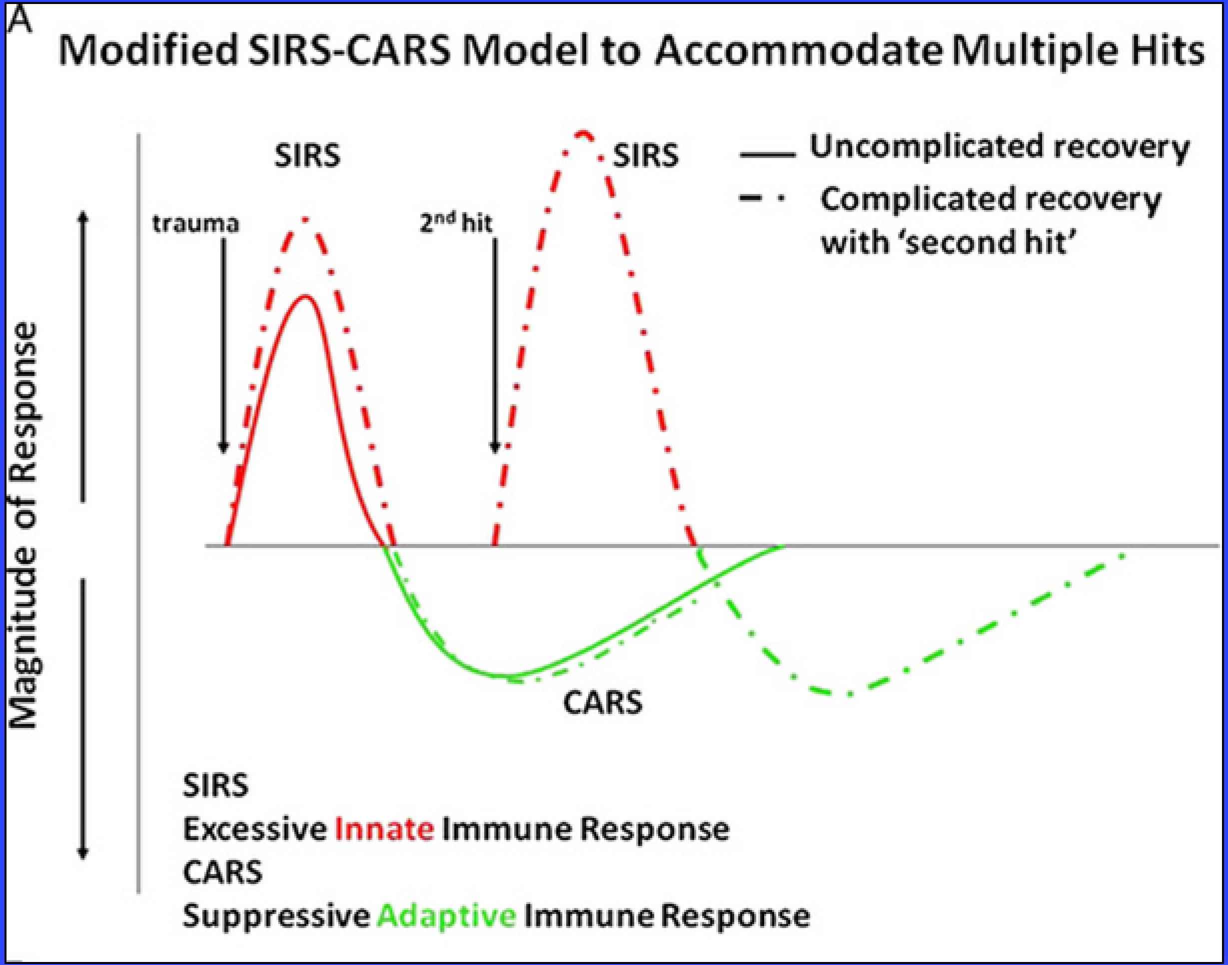
- Skeletal muscle wasting
- Hyperglycemia
- High free fatty acids
- Hypertriglyceridemia
- High lactate levels

Preiser J-C, *et al. Brit J Anaesth.* 2014;113(5):945-54.

Concepts of Inflammation and Immunosuppression in Critical Illness

- These patients are at high risk for severe malnutrition: another risk factor for secondary infections

- Going forward it will be important to understand if nutrition support in PICU might modify **Systemic Inflammatory Response Syndrome (SIRS)** and **Compensatory Anti-inflammatory Response Syndrome (CARS)**



Preiser J-C, *et al. Brit J Anaesth.* 2014;113(5):945-54.

Malnutrition in Critical Illness

- Undernutrition is common in patients admitted to PICU (20-45%)
  - Obesity increasingly common
- Catabolism with rapid loss of protein stores expected in all
  - Greatest risk for undernourished children, neonates and infants
- Muscle loss and loss of muscle function results in sarcopenia, which increases risks:
  - Prolonged ventilation
  - Acquired pneumonia
  - Prolonged length of stay
  - Mortality
  - Prolonged rehabilitation for survivors

Mehta N, *et al. J Pediatr Enteral Nutr.* 2017;41:706-42.

APSPEN Guidelines

Clinical Guidelines

aspen

Journal of Parenteral and Enteral Nutrition
Volume 41 Number 5
July 2017 706–742

DOI: 10.1177/0148607117711387
journals.sagepub.com/home/pen
SAGE

Guidelines for the Provision and Assessment of Nutrition Support Therapy in the Pediatric Critically Ill Patient: Society of Critical Care Medicine and American Society for Parenteral and Enteral Nutrition

Nilesh M. Mehta, MD[1]; Heather E. Skillman, MS, RD, CSP, CNSC[2]; Sharon Y. Irving, PhD, CRNP, FCCM, FAAN[3]; Jorge A. Coss-Bu, MD[4]; Sarah Vermilyea, MS, RD, CSP, LD, CNSC[5]; Elizabeth Anne Farrington, PharmD, FCCP, FCCM, FPPAG, BCPS[6]; Liam McKeever, MS, RDN[7]; Amber M. Hall, MS[8]; Praveen S. Goday, MBBS, CNSC[9]; and Carol Braunschweig, PhD, RD[10]

- Recommend patients in PICU undergo detailed nutritional assessment within 48 hours of admission
- Have regular reassessment at least weekly
- As lack validated screening tools use weight, height, BMI / weight for length
- Be aware fluid shifts and weight can underestimate protein losses

NASPGHAN FOUNDATION

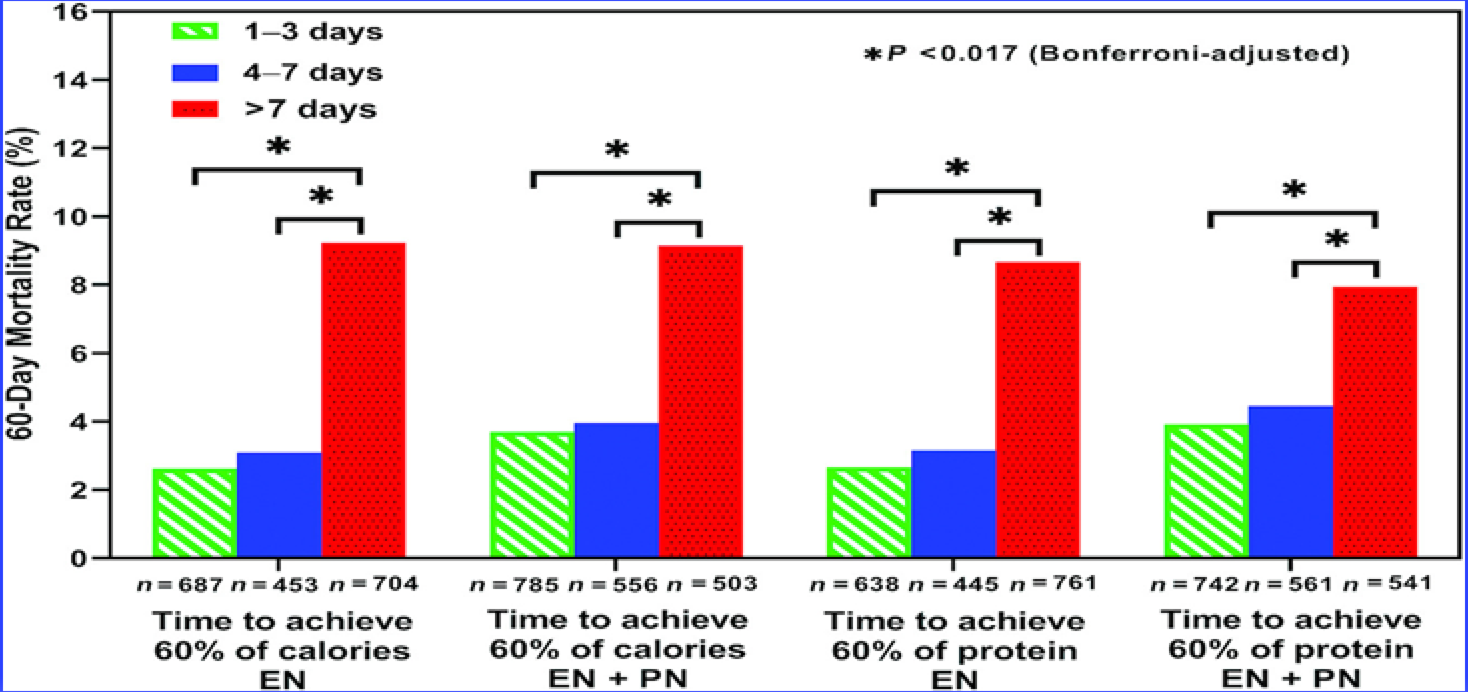
Mehta N, *et al. J Pediatr Enteral Nutr.* 2017;41:706-42.

NASPGHAN

The Role of Nutrition Support

- Malnutrition is associated with worse outcomes in PICU
- Achieving 60% of energy or protein delivery targets within 7 days after PICU admission associated with lower mortality

Regardless of nutrition support strategy



NASPGHAN FOUNDATION

Bechard L, *et al. Am J Clin Nutr.* 2021;114:1859-67.

NASPGHAN

Route of Nutrition Support in Critical Illness

- A functional gut should always be used for enteral nutrition (EN), including in critical illness where early enteral nutrition (EEN: 24 - 48h) is preferred and safe

- EN Contraindicated if: anatomical disruption, obstruction or ischemia

- PN Indicated when cannot use gut

Benefits	Limitations
Reduce gut atrophy	Increase gut oxygen needs; can be contraindicated in severe shock
Improve gut motility	Risk of Aspiration
Reduced infections (enhanced gut immune function and avoidance of translocation)	Frequent interruptions for fasting for diagnostic and other procedures limit efficacy, especially in malnourished patients
Less likely to overfeed	Risk of underfeeding
Cost effective	

Ortiz-Reyes L, *et al. Critical Care* 2022;26:173.
Braunschweig C, *et al. Am J Clin Nutr.* 2001;74:534-42.

What is the Role & Timing of Supplemental PN?

- Based on lack of evidence timing to start supplemental PN when EN intake is insufficient remains controversial
- 2017 Guideline [low quality evidence, weak recommendations]:
  - Start PN If cannot start EN
  - Based on a single RCT, do not start PN within 24h of admission
  - Based on a single RCT, delay supplemental PN until 1 week after PICU admission for patients with normal nutrition and low risk of worsening nutritional status
  - Use caution applying that approach to neonates or children with malnutrition at admission to PICU, who may warrant earlier intervention

Mehta N, *et al. J Pediatr Enteral Nutr.* 2017;41:706-42.

The Early versus Late Parenteral Nutrition in the Pediatric Intensive Care Unit (PEPaNIC) Trial

- Multicenter, prospective, randomized, controlled, parallel-group superiority trial (unblinded)
  - 723 patients receiving early PN within 24 hours after ICU admission
    - 717 patients received late PN on day 8 if still <80% of target EN requirements
  - All patients started early enteral nutrition (EEN) within 24h
  - EN advanced for all per protocol

- Newborn – 17 years (45% infants)
  - Preterm neonates were excluded

NASPGHAN FOUNDATION

Fivez T, *et al. NEJM* 2016;374:1111-22.

NASPGHAN

The Early versus Late Parenteral Nutrition in the Pediatric Intensive Care Unit (PEPaNIC) Trial

- No differences in mortality
- Late PN group had less infections (10.7% vs 18.5%; $p<0.001$)
- Late PN group had shorter ICU stay (9.2 vs 6.5d; $p<0.001$)
- Late PN group had shorter duration ventilation ($p=0.001$)
- Late PN group had less renal replacement therapy ($p=0.04$)
- Late PN group had shorter hospital stay (21.3 vs 17.2d; $p=0.001$)
- Late PN group had more hypoglycemia (9.1% vs 4.8%; $p=0.001$)

Fivez T, *et al. NEJM* 2016;374:1111-22.

Limitations of the PEPaNIC Trial

- 77% of late PN group discharged prior to starting PN
- 55% of early PN group discharged by day 4
  - likely would tolerate EN and not need PN
- Protein and energy provision was estimated so that both groups may have had either over and under feeding
- Parenteral nutrient delivery was not standardized
- Risk of overfeeding particularly high in early PN group
  - Overfeeding known risk factor for infections with PN
- Majority sample did not screen at nutritional risk and were normal weight limiting generalizability to malnourished patients

Fivez T, *et al. NEJM* 2016;374:1111-22.

Risks of Underfeeding in Critical Illness

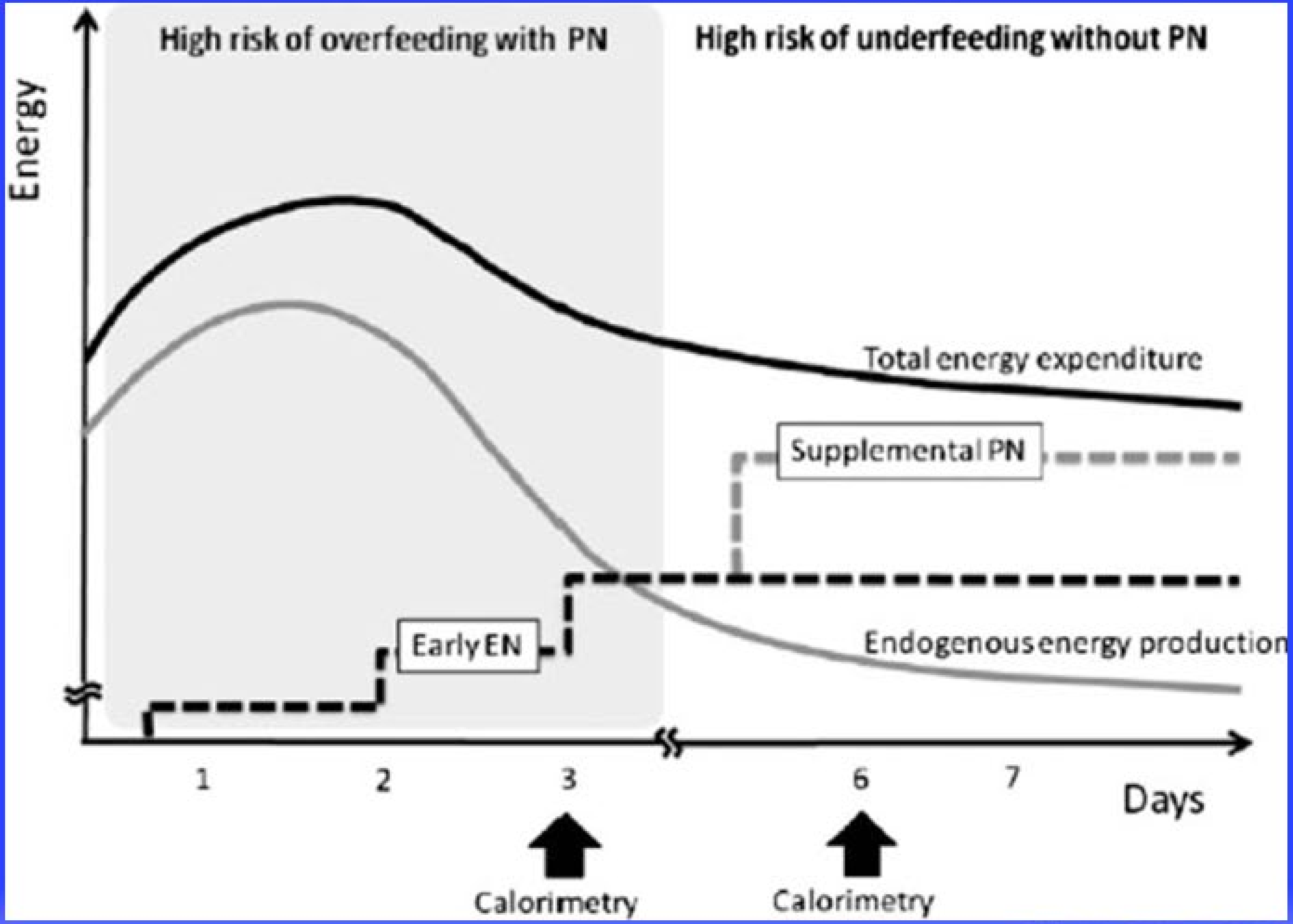
- Hypoglycemia
- Progressive sarcopenia in PICU
- Prolonged ventilation due to sarcopenia
- Increased infection risk
- Poor wound healing
- Prolonged sarcopenia post PICU stay requiring rehabilitation
- Potential to adversely impact neurocognitive and psychomotor development

Risks of Overfeeding in Critical Illness

- Hyperglycemia, which increases risk of sepsis and poor wound healing
- Hypertriglyceridemia
- Hepatic steatosis
- Cholestasis
- Uremia
- Ventilator dependency with hypercapnia from glucose overfeeding

Until the Best Approach is Known Consider an Individualized Approach?

- Delay PN 7 days if risk of overfeeding
- Only use if not meeting 60% of EN goals and advancing
- Consider supplemental PN 3-5 days if risk of underfeeding



NASPGHAN FOUNDATION

Jiminez L, *et al. Curr Opin Clin Nutr Metab Care* 2017;20:227-31.

NASPGHAN

Parenteral Energy Requirements

- Energy requirements are highly variable in PICU
  - Often lower than predicted, e.g., sedation, ventilation, paralysis, PN (NPO)
  - Can be higher, e.g., CNS injury with dysautonomia, burns
- Predictive equations for energy have limited accuracy
  - But due to lack of access to calorimetry are widely used

Mehta N, *et al. J Parenter Enteral Nutr.* 2017;41:706-42.

Parenteral Energy Requirements – Cont'd

- 2017 Guideline [low quality evidence, weak recommendations]
  - Use calorimetry to guide energy goals
  - In the absence of calorimetry use Schofield/FAO/WHO/UNU equations
    - **NOT** Harris Benedict or RDA
    - **DO NOT** add stress factors
  - Target at least 2/3 of goal energy be end of first week in PICU
    - Individualize approach according to baseline nutrition and risk for over or underfeeding

Mehta N, *et al. J Parenter Enteral Nutr.* 2017;41:706-42.

Priority Patients for Measuring Resting Energy Expenditure (REE) in PICU

1. Malnutrition (BMI<5th percentile) or overweight (BMI > 85^{th})
2. > 10% weight gain or loss during PICU stay
3. Failure to consistently meet prescribed caloric goals
4. Failure to wean or escalation in respiratory support
5. Need for muscle relaxants > 7days
6. Need for ventilation > 7days
7. CNS trauma (injury, hypoxia, ischemia) with dysautonomia
8. Oncologic diagnosis
9. PICU stay > 14 days
10. Suspect Hypometabolism (e.g., hypothermia/cooling, drug induced coma) or Hypermetabolism (e.g., SIRS, status epilepticus, hyperthermia)

NASPGHAN FOUNDATION

Albert B, *et al. Minerva Anestesiologica* 2021;87:1025-33.

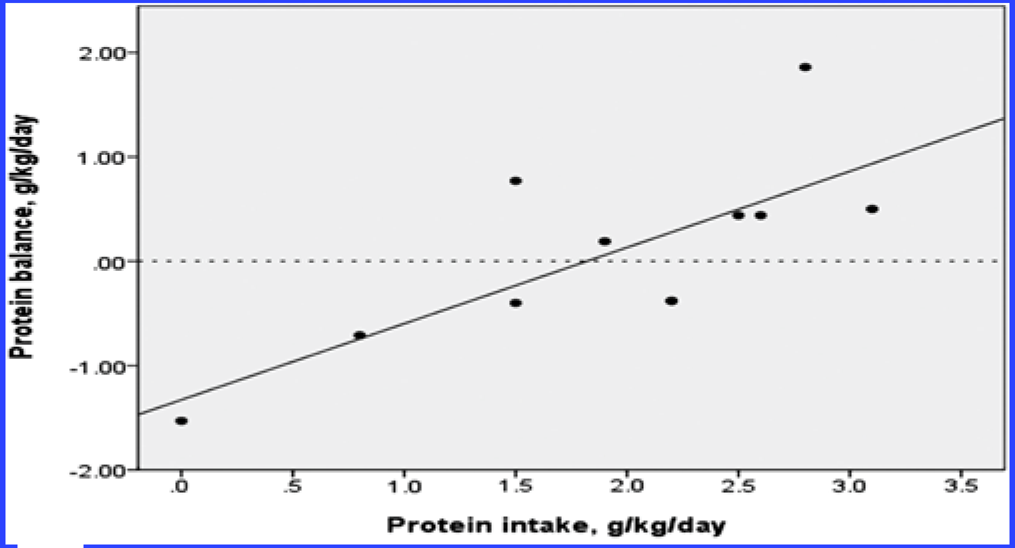
NASPGHAN

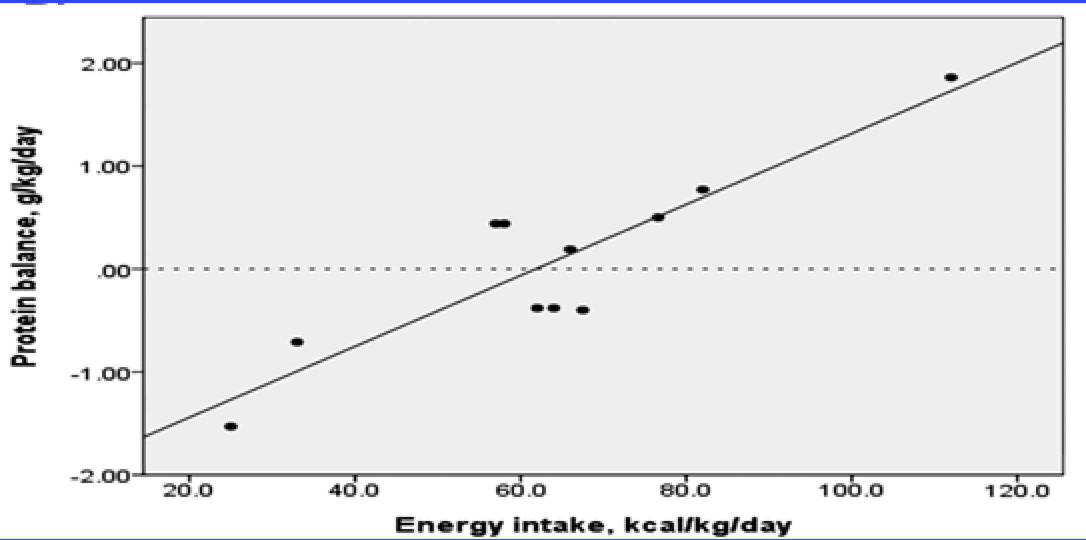
Parenteral Protein Requirements

- Both protein breakdown and synthesis are increased in critical illness
  - Negative nitrogen balance results
- Protein supply is critical and often underestimated
  - Bedside tools to evaluate nitrogen balance limited (especially in renal impairment)
  - Increased requirement in burns, gastrointestinal losses, open wounds, continuous renal replacement therapy
- 2017 Guideline [moderate quality evidence, strong recommendations]
  - Provide a minimum of 1.5g/kg/day protein (and more in infants)
  - **Do not** use RDA (recommended daily allowance) as will be insufficient

Mehta N, *et al. J Parenter Enteral Nutr.* 2017;41:706-42.

Both Important to Achieve Positive Nitrogen Balance





- Systematic review 9 studies 1981-2011 (n=347) children with heterogenous diagnoses admitted to PICU (who had measured protein balance)
- Positive balance with protein intake > 1.5g/kg/d or energy intake > 57Kcal/kg/day

NASPGHAN FOUNDATION

Bechard L, *et al. J Pediatr.* 2012;161:333-9.

NASPGHAN

Extracorporeal Membrane Oxygenation (ECMO)

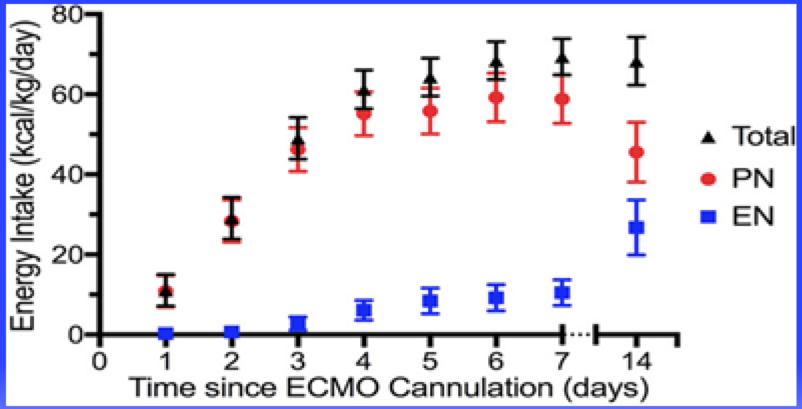
- Indicated for severe cardiac and/or respiratory failure
- Evidence base limited to expert opinion and case series
  - EN safe for 75-90% of patients on ECMO
  - Feeding intolerance is common, up to 50%

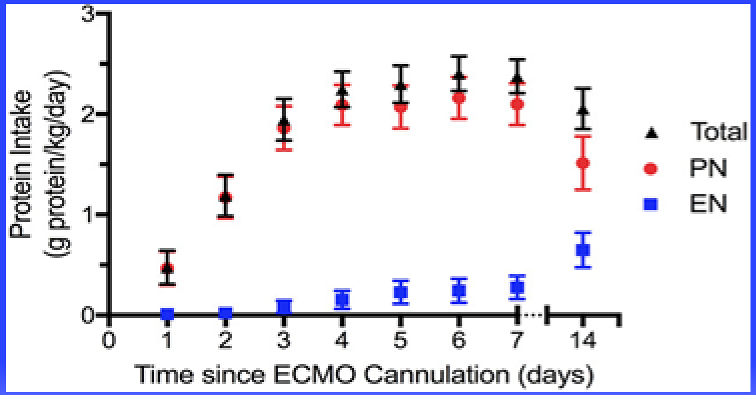
- Acknowledged risk for gut hypoperfusion, although severe GI complications reportedly rare
  - PN (total parenteral nutrition with nil enteral) may be preferred in unstable patients with escalating inotropes or concerning symptoms like bilious emesis, GI bleeding or increasing abdominal distention

Armstrong L, *et al. J Peditatr Enteral Nutr.* 2018;42:1133-8.
Farr B, *et al. Nutr Clin Pract*. 2018;33:747-53.

ECMO – Cont'd

- REE not readily measured or predicted by current equations
- EN has ***risk of underfeeding*** given feeding intolerance
- Supplemental PN can increase protein and energy delivery, but ***risk of overfeeding***
- Start supplemental PN 5-7 days well nourished or 3-5 days in malnourished children





NASPGHAN FOUNDATION

Armstrong L, *et al. J Pediatr Enteral N.* 2018;42:1133-8.

NASPGHAN

Chylothorax

- Common complication in PICU after cardiac surgery, ~5%
- Majority can be managed medically: median chain triglyceride (MCT) enriched EN first line treatment
  - No RCTs comparing MCT-rich EN to PN and nil per os
- PN (with lipids) may be indicated if refractory to EN or high-volume losses >10ml/kg/day
  - More than 80% effective, without further medication or surgery
- Risk of nutritional losses and immunosuppression
  - Chylous fluid has 20-60g/L protein, electrolytes, trace minerals, immune cells and immunoglobulins
  - Monitor for EFAD if extended use of MCT-rich EN, although rare

Duletzke N, *et al. Nutr Clin Pract*. 2023;38:557-63.

Gastrointestinal Surgery & Ostomies

- Massive intestinal resection induces major functional and metabolic changes in the GI tract
  - Loss of inhibitory reflexes of the enteric nervous system including cologastric and ileogastric reflexes, accelerating intestinal motility
  - Decrease in enterohormones leading to accelerated gastric emptying and increased gastric secretion
  - Bile acid loss
- Major net loss of fluids and electrolyte via end-jejunostomy
  - Losses worsened by oral intake
- PN mixture must meet higher hydration needs and compensate nutrition losses

NASPGHAN FOUNDATION

Sobocki J, *et al. British J Nutr.* 2021;125:1125-31.
Nightingale J, *et al. Lancet* 1990;336:765-8.

NASPGHAN

Consider Site Specific Effects of Intestinal Resection for GI Function (and Stoma Losses) and GI Hormones

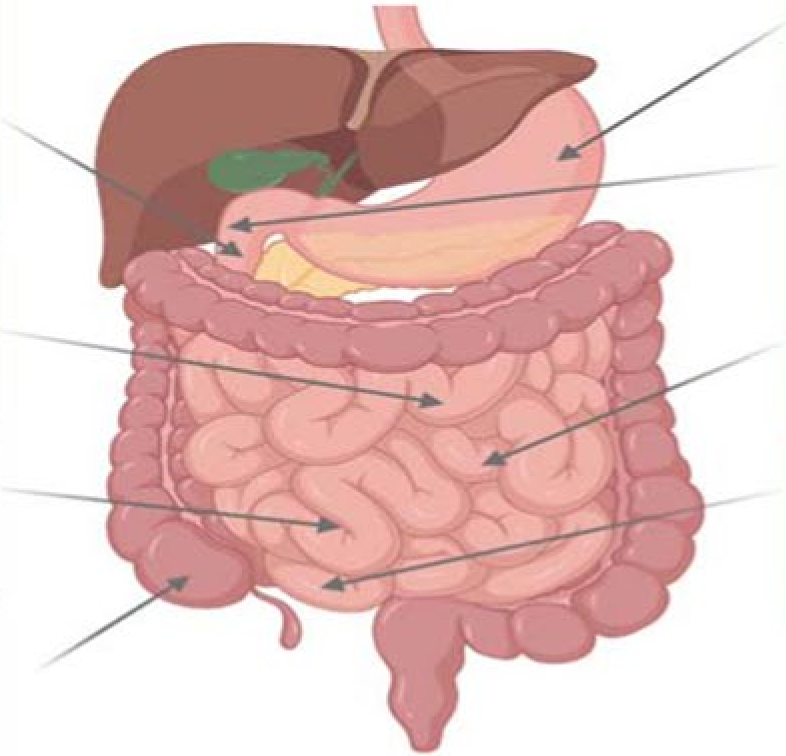
Nutrient Absorption Sites

Duodenum/Proximal Jejunum
- macronutrients
- iron
- folate
- calcium
- vitamins/minerals

Jejunum/Proximal Ileum
- macronutrients
- calcium
- vitamins/minerals

Distal Ileum
- bile salts
- vitamin B_{12}
- SCFA

Colon
- SCFA
- minerals
- vitamin K



Mediator Release Sites

Stomach
- gastrin
- ghrelin

Duodenum
- cholecystokinin
- secretin
- GIP
- VIP

Jejunum/Ileum
- neurotensin

Distal Ileum/Colon
- peptide YY
- GLP-1
- GLP-2

Tappenden KA. *Nutr Clin Prac.* 2023;38:s27-34.

Gastrointestinal Surgery & Ostomies

- PN considerations to compensate for high losses in proximal ostomies
  - Fluid
  - Sodium; patients will not grow until adequately supplemented with sodium. Recommend following urine sodium to guide sodium replacement.
  - Potassium
  - Bicarbonate; incompatible with PN so replaced as acetate in PN; in end stage liver disease may have difficulty converting acetate to bicarbonate
  - Zinc
  - Iron; increased needs in ex-preterm, with chronic GI blood loss and extensive proximal small bowel loss; can be added to PN, but not with sepsis or 3:1 solutions
  - Copper; standard supplementation may be inadequate

Sobocki J, *et al.* *British J Nutr.* 2021;125:1125-31.
Nightingale J, *et al.* *Lancet* 1990;336:765-8.
Adler A, *et al. Nutr Clin Pract*. 2020;35:724-8.

NASPGHAN FOUNDATION

NASPGHAN

Malnutrition in Pediatric Chronic Liver Disease

Decreased energy intake	Anorexia Changes in taste perception Early satiety Nausea / vomiting
Increased energy intake	Increased energy requirement up to 150% EAR Hypermetabolic state in end-stage liver disease Sequelae of CLD (i.e., peritonitis, variceal bleeding) Increased pro-inflammatory cytokines
Endocrine dysfunction	Impaired GH / IGF–1 axis Decreased IGF-1 formation
Malabsorption and disordered substrate metabolism	**Carbohydrate** – hypoglycemia from decreased glycogen stores, hepatocyte loss in fulminant liver failure **Proteins** – increased protein catabolism, impaired protein synthesis **Fats** – malabsorption from decreased bile delivery to small bowel, unconjugation of bile salts with bacterial overgrowth (in children with Kasai portoenterostomy), congested intestinal mucosa.

Yang CH, *et al.* *Nutrients* 2017;9:1127.

Liver Disease

- Supplement
  - Zinc (if deficient)
  - Potassium (especially if on diuretics)
  - Fat soluble vitamins D, E, K (if deficient)
  - Protein (if hypoalbuminemic and not encephalopathic)
- Encephalopathy
  - Reduce protein
  - Monitor ammonia
- Cholestasis
  - Restrict copper, manganese since they are secreted in bile
  - Adjust lipids: consider fish oil lipid emulsion (Omegaven®)
- Immunosuppressant medications can affect nutritional status

Vitamins: Lab Markers and Dosing Recommendations

Vitamin A

Laboratory Markers

Serum retinol level

If available RDR

Recommendations

1000 IU/kg/day, up to 25,000 IU of water miscible formulations

- <10 kg: start with 5000 IU/day
- >10 kg: start with 10,000 IU/day

Vitamin D

Laboratory Markers

Serum 25-OHD

Recommendations

Cholecalciferol

- Weight >40kg
  - Serum level <10 ng/mL: 5000 IU/day
  - Serum level 11-19 ng/mL: 4000 IU/day
  - Serum level 20-29 ng/mL: 3000 IU/day
- Weight <40kg
  - 120-200 IU/kg

Vitamin E

Laboratory Markers

Serum tocopherol level

If available α-tocopherol/total lipids ratio

Recommendations

D-α-tocopherol polyethylene glycol 1000 succinate (TPGS) 15-25 IU/kg/day

Vitamin K

Laboratory Markers

PT/INR

If available PIVKA-II

Recommendations

2.5-5 mg/day 2-7 times weekly; 1-10 mg intravenous as needed

NASPGHAN FOUNDATION

Yang CH, *et al. Nutrients* 2017;9:1127.

NASPGHAN

Nutritional Needs of Children With CLD Before and After Liver Transplant

Liver Transplant

Before

ENERGY INTAKE

- 130-150% EAR

CARBOHYDRATES

- 15-20 g/kg/day given as glucose polymers

PROTEINS

- 3-4 g/kg/day; if acutely encephalopathic may temporarily restrict to <2 g/kg/day. BCAA-enriched formula can be considered

FATS

- 8 g/kg/day, with 30-50% as MCT
- Infants can receive formula containing up to 75% MCT; higher MCT content may result in essential fatty acid deficiency

After

ENERGY INTAKE

- 120% EAR

CARBOHYDRATES

- 6-8 g/kg/day given as glucose polymers

PROTEINS

- 2.5-3 g/kg/day

FATS

- 5-6 g/kg/day LCT
- Children receiving high MCT-containing supplementation pre-transplant can transition to standard formula once bile flow is established post-transplant

Yang CH, *et al. Nutrients* 2017;9:1127.

Nutritional Side-Effects of Immunosuppressive Meds

Immunosuppressant	Nutritional Side-Effects
Calcineurin inhibitors (FK, tacrolimus, cyclosporine)	Hyperlipidemia, Hyperglycemia Hypomagnesemia, Hyperkalemia Hypertension Avoid grapefruit
Corticosteroids (prednisone, methylprednisolone)	Hyperglycemia, Hyperlipidemia Sodium retention, Hypertension Increased appetite, Weight gain Muscle wasting Peptic ulcer disease Impaired wound healing Electrolyte disturbances
Mycophenolate (MMF)	Diarrhea, Nausea
Azathioprine	Nausea, vomiting, sore throat, altered taste acuity
Sirolimus	Hyperlipidemia, GI symptoms

NASPGHAN FOUNDATION

Ikizler TA, *et al. Am J Kidney Dis*. 2009;76(3):S1-S107.

NASPGHAN

Renal Disease

- When to consider PN
  - Peritoneal dialysis complicated by ileus or peritonitis
  - Critically ill patients on hemodialysis
  - Severe malnutrition, intolerance of enteral feeds
  - Intestinal obstruction (mechanical or pseudo-obstruction)
- Acute Kidney Injury (AKI)
  - Fluid intake is often reduced
  - Volume available for PN can impact on caloric intake
  - Protein intake often restricted to meet minimum requirements
  - Electrolytes based on serum levels

Renal Disease – Cont'd

- On dialysis
  - Protein losses are increased by dialysis
  - Dialysis removes excess urea
  - Increase fluid, calorie, and protein provision
  - No longer need to restrict or reduce protein provision

Raina F, *et al. Nat Rev Nephrol*. 2020;16:471-82.

Renal Disease Nutrient Recommendations

Restriction may be required	Supplementation may be required
Deduct dialysate glucose when calculating glucose infusion rate (GIR)	Protein (increased losses with dialysis)
Total fluids (based on fluid status and dialysis settings)	Alkali due to increased losses in 'nonoliguric' renal failure (e.g., congenital hydronephrosis, renal dysplasia)
Sodium (give in small amounts due to diminished excretion)	Sodium due to increased losses in 'nonoliguric' renal failure (e.g., congenital hydronephrosis, renal dysplasia)
Potassium (give in small amounts due to diminished excretion)	Potassium (if on diuretics or depending on dialysate)
Phosphorous (give in small amounts due to diminished excretion)	
Vitamin C to <100 mg/day in pts with hyperoxaluria	
Lipids in patients with hyperlipidemia of renal failure	

Wong Vega M, *et al. Nutr Clin Pract*. 2023;38:S139-57.
Raina R, *et al. Nat Rev Nephrol*. 2020;16:471-82.

Estimated Energy and Protein Requirements in Children with Renal Disease

Age Group	Pre-Dialysis		Hemodialysis		Peritoneal Dialysis	
	Energy Kcal/kg/d	Protein g/kg/d	Energy Kcal/kg/d	Protein g/kg/d	Energy Kcal/kg/d	Protein g/kg/d
0 – 6 m	100 – 110	1.5 – 2.2	100 – 110	1.6	100 – 110	1.8
6 – 12 m	95 – 105	1.2 – 1.7	95 – 105	1.3	95 – 105	1.5
1 – 3 y	90	1.05 – 1.5	90	1.15	90	1.3
4 – 10 y	70	0.95 – 1.35	70	1.05 – 1.6	70	1.1 – 2.0
11 – 14 y (boys)	55	0.95 – 1.35	55	1.05 – 1.4	55	1.1 – 1.8
11 – 14 y (girls)	47	0.95 – 1.35	47	1.05 – 1.4	47	1.1 – 1.8
15 – 18 y (boys	45	0.85 – 1.2	45	0.95 – 1.3	45	1.0 – 1.5
15 – 18 (girls)	40	0.85 – 1.2	40	0.95 – 1.2	40	1.0 – 1.5

NASPGHAN FOUNDATION

National Kidney Foundation. *Am J Kidney Dis*. 2009;53(Suppl 2):S1-S124.

NASPGHAN

Micronutrients in AKI: Energy

Macronutrient	AKI, no RRT	CRRT	PIRRT	HD	PD
Energy	Dictated by disease state, malnutrition, and illness severity				
Key considerations	N/A	• High removal rates of levocarnitine may influence metabolism of free fatty acids • Largely dependent o use of citrate-based anticoagulation and dextrose solutions used within respective institutions • Larger patients likely receive more significant exposure • May be CRRT dose dependent. Higher dose may clear more nonnutritive fluids into effluent than lower doses. • Glucose-free replacement fluids may lead to energy removal • Hyperosmolar, hyperglycemic states may contribute to energy deficit		N/A	• Dextrose is present in dialysate but assessment of exposure cannot be performed without assessment of membrane transporter status • Monitor weight trends and adjust nutrition support accordingly

Note: Suggestions within this table are initial recommendations that should be titrated based on patient progress and reassessment of the patient's nutrition status and medical goals of care.

NASPGHAN FOUNDATION

Wong Vega M, *et al. Nutr Clin Pract.* 2023;38:S139-57.

NASPGHAN

Micronutrients in AKI: Protein

Macronutrient	AKI, no RRT	CRRT	PIRRT	HD	PD
Protein	DRI / age minimum	≥ 2.5 g/kg/day protein or ASPEN/ age + additional 10%–20% to account for removal		ASPEN / age + 0.1 g/kg/day	ASPEN / age + 0.3 g/kg/day
Key considerations	• Temporary protein restrictions may be implemented if AKI recovery expected soon • Inability to obtain dialysis access may limit ability to provide goal protein intake	• No expectation the SUN levels are low or normal • 2.5 g/kg/day is extrapolated from adults	• May require less protein than CRRT, given intermittent nature	• Value is extrapolated from adults receiving HD 3×/week • If HD frequency expected to be higher, adjust for increased frequency	• Values are extrapolated from populations with chronic ESRD

Note: Suggestions within this table are initial recommendations that should be titrated based on patient progress and reassessment of the patient's nutrition status and medical goals of care.

Wong Vega M, *et al.* *Nutr Clin Pract.* 2023;38:S139-57.

Micronutrients in AKI: Fluid

Macronutrient	AKI, no RRT	CRRT	PIRRT	HD	PD
Fluid	Largely dependent on responsiveness to diuretics	• Unrestricted • May be temporarily restricted around initial start	Largely dependent on length of treatment	• < 13-ml/kg/h per treatment • Limit myocardial stunning; may be lower in hemodynamically unstable patients	Unpredictable
Key considerations	• Follow I/Os and fluid balance goals accounting for urine output, volume of medications, and blood products • Concentrate nutrition support when able if not achieving fluid balance goals				

Note: Suggestions within this table are initial recommendations that should be titrated based on patient progress and reassessment of the patient's nutrition status and medical goals of care.

Wong Vega M, *et al. Nutr Clin Pract.* 2023;38:S139-57.

Inborn Errors of Metabolism

- PN should be initiated quickly during metabolic stressors
  - Promote anabolism
  - Diminish catabolism
- Use PN short-term and start enteral nutrition (EN) as soon as clinically feasible
- Metabolic parameters should be monitored closely with adjustment of type and amount of protein when necessary
- Common metabolic stressors
  - Trauma
  - Burns
  - Gastrointestinal (pancreatitis, ileus)
  - Infection
  - Altered mental status
  - Essential fatty acid deficiency

NASPGHAN FOUNDATION

Brusilow SW, *et al.* *NEJM* 1984;310:1630-4.
Haberle J, *et al.* *Orphanet J Rare Dis.* 2012;7:32.

NASPGHAN

Inborn Errors of Metabolism: Phenylketonuria (PKU)

- Hypercatabolism occurs during stress
  - Parallels the extent of infection/injury
- Goal is prevention of prolonged phenylalanine (PHE) elevation
- Interventions to depress catabolic response
  - PN as bridge to enteral nutrition
  - PHE-free parenteral amino-acid solution with some standard parenteral amino acids
    - Not commercially available
    - Needs to be made by a compounding pharmacy

Acosta PB. (2010) Nutrition Management of Patients with Inherited Metabolic Disorders. Boston. Jones and Bartlett. 119-174.

Inborn Errors of Metabolism: Mitochondrial Disorders

- Avoid exposure to PN if possible
- High-glucose diet is a metabolic challenge for impaired oxidative phosphorylation
  - Glucose oxidation is largely aerobic in the liver
- High lipid/low carbohydrate diet recommended in Complex I deficiency
- Carnitine supplementation is recommended in patients with secondary carnitine deficiency
  - Dose of carnitine needed is higher than nutritional doses
  - Carnitine to be administered separately from PN to ensure adequate provision

Munnich *et al*. The Online Metabolic & Molecular Bases of Inherited Disease. McGraw-Hill Education;2019.

Inborn Errors of Metabolism: Propionic Acidemia and Methylmalonic Acidemia (MMA)

Management of acute crisis

- Remove sources of isoleucine (ILE), methionine (MET), threonine (THR), valine (VAL)
- IV glucose and electrolytes: 150 mL/kg; glucose infusion rate (GIR): 10 mg/kg/min
  - Treat metabolic acidosis and maintain normal sodium levels
- Add lipids 2-3 g/kg/day to achieve total caloric goal of 120-150 kcal/kg/day (infant)
- Intravenous L-carnitine 100-300 mg/kg/day to help improve clearance

NASPGHAN FOUNDATION

Forny P, et al. J Inherit Metab Dis. 2021;44:566-92.
Prietsch V, *et al. J Inheirit Metab Dis.* 2002;25:531-46.
Ney D, *et al. J Inherit Metab Dis.* 1985;8:132-42.
Kahler SG, *et al. J Pediatr.* 1989; 115:235-41.

NASPGHAN

Inborn Errors of Metabolism: Propionic Acidemia and MMA – Cont'd

Management of acute crisis

- Combination PN (and EN) within 24 - 48 hours to prevent ILE, MET, THR and VAL deficiency
  - Initiate protein at 0.5 g/kg/day and increase as tolerated not exceeding prescribed amounts
  - Monitor daily plasma amino acids until stable
- Peripheral PN will not provide sufficient energy for anabolism

Forny P, et al. J Inherit Metab Dis. 2021;44:566-92.
Prietsch V, *et al. J Inheirit Metab Dis.* 2002;25:531-46.
Ney D, *et al. J Inherit Metab Dis.* 1985;8:132-42.
Kahler SG, *et al. J Pediatr.* 1989; 115:235-41.

Inborn Errors of Metabolism: Maple Syrup Urine Disease (MSUD)

- Comatose or Neurologically compromised patients
  - Goal calories

    Infants: 120 - 140 kcal/kg/day

    Children: 80 - 100 kcal/kg/day

    Adults: 40 - 45 kcal/kg/day

- Add insulin to treat hyperglycemia (need anabolic GIR)

Heldt K, *et al. Mol Genet Metab.* 2005;84:313-6. Holmes Morton D, *et al. Pediatrics* 2002:109:999-1008.
Elsas *et al. Inherited metabolic disease in Modern Health in Nutrition and Disease.* Philadelphia. Lippincott Williams & Wilkins. 10th Ed. 2006.
www.childrenshospital.org/newenglandconsortium/NBS/MSUD.html.

Inborn Errors of Metabolism: MSUD – Cont'd

- Use branch chain amino acid (BCAA)-free solution and monitor plasma amino acids
  - Neonates: give 2.5 - 3 g/kg/day protein
  - Plasma ILE/VAL decrease more rapidly then, LEU
  - Add ILE/VAL supplement to PN at lower limits of recommended intake
  - Add LEU when plasma LEU reaches 200µmol/L
  - Not commercially available, needs to be made by a compounding pharmacy
- Normalization of all 3 BCAA usually happens in 48 - 72 hours
- When able to tolerate enteral feeds start BCAA-free food

Heldt K, *et al. Mol Genet Metab.* 2005;84:313-6. Holmes Morton D, *et al. Pediatrics* 2002:109:999-1008.
Elsas *et al. Inherited metabolic disease in Modern Health in Nutrition and Disease.* Philadelphia. Lippincott Williams & Wilkins. 10th Ed. 2006.
www.childrenshospital.org/newenglandconsortium/NBS/MSUD.html.

Inborn Errors of Metabolism: Urea Cycle Disorders (UCDs)

- Provide abundant calories with high glucose and lipids to minimize catabolism
- Reduce nitrogen load
  - Restrict nitrogen intake
  - Activate alternate pathways for nitrogen excretion
- Arginine supplementation needed
  - Available as a separate IV infusion for this purpose
- Monitor closely for catabolic stressors and risk factors for hyperammonemia
  - Birth
  - Illness
  - Excess protein intake
  - Surgery

Brausilow SW, *et al. NEJM* 1984;310:1630-4.
Häberle J, *et al. Orphanet J Rare Dis.* 2012;7:32.

Inborn Errors of Metabolism: UCDs – Cont'd

- Early consideration of parenteral support, if emesis is present to diminish catabolic sequelae
  - High parenteral energy provision
  - 80 - 100 kcal/kg/day for infants
  - 10% dextrose and ILE with glucose infusion rate of 6 - 8 mg/kg/min and 1 - 2 g/kg/day fat

- For persistent catabolism use 10 - 35% dextrose along with insulin (to stop catabolism of glucose)

Brausilow SW, *et al. NEJM* 1984;310:1630-4.
Häberle J, *et al. Orphanet J Rare Dis.* 2012;7:32.

Short Bowel Syndrome / Intestinal Failure

- Pediatric Intestinal Failure as defined by NASPGHAN 2017 as,

"The need for PN for > 60 days due to intestinal disease, dysfunction or resection."

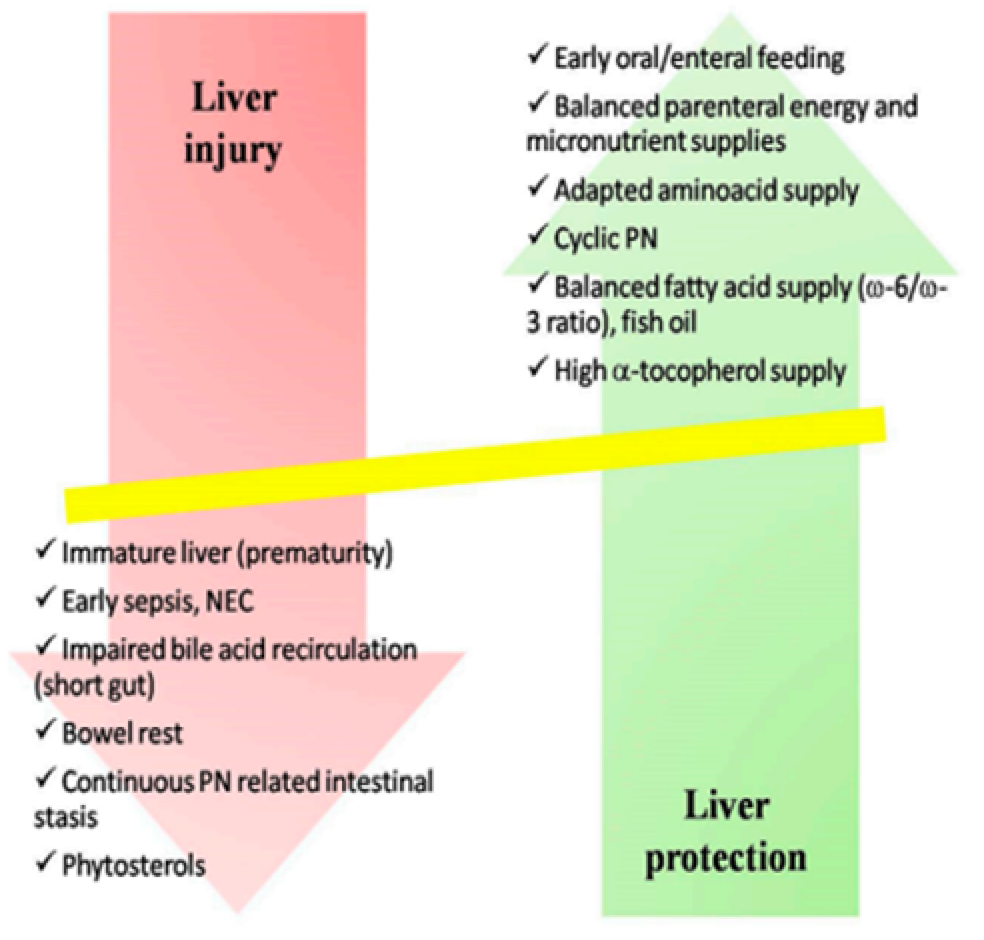
- PN is needed to meet energy, fluid, and nutritional requirements when enteral nutrition (EN) is insufficient or cannot be tolerated

Diagnosis associated with intestinal failure and short bowel syndrome in infants (N=272)	
Diagnosis	**N (%)**
Necrotizing enterocolitis	71 (26)
Gastroschisis	44 (16)
Intestinal atresia (large/small)	27 (10)
Volvulus	24 (9)
Long segment Hirschsprung's disease	11 (4)
Tufting or microvillus inclusion	3 (1)
Other single diagnoses	14 (5)
Unknown	1
Multiple single diagnoses	77 928)

Squires RH, *et al. J Pediatr.* 2012;161:723-8.

Intestinal Failure Associated Liver Disease (IFALD)

- IFALD is seen in up to 2/3rds of patients on long-term PN
- IFALD is defined as ***"hepatobiliary dysfunction as a consequence of medical and surgical management strategies for intestinal failure which can variably progress to end-stage liver disease or can be stabilized or reversed with promotion of intestinal adaptation."***
- Many factors contribute to the development of IFALD



Norsa L, *et al. Nutrients* 2018;10:664.

NASPGHAN FOUNDATION

Kocoshis SA. *Semin Pediatr Surg*. 2010;19:20-6.

NASPGHAN

PN in Intestinal Failure

- Multifactorial etiology
- Macronutrient excess promotes hepatic steatosis
  - High GIR result in increased insulin, triggering hepatic lipogenesis
  - Target required energy for disease state
  - Balance nonprotein calories: 75% as carbohydrate, 25% as fat
- High cumulative infusion of amino acids may also play a role
  - Use of PN amino acid solutions designed for children to avoid nitrogen excess is advised
  - Blood urea nitrogen, acidosis, nitrogen balance and growth can be monitored

Lacaille F, *et al.* *J Pediatr Gastroenterol Nutr.* 2015;60:272-83.

Lipid Emulsions and IFALD

- Soy based intravenous lipid emulsions (ILE) contain high ω-6 long-chain polyunsaturated fatty acids (PUFA), phytosterols and low antioxidant content which promote inflammation and worsen cholestasis
  - Discontinuation or minimizing pure soybean oil lipid emulsions (typically to 1 g/kg/day) may reverse cholestasis
    - Risk of EFAD and compromised growth

Silverman JA, *et al. Pediatr Gastroenterol Nutr.* 2020;71:283-7.
Colomb V, et al. *J Parenter Enteral Nutr.* 2000;24:945-50.
Puder M, *et al. Ann Surg.* 2009;250:395-402.

Lipid Emulsions and IFALD – Cont'd

- Composite lipid emulsions (containing soy, medium chain triglycerides, olive oil and fish oil) provider higher ω-3 to ω-6 fatty acid ratio, increased antioxidants through α-tocopherol and less phytosterols
  - Helps prevent and possibly treat IFALD in infants and children

- Fish oil emulsions provide ω-3 PUFA, DHA and EHA, α-tocopherol and reduced phytosterol load and have been shown to reverse cholestasis
  - Typically dosed at 1g/kg/day; doses of 1.5-2 g/kg/day have been used off label to decrease GIR

NASPGHAN FOUNDATION

Silverman JA, *et al. Pediatr Gastroenterol Nutr.* 2020;71:283-7.
Colomb V, et al. *J Parenter Enteral Nutr.* 2000;24:945-50.
Puder M, *et al. Ann Surg.* 2009;250:395-402.

NASPGHAN

Intestinal Failure Nutritional Considerations

- Start enteral feeds as soon as possible and advance as tolerated
- Cycle PN when possible
- PN is used to meet energy needs and promote normal growth
  - The patient's response is best and PN should be adjusted to meet nutritional needs and promote normal growth
  - Avoid overfeeding
- Care within multidisciplinary intestinal rehabilitation teams is beneficial

Lacaille F, *et al.* *J Pediatr Gastroenterol Nutr.* 2015;60:272-83.

Case

Lucy is a 5-month-old with biliary atresia and progressive end stage liver disease who is listed for transplant. She has been admitted on the GI ward for enteral nutrition to treat worsening malnutrition, however, is now transferred to PICU with fever, tachycardia, poor peripheral perfusion and hypoxia, requiring sedation and mechanical ventilation.

1) What information would you like to assess her nutrition?
2) Would you recommend parenteral nutrition and when?
3) What factors would influence the energy requirements of this patient?

Case Review

Lucy is a 5-month-old with biliary atresia and progressive end stage liver disea … ward for er … trans … and hypo…

1) W…

2) W…

3) W… …ient?

1) What information would you like to assess her nutrition?

- ✓ Anthropometrics like weight, length, weight for length, head circumference; ideally additional measures of body composition like MUAC; recent growth trends
- ✓ Feeding history, including feeding tolerance, vomiting, diarrhea
- ✓ Presence of ascites that can impact feeding tolerance and weight interpretation
- ✓ CRP at admission

Case Review Cont'd

Lucy is a 5-month-old with biliary atresia and progressive end stage liver disea… GI ward for er… ow trans… on and hypox…

> 2) Would you recommend parenteral nutrition and when?
>
> Should recommence enteral nutrition support ideally within 24h and plan to advance to meet 60% of expected or ideally measured energy requirements within a week. However, if not meeting daily goals for EN deliver or experiencing significant feeding intolerance reasonable to consider starting PN in 72h

1) W…
2) Would you recommend parenteral nutrition and when?
3) What factors would influence the energy requirements of this patient?

Case Review Cont'd

Lucy is a 5-month-old with biliary atresia and progressive end stage liver disease who is listed for transplant. She has been admitted on the GI ward

fo

tra d

hy

3) What factors would influence the energy requirements of this patient?

- ✓ Energy requirements are generally increased in liver failure
- ✓ Sepsis can also increase energy requirements
- ✓ Sedation and mechanical ventilation will both decrease energy needs
- ✓ NPO and use of PN will also decrease total energy requirements

1) What information would you like to assess her nutrition?

2) Would you recommend parenteral nutrition and when?

3) What factors would influence the energy requirements of this patient?