GI/Liver/Nutrition PRN Focus Session—Contemporary Issues in the Management of Total Parenteral Nutrition
Activity No. 0217-0000-11-100-L01-P (Knowledge-Based Activity)

Tuesday, October 18
3:30 p.m.–5:30 p.m.
Convention Center: Rooms 302 & 303

Moderator: Joseph V. Ybarra, Pharm.D., BCNSP
Assistant Clinical Professor, Harrison School of Pharmacy, Auburn University, Auburn, Alabama

Agenda

3:30 p.m.  Management of TPN in Patients with Kidney Disease
Sarah Nordbeck, Pharm.D., BCNSP
Nutrition Support Pharmacy Specialist, Beaumont Hospital, Northville, Michigan

4:05 p.m.  Management of TPN in Patients with Obesity
Erin Nystrom, Pharm.D., BCNSP
Clinical Specialist in Nutrition Support, Assistant Professor of Medicine, College of Medicine, Mayo Clinic, Rochester, Minnesota

4:40 p.m.  Micronutrient Supplementation and Long-term Adverse Effects of TPN Therapy
Leslie Hamilton, Pharm.D., BCPS
Assistant Clinical Professor, Department of Pharmacy Practice, Auburn University, Birmingham, Alabama

5:15 p.m.  Panel Discussion
Leslie Hamilton, Pharm.D., BCPS
Sarah Nordbeck, Pharm.D., BCNSP
Erin Nystrom, Pharm.D., BCNSP

Faculty Conflict of Interest Disclosures
Leslie Hamilton: no conflicts to disclose.
Sarah Nordbeck: no conflicts to disclose.
Erin Nystrom: no conflicts to disclose.

Learning Objectives

1. Review current recommendations for dosing and monitoring of TPN in patients with acute, chronic, and end stage kidney disease.
2. Discuss the management of TPN in patients undergoing hemodialysis or continuous renal replacement therapies.
3. Discuss potential complications of TPN therapy in patients with chronic or end stage kidney disease.
4. Review the appropriate roles for both acute and chronic TPN therapy in obese patients.
5. Provide recommendations for dosing and monitoring of TPN in patients with obesity.
6. Discuss potential complications of TPN therapy in patients with obesity.
7. Review the role and appropriateness of micronutrient supplementation in patients receiving TPN therapy.
8. Provide recommendations for dosing and monitoring of micronutrient supplementation in acute and chronic TPN therapy.
9. Discuss strategies for prevention and management of long term adverse effects of TPN therapy.

<table>
<thead>
<tr>
<th>Self-Assessment Questions</th>
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<tbody>
<tr>
<td>Self-assessment questions are available online at <a href="http://www.accp.com/am">www.accp.com/am</a></td>
</tr>
</tbody>
</table>
Management of TPN in Patients with Kidney Disease

Sarah Nordbeck, Pharm.D., BCNSP
Nutrition Support Pharmacy Specialist, Beaumont Hospital, Northville, Michigan
Conflicts of Interest

No conflicts to disclose
Learning Objectives

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- Discuss the management of TPN in patients undergoing hemodialysis or continuous renal replacement therapies.

- Discuss potential complications of TPN therapy in patients with chronic or end stage kidney disease.
Kidney Disease Outcomes Quality Initiative

- 26 million Americans have CKD
- 367,000 with ESRD on dialysis
- Approximately 600,000 cases of AKI annually
Acute Kidney Injury

- Mortality remains > 50%
  - Causes of AKI:
    - Sepsis
    - Trauma
    - Hypotension
    - Contrast dye
    - Medications
    - Pre-existing CKD

ASPEN 2010 Guidelines.
JAMA. 2005;294:313-318
Causes of AKI

- **Prerenal**
  - Hypoperfusion

- **Intrinsic**
  - Damage to the renal parenchyma

- **Postrenal**
  - Urinary obstruction

Patient Case

- 63 yo female admitted on 10/15/09 for pneumonia, severe metabolic acidosis

- PM/SH: ESRD on M/W/F on HD, a fib, metabolic acidosis, depression, gastric bypass in 1999.

- Nutrition hx:
  - 5’3” + 3 edema
  - Admit wt: 67.3 kg Chronic diarrhea
  - IBW: 52.4 kg Pre-albumin < 5
Pt case – initial TPN order

- 2400 ml fluid
- 150 g dextrose
- 20 g fat
- 75 g protein
- 100 meq Na-acetate
- 20 meq Na-phos
- 40 meq K-acetate
- 20 meq Ca Gluconate
- 16 meq Mag Sulfate
- 1 mL Trace Element
- 10 mL MVI
- Thiamine 100 mg
- Zinc chloride 10 mg
Metabolic Alterations in AKI

- Metabolic acidosis
  - Inability to excrete H+ from distal tubule
  - Inadequate bicarbonate synthesis and reabsorption
  - Decreased ammonia production
  - Depletion of available buffers
  - Lactate production
Metabolic Alterations in AKI

- Fluid/electrolyte abnormalities
  - Hyperkalemia
  - Hyperphosphatemia
  - Fluid overload
  - Azotemia
  - Calcium derangements

- Hypercatabolism
  - Glucose intolerance
Protein Energy Wasting

- Occurs in up to 40% of AKI patients

- Associated with
  - Major stress-induced hormonal and metabolic derangements
  - Clearance of most amino acids up to 1.3-1.8 g/kg/day
  - Negative nitrogen balance
  - Depletion of body energy stores

- Poor outcomes:
  - Loss of lean body mass
  - Increase LOS
  - Increase sepsis, bleeding, arrhythmia, resp failure
  - Delayed wound healing

Current Opinion in Critical Care 2009,15:474-480
Goals of Nutrition Therapy

- Provide exogenous fuels to attenuate catabolism thereby maintaining lean body mass.
- Maintenance nutritional status
- Avoidance of worsening metabolic derangements
- Improve wound healing
- Support immune function
- Attenuate inflammation

ASPEN 2010 Guidelines
Tools for evaluating nutrition status

- Albumin
- Pre-albumin
- Lymphocyte count
- BW changes
- Muscle wasting by anthropometrics
- Energy expenditure (EE)

Subjective Global Assessment

A. History
1. Weight change
   Overall loss in past 6 months: amount = # ____________ kg; % loss = # ____________
   Change in past 2 weeks ____________ increase,
   ____________ no change,
   ____________ decrease.

2. Dietary intake change (relative to normal)
   ____________ No change
   ____________ Change duration = # ____________ weeks.
   ____________ type: ____________ suboptimal solid diet, ____________ full liquid diet
   ____________ hypocaloric liquids, ____________ starvation.

3. Gastrointestinal symptoms (that persisted for >2 weeks)
   ____________ none, ____________ nausea, ____________ vomiting, ____________ diarrhea, ____________ anorexia.

4. Functional capacity
   ____________ No dysfunction (e.g., full capacity),
   ____________ Dysfunction duration = # ____________ weeks.
   ____________ type: ____________ working suboptimally,
   ____________ ambulatory,
   ____________ bedridden.

5. Disease and its relation to nutritional requirements
   Primary diagnosis (specify) ____________
   Metabolic demand (stress): ____________ no stress, ____________ low stress,
   ____________ moderate stress, ____________ high stress,

B. Physical (for each trait specify: 0 = normal, 1+ = mild, 2+ = moderate, 3+ = severe).
   # ____________ loss of subcutaneous fat (triceps, chest)
   # ____________ muscle wasting (quadriceps, deltoids)
   # ____________ ankle edema
   # ____________ sacral edema
   # ____________ ascites

C. SGA rating (select one)
   ____________ A = well-nourished
   ____________ B = moderately (or suspected of being) malnourished
   ____________ C = severely malnourished
Standard amino acid parenteral formulas should be used in AKI (Grade: C)

Intradialytic parenteral nutrition **should not be used** as a supplement in malnourished CKD-V hemodialysis patients (Grade: C)
2010 ASPEN Guidelines

- Renal failure patients requiring nutrition support should receive enteral nutrition if intestinal function permits (Grade: E)

- Energy requirements in patients with renal disease should be evaluated using indirect calorimetry when possible. If not possible, individualized assessment of energy intake goals is recommended. (Grade: D)
To promote positive nitrogen balance in patients with AKI, protein intake should be adjusted according to catabolic rate, renal function, and dialysis losses (Grade D)

Electrolyte intake in patients should be adjusted by monitoring serum concentrations of K, Mg, P, and Ca (Grade D)
Indications for Nutritional Support

“Individuals undergoing maintenance dialysis who are unable to meet their protein and energy requirements with food intakes for an extended period of time should receive nutrition support”

“If tube feedings are not used, intradialytic parenteral nutrition (IDPN; for hemodialysis) should be considered”

So how do we accomplish this?
Dialysis Modalities

- Intermittent hemodialysis (HD)
- CAPD
- CRRTs
Intermittent Hemodialysis

- Typically 3-4 hour session three times weekly
- Diffusion
Solute movement in dialysis

Schematic representation of the movement of solute from blood to dialysate across the dialysis membrane. Blood and dialysate move in opposite directions (i.e., flow in a countercurrent fashion) to maximize the clearance of solute.
Concentrations of dialysate components used in hemodialysis

<table>
<thead>
<tr>
<th>Component</th>
<th>Concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium (meq/L)</td>
<td>135 to 155</td>
</tr>
<tr>
<td>Potassium (meq/L)</td>
<td>0 to 4</td>
</tr>
<tr>
<td>Calcium (mmol/L)</td>
<td>1.25 to 1.75 (2.5 to 3.5 meq/L)</td>
</tr>
<tr>
<td>Magnesium (mmol/L)</td>
<td>0 to 0.75 (0 to 1.5 meq/L)</td>
</tr>
<tr>
<td>Chloride (meq/L)</td>
<td>87 to 120</td>
</tr>
<tr>
<td>Bicarbonate (meq/L)</td>
<td>25 to 40</td>
</tr>
<tr>
<td>Glucose (g/dL)</td>
<td>0 to 0.20</td>
</tr>
</tbody>
</table>

Continuous renal replacement therapies

- Proposed advantages over intermittent procedures:
  - Better hemodynamic stability
  - Slow volume shifts
  - Progressive elimination of urea
  - Possible elimination of inflammatory mediators

CRRTs

- Continuous venovenous hemofiltration (CVVH)
- Continuous filtration of blood via a pump using the vein as entry and exit
- Convection/solvent drag

## Replacement Fluids

<table>
<thead>
<tr>
<th></th>
<th>Na (mg/dL)</th>
<th>K (mEq/L)</th>
<th>Ca (mEq/L)</th>
<th>Cl (mEq/L)</th>
<th>HCO3 (mEq/L)</th>
<th>Lactate (mEq/L)</th>
<th>Mg (mEq/L)</th>
<th>Glucose (mg/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>#1</td>
<td>130</td>
<td>2</td>
<td>0</td>
<td>108.5</td>
<td>25</td>
<td>0</td>
<td>1.5</td>
<td>100</td>
</tr>
<tr>
<td>#2</td>
<td>130</td>
<td>4</td>
<td>0</td>
<td>110.5</td>
<td>25</td>
<td>0</td>
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<td>100</td>
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<tr>
<td>#3</td>
<td>140</td>
<td>4</td>
<td>3</td>
<td>113</td>
<td>35</td>
<td>0</td>
<td>1</td>
<td>100</td>
</tr>
</tbody>
</table>
Protein losses in RRT

- Higher losses in convection techniques
- Amino acid losses up to 15 grams/day
- Nitrogen balance highly correlated with protein intake

Harris-Benedict
- ABW vs. IBW vs. TBW?

Stable renal failure
- 20-30 kcals/kg

AKI
- 25-35 kcals/kg
  - or 1.3 X the REE
- Indirect calorimetry
Energy requirements during acute illness

- Acutely ill maintenance dialysis patients should receive > 35 kcal/kg/day for those < 60 years of age

- 30-35 kcals/kg/day for those > 60 years of age

KDOQI 2011
Historic practice

- Late 80s and early 90s, practice was < 1 g/kg/day and 30-45 kcals/kg

- Recommended energy intakes for AKI patients have progressively lowered to 25-30 kcals/kg per day and higher amounts of protein

Nutrition in Clinical Practice 26;143-150:2011.
Recommended amount of protein during acute illness

- 1.8-2.5 g/kg for CRRT
- AKI requiring HD 1.5 g/kg
- 1.2 g/kg for stable ESRD on HD
- 1.3 g/kg for CAPD
Fluid and Sodium

- Must be monitored closely in all RF patients
- Anuric pts
  - (urine output < 75 mL/day) are typically restricted to 1000 – 1500 mL/day
- Oliguric patients
  - (urine output < 400 ml/day) can tolerate a bit more fluid
    - < 2 liters/day
- CRRTs even more removal
  - No fluid restriction
Effects on Electrolytes

- Potassium, magnesium, phosphorus accumulate in renal failure

- Calcium-phosphate precipitation
  - More problematic in chronic dialysis patients
  - Concern for calciphylaxis
  - Keep calcium phosphate product < 55
Vitamin Requirements

- Not well established in renal pts
- Standard additives
- Vitamin C
  - Limit to < 200 mg/day
- Fat soluble vitamins

Estimated 10% of ESRD pts are severely malnourished
- 33% are moderately malnourished

Serum albumin < 3.5 mg/dL
- 2x mortality than albumin > 4

Serum albumin < 2.5
- linked to 10 fold increase in mortality.

Chronic Kidney Disease

- Balanced energy requirements
  - Protein 10-15% total calories
  - Carbohydrate 55-70% calories
  - Fat 20-30% of calories
- Avoid excessive lipid calories due to diminished clearance rates
- Fluid restriction for oliguria or anuria
- Must account for glucose from PD
Chronic Kidney Disease

MDRD trial

- Low protein (0.6-0.8g/kg) historically used to reduce uremia
  - Intended to slow the progression of renal disease
- Intent to treat analysis following 585 patients with CKD
  - Disease progression in Stage 3 or 4 patients not slowed by dietary protein restriction to 0.3 or 0.6 g/kg/day when compared to 1.3 g/kg

Protein Restriction

- Practice used for stages 1 - 4 CKD to postpone kidney disease progression

- Concern for malnutrition when extended over a period of time

KDOQI 2011.
NCP 2011;26:143-150.
## Adult Renal Failure PN Requirements

<table>
<thead>
<tr>
<th></th>
<th>Pre-dialysis</th>
<th>PD</th>
<th>HD/CRRT</th>
</tr>
</thead>
</table>
| **Energy**           | CRF/ARF: Harris Benedict | ARF: Stress factor 1.5 - 2  
CRF: Stress factor 1.1 – 1.2 | Same          |
| **Protein**          | 0.6-0.8 g/kg | 1.2-1.3 g/kg  
Up to 1.5-1.8 g/kg for ARF | 1.2 – 1.3 g/kg  
ESRD  
1.5-1.8 for ARF on HD  
1.5-2.5 for CRRTS |
| **Fluid**            | As tolerated | As tolerated               | As tolerated  |
| **Electrolytes**     |              |                           |               |
| Na                   | 35-75 mEq/L  | Same                      | Same          |
| K                    | 10-40 mEq/L  |                           | 2007 ASPEN Core Curriculum |
Patient case revisited...

- Patient on TPN x 2 weeks then discharged home

- Re-admitted 7 days later
  - Nephrologist orders intra-dialytic TPN
    - concern for malabsorption
    - no central line due to risk of infection
Intradialytic PN

- Provides 1000-1200 kcals/treatment

- For patients who cannot tolerate or have not responded to enteral supplements

- Indicated:
  - Serum albumin < 3.4
  - Dietary protein intake < 0.8 g/kg
  - Dietary intake < 25 kcals/kg/day

Efficacy of Intradialytic PN

- 4 studies demonstrate weight gain and improved serum albumin

- Adverse events: Excess fluid gain
  Hyperglycemia

Am J Kidney Dis. 1994;23:808-816
Cano et al.

- Prospective study, n = 186
- IDPN + oral supplements, n = 93
- Oral supplements alone, n = 93

Primary endpoint

- No difference in mortality at 2 years
- 36 deaths in control group
- 40 in IDPN group

Intradialytic TPN order

- 400 cc/hr x 3 hrs during HD three times weekly
  - 100 grams dextrose
  - 20 grams fat
  - 100 grams protein  **Total 940 kcals/session**

- Continues on intra-dialytic TPN for 4 months
  - HD session increased to 4 hours due to fluid overload
Complications of Parenteral Nutrition

- Refeeding syndrome
- Overfeeding
  - Increased CO2 production, respiratory acidosis
- Hyperglycemia
- Electrolyte abnormalities
- Fluid overload
- Azotemia

Patient case

- Pt re-admitted with malabsorption, calciphylaxis
- Physician requests daily TPN while admitted
- Daily TPN x 2 weeks until patient is febrile
- BC x 2 drawn
  - 2/2 + GPC
- TEE negative to r/o endocarditis
- Transfer to ICU for traumatic pneumothorax, intubated, CRRTs started
- Patient recovered and discharged home after inpatient rehab
Patient case

- Re-admitted 3 months later with toxic megacolon
- Taken to OR for colectomy
Benefits of Enteral vs. Parenteral Nutrition

- For all patient populations, enteral nutrition generally considered preferred route due to decreased cost and infectious complications.

- For AKI, 1 study demonstrated greater mortality, infection with PN
  - EN (n = 45), mortality 42%, infection 64%
  - PN (n = 19), mortality 69%, infection 84%
    - (p = 0.05)

References:
Nutrition 2004;20:843-848
JPEN 2009;33:277-316.
Infection Risk of Parenteral Nutrition

- Incidence of TPN associated catheter-related bloodstream infections in critical care ranges from 1.5 – 21%

- A general hospitalized population found 1.4 – 2% per patient day rate of catheter-related sepsis

Risk factors for invasive candidiasis

Host Factors
- Extremes of age
- Neutropenia
- Renal failure
- Higher APACHE II Score
- Trauma/burns
- Bowel perforation

Medical intervention
- Chemotherapy
- Dialysis
- Central venous catheters
- Antibiotic use
- Parenteral nutrition
- Abdominal surgery
- Length of ICU stay > 7 days
- Nasogastric tubes
- Gastric acid suppression

Crit Care Med 2010 Vol 38, S380-387
Factors independently associated with candidemia

<table>
<thead>
<tr>
<th>Prior surgery</th>
<th>RR</th>
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<tbody>
<tr>
<td>Prior surgery</td>
<td>7.3</td>
</tr>
<tr>
<td>Acute renal failure</td>
<td>4.2</td>
</tr>
<tr>
<td>Parenteral nutrition</td>
<td>3.6</td>
</tr>
<tr>
<td>Presence of TLC</td>
<td>5.4</td>
</tr>
</tbody>
</table>

Clin Infect Dis 2001; 33:177-186.
Conclusions

- Enteral nutrition preferred over parenteral nutrition when possible.
- Protein requirements are different for AKI vs CRF.
- Protein requirements differ depending on dialysis modality.
- Risks vs. benefits must be weighed in initiating parenteral nutrition.
Parenteral Nutrition in the Obese Patient

Erin Nystrom, Pharm.D., BCNSP
Clinical Pharmacist in Nutrition Support
Mayo Clinic
Rochester, Minnesota
Conflicts of Interest

- No conflicts to disclose
Learning Objectives

• Review the appropriate roles for both acute and chronic PN in obese patients
• Provide recommendations for dosing and monitoring of PN in patients with obesity
• Discuss potential complications of PN in patients with obesity
Obesity

- Definitions
  - Excessive adipose tissue in relation to lean body mass
  - NIH/WHO classification
    - Obese: BMI $\geq 30$ kg/m$^2$
      - Obese class I   $30 - 34.9$ kg/m$^2$
      - Obese class II  $35 - 39.9$ kg/m$^2$
      - Obese class III $\geq 40$ kg/m$^2$
    - Overweight/Pre-obese: BMI 25 to 29.9 kg/m$^2$
- 33.8% of Americans are obese (CDC 2010)
Trust for America’s Health & Robert Wood Johnson Foundation: 
F as in Fat 2011

• Two-thirds of adults and one-third of children are overweight or obese
• Since 2010, obesity rates increased in 16 states; 12 states over 30%
• In the last 15 years…
  – 7 states’ obesity rates doubled
  – 10 states increased at least 90%
  – 22 states increased at least 80%
Obesity Trends* Among U.S. Adults
BRFSS, 1990, 2000, 2010
(*BMI ≥30, or about 30 lbs. overweight for 5’4” person)

1990

2000

2010

Source: Behavioral Risk Factor Surveillance System, Centers for Disease Control.
Obesity Rates* Among U.S. Adults 2010
(*BMI ≥30, or about 30 lbs. overweight for 5’4” person)

Source: Behavioral Risk Factor Surveillance System, Centers for Disease Control.
Obesity-Associated Morbidity

• TFAH/RWF 2011 Report
  – Type 2 Diabetes: Rates increased in 11 states in past year; 8 states with over 10% of adults
  – Hypertension: Every state over 20% of adults with hypertension; 9 states over 30%
Obesity-Associated Morbidity

- Type 2 diabetes; insulin resistance
- Dyslipidemia
- Gastrointestinal
  - Nonalcoholic fatty liver disease: steatosis, nonalcoholic steatohepatitis
  - Gall stones, cholelithiasis
  - Pancreatitis
- Obstructive sleep apnea
- Osteoarthritis

- Cardiovascular
  - Hypertension
  - Coronary artery disease
  - Congestive heart failure
  - Stroke
  - Deep vein thrombosis, pulmonary embolism

- Cancer
  - Breast
  - Colon
  - Endometrium
  - Esophagus
  - Stomach

PN in Obesity: Goals of Care

• Minimize risk of metabolic complications
  – Do No Harm
  – Metabolic Control

• Preserve lean body mass

• Promote gradual loss of fat tissue

• When, how much, what to monitor?

When to Initiate PN?

• Body weight is not a good indicator of underlying nutrition status
  – “Reserves” do not place a patient at lower nutritional risk
  – Acute illness vs. chronic starvation

• Risks of malnutrition: impaired wound healing, immune function, ventilator weaning and increased infection risk
How Much to Feed?

- Body composition in obesity
  - Adipose tissue is metabolically inactive
  - Lean mass increases with weight gain; neither fat nor lean mass gain is linear with weight gain
  - Mobilization of fat stores in acute illness
  - Energy expenditure vs. requirement

- Feed to metabolic control
Metabolic Complications: Risks of Overfeeding

- Hyperglycemia, glucose intolerance, hyperinsulinemia
- Volume overload
- Hypercarbia
- Hypertriglyceridemia
- Inflammation

- Impaired fat mobilization and oxidation
- Lipogenesis, hepatic steatosis
- Infection, immunosuppression
Advantages of Hypocaloric, Protein-Sparing Feeding

- Reduced carbon dioxide production
- Reduced hyperglycemia, hyperinsulinemia
- Improved diuresis
- Enhanced wound healing and immune function
How Much to Feed?

• Total energy expenditure
  – Resting/basal energy expenditure (REE/BEE) \( \sim 70\% \)
  – Thermic effect of food \( \sim 10\% \)
  – Physical activity \( \sim 20\% \)

• REE greater in obesity

• Best way to estimate BEE?
Predictive Equations
(BEE, kcal/day)

- **Harris Benedict**
  - Females: 655 + 9.6(wt, kg) + 1.8(ht, cm) − 4.7(age, yr)
  - Males: 66.5 + 13.8(wt, kg) + 5(ht, cm) − 6.8(age, yr)

- **Ireton-Jones**
  - Ventilated: 1784 - 11(age, yr) + 5(wt, kg) + 244(S) + 239(T) + 804(B)
  - Spontaneous breathing: 629 − 11(A) + 25(W) − 609(O)
    
    S = sex (female = 0, male = 1), V = ventilator (absent = 0, present = 1);
    T = trauma (absent = 0, present = 1), B = burn (absent = 0, present = 1)

- **Mifflin-St.Jeor**
  - Females: 10(wt, kg) + 6.25(ht, cm) - 5(age, yr) - 161
  - Males: 10(wt, kg) + 6.25(ht, cm) − 5(age, yr) + 5

- **21 kcal/kg** (Amato 1995)
Which Weight to Use?

- Ideal weight (IBW), e.g., Hamwi
- Adjusted body weight
  - 
  - (Actual weight – IBW) x estimated LBM contribution + IBW
  - Lean body mass accrual is not linear with weight gain; lack of scientific data to support “adjustment” factor
- Weight measurement limitations in obesity
Predicting Energy Expenditure

• Limitations of predicted energy expenditure trials
  – Indirect calorimetry
  – Healthy controls not included
  – Fed vs. fasting; degree of illness; other variables
  – Small numbers, heterogeneous

• Reported correlations between measured and predicted REE do not equal accuracy in the individual patient
Predicting Energy Expenditure

ASPEN-SCCM, 2009
Nutrition in Critical Illness Guidelines:
“Predictive equations should be used with caution, as they provide a less accurate measure of energy requirements than indirect calorimetry in the individual patient.”
Indirect Calorimetry: REE

- Measures O2 consumption and CO2 production
- Weir equation
  - \( \text{REE (kcal/24h)} = (3.9 \ \text{VO}_2 + 1.1 \ \text{VCO}_2) \times 1.44 \)
- Respiratory Quotient (RQ)
  - \( RQ = \frac{\text{VCO}_2}{\text{VO}_2} \)
    - Validates IC if within physiologic range
    - CHO = 1
    - Pro = 0.8
    - Fat = 0.7
    - Lipogenesis = 1.1 – 1.2

http://www.icts.uiowa.edu/drupal/
Indirect Calorimetry Limitations

- Point-in-time analysis
- Confounders
  - Activities/cares
  - Respiratory status
  - Acid/base disturbances
  - Air leaks
  - Fever, sepsis
- $\text{FiO}_2 < 60\%$; no nasal cannula

- Operator experience
- RQ correlates with substrate use and under- or overfeeding, but low sensitivity, specificity
- Not widely available
Parenteral Nutrition in Obesity: The Evidence
Dickerson et al. 1986

- Thirteen obese surgical patients; Prospective, single-arm
- PN program: 50% REE as non-protein calories + protein of 2 g/kg (IBW)
  - Average: 881 npc/day + protein
  - PN duration: 48.2 +/- 31.4 (12 – 190) days
- Outcomes
  - RQ consistent with fat oxidation
  - Weight loss: 2.3 +/- 2.7 kg/wk
  - Nitrogen balance: all patients positive or even
  - All patients demonstrated complete tissue healing
Burge et al. 1994

- Sixteen patients; Prospective, double-blind randomized trial
  - Hypocaloric group, n = 9: npc of 50% REE + protein 2 g/kg IBW
    - Avg 1285 kcal/day or 14 kcal/kg ABW
    - Avg 110 g protein
  - Control group, n = 7: npc of 100% REE + protein 2 g/kg IBW
    - Avg 2592 kcal/day or 25 kcal/kg ABW
    - Avg 130 g protein
  - PN duration: 9.6 +/- 3 (5 – 15) days

- Outcomes
  - RQ also consistent with oxidation of endogenous fat stores
  - N balance positive in both groups
Choban et al. 1997

• Thirty patients; Randomized, double-blind study
  – Isonitrogenous formulas, 2 g/kg IBW
  – Hypocaloric, n = 16: kcal:N = 75:1 (33% kcal as protein)
    • 1292 +/- 298 kcal/d; 14 kcal +/- 3 kcal/kg ABW
  – Control, n = 14: kcal:N = 150:1 (17% kcal as protein)
    • 1934 +/- 198 kcal/d; 22 +/- 5 kcal/kg ABW
  – PN duration: 10.5 +/- 2.6 (6 – 15) days

• Results
  – No difference in N balance
  – Better glycemic control and lower insulin requirement in hypocaloric group
State of the Data

- Total number of obese patients on PN studied = 89
  - Two RCTs (n = 46)
  - One retrospective study (n = 30)*
  - Two studies used indirect calorimetry to predict REE
- Non-protein calories vs. total calories

Macronutrient Balance

• Mixed fuel source is best
• Protein-sparing properties: dextrose, fat, and protein
  – Elwyn 1980: Brain requires about 125 g/day dextrose; else gluconeogenesis to meet obligatory glucose needs is achieved by muscle catabolism
  – Sparing lean mass can not occur independently of non-protein calorie provision
• Dextrose overfeeding in absence of fat promotes lipogenesis (Paluzzi, Meguid 1987)
Unanswered Questions

• Clinical outcomes with hypocaloric, high protein regimens
• Specific patient populations
  – Kidney failure, renal replacement therapy
  – Liver disease; hepatic encephalopathy
  – Burns, trauma
  – Higher obesity classifications
  – Long-term PN
• Markers of adequacy of nutrition
Surrogate Markers vs. Clinical Outcomes

- Reviewed 99 RCTs of nutrition support vs. no nutrition support and clinical outcome vs. surrogate marker association

**Surrogate**
- Albumin
- Transferrin
- Prealbumin
- Nitrogen balance

**Clinical**
- Mortality
- Infections
- Total complications
- Hospital length of stay
<table>
<thead>
<tr>
<th>Concordance (%)</th>
<th>Partial Discordance (%)</th>
<th>Complete Discordance (%)</th>
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<tbody>
<tr>
<td></td>
<td>Nutrition better</td>
<td>Clinical better</td>
</tr>
<tr>
<td><strong>Albumin</strong></td>
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</tr>
<tr>
<td>Mortality</td>
<td>29</td>
<td>18</td>
</tr>
<tr>
<td>Infections</td>
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<td>16</td>
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<tr>
<td><strong>Prealbumin</strong></td>
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<td>33</td>
<td>39</td>
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<tr>
<td>Infections</td>
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<td>6</td>
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<td><strong>N Balance</strong></td>
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<tr>
<td>Mortality</td>
<td>36</td>
<td>42</td>
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<tr>
<td>Infections</td>
<td>43</td>
<td>17</td>
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</table>
Minnesota Starvation Experiment

- Conducted by University of Minnesota from Nov. 1944 to Dec. 1945
- 32 male participants; 3 phases, including 24-week ‘semi-starvation’ phase

<table>
<thead>
<tr>
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<th>Baseline*</th>
<th>6 mos*</th>
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<tbody>
<tr>
<td>Weight</td>
<td>69.4 ± 5.9</td>
<td>52.6 ± 4.0</td>
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<tr>
<td>BMI</td>
<td>21.7 ± 1.7</td>
<td>16.4 ± 0.9</td>
</tr>
<tr>
<td>Albumin</td>
<td>4.3 ± 0.5</td>
<td>3.9 ± 0.5</td>
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</tbody>
</table>

*Mean ± standard deviation.

## Visceral Proteins

<table>
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<tr>
<th></th>
<th>Albumin</th>
<th>Prealbumin (Transthyretin)</th>
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<tr>
<td><strong>Half-life</strong></td>
<td>20 days</td>
<td>2-3 days</td>
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<tr>
<td><strong>Normal</strong></td>
<td>3.5-5 g/dL</td>
<td>16-40 ng/dL</td>
</tr>
<tr>
<td><strong>Factors that</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Increase Levels</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dehydration</td>
<td></td>
<td>Corticosteroids</td>
</tr>
<tr>
<td>Exogenous albumin</td>
<td></td>
<td>Renal failure</td>
</tr>
<tr>
<td><strong>Factors that</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Decrease Levels</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stress/Acute Phase</td>
<td></td>
<td>Stress/Acute Phase</td>
</tr>
<tr>
<td>Response</td>
<td></td>
<td>Response</td>
</tr>
<tr>
<td>Volume overload</td>
<td></td>
<td>Dialysis</td>
</tr>
<tr>
<td>Liver disease</td>
<td></td>
<td>Liver disease</td>
</tr>
</tbody>
</table>

Hepatic proteins are better indicators of inflammation and severity of illness.
Nitrogen Balance

\[ N \text{ balance} = N_{\text{in}} \text{ minus } N_{\text{out}} \]
\[ = \left( \frac{g \text{ pro}}{6.25} \right) - (UUN + 4) \]

N balance is not N utilization

Slide: Adapted from M. Kochevar.
N Balance Limitations

- 24-hour urine collection; requires steady state
- Unaccounted nitrogen losses
- Factors that alter urine urea nitrogen (UUN) content
  - Renal disease
  - Liver disease, hyperammononemia
  - Stress, protein catabolism
  - Preexisting state of nutrition
  - Acidosis
  - Hematuria, bacteruria
PN in Obesity

- Data support
  - Fat stores are mobilized in acute illness
  - Underfeeding is effective
    - Preservation of lean body mass (N balance)
    - Successful wound healing
  - Underfeeding reduces metabolic complications
- More research needed
Best Practice

• Matching energy expenditure risks overfeeding
• Hypocaloric, high-protein regimen
  – Protein 1.5 - 2 g/kg ideal weight
  – 60 – 75% of BEE/REE; daily calorie deficit
• Indirect calorimetry?
• ASPEN/SCCM Guidelines in ICU
  – Protein of 2 – 2.5 g/kg ideal weight
  – Avoid exceeding 60 – 70% energy requirements or 11 – 14 kcal/kg actual weight

Case

GL, 52 y/o male admitted with 1-week history of N/V/abdominal pain, found to have SBO. PMH: Crohn’s disease, hyperlipidemia, hypertension, osteoarthritis.

Wt: 92 kg   Ht: 179 cm
BMI: 29.6
IBW: 76.7 kg
Harris Benedict BEE: 1917 kcal/day

PN Program?
Monitoring parameters?
Case: PN Program

- Energy/Protein: 75% HB = 1400 - 1450 kcal/day; includes protein of 1.5 – 2 g/kg IBW or 115 – 150 g/day
- PN Program: 120 g protein, 150 g dextrose, 40 g fat
- Monitor: Glucose, triglycerides
- Day 3 PN: TG = 390… Next step?
- What if hyperglycemia?
Summary

- Nutrition prescription in the obese patient warrants an individualized approach
- Predictive equations lack validation in obesity, but are a starting point for estimating energy expenditure
- Hypocaloric, high-protein approach is recommended to minimize overfeeding risks
- Close monitoring is essential to optimize metabolic control
- More research is needed to define optimal energy prescription and markers of adequacy of nutrition support
References


References


Global database on body mass index. World Health Organization.


References


Micronutrient Supplementation and Long Term Adverse Effects of TPN Therapy

Leslie A. Hamilton, Pharm.D., BCPS

10/18/2011
Conflicts of Interest

- No conflicts of interest to report.
Objectives

- Review the role and appropriateness of micronutrient supplementation in patients receiving TPN therapy.
- Provide recommendations for dosing and monitoring of micronutrient supplementation in acute and chronic TPN therapy.
- Discuss strategies for prevention and management of long term adverse effects of TPN therapy.
Trace Elements

- Given daily as a mixture of four to five trace elements
- Trace elements can also be given individually for supplementation
- Direct antioxidant activity and cofactors for antioxidant enzymes
# Requirements

![ACCP logo](https://example.com/accp_logo.png)

<table>
<thead>
<tr>
<th>Trace Element</th>
<th>Preterm Neonates (&lt;3 kg) (mcg/kg/d)</th>
<th>Term Neonates (3 – 10 kg) (mcg/kg/d)</th>
<th>Children (10 – 40 kg) (mcg/kg/d)</th>
<th>Adolescents Standard Daily Intake (&gt;40 kg)</th>
<th>Adult Standard Daily Intake</th>
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</thead>
<tbody>
<tr>
<td>Zinc</td>
<td>400</td>
<td>50 – 250</td>
<td>50 – 125</td>
<td>2.5 – 5 mg</td>
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<td>Copper</td>
<td>20</td>
<td>20</td>
<td>5 – 20</td>
<td>0.2 – 0.5 mg</td>
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<td>1</td>
<td>1</td>
<td>40 – 100 mcg</td>
<td>60 – 100 mcg</td>
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## Requirements

<table>
<thead>
<tr>
<th>Trace Element</th>
<th>Preterm Neonates (&lt;3 kg) (mcg/kg/d)</th>
<th>Term Neonates (3 – 10 kg) (mcg/kg/d)</th>
<th>Children (10 – 40 kg) (mcg/kg/d)</th>
<th>Adolescents Standard Daily Intake (&gt;40 kg)</th>
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<tr>
<td>Chromium</td>
<td>0.05 – 0.2</td>
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<td>1 – 2</td>
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<td>Trace Element</td>
<td>Amount per unit dose</td>
<td>Manufacturer</td>
<td>American Regent</td>
<td>Hospira</td>
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<td>---------------</td>
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</tr>
<tr>
<td></td>
<td></td>
<td>Multitrace-5 Concentrate</td>
<td>Multitrace-5 Concentrate</td>
<td>Multitrace-4 Concentrate</td>
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<td>0.4 mg</td>
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## Pediatric Products

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<td>Copper</td>
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<tr>
<td></td>
<td>30 mcg</td>
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<tr>
<td></td>
<td>1 mcg</td>
</tr>
<tr>
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</tr>
<tr>
<td></td>
<td>1 mg</td>
</tr>
<tr>
<td></td>
<td>0.1 mg</td>
</tr>
<tr>
<td></td>
<td>25 mcg</td>
</tr>
<tr>
<td></td>
<td>1 mcg</td>
</tr>
<tr>
<td></td>
<td>None</td>
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</tbody>
</table>
Zinc

- Reduced gastric acidity decreases zinc availability for absorption
- Most zinc is intracellular
- Mostly absorbed in duodenum and jejunum
- Transported by albumin to the liver
- Hypoalbuminemia can impair hepatic release of zinc
Zinc homeostasis affected by:

- Dietary zinc intake
- Fasting
- Acute infection
- Minerals and vitamins
- Alcohol
- Calcium and milk proteins
- Copper and iron competition
Zinc

- Catalyst for more than 200 enzymes
- Involved in apoptosis, cellular proliferation and differentiation, and immune function
Zinc Deficiency

- Difficult to diagnosis
  - Redistributed during acute phase response
- Skin lesions
- Impaired night vision
- Anorexia
- Diarrhea
- Impaired immune function
- Impaired wound healing
Zinc Deficiency

- Decreases retinol mobilization from the liver
- Decreased in elderly, alcoholics, post-operative and burn patients, patients with malabsorption, and renal disease
- Can worsen respiratory muscle function, hepatic dysfunction, and glucose intolerance
Zinc Toxicity

- Gastric distress
- Nausea
- Dizziness
- Decreased immune function
- Decreased HDL
- High doses can induce copper deficiency
Zinc

- In SIRS, also draw a CRP level
  - Will help determine if acute phase reaction or increased zinc requirements
- Serum zinc levels < 70 mcg/dL: low
- Serum zinc levels 70 – 85 mcg/dL: marginal zinc status
Zinc

- Extra zinc should be given to patients with high-output ostomies, chronic diarrhea, and thermally burned patients receiving PN
  - Zinc 12 mg can be added per liter of gastrointestinal loss
  - Up to 36 mg per day of zinc has been given to benefit patients with severe burns without toxicity
Copper

- Digestion releases copper to free it for absorption
- Gastric secretions, HCl, and pepsin assist in release of bound copper in the stomach
- Most absorption occurs in the small intestine, mostly in the duodenum
Copper

- Absorption negatively affected by:
  - Dietary fiber
  - Zinc
  - Iron
  - Large doses of calcium gluconate
  - Large doses of vitamin C
  - H₂ antagonists and PPI’s
- Transported by albumin
- Involved in iron transfer
Copper

- Responsible for:
  - Manganese oxidation
  - Ferrous and ferric iron oxidation
  - Conversion of dopamine to norepinephrine
  - Cholesterol and glucose metabolism
Copper Deficiency

- Microcytic anemia
- Leukopenia
- Neutropenia
- Hypercholesterolemia
- Abnormal ECG
- Menkes disease
- Occurs in patients with chronic diarrhea, post-intestinal surgery, and in chronic HD
Copper Toxicity

- Uncommon, except in impaired biliary excretion or cholestasis
- Wilson’s disease (cirrhosis)
Manganese

- Competes with iron for binding sites
- Enters liver via portal circulation
- Almost 100% is excreted via bile into feces
- Part of metalloenzymes
  - Arginase (urea formation)
  - Pyruvate carboxylase (carbohydrate synthesis)
  - Mn superoxide dismutase (antioxidant)
Manganese Deficiency

- Rare
- Reproductive difficulties
- Abnormal bone and cartilage formation
- Defects in lipid and carbohydrate metabolism
Manganese Toxicity

- CNS abnormalities
  - Hallucinations
  - Ataxia
  - Hyperirritability
  - Parkinson-like
- Reproductive dysfunction
- Nephritis
- Hepatic Damage
Manganese Toxicity

- Risk
  - Long-term PN ( > 30 days)
  - Biliary tract obstruction

- Difficult to determine manganese status
  - Whole blood manganese levels
  - MRI

- Contamination product from calcium gluconate, magnesium sulfate, and potassium chloride
Manganese and Cholestasis

- IV Manganese delivery bypasses normal regulatory mechanism
- Predisposes long-term PN patients to tissue and/or brain accumulation of Manganese
Chromium

- Required for glucose and lipid metabolism
- Poor absorption
  - 0.4 – 3%
- Transported with iron
- Competes for binding sites with transferrin
Chromium Deficiency

- Impaired glucose and amino acid utilization
- Increased plasma LDL
- Peripheral neuropathy
- Only seen in PN patients without adequate chromium replacement
- Weight loss
- Hyperglycemia refractory to insulin
Chromium Toxicity

- Rhabdomyolysis (1200 mcg/day)
- Liver dysfunction
- Renal failure (600 mcg – 2400 mcg/day)
- Compromised iron status
  - Ferritin decreases with chromium intake of 200 mcg/day
Chromium Levels

- Serum: 0.05 – 0.5 mcg/L
- Erythrocyte: 20 – 36 mcg/L
- Urine: 0.1 – 2 mcg/L
Chromium

- Levels are decreased in critically ill patients and during acute infection
- Some literature of using chromium infusions in critically ill patients with extreme insulin resistance
  - One case report of 3 mcg/hour (100 mcg of elemental chromium) in a patient requiring > 2000 units of insulin
  - Insulin requirements dropped dramatically and insulin infusion was discontinued within 12 hours
Selenium

- Excreted renally and through fecal excretion
- Cofactor in glutathione, iodine, and thyroid metabolism
  - Eliminate hydrogen peroxide
  - Catalyze deiodination of iodine
  - Oxidative defense
Selenium Deficiency

- Oxidative injury
- Increased susceptibility to mercury injury
- Altered thyroid hormone metabolism
- Increased glutathione levels
- Keshan disease (cardiomyopathy)
Selenium Toxicity

- Nausea/vomiting
- Fatigue
- Tooth decay
- Hair and nail loss
- Peripheral neuropathy
Selenium

- Additional selenium (60 – 100 mcg/day) should be given to home PN patients
- Erythrocyte levels < 10.5 U/mL suggests deficiency
- Serum levels > 100 mcg/L suggest adequate selenium status
Selenium

- Often depleted in trauma and SIRS patients
  - Additional supplementation has been studied at doses from 155 – 400 mcg/day
- Trend toward reducing mortality in sepsis and septic shock
Contamination

- Many PN components are contaminated with trace elements:
  - Aluminum
  - Chromium
  - Copper
  - Manganese
- Patients on long-term PN are at higher risk of toxicities and should have serum monitoring
Iron

- Iron is not routinely added to PN formulations
  - Cannot be added to PN with IVFE as it causes destabilization of IVFE
  - Can be added to Two-in-One formulations
Liver Disease and Trace Elements

- Remove copper and manganese from PN for patients with hepatobiliary disease
  - Elevated direct and total bilirubin levels
- Advanced liver disease is often accompanied by zinc deficiency
  - Replacement may improve amino acid metabolism and grade of encephalopathy
Renal Disease and Trace Elements

- Chronic HD can deplete copper stores
- Zinc is often depleted in renal disease
- Selenium is often depleted in CKD patients
- Selenium, chromium, copper, and zinc are removed by CRRT
Burn Injury

- May benefit from additional selenium
  - Reports of 210 mcg/day to maintain balance
  - Up to 380 mcg/day to help prevent nosocomial pneumonia
- Additional zinc is beneficial
- Improves wound healing, reduces infections
Fistulas

- Additional zinc supplementation is needed, especially for high-output fistulas
  - 12mg of zinc/liter lost
Bariatric Surgery

- Biliopancreatic diversion or duodenal switch
  - Additional zinc supplementation is needed
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