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ENTERAL NUTRITION IN THE CRITICALLY ILL CHILD

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Work supported by S.K. Wellman Foundation, Cleveland, Ohio
ENTERAL NUTRITION IN THE CRITICALLY ILL CHILD

Part I

Starvation vs. Injury
Nitrogen Dynamics
Major Burns
Skeletal Trauma
Severe Sepsis
Infection
Elective Operation
Partial Starvation
Total

Changes in metabolic rate and nitrogen excretion with various types of physiologic stress

Normal Range


3
Hypermetabolic Response
+ Limited Energy Reserves
+ High Incidence of Malnutrition

= MAGNIFIED IMPACT

In hospital malnutrition 60% (PICU)

Irving BY et al., 2006. Oosterveld MJ et al., 2006.

MALNUTRITION

- Impaired immunity
  - T-cell function
  - Phagocytic cell activity
  - Secretory immunoglobulin A (IgA) response
- Increased risk of infection
- Poor wound healing
- Death

OVERFEEDING

- Diet-induced thermogenesis
- \( \uparrow \text{CO}_2 \) production
- Prolonged ventilation
- Fatty deposition of the liver (steatosis)
- Risk of infection


PRIMARY FACTORS LEADING TO POOR NUTRITIONAL OUTCOME

- Inadequate initial nutritional assessment
- Inaccurate prediction of energy and protein needs
- Inconsistent nutrient delivery

da Oliveira Iglesias SB et al., 2007.
Several general principles have emerged that are increasingly guiding management in the ICU:

- early nutritional intervention
- avoidance of overfeeding
- preferential utilization of enteral relative to parenteral support

PURPOSE OF PRESENTATION

To discuss the role of enteral nutrition in the pathophysiology and treatment of critical illness in the pediatric population.
METABOLIC RESPONSE TO INJURY AND STRESS

NUTRIENT PARTITIONING

CARBOHYDRATE, FAT

Energy Depot
(Fat)

Energy Production
(ATP)

PROTEINS

Protein Synthesis
(Lean Body Mass)

Excess Amino Acids

Excess Amino Acids
Normal metabolic vs hypermetabolic response in children

Normal Metabolism

- Normal organ function present
- Hormones are balanced
- All functions supported by oxygen, micronutrients, anabolic and catabolic stimuli

- Carbohydrate (50-60% of kcal)
- Fat (25-35% of kcal)
- Protein (15-15% of kcal)

Energy storage in fat mass

Liver initiates gluconeogenesis to provide energy

Lean body mass maintains: Physical and metabolic functions

Lean body mass:
- Extract protein from muscle mass
- Loss of visceral protein for function

Glucose
- Mainly glucose and amino acids

Protein and energy production are abnormal
- Accelerated with increased temperature

Overall result
- Glutamine depletion
- Micronutrient depletion
- Antioxidant depletion
- Protein depletion

Normal growth and development

Catabolism due to Hypermetabolism

- Inadequate nutrition intake for function
- Energy utilization from fat mass (30% fatty acids used; 70% recycled)

Lean body mass:
- Extract protein from muscle mass
- Loss of visceral protein for function

Glucose
- Mainly glucose and amino acids

Energy utilization for:
- Cell function
- Muscle function
- Tissue repair
- Protein synthesis

Proinflammatory
- Promotes inflammation
- Leukocyte adhesion
- Release of arachidonic acid metabolites
- Complement activation
- Neutrophil chemotaxis
- Promotes coagulation
- Increases tissue factors
- Increases membrane coagulants
- Inhibits anticoagulant
- Decreases thrombomodulin
- Increases α1-antitrypsin
- Inhibits fibrinolysis
- Increases PAI-1

Proinflammatory
- Monocyte-Derived Cytokine Release (TNF-α, IL-1, IL-6, IL-8, INF)
- Death

Antinflammatory
- Inhibits inflammation
- Inhibits TNF-α
- Augments acute phase reactants
- Augments immunoglobulins
- Inhibits T-lymphocyte
- Inhibits Monocytes
- Inhibits coagulation
- Inhibits activation of coagulation by cytokines

Multiple Organ Dysfunction Syndrome (MODS)

- Sepsis or Septic Shock
- Severe Sepsis or Septic Shock

Figure 2. Sepsis cascade illustrates the balance between proinflammatory (SIRS) and antinflammatory (CARS) forces.


TNF = tumor necrosis factor, IL = interleukin, INF = interferon, PAI = plasminogen activator inhibitor.
**Stress Response**

- Increased cholesterol and fatty acids in blood for energy production systems
- Decreased protein synthesis; intestinal movement (digestion); Immune and allergic response systems
- Increased blood pressure
- Increased metabolism; e.g., faster heartbeat, faster respiration
- Localized inflammation (redness, swelling, heat and pain)
- Faster blood clotting
- Increased production of blood sugar for energy
- Increased stomach acids
- Leukocytosis
- Hyperglycemia
- Fever

**Balanced Response**

- Leukocyte activation
- Sepsis-associated tissue injury
- Systemic inflammatory response (SIRS)

**Septic Shock/Organ dysfunction**

- Leukocyte deactivation
- Sepsis-associated immunosuppression
- Compensatory anti-inflammatory response (CARS)

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Metabolic Response to Stress & Injury

Fat Stores → Free fatty acids → Energy + CO₂ → Fatty acids → Amino acids → Protein

Brain → Glucose → Ketone bodies → Amino acids → Acute-phase proteins

Liver → Fatty acids → Acetylcholine

Hypothalamus → Increased breathing rate → Increased blood pressure

Spinal Cord → Increased metabolic rate

Adrenal medulla → Norepinephrine → Epinephrine

Increased blood flow to muscle and liver

Decreased blood flow to kidney and intestines

Glycogen broken down to glucose

Increased blood glucose levels
Injury (Trauma) or Stress

Acute Phase Response

Liver

Increased synthesis
C-reactive protein
α1-Acid Glycoprotein

Decreased synthesis
α1-Antitrypsin

Transferrin

Albumin

THE ACUTE PHASE RESPONSE

Infection → Monocytes, Macrophages & Fibroblasts → Cancer
Inflammation → Cytokines & Inflammatory Mediators → Trauma

Physiologic Responses to Inflammation

Fever, Lethargy, Weight Loss
Neutrophilia, WBC adhesion
Capillary Permeability
Antibody Production

Hepatocytes

Acute Phase Proteins
Haptoglobin (Hp), Amyloid A, C-Reactive Protein (CRP), α1 Acid Glycoprotein (AGP), Fibrinogen (Fb)

Fever, Lethargy, Weight Loss, Neutrophilia, Capillary Permeability

**Catabolic Insult-Induced Protein-Energy Malnutrition**
(Protein and Energy Production Abnormal)
- No adaptive responses activated
- Increase metabolic rate 35-40 kcal/kg/d
- Increase glucose production in excess of need
- Increase use of protein for fuel (glucose)
- Inefficient use of fat for energy

Prior to Nutrition Support
Glucose

**Metabolic Stages Post Injury and Stress**

<table>
<thead>
<tr>
<th>Day</th>
<th>Phase</th>
<th>Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-2</td>
<td>Shock</td>
<td>Low metabolism</td>
</tr>
<tr>
<td>2-25</td>
<td>Catabolic</td>
<td>Extremely high metabolism&lt;br&gt;Extremely high nitrogen consumption&lt;br&gt;Redirection of protein synthesis</td>
</tr>
<tr>
<td>&gt;25</td>
<td>Anabolic</td>
<td>Lower metabolism&lt;br&gt;Return to normal protein synthesis</td>
</tr>
</tbody>
</table>

### NEGATIVE ACUTE PHASE PROTEINS

<table>
<thead>
<tr>
<th>Protein</th>
<th>Half-Life</th>
<th>Binds With</th>
<th>2-Day Trauma Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>Albumin</td>
<td>20 days</td>
<td>Anions, Drugs, Free Fatty Acids</td>
<td>Negative Acute Phase</td>
</tr>
<tr>
<td>Transferrin</td>
<td>8 days</td>
<td>Iron</td>
<td>Negative Acute Phase</td>
</tr>
<tr>
<td>Ceruloplasmin</td>
<td>5-7 days</td>
<td>Copper</td>
<td>Weak Acute Phase</td>
</tr>
<tr>
<td>Pre-albumin</td>
<td>2 days</td>
<td>Thyroxine, Retinol Binding</td>
<td>Negative Acute Phase</td>
</tr>
<tr>
<td>Retinol</td>
<td>12 hours</td>
<td>Vitamin A</td>
<td>Negative Acute Phase</td>
</tr>
</tbody>
</table>

### POSITIVE ACUTE PHASE PROTEINS

<table>
<thead>
<tr>
<th>Protein</th>
<th>Half-Life</th>
<th>Binds With</th>
<th>2-Day Trauma Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\alpha_1$-antitrypsin</td>
<td>16 days</td>
<td>Proteases</td>
<td>Strong Positive Acute Phase</td>
</tr>
<tr>
<td>$\alpha_1$-Acid glycoprotein</td>
<td>6 days</td>
<td>Drugs</td>
<td>Strong Positive Acute Phase</td>
</tr>
<tr>
<td>$\alpha_2$-macroglobulin</td>
<td>2-4 days</td>
<td>Endopeptidases and Proteases</td>
<td>Neutral/No Change in Concentration</td>
</tr>
<tr>
<td>C-reactive protein (C-RP)</td>
<td>5 hours</td>
<td>Damaged cells, Bacteria, Platelets, Lymphocytes</td>
<td>Very Strong/Rapid Increase in (usually 20 -1000 fold)</td>
</tr>
</tbody>
</table>
Fig. 1. Alterations in some acute phase reactants following tissue injury. Note that CRP levels rise the highest and the fastest.

- **C-REACTIVE PROTEIN (CRP)**
  - Opsonization
  - Complement activation
  - Enhances chemotaxis and phagocytosis
  - Enhanced Natural Killer cell activity
  - Modulates platelet activation
  - Enhances macrophage anti-tumoricidal activity
NUTRITION ASSESSMENT

NUTRITION SUPPORT GOALS IN PEDIATRIC CRITICAL CARE

- Maximal preservation of major organ system function
- Minimization of the catabolic response
- Prompt restoration of the premorbid nutritional state
NUTRITIONAL ASSESSMENT PROCEDURES

Initial Screening on Admission

Patient Evaluation: Weight (compare vs. standard for height)
Patient history – look for recent weight loss, loss of appetite, gastrointestinal problems, chronic illness, etc.

Other lab measures:
- Hematocrit
- Total lymphocyte count
- WBC

Plasma protein markers:
- Albumin
- Prealbumin
- Retinol-binding protein
- Transferrin
- Prealbumin
- Total lymphocyte count

Adequately Nourished Patients
Repeat above assessment every 14 days

Patients with Moderate Malnutrition:
Repeat above assessment every 7 days until stabilized; adjust nutrition support as necessary

Patients with Severe Malnutrition:
Repeat above assessment twice weekly until stabilized; adjust nutrition support as necessary

NUTRITIONAL ASSESSMENT OF THE CRITICALLY ILL CHILD

I. History
   - Past medical history
   - Diagnosis
   - Medications
   - Supplements
   - Allergies
   - Diet history

II. Anthropometrics

III. Body composition

IV. Biochemical profile
   - Basic metabolic profile (BMP)
   - Liver function tests (LFTs)
   - Complete blood count (CBC)
   - Prothrombin time (PT)
   - Minerals and trace elements
   - Vitamins

Component Guidelines

<table>
<thead>
<tr>
<th>Component</th>
<th>Guidelines</th>
</tr>
</thead>
<tbody>
<tr>
<td>I. History</td>
<td></td>
</tr>
<tr>
<td>Past medical history</td>
<td>Should be detailed</td>
</tr>
<tr>
<td>Diagnosis</td>
<td>Assess the effects on metabolic rate</td>
</tr>
<tr>
<td>Medications</td>
<td>Prescribed and over-the-counter</td>
</tr>
<tr>
<td>Supplements</td>
<td>Nutritional and herbal</td>
</tr>
<tr>
<td>Allergies</td>
<td>Environmental and food related as well as drug</td>
</tr>
<tr>
<td>Diet history</td>
<td>Assess adequacy, risk for deficiencies, premorbid malnutrition (/&gt;10% weight loss)</td>
</tr>
</tbody>
</table>
## NUTRITIONAL ASSESSMENT OF THE CRITICALLY ILL CHILD

<table>
<thead>
<tr>
<th>Component</th>
<th>Guidelines</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>II. Anthropometrics</strong></td>
<td></td>
</tr>
<tr>
<td>Height</td>
<td>Knee-height measurement, arm span, segmental measures</td>
</tr>
<tr>
<td>Weight</td>
<td>Calculate weight-for-height ratios, % ideal body weight</td>
</tr>
<tr>
<td>Head circumference</td>
<td>If &lt; 2 years of age</td>
</tr>
<tr>
<td>Triceps skinfold (TSF)</td>
<td>To assess body fat</td>
</tr>
<tr>
<td>Mid arm circumference (MAC)</td>
<td>Use to determine somatic protein stores</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Component</th>
<th>Guidelines</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>III. Body composition</strong></td>
<td></td>
</tr>
<tr>
<td>Bioimpedence analysis (BIA)</td>
<td>Use to measure lean body mass, fat mass and bone density</td>
</tr>
<tr>
<td>Dual energy X-ray absorptiometry (DEXA)</td>
<td>Use to measure bone density</td>
</tr>
</tbody>
</table>
## NUTRITIONAL ASSESSMENT OF THE CRITICALLY ILL CHILD

### IV. Biochemical profile

#### Basic metabolic panel (BMP)

<table>
<thead>
<tr>
<th>Component</th>
<th>Guidelines</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium (Na)</td>
<td>2-6 mEq/kg/d; ↑ needs diuretic rx, SIADH; needs fluid overload</td>
</tr>
<tr>
<td>Potassium (K)</td>
<td>2-3 mEq/kg/d; ↑ needs refeeding, diuretics, ↓ needs renal failure 2-4 mEq/kg/d</td>
</tr>
<tr>
<td>Chloride (Cl)</td>
<td>2-5 mEq/kg/d; ↑ needs with (nasogastric losses or vomiting)</td>
</tr>
<tr>
<td>Bicarbonate (HCO3)</td>
<td></td>
</tr>
<tr>
<td>Blood Urea Nitrogen (BUN)</td>
<td></td>
</tr>
<tr>
<td>Creatinine (Cr)</td>
<td></td>
</tr>
<tr>
<td>Glucose</td>
<td></td>
</tr>
</tbody>
</table>

Use to assess hydration, renal function

#### Liver Function Tests (LFTS)

<table>
<thead>
<tr>
<th>Component</th>
<th>Guidelines</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alkaline Phosphatase (Alk)</td>
<td>↑ in bone disease or biliary obstruction</td>
</tr>
<tr>
<td>Aspartate aminotransferase</td>
<td>↑ in hepatocellular injury ie, trauma, drugs, toxins, TPN</td>
</tr>
<tr>
<td>Alanine aminotransferase</td>
<td>↑ in hepatocellular injury ie, trauma, drugs, toxins, TPN</td>
</tr>
<tr>
<td>Lactate dehydrogenase</td>
<td>normal range varies with age of child; elevations imply hepatic disease</td>
</tr>
<tr>
<td>Total bilirubin</td>
<td>↑ intra- or extra-hepatic ductal obstruction i.e. decreased secretion</td>
</tr>
<tr>
<td>Albumin</td>
<td>↑ levels may suggest liver synthetic dysfunction or malnutrition</td>
</tr>
<tr>
<td>Total protein</td>
<td>↑ levels present with loss of visceral and somatic protein stores</td>
</tr>
<tr>
<td>Triglyceride level</td>
<td>↑ levels present in malnutrition/metabolic disease, ↑ obesity</td>
</tr>
</tbody>
</table>

Use to assess hepatic function
# NUTRITIONAL ASSESSMENT OF THE CRITICALLY ILL CHILD

## IV. Biochemical profile

<table>
<thead>
<tr>
<th>Component</th>
<th>Guidelines</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Complete Blood Count (CBC)</strong></td>
<td>To help identify micronutrient deficiencies</td>
</tr>
<tr>
<td>Hemoglobin/Hematocrit (Hgb/Hct)</td>
<td>↓ levels in anemia of chronic disease, iron deficiency, malnutrition</td>
</tr>
<tr>
<td>Platelet count</td>
<td>Thrombocytopenia may indicate hepatic dysfunction or bone marrow failure</td>
</tr>
<tr>
<td>Mean corpuscle volume (MCV)</td>
<td></td>
</tr>
<tr>
<td><strong>Prothrombin time (PT)</strong></td>
<td>Prolongation indicative of coagulopathy, possibly secondary to hepatic synthetic dysfunction</td>
</tr>
</tbody>
</table>

## Minerals and Trace Elements

<table>
<thead>
<tr>
<th>Component</th>
<th>Guidelines</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium</td>
<td>1–2.5 mEq/kg/d; ↓ levels cause tetany,</td>
</tr>
<tr>
<td>Phosphorus</td>
<td>0.5–1 mmol/kg/d; ↓ levels cause weakness</td>
</tr>
<tr>
<td>Magnesium</td>
<td>0.3–0.5 mEq/kg/d; ↓ levels cause seizures</td>
</tr>
<tr>
<td>Iron</td>
<td>↓ levels cause anemia</td>
</tr>
<tr>
<td>Zinc</td>
<td>2–5 mg/d; (normal plasma level 90–110 mcg/dL)</td>
</tr>
<tr>
<td>Copper</td>
<td>200–500 mcg/d; (normal plasma level 80–163 mcg/dL)</td>
</tr>
<tr>
<td>Selenium</td>
<td>30–40 mcg/d; (normal plasma level 50–150 mcg/dL)</td>
</tr>
<tr>
<td></td>
<td>↓ levels cause muscle tenderness, kwashiorkor</td>
</tr>
</tbody>
</table>
NUTRITIONAL ASSESSMENT OF THE CRITICALLY ILL CHILD

Component Guidelines

IV. Biochemical profile

<table>
<thead>
<tr>
<th>Vitamin</th>
<th>Guidelines</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>↓(deficiency) scaly skin, night blindness</td>
</tr>
<tr>
<td>D</td>
<td>↓rickets, craniotabes, tetany</td>
</tr>
<tr>
<td>E</td>
<td>↓peripheral neuropathy, ataxia, nystagmus</td>
</tr>
<tr>
<td>B₁₂</td>
<td>↓pernicious anemia, neuropathy</td>
</tr>
<tr>
<td>Folate</td>
<td>↓macrocytic anemia</td>
</tr>
</tbody>
</table>

NUTRITION SUPPORT
NUTRITIONAL ASSESSMENT OF THE CRITICALLY ILL CHILD

• Provision of nutrients, calories and fluids for the preservation of tissue integrity
• Fulfillment of energy supply to meet organ needs and prevent major dysfunction

NUTRITIONAL ASSESSMENT OF THE CRITICALLY ILL CHILD

• Rapid repletion of protein deficits
• Restore normal physiology and homeostasis
• Decrease injury-related morbidity and mortality
• Facilitate physical growth in recovery
## RESTING ENERGY EXPENDITURE EQUATIONS

<table>
<thead>
<tr>
<th>Age</th>
<th>Gender</th>
<th>WHO</th>
<th>Schofield</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-3 years</td>
<td>Male</td>
<td>60.7W – 54</td>
<td>0.17W + 1.517H – 617.6</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>61W – 51</td>
<td>16.25W + 10.232H – 413.5</td>
</tr>
<tr>
<td>3-10 years</td>
<td>Male</td>
<td>22.7W + 495</td>
<td>19.6W + 0.1303H + 414.9</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>22.5W + 499</td>
<td>16.97W + 1.618H + 371.2</td>
</tr>
<tr>
<td>10 -18 years</td>
<td>Male</td>
<td>17.5W + 651</td>
<td>16.25W + 1.1372H + 515.5</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>12.2W + 746</td>
<td>8.365W + 4.65H + 200.0</td>
</tr>
</tbody>
</table>

W= Weight (kg), H= Height (cm)

---

## INDIRECT CALORIMETRY

- Many PICUs may lack resources
- Difficult in the intubated child
- Inaccurate in child <5kg
- Unreliable if FiO$_2$ > 60%
- Endotracheal tube leakage >10%
“Dynamic clinical judgment and reassessment should be the principal tools utilized to guide the ongoing adequacy of nutritional support therapy”
NUTRITION SUPPORT GOALS IN PEDIATRIC CRITICAL CARE

• Maximal preservation of major organ system function
• Minimization of the catabolic response
• Prompt restoration of the premorbid nutritional state

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