Malnutrition & the Refeeding Syndrome: Why all the Phos?

Presented by
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Disclosures

- Nothing to Disclose.
Objectives

- 1. List two markers of malnutrition.
- 2. Identify patients at risk for developing refeeding syndrome.
- 3. Outline the treatment of refeeding syndrome.
1. Markers of malnutrition include all of the following EXCEPT:
   - A. unintended weight loss
   - B. decreased functional strength
   - C. muscle wasting
   - D. low prealbumin

2. Refeeding syndrome (RFS) is characterized by
   - A. increased serum phosphorus
   - B. salt and fluid retention
   - C. thiamine toxicity
   - D. decreased insulin levels

3. Complications of RFS include which of the following?
   - A. cardiac arrythmias
   - B. respiratory failure
   - C. heart failure
   - D. all of the above

4. In patients at very high risk of developing RFS, energy should initially be restricted to:
   - A. 5-10 kcal/kg
   - B. 15-20 kcal/kg
   - C. 25-30 kcal/kg
   - D. They’re malnourished; there should be no restriction.
Malnutrition

- Any nutritional imbalance
  - Overnutrition
  - Undernutrition
Undernutrition

- A lack of proper nutrients to sustain tissue growth, maintenance & repair

- Caused by
  - Inadequate intake &/or increased requirements
  - Impaired absorption
  - Altered transport
  - Altered nutrient utilization
Pathophysiology of Starvation

- Decreased carbohydrate intake
  - ↓ insulin secretion
- Glycogen stores are reduced
  - ↑ glucagon release → initiation of gluconeogenesis & proteolysis
    - ↓ lean muscle mass → functional weakness, weight loss
- Increased lipolysis
  - Shift from glucose metabolism to fat metabolism (ketogenesis)
  - Phosphate is not required for fat oxidation
- Metabolic rate decreases (30-50% of normal)
- ↓ Intracellular vitamin & electrolyte stores
  - Transient increase in circulating levels → immediate urinary excretion in exchange with Na
  - Net loss of K+, Mg, Phos accompanied by Na retention
Metabolism during Starvation

https://www.namrata.co/case-study-starvation/
Risks of Malnutrition

- A major contributor to increased morbidity & mortality, decreased function & quality of life
- Increases the risk of healthcare-associated infections
- Increases the risk of pressure ulcer development
- Associated with increased risk of mortality, hospital LOS, & cost of hospitalization
Identification of Malnutrition

- No single, universally accepted approach to diagnosis & documentation
  - Appetite
  - Weight loss
  - Laboratory values
  - Anthropometrics

- Screening Tools
  - Malnutrition Screening Tool (MST)
  - Nutrition Risk in the Critically Ill (NUTRIC)
  - Malnutrition Universal Screening Tool (MUST)
  - Mini Nutritional Assessment - Short Form (MNA-SF)
  - Patient-generated Subjective Global Assessment (PG-SGA)
  - Short Nutritional Assessment Questionnaire (SNAQ)

- Comprehensive Nutrition Assessment tools
  - Mini Nutrition Assessment (MNA)
  - Subjective Global Assessment (SGA)
  - AND-ASPEN Criteria
ASPEN-AND Criteria

- Identification of 2+ characteristics
  - Insufficient energy intake
  - Weight loss
  - Loss of muscle mass
  - Loss of subcutaneous fat
  - Localized or generalized fluid accumulation
  - Diminished functional status (as measured by hand grip strength)

- ***Serum proteins such as albumin and prealbumin are not included as defining characteristics of malnutrition because recent evidence analysis shows that serum levels of these proteins do not change in response to changes in nutrient intake.***
# Malnutrition in Acute Illness/Injury

<table>
<thead>
<tr>
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<th>Severe Malnutrition</th>
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<tbody>
<tr>
<td><strong>Energy Intake</strong></td>
<td>&lt;75% of needs for &gt;7 days</td>
<td>&lt;50% of needs for ≥5 days</td>
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<td><strong>Weight loss</strong></td>
<td>1-2% in 1 week OR 5% in 1 month OR 7.5% in 3 months</td>
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<td><strong>Grip Strength</strong></td>
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Malnutrition in Social or Environmental Circumstances

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Nutrition-focused Physical Exam

**Exam Areas: Head and Face (Fat and Muscle)**

- **Normal**
  - Orbital Region: Orbital Fat Pads
    - Slightly bulged fat pads
  - Temple Region: Temporalis Muscle
    - Well-defined muscle, flat or slight bulge

- **Mild – Moderate**
  - Orbital Region: Orbital Fat Pads
    - Slightly dark circles, somewhat hollow look
  - Temple Region: Temporalis Muscle
    - Slight depression

- **Severe**
  - Orbital Region: Orbital Fat Pads
    - Hollow look, depressions around eye, dark circles, loose saggy skin
  - Temple Region: Temporalis Muscle
    - Deep hollowing/scooping, lacking muscle to the touch, facial bone structures very defined

**Exam Area: Upper Chest (Muscle)**

- **Normal**
  - Clavicle Bone Region: Pectoralis major, deltoid, trapezius
    - Well-defined muscle surrounding bone, clavicle bone typically not visible in males and may be slightly prominent in females
  - Acromion Bone Region: Deltoid
    - Rounded curves at arms, shoulder, and neck

- **Mild – Moderate**
  - Clavicle Bone Region: Pectoralis major, deltoid, trapezius
    - More prominent clavicle bone, less prominent muscle when palpated
  - Acromion Bone Region: Deltoid
    - Acromion process may slightly protrude

- **Severe**
  - Clavicle Bone Region: Pectoralis major, deltoid, trapezius
    - Protruding and prominent bone with low surrounding muscle mass when palpated
  - Acromion Bone Region: Deltoid
    - Shoulder to arm joint looks square, bones more prominent, acromion process very prominent
Nutrition-focused Physical Exam

**EXAM AREA: UPPER BACK (MUSCLE)**

**Normal**
- Scapular Bone Region: Trapezius, supraspinatus, infraspinatus
  - Bones not prominent, no significant depressions

**Mild – Moderate**
- Scapular Bone Region: Trapezius, supraspinatus, infraspinatus
  - Mild depression around scapula or bone may slightly show

**Severe**
- Scapular Bone Region: Trapezius, supraspinatus, infraspinatus
  - Prominent, visible scapula bone; notable depressions between ribs, scapula, and/or shoulder/spine

**EXAM AREA: MIDAXILLARY LINE (FAT)**

**Normal**
- Thoracic and Lumbar Region: Ribs, lower back, midaxillary line at iliac crest
  - Chest is full, ribs do not show, slight to no protrusion of the iliac crest

**Mild – Moderate**
- Thoracic and Lumbar Region: Ribs, lower back, midaxillary line
  - Ribs somewhat more apparent, depressions not very pronounced, iliac crest somewhat prominent

**Severe**
- Thoracic and Lumbar Region: Ribs, lower back, midaxillary line
  - Depression between ribs very apparent, iliac crest is very prominent
Nutrition-focused Physical Exam

**EXAM AREA: ARMS (FAT)**

**Normal**
Upper Arm Region: Area under the tricep muscles
- Ample fat tissue obvious between folds of skin pinched between finger

**Mild – Moderate**
Upper Arm Region: Area under the tricep muscles
- Some depth to pinch, not ample

**Severe**
Upper Arm Region: Area under the tricep muscles
- Very little space between folds, fingers practically touching

**EXAM AREA: HANDS (MUSCLE)**

**Normal**
**Palmar:** Opponens pollicis, adductor pollicis, first dorsal interossi
- Muscle bulges, could be flat in some well-nourished individuals

**Mild – Moderate**
**Palmar:** Opponens pollicis, adductor pollicis, first dorsal interossi
- Slight depression

**Severe**
**Palmar:** Opponens pollicis, adductor pollicis, first dorsal interossi
- Depressed areas, particularly between thumb and forefinger

**Dorsal:** Interosseous muscles
- Flat/mild bulge between dorsal bones, bulging/flat muscle between index finger and thumb

**Dorsal:** Interosseous muscles
- Slight depression between dorsal bones

**Dorsal:** Interosseous muscles
- Depressed areas between dorsal bones, particularly between thumb and forefinger; bones very prominent
Nutrition-focused Physical Exam

**Normal**
- **Anterior Thigh Region:** Quadriceps
  - Well rounded, well developed
- **Patellar Region:** Quadriceps
  - Muscles protrude, kneecap not prominent
- **Posterior Calf Region:** Gastrocnemius
  - Well-developed bulb of muscle

**Mild – Moderate**
- **Anterior Thigh Region:** Quadriceps
  - Mild depression on inner thigh
- **Patellar Region:** Quadriceps
  - Kneecap more prominent
- **Posterior Calf Region:** Gastrocnemius
  - Not well developed

**Severe**
- **Anterior Thigh Region:** Quadriceps
  - Depression/line on thigh, not well developed
- **Patellar Region:** Quadriceps
  - Kneecap prominent, little sign of muscle around knee
- **Posterior Calf Region:** Gastrocnemius
  - Thin, minimal to no muscle definition
Feed them!*

*Treatment of Malnutrition

*Except…it’s not quite that simple.

Refeeding

- Shift from catabolic state to anabolic state
- Shift from fat oxidation to carbohydrate utilization
- $\uparrow$ insulin secretion $\uparrow$ carbohydrate intake
  - $\uparrow$ production of glycogen, fat, & protein
- Electrolyte shift from extracellular to intracellular as glucose is metabolized
Refeeding Syndrome (RFS)

- First described post-WW2
- A normal physiologic reaction
- Usually occurs within the first 72h of refeeding
- Pts on enteral or parenteral nutrition support at higher risk

Characterized by:
- Low serum electrolytes (K+, Mg, and P)
- Increased serum glucose
- Vitamin depletion
- Fluid imbalance
- Salt retention
- Impaired organ function
- Cardiac arrhythmias

No standardized definition
- Depletion of electrolytes occur at varying degrees and therefore variable clinical effects
- Unknown incidence/prevalence
- Central defining criteria is severe hypophosphatemia (<0.32 mMol/L or <1 mg/dl)
- Severity is associated with the degree of malnutrition
Hypokalaemia
Hypomagnesaemia
Hypophosphataemia
Thiamine deficiency
Salt and water retention - oedema

Starvation / Malnutrition

Glycogenolysis, gluconeogenesis and protein catabolism

Protein, fat, mineral, electrolyte and vitamin depletion – salt and water intolerance

Refeeding (switch to anabolism)

Fluid, salt, nutrients (CHO major energy source)

↑ Glucose uptake
↑ Utilization of thiamine
↑ Uptake of K⁺, Mg²⁺ & PO₄²⁻

↑ Protein and glycogen synthesis

Refeeding syndrome

↑ Insulin secretion

Phosphorus

- ATP production
- 2,3-diphosphoglycerate
  - Regulates the release of oxygen from Hgb
- Phosphorylation of glucose (required for glycolysis)
- NOT required for fat oxidation

Hypophosphatemia

- All-cause mortality of 18.2% compared to 4.6% in pts without hypophosphatemia
- Impaired neuromuscular fn (paresthesia, seizures, hypoventilation → respiratory failure)
- Increased insulin resistance
- Impaired ability to release O₂ to target organs
Magnesium & Potassium

- **Potassium**
  - Main intracellular cation
  - Balances negative charges on intracellular proteins

- **Magnesium**
  - Acts as a cofactor for final phosphorylation of ATP

- **Hypokalemia & hypomagnesemia**
  - Rapid cellular uptake 2’ insulin
  - May be worsened by diarrhea 2’ gut atrophy associated w/underlying malnutrition
  - Neuromuscular dysfunction
  - Cardiac arrhythmias & cardiac arrest
    - The most common cause of death in RFS
Sodium & Fluid Balance

- **Salt & Fluid retention**
  - Na is retained during periods of starvation, stress, & inflammation
  - Na-K+-ATPase: as K+ is pumped back into the cell during refeeding, Na is pumped out
  - Introduction of CHO/high concentrations of insulin $\rightarrow$ decreased renal sodium excretion and increased water retention
  - Excess fluid retention $\rightarrow$ peripheral edema, heart failure, pulmonary & brain edema

- **Can further aggravate pre-existing pathology**
  - Peripheral edema due to low protein stores
  - Cardiac atrophy 2' prolonged malnutrition
  - Alcoholic cardiomyopathy
  - Thiamine deficiency (wet beriberi)
Thiamine

- Water-soluble vitamin; half-life 9-18 days
- Required to convert pyruvate to acetyl-coA (TCA cycle)
  - Without thiamine, pyruvate & lactic acid accumulate
  - Lactic acidosis → N/V, abd pain

Thiamine deficiency
- Wernicke’s encephalopathy
- Peripheral neuropathy
- Volume overload, peripheral edema
- CHF 2’ thiamine deficiency is more pronounced in pts with reduced cardiac muscle mass 2’ malnutrition
Outcomes

- Increased mortality
- Higher incidence of adverse clinical outcomes
  - Unplanned readmissions
  - Transfer to ICU
  - Prolonged hospital stay
Can you identify it?

- Respiratory failure
- Seizures
- Cardiac arrhythmias
- Peripheral edema
- Heart failure
- Peripheral neuropathy
- Altered mental status
- Electrolyte disturbances

- In a 2019 study, only 14% of 4th-year medical students and young physicians were able to identify RFS when given a case vignette.

Prevention & Treatment of RFS

- 1. Identify patients at risk.
- 2. Prevent RFS during nutrition therapy
<table>
<thead>
<tr>
<th>Pt has 2 or more MINOR risk factor</th>
<th>Pt has 1 or more MAJOR risk factors</th>
<th>Pt is at VERY HIGH RISK</th>
</tr>
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<tbody>
<tr>
<td>BMI &lt;18.5</td>
<td>BMI &lt;16</td>
<td>BMI &lt;14</td>
</tr>
<tr>
<td>Unintentional wt loss &gt;10% x3-6 months</td>
<td>Unintentional wt loss &gt;15% x3-6 months</td>
<td>Unintentional wt loss &gt;20%</td>
</tr>
<tr>
<td>Little or no nutritional intake &gt;5 days</td>
<td>Little or no nutritional intake &gt;10 days</td>
<td>Little or no nutritional intake &gt;15 days</td>
</tr>
<tr>
<td>History of EtOH or drug use (insulin, chemotherapy, diuretics)</td>
<td>Low serum levels of K+, PO4, or Mg prior to feeding</td>
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Specific populations at high risk:

- Hunger strike
- Recent severe diet
- Hx bariatric surgery
- Short bowel syndrome
- Cancer patients
- Frail elderly pts w/chronic debilitating disease
Nutrition Therapy

- Calorie restriction
  - Decreased 60-day mortality w/hypocaloric feeds in critically ill pts w/RFS
- Fluid & Electrolyte Management
- Micronutrient Repletion

Calorie Restriction

- Low risk (1 minor risk factor)
  - 15-25 kcal/kg x3 days
  - Increase to goal rate by day 5

- High risk (1 major or 2 minor risk factors)
  - 10-15 kcal/kg x3 days, then
  - 15-25 kcal/kg x2 days, then
  - 30 kcal/kg x1 day, then
  - Goal kcals by day 7

- Very high risk
  - 5-10 kcal/kg x3 days, then
  - 10-20 kcal/kg x3 days, then
  - 20-30 kcal/kg x3 days, then
  - Goal kcals by day 10
Fluid Management

- Strive to maintain zero balance
- Low risk
  - 30-35 ml/kg
  - No sodium restriction
- High risk
  - 25-30 ml/kg x3 days, then
  - 30-35 ml/kg
  - Restrict Na to 1 mMol/kg/day x7 days
- Very high risk
  - 20-25 ml/kg x3 days, then
  - 25-30 ml/kg x3 days, then
  - 25-35 ml/kg thereafter
  - Restrict Na to 1 mMol/kg/day x10 days
Electrolyte management

- Aggressive monitoring
  - At least daily x3 days, depending on risk
- Consider empiric phosphorus supplementation in high risk pts
  - 0.3-0.6 mMol P/kg/day
- Replete K+/Mg only when low
  - 1-1.5 mMol K+/kg/day
  - 0.2-0.4 mMol Mg/kg/day
Micronutrient Repletion

- 200-300 mg thiamine daily x5 days
  - Start prior to dextrose or nutrition initiation
- MVI daily x10 days
- Check other values and replace PRN
  - Vit D
  - B12
  - Folate
- Do NOT replace Fe in the 1st 7 days
  - May worsen hypokalemia
  - Parenteral Fe may induce or prolong hypophosphatemia
Due to a lack of large, randomized trials, the current literature confirms the clinical consequences but not the efficacy of measures used to prevent and treat refeeding syndrome.”

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