Pharmacy Implications with Enteral Nutrition
Objectives

- Compare and contrast enteral nutrition (EN) formulations and feeding approaches and discuss appropriateness in given patient populations
- Describe how to transition from total parenteral nutrition (TPN) to EN and when supplemental TPN is necessary
- Analyze key drug interactions with EN and how to prevent and manage these interactions
- Identify complications of EN and provide pharmacologic recommendations for resolving complications
• **Enteral nutrition** – Providing nutrition with a combination of calories, protein, electrolytes, vitamins, minerals and fluids via an intestinal route

• Classified by the FDA as a “medical food”

• Used when oral feeding is impossible, inadequate or unsafe

• Less risk of infection, cheaper cost, more physiologic way of feeding patients compared to TPN
  – Preserves gut function and integrity
  – Enhances mucosal immunological functions
### Indications/Contraindications

<table>
<thead>
<tr>
<th>Indications</th>
<th>Contraindications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Functional GI tract but oral feedings not adequate</td>
<td>Complete intestinal obstruction</td>
</tr>
<tr>
<td>Poor appetite – associated with chronic medical condition</td>
<td>GI fistula (high-output)</td>
</tr>
<tr>
<td>Impaired swallowing function</td>
<td>Severe GI bleed</td>
</tr>
<tr>
<td>Major trauma/burn wounds</td>
<td>Extreme short bowel</td>
</tr>
<tr>
<td>Critical illness</td>
<td>Severe diarrhea or vomiting</td>
</tr>
<tr>
<td></td>
<td>Intestinal ischemia or paralysis</td>
</tr>
</tbody>
</table>

The ASPEN Guidelines recommend that nutrition support should be initiated for patients with inadequate oral intake for 7 to 14 days or in patients for whom inadequate oral intake is expected for 7 to 14 days.

ASPEN= American Society of Parenteral and Enteral Nutrition
ASPEN Algorithm

NUTRITION ASSESSMENT
Decision to Initiate Specialized Nutrition Support

FUNCTIONAL GI TRACT
YES

ENTERAL NUTRITION
Long-term Gastrostomy, Jejunostomy
Short-term Nasogastric, Nasoduodenal, Nasojejunal

GI Function
Normal, Compromised

Intact Nutrients
Defined Formula

NUTRIENT TOLERANCE
Adequate Progress to Oral Feedings
Inadequate PN Supplementation
Adequate Progress to More Complex Diet and Oral Feedings as Tolerated

PARENTERAL NUTRITION
Short-Term
Peripheral PN
Long-Term or Fluid Restriction
Central PN

GI FUNCTION
YES
NO
## EN Formulations

<table>
<thead>
<tr>
<th>Nestle Nutrition®</th>
<th>Abbott/Ross Nutrition®</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nutren® 1.0</td>
<td>Nepro®</td>
</tr>
<tr>
<td>Nutren® 2.0</td>
<td>Promote®</td>
</tr>
<tr>
<td>Isosource® HN</td>
<td>Twocal® HN</td>
</tr>
<tr>
<td>Crucial®</td>
<td>Glucerna®</td>
</tr>
<tr>
<td>Nutren® 1.0 Fiber</td>
<td>Polycose®</td>
</tr>
<tr>
<td>Impact® Glutamine</td>
<td>Pulmocare®</td>
</tr>
<tr>
<td>Fibersource® HN</td>
<td>Vital®</td>
</tr>
<tr>
<td>Peptamen AF™</td>
<td>Promod®</td>
</tr>
<tr>
<td>Isosource® 1.5 cal</td>
<td>Suplena®</td>
</tr>
<tr>
<td>Vivonex® RTF</td>
<td>Jevity®</td>
</tr>
<tr>
<td>Nutren® Replete® Fiber</td>
<td>Optimental®</td>
</tr>
<tr>
<td>Nutrihep®</td>
<td>Osmolite®</td>
</tr>
<tr>
<td>Diabetisource® AC</td>
<td>Oxepa®</td>
</tr>
<tr>
<td>Novasource® Renal</td>
<td>Pivot®</td>
</tr>
<tr>
<td>Nutren® Junior</td>
<td></td>
</tr>
<tr>
<td>Component</td>
<td>Range</td>
</tr>
<tr>
<td>---------------------------------</td>
<td>-----------</td>
</tr>
<tr>
<td>Calories (kcal/mL)</td>
<td>1.0 – 2.0</td>
</tr>
<tr>
<td>Protein (gm/L)</td>
<td>40 – 94</td>
</tr>
<tr>
<td>Carbohydrates (gm/L)</td>
<td>100 - 300</td>
</tr>
<tr>
<td>Fiber (gm/L)</td>
<td>0 - 16</td>
</tr>
<tr>
<td>Fat (gm/L)</td>
<td>10 - 100</td>
</tr>
<tr>
<td>Sodium (mg/L)</td>
<td>150 – 1300</td>
</tr>
<tr>
<td>Potassium (mg/L)</td>
<td>1100 - 2200</td>
</tr>
<tr>
<td>Osmolality (mOsm/kg)</td>
<td>310-960</td>
</tr>
<tr>
<td>Free water (%)</td>
<td>71% to 84%</td>
</tr>
</tbody>
</table>
Choosing EN For Your Patient

- Choose the best formula based on patient specific characteristics
  - Calorie requirement (protein)
  - Co-morbidities/acute illness
  - Renal function/hepatic function
  - Fluid status/electrolytes

- Renal patients
  - Protein content, Calories/L \( \rightarrow \) fluid status
  - Potassium content

- Diabetic patients
  - Carbohydrates

- Congestive heart failure patients
  - Calories/L \( \rightarrow \) fluid status

- Other considerations
  - Lactose intolerance
  - Gluten content and Celiac’s disease
  - Kosher vs. non-kosher
  - Medications that contain fats or modify electrolytes
Elemental vs. Non-Elemental

- EN formulations differ in protein and fat content
  - **Elemental (monomeric)**
    - Individual AA, glucose polymers, low fat with ~ 2% LCT’s
  - **Semi-elemental (oligomeric)**
    - Varying AA chains, glucose polymers, low fat with MCT’s
  - **Standard (polymeric)**
    - Intact AA, complex carbs, mainly LCT’s
  - **Immunostimulating**
    - Added nutrients such as glutamine, arginine and EFA’s

**Definitions:**
- AA = Amino acids
- LCT = Long chain triglycerides
- MCT = Medium chain triglycerides
- EFA = Essential fatty acids
<table>
<thead>
<tr>
<th>Product (elemental)</th>
<th>AWP Cost($)/1000 calories</th>
<th>Product (standard)</th>
<th>AWP Cost($)/1000 calories</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peptamen</td>
<td>24.06</td>
<td>Fibersource HN</td>
<td>3.73</td>
</tr>
<tr>
<td>Peptamen 1.5</td>
<td>24.22</td>
<td>Isosource 1.5</td>
<td>4.44</td>
</tr>
<tr>
<td>Vivonex Plus</td>
<td>31.30</td>
<td>Novasource 2.0</td>
<td>3.04</td>
</tr>
<tr>
<td>Crucial</td>
<td>38.48</td>
<td>Replete</td>
<td>7.35</td>
</tr>
</tbody>
</table>

AWP= average wholesale price
Patients: 205 well-nourished patients post upper GI surgery

Methods: Randomized 2 x 2 factorial design into standard EN (polymeric), immunomodulating EN, TPN or immunomodulating TPN

Outcomes: Incidence of infectious complications, tolerance of feeding, mortality and hospital LOS

LOS = length of stay
<table>
<thead>
<tr>
<th></th>
<th>EN</th>
<th>Immune EN</th>
<th>p-value</th>
<th>TPN</th>
<th>Immune TPN</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rate of Infection</td>
<td>28 (27%)</td>
<td>25 (24%)</td>
<td>0.498</td>
<td>25 (25 %)</td>
<td>28 (27%)</td>
<td>0.672</td>
</tr>
<tr>
<td>Morbidity (post-op complications)</td>
<td>36 (35%)</td>
<td>37 (36%)</td>
<td>0.804</td>
<td>35 (35%)</td>
<td>38 (36%)</td>
<td>0.577</td>
</tr>
<tr>
<td>Mortality</td>
<td>2 (2%)</td>
<td>2 (2%)</td>
<td>0.992</td>
<td>2 (2%)</td>
<td>2 (2%)</td>
<td>0.960</td>
</tr>
<tr>
<td>Hospital LOS, days (mean)</td>
<td>12.8</td>
<td>12.5</td>
<td>0.746</td>
<td>12.9</td>
<td>12.4</td>
<td>0.656</td>
</tr>
</tbody>
</table>
• The addition of glutamine to an EN regimen should be considered in burn, trauma, and mixed ICU patients (Grade B)
  – Use caution in patients with sepsis
  – Glutamine also comes in supplemental packets (Glutasolve®)
• Patients with ARDS should be placed on a formula with anti-inflammatory lipids (Grade A)
  – Omega-3 fish oils
• To receive benefit from any immune-modulating formulas, must feed > 50 % of goal calories (Grade C)

ARDS=Acute Respiratory Distress Syndrome

Immunostimulating Nutrition

Martindale RG. Crit Care Med 2009; 37: 5
Williams NT. AJHP 2008; 65: 2347-2357.
JS is a 54 year old, nutritionally compromised male admitted for pneumonia. The physician wants to start EN, but the dietician is gone for the day and asks your recommendation. Which EN ingredient should you be most concerned about when choosing a formula?

PMH – DM, asthma, hypothyroidism, hyperlipidemia

A. Carbohydrates
B. Potassium
C. Glutamine
D. Fluid concentration (i.e. Kcal/ml)
E. Sodium

Correct Answer: A. Carbohydrates
Placement of EN Feeding Tubes
Placement of EN Feeding Tubes

Nasogastric
Orogastric

Stomach
Duodenum
Jejunum

Gastrostomy
Percutaneous endoscopic gastrostomy
Jejunostomy

## Gastric vs. Post-Pyloric Feeding

<table>
<thead>
<tr>
<th></th>
<th>Gastric feeding</th>
<th>Post-pyloric feeding</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Indications</strong></td>
<td>Indication for EN</td>
<td>Gastroparesis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Recurrent aspiration</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Pancreatitis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Hyperemesis gravidarum</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Proximal enteric fistula</td>
</tr>
<tr>
<td><strong>Insertion technique</strong></td>
<td>Easier placement</td>
<td>More advanced placement</td>
</tr>
<tr>
<td><strong>Physiology</strong></td>
<td>More physiological, maintain</td>
<td>Less physiological, less motility</td>
</tr>
<tr>
<td></td>
<td>motility and gut hormone control</td>
<td>Less motility and gut hormone control</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Less pancreatic stimulation</td>
</tr>
<tr>
<td><strong>Feeding mode</strong></td>
<td>Continuous or bolus</td>
<td>Continuous only</td>
</tr>
<tr>
<td><strong>Aspiration risk</strong></td>
<td>Greater than post-pyloric</td>
<td>Lower than gastric</td>
</tr>
<tr>
<td><strong>Clogging rate</strong></td>
<td>Lower – usually larger diameter</td>
<td>Higher – usually smaller diameter tube</td>
</tr>
<tr>
<td></td>
<td>tube</td>
<td></td>
</tr>
</tbody>
</table>
Gastric vs. Post-Pyloric Feeding

Multicenter, prospective, randomized, single-blind study comparing the efficacy and gastrointestinal complications of early jejunal feeding with early gastric feeding in critically ill patients

Juan C. Montejo, MD; Teodoro Grau, MD; Jose Acosta, MD; Sergio Ruiz-Santana, MD; Mercé Planas, MD; Abelardo García-de-Lorenzo, MD; Alfonso Mesejo, MD; Manuel Cervera, MD; Carmen Sánchez-Álvarez, MD; Rafael Núñez-Ruiz, MD; Jorge López-Martínez, MD; for the Nutritional and Metabolic Working Group of the Spanish Society of Intensive Care Medicine and Coronary Units

- **Design:** Prospective, RCT at 11 hospitals in Spain
- **Patients:** 110 ICU patients predicted to receive EN for at least 5 days
- **Intervention:** EN started in the first 36 hours, patients were either fed with a NG tube or a NJ tube
- **Outcome Measures:** ICU length of stay, mortality, feeding complications
## Gastric vs. Post-Pyloric Feeding

<table>
<thead>
<tr>
<th>Primary Outcomes</th>
<th>All patients</th>
<th>Gastric</th>
<th>Post-pyloric</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality (%)</td>
<td>41 (41)</td>
<td>22 (43)</td>
<td>19 (38)</td>
<td>0.60</td>
</tr>
<tr>
<td>ICU length of stay, days</td>
<td>16 ± 13</td>
<td>18 ±16</td>
<td>15 ±10</td>
<td>0.20</td>
</tr>
<tr>
<td>Incidence of pneumonia (%)</td>
<td>36 (36)</td>
<td>20 (40)</td>
<td>16 (32)</td>
<td>0.40</td>
</tr>
<tr>
<td>MODS score at discharge</td>
<td>4.5 ± 3.9</td>
<td>4.2 ± 3.8</td>
<td>4.9 ± 3.9</td>
<td>0.40</td>
</tr>
</tbody>
</table>

- Increased rate of “high gastric residuals” with the gastric group (49%) vs. post pyloric group (2%) (p < 0.001)
- No difference found in incidence of vomiting, diarrhea, constipation or abdominal distension (p > 0.05)

MODS= Multi organ dysfunction score

• During acute pancreatitis, must allow the pancreas to rest and recover
• 4 metabolic phases of pancreatic secretion
  – Basal
  – Cephalic
  – Gastric
  – Duodenal
• EN via nasojejunal route appears to be an attractive option for acute pancreatitis
  – Feed past the ligament of Treitz → point of transition from the duodenum to the jejunum
# EN vs. TPN in Pancreatitis

<table>
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<tr>
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<tbody>
<tr>
<td></td>
<td>34 patients with acute pancreatitis (stratified by disease severity)</td>
<td>70 patients with acute pancreatitis randomized</td>
<td>50 patients with acute pancreatitis randomized</td>
</tr>
</tbody>
</table>

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</thead>
<tbody>
<tr>
<td></td>
<td>Primary - SIRS Secondary - sepsis, ICU stay, MODS, mortality</td>
<td>Pancreatic infectious complications (necrosis/abscess), MODS, mortality</td>
<td>C-RP, surgical intervention, infections, LOS and mortality</td>
</tr>
</tbody>
</table>

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<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>SIRS</td>
<td>SIRS – 2 vs. 10 pts (p &lt; 0.05)</td>
<td>Infections – 7 vs. 16 pts (p=0.02)</td>
<td>C-RP – 10.0 vs. 14.0 (p=NS)</td>
</tr>
<tr>
<td>Sepsis</td>
<td>Sepsis – 0 vs. 3 pts (NS)</td>
<td>MODS – 7 vs. 17 (p=0.02)</td>
<td>Surg intervention – (p=NS)</td>
</tr>
<tr>
<td>MODS</td>
<td>MODS – 0 vs. 5 pts (NS)</td>
<td>Mortality – 2 vs. 12 (p &lt; 0.01)</td>
<td>Infections – 16 vs. 15, (p=NS)</td>
</tr>
<tr>
<td>Mortality</td>
<td>Mortality – 0 vs. 2 pts (NS)</td>
<td></td>
<td>LOS (days) – 42 vs. 36, (p=NS)</td>
</tr>
</tbody>
</table>

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</thead>
<tbody>
<tr>
<td></td>
<td>EN improves disease severity and outcome with no pancreatic injury</td>
<td>EN should be used as therapy for pancreatitis</td>
<td>EN and TPN have comparable incidences in primary outcomes</td>
</tr>
</tbody>
</table>

**C-RP = C-reactive protein**  
**SIRS= Systemic inflammatory response syndrome**

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FIGURE 29-1 Algorithm for Nutritional Management of Acute Pancreatitis

- Acute Pancreatitis
- Abdominal pain
- Abn amylase/lipase
  - Intravenous fluid resuscitation
  - Analgesia

- APACHE II (AII)
- Ranson Criteria (RC)
- CT Scan
  - AII ≤ 9
  - RC ≤ 2
  - No necrosis on CT
  - Continue Supportive Care
  - Intravenous fluids
  - Analgesia

- AII ≥ 10
- RC ≥ 3
- Necrosis on CT
  - Place nasojejunal tube
  - Initiate enteral feeding

- Unable to place tube
- Intolerant to EN
  - Complication develops
  - (which increases disease severity or hosp LOS)
  - Or failure to advance to oral diet within 7 days

- Able to place tube
- Tolerant of EN
  - Assess tube placement and tolerance to EN

- Initiate PN
  - (After hosp day 5)
  - Abdominal pain resolves
  - Decreasing amylase/lipase toward normal
  - Advance to clear liquid diet

- Remains asymptomatic
  - Advance to Regular Diet
  - Discharge from hospital

- Symptoms recur
  - Reevaluate feasibility of EN

CT, computerized tomography; EN, enteral nutrition; PN, parenteral nutrition; LOS, length of stay; APACHE, acute physiology and chronic health evaluation.
KD is a 27 year old male with severe pancreatitis admitted to the ICU. On day 5 the team would like to start nutrition as he is severely malnourished. He has a history of gastric bypass and interventional radiology is unable to place a feeding tube in the jejunum for structural reasons. The feeding tube is in the stomach. What is the most appropriate option for starting nutrition?

A. Begin enteral nutrition with a standard formula
B. Wait to take the patient back to IR for proper placement
C. Begin total parenteral nutrition
D. Hold off on nutrition for 7 days per guidelines
Using Enteral Nutrition with Parenteral Nutrition
Transition from TPN to EN

- Begin tapering TPN when EN is providing 33 – 50% of nutrition requirements.
- Balance TPN & EN so that patient is meeting 100% of daily goals (do not overfeed).
- When EN is well tolerated and providing > 75% of nutrition requirements, TPN can be stopped.
Supplementing EN with TPN

Early versus Late Parenteral Nutrition in Critically Ill Adults

- **Design:** Prospective, multi-center, RCT
- **Patients:** 4640 ICU patients with nutrition risk score > 3
- **Intervention:** Patients in the early group received TPN on day 3 to supplement EN calories, patients in the late group did not receive TPN until day 8 if they were not at calorie goal
- **Outcomes:** ICU LOS, mortality, infection risk, time on ventilator, healthcare cost

Casaer MP. NEJM 2011; 365: 506-517.
Supplementing EN with TPN

Casaer MP. NEJM 2011; 365: 506-517.
## Outcome

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Late-Initiation group (N=2328)</th>
<th>Early-Initiation group (n=2312)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICU LOS (median), days</td>
<td>3 (2-7)</td>
<td>4(2-9)</td>
<td>0.02</td>
</tr>
<tr>
<td>Mortality (%)</td>
<td>141 (6.1)</td>
<td>146 (6.3)</td>
<td>0.76</td>
</tr>
<tr>
<td>New infection, any (%)</td>
<td>531 (22.8)</td>
<td>605 (26.2)</td>
<td>0.008</td>
</tr>
<tr>
<td>Mechanical ventilation duration &gt; 2 days (%)</td>
<td>846 (36.3)</td>
<td>930 (40.2)</td>
<td>0.006</td>
</tr>
<tr>
<td>Mean total incremental cost (Euros)</td>
<td>16,863 (8,793 – 17,774)</td>
<td>17,973 (8,749 – 18,677)</td>
<td>0.04</td>
</tr>
</tbody>
</table>

Casaer MP. NEJM 2011; 365: 506-517.
Drug Interactions with EN
• Interactions between EN and medications can significantly impact patient outcomes
  – Loss of feeding access
  – Loss of drug administration access
  – Decreased medication efficacy
  – Altered absorption of drugs or nutrients

• Drug-nutrient interactions (DNI) have not been extensively studied
  – Strength of evidence is poor
  – DNI’s rely on understanding mechanism of action
• FDA has 5 classifications for DNI’s
  – Physical $\rightarrow$ precipitates formed, altered viscosity, clumping of EN or medication
  – Pharmaceutical $\rightarrow$ +/- drug activity
  – Pharmacokinetic $\rightarrow$ +/- drug activity
  – Pharmacodynamic $\rightarrow$ +/- drug activity
  – Pharmacological $\rightarrow$ inability to provide EN because of medication adverse drug reactions
## Example medications physically incompatible with EN

<table>
<thead>
<tr>
<th>Medication</th>
<th>pH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brompheniramine</td>
<td></td>
</tr>
<tr>
<td>Calcium glubionate</td>
<td></td>
</tr>
<tr>
<td>Ferrous sulfate elixir (Feosol) pH=2.2</td>
<td></td>
</tr>
<tr>
<td>Guaifenesin</td>
<td></td>
</tr>
<tr>
<td>Lithium citrate pH=4.7</td>
<td></td>
</tr>
<tr>
<td>Monobasic sodium phosphate (Fleet Phosphosoda)</td>
<td></td>
</tr>
<tr>
<td>Potassium chloride liquid</td>
<td></td>
</tr>
<tr>
<td>Pseudoephedrine pH=2.5</td>
<td></td>
</tr>
</tbody>
</table>
Drug Interactions with EN

• **Site of delivery** → many medications require administration to a certain “site” to be effective
  – Antacids/ sucralfate
    • Require administration to the stomach

• **Delivery environment** → environmental changes in pH have an effect on drug absorption
  – Digoxin, tetracycline & carbamazepine → poorly soluble
    • Require acidic environment for dissolution & benefit from increased time in gastric environment
    • Have reduced bioavailability with post-pyloric administration or concurrent gastric EN

Williams NT. *AJHP* 2008; 65: 2347-2357.
• Hyperosmolar medications require gastric dilution before transferred to the intestine
  – If feeding past the stomach, miss this step
• Hyperosmolar solutions administered into the intestine may be dumped into small bowel
  – Results in osmotic diarrhea

### Example medications with osmolality of > 3000 mOsm/kg

<p>| | | | | |</p>
<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>Acetaminophen elixir 65mg/ml</td>
<td>Acetaminophen w/ codeine elixir</td>
<td>Amantadine solution</td>
<td>Chloral hydrate</td>
<td>Dexamethasone solution</td>
</tr>
<tr>
<td>Docusate sodium syrup</td>
<td>Ferrous sulfate liquid</td>
<td>Hydroxyzine syrup</td>
<td>Lactulose syrup</td>
<td>Lithium citrate</td>
</tr>
<tr>
<td></td>
<td>Potassium chloride liquid 10%</td>
<td>Promethazine syrup</td>
<td>Sodium phosphate liquid</td>
<td></td>
</tr>
</tbody>
</table>
Phenytoin and EN

• **Phenytoin → absorption altered up to 70%**
  – Phenytoin adhering to EN tube, or binding to component of EN
  – Account for decreased absorption and increase dose
  – Monitor phenytoin levels
  – Hold EN for 1-2 hours before and after administration, flush medication

• No difference found in phenytoin recovery when compared with two different EN protein formulations
• Fluoroquinolones → decreased bioavailability when mixed with cations such as calcium, magnesium, aluminum and iron

• Ciprofloxacin and other fluoroquinolones primarily absorbed in the duodenum
  – Gastric feeding preferred over jejunum

• Class effect?
  – Wright et al → Ciprofloxacin loss greatest compared to levofloxacin and ofloxacin
  – Burkhardt, et al → No clinically relevant effect with moxifloxacin and EN
• Carbamazepine → poorly soluble drug, EN administration may affect bioavailability
  – In vitro study showed 59% recovery of carbamazepine when concurrent EN used compared to 79% without EN
  – Slower gastric emptying increases bioavailability
  – Post-pyloric administration appears to be a poor option
  – Should monitor levels in patients on EN
  – Dilute medication with water to prevent drug loss in feeding tube

• **Warfarin** → DNI was attributed to high amounts of vitamin K in EN formulations
  – Warfarin also highly protein bound, may bind to proteins in EN or feeding tube
• INR should be monitored or switch to alternative anticoagulant if necessary
• Hold EN for 1-2 hours before and after administration
• May require a reduction in dose when EN stopped
  – Important for transitioning dose for outpatient
• Clinical pearls - DNI’s
  – Consider frequency of medications and if medications need to be taken on an empty stomach
    • If stopping EN, will need to compensate for missed nutrition
    • May worsen malnourished state
  – Most interacting medications can be monitored for efficacy with levels
  – Remember location of feeding tube and effect on medications
DL is a 45 year old female with CAP and pancreatitis started on EN for severe malnutrition. Her feeding tube is placed in her jejunum. She is being treated with levofloxacin and the physician asks what we should do about this interaction. Which one of the following is the most appropriate recommendation?

a. Initiate parenteral nutrition
b. Adjust the EN formula to an elemental formula
c. Hold EN for 1 hour before and 2 hours after levofloxacin

✓ d. Change the levofloxacin to IV formulation
e. Hold the levofloxacin until the patient resumes normal diet
Complications with Enteral Nutrition
Complications with EN

- Clinical problems with EN
  - Diarrhea
  - Aspiration
  - Metabolic disturbances
- Clogged feeding tubes
- High gastric residuals
- Delayed gastric emptying
Diarrhea

• Diarrhea is the #1 side effect in patients on EN
  – Incidence 5-60% in acute care, higher in ICU
  – No universal definition

• Many confounding factors influence diarrhea
  – Medications
    • Antibiotics
    • Inactive ingredients
  – Infection
  – Malabsorption
  – Comorbid conditions
Diarrhea

• Treatment approaches
  – Remove offending medications
    • Hyperosmolar medications
    • Sorbitol based medications
  – Probiotic supplements
  – Anti-diarrheal medications
  – Change EN formulation
    • Lower osmolality formulation
    • Elemental/semi-elemental formulation
  – Assess fat content in stool
• Most feared complication of EN
  – May lead to pneumonia, empyema, bronchitis, lung injury and ARDS
• Incidence of aspiration varies widely
• Symptoms include dyspnea, wheezing, frothy sputum, fever, cyanosis and agitation
  – May also be asymptomatic
• No routine method to detect aspiration
  – Chest x-ray non specific, dye’s not effective nor recommended
  – Use clinical picture after possible aspiration event
Aspiration

• Important to prevent aspiration and identify high risk patients
  – Raising head of bed 45 degrees (gastric feeding)
    • Reduces reflux of gastric contents
  – Feed post-pyloric if possible
  – Gastric residuals have no correlation with aspiration pneumonia

• EN unlikely to be primary cause of metabolic disturbances
  – Exceptions:
    • Re-feeding syndrome
    • Hyperglycemia
• Electrolyte monitoring
  – Supplemental therapy if low levels
  – May alter EN formula if elevated levels
• “Tube feeding syndrome”
  – Azotemia, hypernatremia and dehydration
  • Results from high protein formulations with inadequate hydration
Common mechanical problem associated with feeding tubes

- **Factors**
  - Small diameter tubes > larger diameter tubes
  - Powdered or crushed medications
  - Highly acidic or alkaline medications used
  - Tubes not properly flushed

- Less clogging with intestinal feeds compared to gastric feeds
  - Digestive enzymes and alkaline secretions
Efficacy of agents to prevent and treat enteral feeding tube clogs

- Meta-analysis conducted from 1970 – 2011
  - 3 in-vitro studies, 1 RCT and 1 descriptive report
    - Water comparable in efficacy when compared to Coca-cola®, both superior to cranberry juice
    - No studies looking at newer formulations of pancreatic enzymes

• Long served as a surrogate for gastric motility
  – Has been a common method to assess EN tolerance
• GRV’s from 100 to 600 have been used as cutoff limits
• Only followed when feeding into the stomach

GRV= Gastric residual volume
Design: Open label, prospective, randomized

Patients: 329 intubated and mechanically ventilated patients in 28 ICU’s in Spain

Interventions: GRV of 200 ml (control) compared to 500 ml (active)

Outcome measures: GI complications, ICU pneumonia, days on vent, ICU LOS, diet received/prescribed ratio
<table>
<thead>
<tr>
<th>Outcome variable</th>
<th>Control (200 ml GRV)</th>
<th>Active (500 ml GRV)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>GI complication</td>
<td>105 (63%)</td>
<td>75 (48%)</td>
<td>0.004</td>
</tr>
<tr>
<td>Mechanical ventilation (days)</td>
<td>14.7 ± 13.1</td>
<td>15.6 ± 13.6</td>
<td>0.36</td>
</tr>
<tr>
<td>ICU los (days)</td>
<td>19.8 ± 15.8</td>
<td>20.7 ± 16.2</td>
<td>0.50</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>27.3%</td>
<td>28.0%</td>
<td>0.88</td>
</tr>
<tr>
<td>Mortality</td>
<td>33.6%</td>
<td>33.9%</td>
<td>0.53</td>
</tr>
</tbody>
</table>

Example Policy on GRV

- GRV measured every 8 hours in patients with gastric feeds
  - Not measured if tube is post-pyloric

- What to do with GRVs?
  - **Acute Care Units**
    - If the GRV < **500** mL, return residuals to patient
    - If the GRV > **500** mL,
      - Stop the tube feeding for two hours
      - Return **500** mL to the patient and discard the remaining GRV
      - Restart the tube feeds at the previous rate after holding for two hours

- Same process for ICU but the GRV cutoff is **400** mL

- Notify prescriber if patient experiences N/V, diarrhea, abdominal distention/pain, two elevated GRV’s
<table>
<thead>
<tr>
<th>Agent</th>
<th>Mechanism of Action</th>
<th>Effect</th>
<th>Dosing</th>
<th>Monitoring</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cisapride</td>
<td>Cholinergic agent</td>
<td>↑ LES pressure</td>
<td>10 mg PO every 6 hours</td>
<td>• Prolongs QTc interval</td>
</tr>
<tr>
<td></td>
<td></td>
<td>↑ gastric emptying</td>
<td></td>
<td>• Many drug interactions</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>Motilin agonist</td>
<td>NO effect on LES pressure</td>
<td>500 mg IV/PO every 6 hours</td>
<td>• Prolongs QTc interval</td>
</tr>
<tr>
<td></td>
<td></td>
<td>↑ gastric emptying</td>
<td></td>
<td>• Many drug interactions</td>
</tr>
<tr>
<td>Metoclopramide</td>
<td>Dopamine antagonist</td>
<td>↑ LES pressure</td>
<td>10 mg IV/PO every 6 hours</td>
<td>• Extrapyramidal effects</td>
</tr>
<tr>
<td></td>
<td></td>
<td>↑ gastric emptying</td>
<td></td>
<td>• Contains sorbitol</td>
</tr>
<tr>
<td>Naloxone</td>
<td>Opioid Antagonist</td>
<td>Decreases opioid induced bowel dysfunction</td>
<td>3-10 mg PO three times daily</td>
<td>• No effect on analgesia</td>
</tr>
</tbody>
</table>

LES = Lower esophageal sphincter

Elevated plasma cholecystokinin (CCK) associated with delayed gastric emptying
  - CCK-1 receptor antagonists
    - Cerulein, dexloxiglumide and loxiglumide
    - Stimulate CCK receptors and increase motility

Mitemcinal
  - Oral motilin agonist
  - Studied in insulin-related gastroparesis, better than placebo

Ghrelin
  - Motilin-related peptide
  - Increases appetite and GI motility
• ASPEN Core curriculum and guidelines

• Excellent reading about post-pyloric feeding

• Elemental and Semi-Elemental Formulas: Are They Superior to Polymeric Formulas?

• Medication administration through enteral feeding tubes
Questions?

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