Total Parenteral Nutrition is ...

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University of Colorado Hospital
Department of General Surgery
Totally AWESOME!!!
Objectives

- History of TPN
- Dichotomies of Perception
- Pitfalls of TPN Studies
- Canadian Clinical Practice Guidelines
- The Surgical Patient
- Preoperative TPN
- Malnourishment
- Summary and Future Directions
History of TPN

- William Harvey 1628 – Circulation
- Sir Christopher Wren 1665 – Wine, ale, opiates
- William Courten 1712 – Olive oil
- T. Latta 1831 – Water and salts during cholera
- Claude Bernard 1859 – Glucose and metabolism
- Edward Hodder 1873 – Milk
- Paul Friedrich 1904 – Subcutaneous nutrients

History of TPN continued

- Whipple, Holman, Madden 1930’s – protein
- Robert Elman 1937 – IV infusion of AA’s
- Wretlind 1961 – Lipid emulsion
- Dudrick 1968 – SVC catheter delivery of “glucose system”

General Indications

- Patients who can’t eat
- Patients who won’t eat
- Patients who shouldn’t eat

“If the gut works, use it.”

http://pharmacy.umkc.edu/New/pharm/Pharm377/Pharm377F06/TOTAL%20PARENTERAL%20NUTRITION.ppt
Dichotomies of Perception

TPN as a Therapy
- Chemical agent which affects living processes is a drug
- MDs and medical societies view TPN as therapy
- TPN is medical therapy for ill people

TPN as a Support
- Nutrition “natural” affects living processes (intrauterine PN)
- Nourishment is viewed by relatives as an act of love and care
- Nutrition is essential to both the ill and the healthy

What about tube feeds?

Bozzetti F. Clinical Nutrition 2009; xxx 1-6 (article in press)
Problems with TPN Studies

- No placebo controlled trials
- Those who truly need it cannot be randomized
- Diverse patient populations
- Hyperalimented patients
- Carbohydrates only as nutrition source
- Lack of proper glucose control
- Formulation changes

Braga M et al. Clinical Nutrition 2009; xxx 1-9 article in press
Canadian Clinical Practice Guidelines for Nutrition Support in the Mechanically Ventilated, Critically Ill Adult Patients

- Meta-analysis
- 12 level 2, one level 1 study
- EN vs PN is **NOT** associated with a reduction in mortality
- EN vs PN associated with fewer infectious complications
- No difference in LOS or ventilator days

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## Mortality

### Review:
**Enteral Nutrition vs Parenteral Nutrition**

### Comparison:
01. EN vs PN

### Outcomes:
02. Mortality

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>EN n/N</th>
<th>PN n/N</th>
<th>RR (random)</th>
<th>95% CI</th>
<th>Weight</th>
<th>RR (random)</th>
<th>95% CI</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adams</td>
<td>1/23</td>
<td>3/23</td>
<td>3.89</td>
<td>0.33 [0.04, 2.97]</td>
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<td></td>
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<td>1986</td>
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<td>1/21</td>
<td>4.28</td>
<td>3.75 [0.47, 39.75]</td>
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<td>Cerra</td>
<td>7/33</td>
<td>8/35</td>
<td>14.74</td>
<td>0.99 [0.40, 2.41]</td>
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<td>Dunham</td>
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<td>1/15</td>
<td>2.72</td>
<td>1.25 [0.09, 17.98]</td>
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<td>Hadidichel</td>
<td>2/13</td>
<td>6/11</td>
<td>0.27</td>
<td>0.20 [0.07, 1.13]</td>
<td></td>
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<td>1995</td>
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<tr>
<td>Kakar et al.</td>
<td>1/10</td>
<td>2/20</td>
<td>0.52</td>
<td>0.56 [0.05, 5.62]</td>
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<td>Kudsk</td>
<td>1/51</td>
<td>1/45</td>
<td>2.59</td>
<td>0.66 [0.65, 13.70]</td>
<td></td>
<td></td>
<td></td>
<td>1992</td>
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<tr>
<td>Moore 1992</td>
<td>8/116</td>
<td>11/112</td>
<td>15.09</td>
<td>0.69 [0.29, 1.65]</td>
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<tr>
<td>Rapp</td>
<td>9/18</td>
<td>3/20</td>
<td>10.89</td>
<td>3.33 [1.07, 10.43]</td>
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<td></td>
<td>1983</td>
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<tr>
<td>Woodcock</td>
<td>9/17</td>
<td>5/21</td>
<td>14.84</td>
<td>2.22 [0.92, 5.40]</td>
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<td></td>
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<td>2001</td>
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<tr>
<td>Young</td>
<td>10/28</td>
<td>10/23</td>
<td>19.18</td>
<td>0.82 [0.42, 1.62]</td>
<td></td>
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<td>1987</td>
</tr>
</tbody>
</table>

| Total (95% CI)        | 357    | 346    | 100.00      | 1.00 [0.66, 1.66] |        |             |        |      |

Total events: 54 (EN), 51 (PN)

Test for heterogeneity: Chi² = 21.29, df = 10, P = 0.16, P = 30.5%

Test for overall effect: Z = 0.13 (P = 0.85)
Infectious Complications

<table>
<thead>
<tr>
<th>Study</th>
<th>EN</th>
<th>PN</th>
<th>RR (random)</th>
<th>Weight %</th>
<th>RR (random)</th>
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<tbody>
<tr>
<td>Adams</td>
<td>15/23</td>
<td>17/23</td>
<td>29.23</td>
<td>0.66</td>
<td>[0.60, 1.30]</td>
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<tr>
<td>Kalaremos</td>
<td>5/16</td>
<td>10/20</td>
<td>10.27</td>
<td>0.56</td>
<td>[0.23, 1.92]</td>
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<tr>
<td>Kudsk</td>
<td>9/51</td>
<td>18/45</td>
<td>14.48</td>
<td>0.44</td>
<td>[0.22, 0.88]</td>
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<tr>
<td>Moore 1992</td>
<td>13/113</td>
<td>38/112</td>
<td>23.12</td>
<td>0.46</td>
<td>[0.29, 0.75]</td>
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<tr>
<td>Peterson</td>
<td>2/31</td>
<td>8/25</td>
<td>4.23</td>
<td>0.30</td>
<td>[0.07, 1.25]</td>
</tr>
<tr>
<td>Woodcock</td>
<td>6/16</td>
<td>11/21</td>
<td>12.77</td>
<td>0.72</td>
<td>[0.34, 1.62]</td>
</tr>
<tr>
<td>Young</td>
<td>5/20</td>
<td>4/23</td>
<td>5.93</td>
<td>1.00</td>
<td>[0.31, 2.99]</td>
</tr>
</tbody>
</table>

Total (95% CI): 275 and 269

Test for heterogeneity: Chi^2 = 8.32, df = 6 (p = 0.22), I^2 = 27.9%

Test for overall effect: Z = 3.09 (p = 0.002)

but wait a minute...

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### Infections in studies where the PN group received more calories than the EN group

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>EN nN</th>
<th>PN nN</th>
<th>RR (random) 95% CI</th>
<th>Weight %</th>
<th>RR (random) 95% CI</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kudek</td>
<td>9/61</td>
<td>16/45</td>
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<td></td>
<td>1992</td>
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<td>6/16</td>
<td>11/21</td>
<td></td>
<td></td>
<td></td>
<td>2001</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td>205</td>
<td>203</td>
<td>100.00</td>
<td>0.49</td>
<td>[0.35, 0.63]</td>
<td></td>
</tr>
</tbody>
</table>

Test for heterogeneity: Ch² = 5.97, df = 3, P = 0.15
Test for overall effect: Z = 1.50 (P = 0.07)

### Infections in studies where the PN group received similar calories to the EN group

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>EN nN</th>
<th>PN nN</th>
<th>RR (random) 95% CI</th>
<th>Weight %</th>
<th>RR (random) 95% CI</th>
<th>Year</th>
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<tbody>
<tr>
<td>Adams</td>
<td>15/23</td>
<td>17/23</td>
<td></td>
<td></td>
<td></td>
<td>1996</td>
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<tr>
<td>Kallensteinos</td>
<td>5/15</td>
<td>10/20</td>
<td></td>
<td></td>
<td></td>
<td>1997</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td>41</td>
<td>48</td>
<td>100.00</td>
<td>0.81</td>
<td>[0.56, 1.18]</td>
<td></td>
</tr>
</tbody>
</table>

Test for heterogeneity: Ch² = 1.06, df = 1, P = 0.30
Test for overall effect: Z = 1.00 (P = 0.31)
What About the Surgical Patient?
ESPEN

(European Society for Clinical Nutrition and Metabolism)
ESPEN Guidelines on Parenteral Nutrition: Surgery

- Preoperative TPN is indicated in severely undernourished patients who cannot be adequately orally or enterally fed.
- Postoperative TPN is beneficial in undernourished patients in whom enteral nutrition is not feasible or tolerated.
- Postoperative TPN is beneficial in patients with postoperative complications impairing GI function for at least 7 days.

Braga M et al. Clinical Nutrition 2009; xxx 1-9 article in press
Parenteral vs Enteral Nutrition in the Critically Ill Patient: A Metaanalysis of Trials Using the Intention to Treat Principle

- 465 papers reviewed, 11 accepted
- 9 out of 11 trials had surgical patients
- PN vs early EN – NO Mortality difference (p=0.89)
- PN vs late EN – **Favored PN** (p=0.006)
- PN associated with more infectious complications (p<0.05)

“Clinical importance of this finding is open to interpretation”

Simpson F. Intensive Care Medicine 2005; 31:12-23
Mortality

Simpson F. Intensive Care Medicine 2005; 31:12-23
Grade B+ Evidence-Based Recommendation:

Parenteral nutrition use in patients in whom enteral nutrition cannot be initiated within 24-hours of ICU admission or injury

Simpson F. Intensive Care Medicine 2005; 31:12-23
Perioperative Total Parenteral Nutrition in Malnourished, Gastrointestinal Cancer Patients

- Randomized control trial
- 90 patients with gastric or colorectal carcinoma
- >10% wt loss in past 6 months, elective operation
- 2 groups:
  1. TPN (10 days pre op + 9 days post op)
  2. Standard diet with parenteral solution (940 kcal nonprotein, 85 g AA)
- Equally matched in demographics

# Results

<table>
<thead>
<tr>
<th></th>
<th>TPN</th>
<th>Control</th>
<th>Statistics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall Complications</td>
<td>37%</td>
<td>57%</td>
<td><em>p</em> = 0.03</td>
</tr>
<tr>
<td>Infectious Complications</td>
<td>33%</td>
<td>45%</td>
<td><em>p</em> = 0.22</td>
</tr>
<tr>
<td>Mortality</td>
<td>0%</td>
<td>10%</td>
<td><em>p</em> = 0.05</td>
</tr>
</tbody>
</table>

- No line infections
- Length of post-operative hospital stay same (*p*=0.98)

Degree of Undernourishment?

- **Von Meyenfeldt et al. 1992**¹
  Decrease in septic complications from 18.8% to 5.5% (p <0.05) in 29 patients with weight loss >10%

- **Veterans Affairs TPN Cooperative Study**²
  Decrease in noninfectious complications from 42.9% to 5.3% (p = 0.03) in 33 severely undernourished patients

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Is there an ideal BMI/nutrition status for TPN?
Which Patient is Malnourished?
Future Directions

- “Optimal candidate”
- Glutamine
- Omega-3 fatty acids
- Zinc
- Selenium
- Lipid Delivery
- Insulin and glucose control
Summary

- TPN plays a critical role in surgical patients
- When the gut does not work...
- No mortality difference
- How significant are the infections?
- Undernourished benefit the most
- Nutrition is NOT an after thought
References