Lipids in Parenteral Nutrition: How Much Fat Do We Really Need?

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Objectives:
- Know the history of parenteral nutrition and essential fatty acid (EFA) deficiency.
- Know the time course of the recent intravenous fat emulsion (IVFE) shortage and currently available formulations.
- Be able to describe EFAs, their metabolism and what happens in deficiency.
- Know the current guideline recommendations for parenteral lipid supplementation.
- Understand the data supporting minimal lipid supplementation.
**History**
1929- EFA deficiency first described in rats
1968- 1st total parenteral nutrition (TPN) formulation to promote growth, development, and positive nitrogen balance; 1st formulations were fat-free
1972- 1st naturally occurring reported cases of EFA deficiency in infants receiving long-term TPN
1975- 1st naturally occurring reported cases of EFA deficiency in adults receiving long-term TPN
1982- 1st case report of linolenic acid (18:3w3) deficiency

**Intravenous Fat Emulsion (IVFE)**

<table>
<thead>
<tr>
<th>Product &amp; Manufacturer</th>
<th>Oil (%)</th>
<th>Fatty acid content (%)</th>
<th>Egg yolk phospholipid</th>
<th>Glycerin %</th>
<th>Kcal/mL</th>
<th>Osmolarity mOsm/L</th>
<th>How supplied (mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intralipid (Baxter)</td>
<td>20%</td>
<td>-</td>
<td>20</td>
<td>50</td>
<td>26</td>
<td>10</td>
<td>9</td>
</tr>
<tr>
<td></td>
<td>20%</td>
<td></td>
<td>50</td>
<td>65.8</td>
<td>17.7</td>
<td>8.8</td>
<td>4.2</td>
</tr>
<tr>
<td>Liposyn II ( Hospira)</td>
<td>10%</td>
<td>discontinued</td>
<td></td>
<td>54.5</td>
<td>22.4</td>
<td>10.5</td>
<td>8.3</td>
</tr>
<tr>
<td></td>
<td>20%</td>
<td>discontinued</td>
<td></td>
<td>54.5</td>
<td>22.4</td>
<td>10.5</td>
<td>8.3</td>
</tr>
<tr>
<td>Liposyn III ( Hospira)</td>
<td>10%</td>
<td>backorder</td>
<td>10</td>
<td>54.5</td>
<td>22.4</td>
<td>10.5</td>
<td>8.3</td>
</tr>
<tr>
<td></td>
<td>20%</td>
<td>backorder</td>
<td>20</td>
<td>54.5</td>
<td>22.4</td>
<td>10.5</td>
<td>8.3</td>
</tr>
<tr>
<td></td>
<td>30%</td>
<td>backorder</td>
<td>30</td>
<td>54.5</td>
<td>22.4</td>
<td>10.5</td>
<td>8.3</td>
</tr>
</tbody>
</table>

Adapted from Drugs Facts and Comparisons

- IVFE components (currently available formulations): Soybean oil: provides EFAs, Egg yolk: emulsifier and provides calories (IVFE provides 10 kcal/g, instead of 9 kcal/g expected from lipids), Glycerin: creates an isotonic solution, Vitamin K and sodium hydroxide: adjusts final pH
- Drug shortage: November 6, 2009: Liposyn II and III were recalled by Hospira, Liposyn II was then discontinued due to lack of raw material, Currently, Liposyn III is on backorder with no estimated time of resolution, Intralipid was recently removed from allocation distribution by Baxter and is now available through normal distribution methods, Solution: Many hospitals were forced to limit the amount of lipid supplementation in TPNs...BUT HOW MUCH DO WE REALLY NEED?
**IVFE recommendations**
- A.S.P.E.N recommends a minimum of 1-2% total calories as linoleic acid and 0.5% as linolenic acid
- Minimum: 100 gm IVFE weekly (500 mL 10% IVFE twice weekly, 250 mL 20% IVFE twice weekly or 500 mL 20% IVFE once weekly)
- Maximum: ≤1-2.5 gm/kg/d
- Benefits of higher amounts of fat
  - Higher energy yield per weight compared to protein and carbohydrates (10kcal/gm vs 4 kcal/gm and 3.9 kcal/gm, respectively)
  - Less CO₂ production with metabolism compared to glucose
  - Limit hyperglycemia associated with high glucose infusion
- Reasons for fat-free parenteral nutrition
  - Hypertriglyceridemia (TG >500)
  - IVFE allergy (caution with severe egg allergy)
  - Recent nationwide drug shortage

**Essential Fatty Acids (EFAs)**

![Fatty acid metabolism](Image)

*Figure 1: Fatty acid metabolism*  
(adapted from 11)
• Biochemistry\textsuperscript{10}
  o Essential fatty acids: ω3 and ω6
  o First 3 metabolic steps for all 3 families utilize the same enzymes
    ▪ Substrate metabolism prefers ω3 > ω6 > ω9. Mead acid (20:3w9) is only produced in appreciable amounts when linoleic acid is deficient.

Figure 2: Fatty acid structure\textsuperscript{12}

Figure 3: Function of EFAs\textsuperscript{12}

Lipids in Parenteral Nutrition
EFA Deficiency

- Mechanism of action\textsuperscript{13}
  - EFAs can be obtained endogenously from fat stores or exogenously from diet
  - In fat-free TPN patients:
    - Continuous glucose infusion $\rightarrow$ increased insulin release $\rightarrow$ prevents lipolysis of endogenous fat stores to fatty acids
    - No exogenous EFAs
  - Timeframe to development of EFA deficiency is dependent on
    - EFA content of diet
    - Available endogenous fat stores
    - Continuous versus cyclic glucose infusion (e.g. nocturnal infusion)

- Biochemical Diagnosis
  - Triene:tetraene or T:T ratio $>$ 0.2 (defined as T:T $>$ 0.4 before 1979)\textsuperscript{14, 15}
    - Triene:tetraene ratio refers to the mead acid:arachidonic acid ratio
    - EFA deficiency: mead acid increases and arachidonic acid decreases
    - Rationale: Omega 3 and omega 6 are preferred substrates over omega 9. In the absence of EFAs, omega 9 is metabolized to mead acid, thus increasing the T:T ratio.

- Linoleic acid (\omega 6) deficiency\textsuperscript{3, 4, 16, 13, 17, 18}
  - Well documented
  - Clinical symptoms: dermatitis (scaling, thinning and dryness of skin) and alopecia
    - Less evidence for hepatomegaly, thrombocytopenia and anemia\textsuperscript{7}

- Linolenic acid (\omega 3) deficiency\textsuperscript{5}
  - Only 1 case report
  - Neurological side effects: numbness, paresthesia, weakness, blurred vision, pain in legs, inability to walk
  - Symptoms resolved in 12 weeks with 0.54\% of calories as linolenic acid
I. Timeframe for development and correction of EFA deficiency

| Objective | To examine time to development of EFA deficiency in patients receiving fat-free TPN and determine the time and dose of IVFE needed to correct EFA deficiency in these patients |
| Design | Prospective study in Nashville, TN |
| Population | 28 surgical patients expected to receive TPN for > 14 days  
- 9 patients < 3 months old, 5 patients age 3 to 14 years, 14 patients age 18 to 66 years  
- Received TPN from 13 days to 7 months |
| Intervention | Patients with a T:T ratio > 0.4 were given IVFE (Intralipid 10%) as 25% of total calories |
|Endpoints | T:T ratio was assessed on a regular basis (usually weekly), EFA deficiency defined as T:T ratio > 0.4  
- Signs of dermatitis and alopecia were assessed daily |
| Statistics | Not addressed |
| Results | 20 of 28 developed T:T ratio > 0.4  
- 17 of these 20 developed dermatitis and/or alopecia  
- Infants: 8 of 9 developed EFA deficiency, mean time 13 days  
  - 7 of these 8 developed dermatitis and/or alopecia 7 days later  
- Children: 4 of 5 developed EFA deficiency after 20-35 days, 5th child had T:T ratio of 0.19  
- Adults: 8 of 14 developed EFA deficiency, mean time 30 days (10-58 days)  
  - 6 of these 8 developed dermatitis  
- T:T ratio correction required 7 to 10 days, correction of dermatitis and/or alopecia required an additional 5 to 7 days |
Discussion/Conclusions

- Average time to EFA deficiency:
  - Infants: 2 weeks
  - Children: 3 to 4 weeks
  - Adults: 4 weeks
- Clinical signs developed about a week after the T:T ratio exceeded 0.4
- IVFE corrected EFA deficiency in 7 to 10 days
  - If IVFE was then removed, EFA deficiency returned in 2 weeks
- TPNs in the 1970’s often did not include IVFE due to limited availability
- Dermatitis presented as scaling, dryness and thinning of skin. Alopecia may precede dermatitis. However, in these complex patients, many factors may have contributed, including weight loss, protein depletion and infection.

Strengths

- Assessed time to development of EFA deficiency
- Assessed clinical and biochemical signs of EFA deficiency
- Methods of laboratory analysis were addressed

Limitations

- Small patient population
- Only one dose of IVFE was studied/mentioned
- Methods of statistical analysis were not addressed

II. Amount of IVFE needed to prevent EFA deficiency


Objective

To define the minimal fat requirements for patients who are receiving continuous parenteral nutrition

Design

Prospective study at Clinical Center of the National Institutes of Health

Population

- 77 patients receiving TPN for ≥ 14 days (age: 8 to 68 years)
  - 69 required TPN due to malignant disease

Intervention

- Initial T:T ratio at 14+ days of TPN therapy
- No IVFE
- IVFE as 10% soybean oil at fixed dose (54% linoleic acid)
- Fat from oral diet (linoleic acid content of 7.5% total calories assumed)
- IVFE and fat from oral diet

Endpoints

- Fatty acid profile: baseline
- EFA deficiency defined as T:T ratio > 0.4

Statistics

Not addressed

Results

- No IVFE
  - 71% had EFA deficiency by 2 weeks
  - All except 1 pt developed EFA deficiency by 3 weeks
- 50 g IVFE per week or less
  - 70% developed EFA deficiency
  - IVFE as ≤ 3% of calories delayed EFA deficiency by 6 weeks
- 100 g IVFE per week or more (≥ 5.6% total calories)
  - No EFA deficiency
  - T:T ratio of 0.4 corresponds with IVFE as 1.9% total calories (see Fig.4 below)
Barr et al., cont.

**Results, cont.**

- IVFE as ≥ 3.2% total calories
  - No EFA deficiency
- Fat by mouth
  - < 15% total calories as fat by mouth: 75% developed EFA deficiency in 3 wks
  - >15% total calories as fat by mouth: NO EFA deficiency

<table>
<thead>
<tr>
<th>IVFE (units/wk)</th>
<th>N</th>
<th>T:T ratio (Mean ± SEM)</th>
<th>Percent abnormal †</th>
<th>Percent Calories as fat ‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>19</td>
<td>1.17 ± 0.21</td>
<td>95</td>
<td>0</td>
</tr>
<tr>
<td>0.1 - 1.0</td>
<td>10</td>
<td>0.64 ± 0.12</td>
<td>70</td>
<td>2.1±0.2</td>
</tr>
<tr>
<td>1.1 - 2.0</td>
<td>3</td>
<td>0.10 ± 0.04</td>
<td>0</td>
<td>6.4±0.4</td>
</tr>
<tr>
<td>&gt; 2.0</td>
<td>12</td>
<td>0.06 ± 0.01</td>
<td>0</td>
<td>10±1.1</td>
</tr>
<tr>
<td>Controls</td>
<td>10</td>
<td>0.08 ± 0.01</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*One unit of fat = 50 g soybean oil emulsion
†Percent of total nonprotein calories as fat, mean ± SEM

**Discussion/Conclusions**

- EFA deficiency can be prevented by at least 3.2% of calories as IVFE (1.7% as linoleic acid) or 15% of calories as fat by mouth
  - Lesser amounts delayed but did not prevent EFA deficiency
  - **100 g IVFE is sufficient to prevent EFA deficiency**
- All patients on fat-free TPN developed EFA deficiency after 21 days
  - Infants developed EFA deficiency after as few as 7 days of fat-free TPN
  - Children and adults developed EFA deficiency after 3 to 5 weeks of fat-free TPN

**Strengths**

- Various concentrations and routes of fat were studied
- Methods of laboratory analysis were described

**Limitations**

- Outdated definition of EFA deficiency: T:T>0.4 (1960 definition) instead of 0.2 (1979 definition)
- Clinical findings of EFA deficiency were not addressed in this study (dermatitis, alopecia, etc.)
- Methods of statistical analysis were not addressed

Fig. 2. Triene:tetraene ratio during TPN in eight patients who received up to 3% of their calories as intravenous fat. The rate of development of EFA deficiency is delayed compared with Figure 1.
III. Timeframe to develop and minimal dose needed for correction of EFA deficiency

|---|

**Objective**
To assess the time to development of EFA deficiency, time to correction of EFA deficiency and the most appropriate dose of IVFE in home parenteral nutrition (HPN) patients.

**Design**
Prospective, non-blinded study in Boston, MA

**Population**
- 12 patients receiving HPN for ≥ 4 months (age: 29-72 years)
  - HPN delivered to patients every 2 weeks. Providers suspected non-compliance with weekly IVFE infusion due to infusion side effects and time requirements. Researchers proposed a biweekly 3-in-1 TPN to increase compliance.
  - Oral diet unrestricted (all patients had short bowel syndrome)

**Intervention**
- Phase I: IVFE held until T:T ratio > 0.2, then patients entered phase II
- Phase II: IVFE 0.6 g/kg every other week (eg. 56 kg pt: 17 g/wk)
  - Phase ended when T:T ratio < 0.1 or decreased by half; patient entered phase III if EFAD did not resolve after 6 months of treatment (similar in phase III and IV)
- Phase III: IVFE 1.2 g/kg every other week (eg. 56 kg pt: 34 g/wk)
- Phase IV: IVFE 1.8 g/kg every other week (eg. 56 kg pt: 50 g/wk)
- Phase V: IVFE 2.4 g/kg every other week (eg. 56 kg pt: 67 g/wk)

**Endpoints**
- Fatty acid profile: 2 baseline profiles, then every 3 to 4 weeks

**Statistics**
Not discussed

**Results**
- Initiation:
  - 6 of 12 pts had EFAD on initiation
  - 2 of 12 pts developed EFAD during phase I (in 20-25 wks)
  - 3 of 12 pts never developed EFAD after 6-12 months without IVFE; 1 died after 26 wks
    - Gut absorption of fat was apparently adequate in these patients
  - Dose required to replete fatty acid stores
    - 0.6 g/kg every other week: 1 pt
    - 1.2 g/kg every other week: 2 pts
    - 1.8 g/kg every other week: 4 pts
    - 2.4 g/kg every other week: 1 pt
    - None reported infusion side effects with 3-in-1 HPN
Mascioli et al, cont.

<table>
<thead>
<tr>
<th>Pt #</th>
<th>Prestudy fat dose (g)</th>
<th>Prestudy T:T ratio</th>
<th>Maximum T:T ratio</th>
<th>Current fat dose (g)</th>
<th>Correcting dose rate (g/kg q 2 wk)</th>
<th>Total # weeks given fat</th>
<th>Week of correcting dose</th>
<th>Current T:T ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>60 q 2 wk</td>
<td>0.06</td>
<td>0.19, 0.26</td>
<td>72 q 2 wk</td>
<td>1.2</td>
<td>8</td>
<td>2</td>
<td>0.10</td>
</tr>
<tr>
<td>2</td>
<td>75 q 2 wk</td>
<td>0.09</td>
<td>0.23, 0.29</td>
<td>93 q 2 wk</td>
<td>1.8</td>
<td>37</td>
<td>8</td>
<td>0.09</td>
</tr>
<tr>
<td>7</td>
<td>50 q 2 wk</td>
<td>0.20</td>
<td>0.43, 0.35</td>
<td>45 q 1 wk</td>
<td>1.8</td>
<td>74</td>
<td>33</td>
<td>0.09</td>
</tr>
<tr>
<td>8</td>
<td>None</td>
<td>0.23</td>
<td>0.22, 0.38</td>
<td>32 q 2 wk</td>
<td>0.6</td>
<td>22</td>
<td>22</td>
<td>0.12</td>
</tr>
<tr>
<td>3</td>
<td>None</td>
<td>0.24</td>
<td>0.23, 0.16</td>
<td>30 q 1 wk</td>
<td>1.2</td>
<td>31</td>
<td>8</td>
<td>0.06</td>
</tr>
<tr>
<td>4</td>
<td>75 q 2 wk</td>
<td>0.24</td>
<td>0.32, 0.34</td>
<td>82 q 1 wk</td>
<td>1.8</td>
<td>36</td>
<td>6</td>
<td>0.10</td>
</tr>
<tr>
<td>5</td>
<td>24 q 2 wk</td>
<td>0.41</td>
<td>0.34, 0.28</td>
<td>78 q 2 wk</td>
<td>1.8</td>
<td>52</td>
<td>6</td>
<td>0.09</td>
</tr>
<tr>
<td>9</td>
<td>88 q 1 wk</td>
<td>0.64</td>
<td>0.38, 0.37</td>
<td>88 q 1 wk</td>
<td>2.4</td>
<td>64</td>
<td>29</td>
<td>0.17</td>
</tr>
</tbody>
</table>

**Discussion/Conclusions**

- Correction of EFA deficiency required 2 to 8 weeks once the appropriate dose was found.
- For most patients, 1.2 to 1.8 g/kg every other week was sufficient to prevent EFA deficiency.
- 3 of 12 patients no longer required IVFE at the end of the trial due to adequate gut absorption. Although these patients had received IVFE for ≥ 1.5 yrs, they never developed EFA deficiency when IVFE was discontinued.

**Strengths**

- Study design allowed for individualized dose determination
- Methods of laboratory analysis were described

**Limitations**

- Small sample size
- Fat absorption through the gut was not assessed
- Assessment of clinical symptoms was not addressed
- Methods of statistical analysis were not discussed

**IV. Prevalence of EFA deficiency in HPN patients in relation to IVFE dose and small intestine length, evaluation of current definition of EFA deficiency**


**Objective**

To examine the correlation between small intestine length, amount of IVFE received, presence of biochemical EFA deficiency and clinical symptoms of EFA deficiency in patients receiving HPN.

**Design**

Observational study in Copenhagen, Denmark

**Population**

- 56 patients on HPN (age: 16 to 76 years)
- 37 healthy control subjects (age: 25 to 60 years)

**Methods**

- Nocturnal HPN 3 to 7 times per week, duration ranged from 2 months to 25 years
  - Subgroups: <100 cm, 100-200 cm or >200 cm remaining small intestine (normal = 350 cm)
  - Subgroups: no IVFE, 50-100 gm IVFE weekly or ≥ 100 g IVFE weekly (Intralipid 10% or 20%)
- Oral intake over 48 hours was assessed prior to the study

**Endpoints**

- Amount of HPN, blood tests, skin problems (scaling and dryness, assessed via questionnaire)

**Statistics**

- Subgroup assignment and data collection performed after characteristics of patient population had been determined
- Nonparametric testing

Lipids in Parenteral Nutrition
Lipids in Parenteral Nutrition

<table>
<thead>
<tr>
<th>Results</th>
<th>Jeppessen et al, cont.</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Only 22 of 56 patients received IVFE (4 to 59% of basal metabolic rate)</td>
<td></td>
</tr>
<tr>
<td>• Patients receiving IVFE had lower oral intake and higher HPN intake</td>
<td></td>
</tr>
<tr>
<td>• Skin problems:</td>
<td></td>
</tr>
<tr>
<td>o 2 of 37 control subjects reported problems (psoriasis)</td>
<td></td>
</tr>
<tr>
<td>o 25 of 56 patients reported problems in the past 3 months (no difference shown between patients who did and did not received IVFE)</td>
<td></td>
</tr>
<tr>
<td>o Note: HPN patients were older and more medically complex in comparison to the healthy control subjects</td>
<td></td>
</tr>
<tr>
<td>• T:T ratio</td>
<td></td>
</tr>
<tr>
<td>o 14 of 56 HPN patients had a T:T ratio &gt; 0.2</td>
<td></td>
</tr>
<tr>
<td>▪ 13 of these patients did not receive IVFE</td>
<td></td>
</tr>
<tr>
<td>o HPN patients: 0.7; healthy control subjects: 0.1</td>
<td></td>
</tr>
<tr>
<td>o Arachidonic acid was higher in HPN patients; however, total omega-6 levels were lower</td>
<td></td>
</tr>
<tr>
<td>o Mead acid was 8 times higher in HPN patients which created an elevated ratio</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Discussion/Conclusions</th>
<th>100 g/wk is sufficient to prevent T:T ratio &gt; 0.2 (EFA deficiency)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Presence of skin problems lacked association with T:T ratio &gt; 0.2. Perhaps a lower T:T ratio or another fatty acid measurement may be a better indicator of EFA deficiency.</td>
<td></td>
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</table>

<table>
<thead>
<tr>
<th>Strengths</th>
<th>Assessed clinical symptoms of EFA deficiency</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Laboratory analysis and statistical analysis were described</td>
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</table>

<table>
<thead>
<tr>
<th>Limitations</th>
<th>Unlimited oral intake was permitted</th>
</tr>
</thead>
<tbody>
<tr>
<td>• No intervention made</td>
<td></td>
</tr>
</tbody>
</table>

V. Prevalence of EFA deficiency in HPN patients, evaluation of current definition of EFA deficiency

<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td>Design</td>
<td>Prospective, placebo-controlled, observational study in Boston, MA</td>
</tr>
<tr>
<td>Population</td>
<td>• Treatment group: 11 patients receiving HPN for 6 months to 19 years (age: 25 to 73 years)</td>
</tr>
<tr>
<td></td>
<td>• Control group: 10 healthy control subjects (age: 30 to 55 years)</td>
</tr>
<tr>
<td></td>
<td>• Oral diet was unrestricted</td>
</tr>
<tr>
<td>Endpoint</td>
<td>Comparison of serum fatty acids between patients and healthy control subjects</td>
</tr>
<tr>
<td>Statistics</td>
<td>• Results reported as mean ± SEM (standard error of mean)</td>
</tr>
<tr>
<td></td>
<td>• Statistical significance determined by unpaired Student’s t test</td>
</tr>
</tbody>
</table>
### Results

- Mean HPN (kcal/d) : 520-2050 kcal/d
- Mean IVFE intake: 11.5 ± 6.3 g/d
  - 30-50 g IVFE 1-4 times per week
  - Mean 6.5% ± 3.7% total energy intake, linoleic acid: 50% total IVFE
- T:T ratio < 0.2 for all patients and volunteers
  - Although mead acid was elevated in patients, arachidonic acid was also elevated, creating a near normal ratio

### Fatty acids

<table>
<thead>
<tr>
<th>Fatty acids</th>
<th>Patients (n=11) (nmol/mL)</th>
<th>Controls (n=10) (nmol/mL)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Triglyceride</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20:3w9</td>
<td>7.12 ± 1.51</td>
<td>4.25 ± 1.65</td>
<td>0.17</td>
</tr>
<tr>
<td>20:4w6</td>
<td>75.15 ± 8.08</td>
<td>32.84 ± 4.22</td>
<td>0.003</td>
</tr>
<tr>
<td>Phospholipid</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20:3w9</td>
<td>11.86 ± 2.16</td>
<td>7.58 ± 0.92</td>
<td>0.10</td>
</tr>
<tr>
<td>20:4w6</td>
<td>233.75 ± 24.10</td>
<td>171.99 ± 12.14</td>
<td>0.06</td>
</tr>
<tr>
<td>18:2w6/20:4w6</td>
<td>1.67 ± 0.20</td>
<td>3.37 ± 0.29</td>
<td>0.0002</td>
</tr>
<tr>
<td>T:T ratio</td>
<td>0.05 ± 0.01</td>
<td>0.05 ± 0.01</td>
<td>0.62</td>
</tr>
</tbody>
</table>

*Values are mean ± SEM. P values by Student t test*

### Discussion/Conclusions

- Linoleic acid as 3.2% of total calories is sufficient to prevent EFA deficiency in patients on long-term HPN (lipids as 6% of total calories)
  - There was no significant difference in T:T ratio between patients and control subjects.
  - Since these patients received nocturnal feedings, lipolysis should have increased during the day allowing for breakdown of available endogenous fat stores. However, chronic cycling eventually leads to depletion of endogenous fat stores.
  - This patient population received twice the amount of IVFE needed to prevent EFA deficiency. However, this amount is still lower than the average HPN patient receives.
  - The author proposed that a T:T ratio is not an accurate assessment of EFA deficiency since patients in this study had other abnormal labs. However, no other measurement is suggested by the authors and no patient in this study had EFA deficiency.

### Strengths

- Most recent analysis of EFA deficiency in HPN patients
- Placebo controlled
- Described, in detail, methods of laboratory analysis and statistical analysis

### Limitations

- Small sample size
- No intervention was made
- Linoleic acid content of diet was twice that demonstrated to prevent EFA deficiency
- Quantity of oral intake was not assessed. Considering that HPN provided as few as 520 kcal/day, oral intake may have been significant in some patients.
Recommendations

- A.S.P.E.N. currently recommends EFAs be supplemented in patients on TPN as a minimum of 100 g weekly of IVFE. This may be accomplished with 250 mL of Intralipid 20% twice weekly.
  - This amount is supported by Jeppesen, et al and Barr, et al.
- During times of drug shortage, initiation of IVFE supplementation may be delayed for up to one week if needed.
  - Fat-free TPN cycling allows breakdown of endogenous fat stores. This may temporarily prevent EFA deficiency until endogenous sources have been depleted.
- If a sufficient supply of IVFE is available, a maximum of 1 g/kg/day IVFE or 40% of total calories (based on 25 kcal/kg/day) may be provided.

Areas for further study

- Current methods of biochemical assessment of EFA deficiency may require revision. Although clinical symptoms usually follow initial development of a T:T ratio > 0.2, clinical symptoms of long term EFA deficiency can be present at lower T:T ratios.
  - Perhaps a more accurate biochemical definition would include analysis of only omega 6 rather that a ratio in comparison to omega 9, since omega 6 is the fatty acid that contributes most to clinical symptoms of EFAD deficiency.
REFERENCES


Appendix I: Abbreviations

- IVFE intravenous fat emulsion
- TPN total parenteral nutrition
- EFA essential fatty acids
- A.S.P.E.N. American Society for Parenteral and Enteral Nutrition
- T:T ratio triene:tetraene, first described by RT Holman
- HPN home parenteral nutrition
## Appendix II: Summary of Trials

<table>
<thead>
<tr>
<th>Methods</th>
<th>Conclusion</th>
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<tr>
<td><strong>O’Neill, et al. 1977</strong></td>
<td>- Adults acquire EFAD in 4 weeks on fat-free TPN, infants in 2 weeks&lt;br&gt;- EFAD was corrected in 7 to 10 days of IVFE</td>
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<td><strong>Barr, et al. 1981</strong></td>
<td>- IV linoleic acid as 1.7% of calories is the minimal amount necessary to prevent EFAD&lt;br&gt;- 100 g IVFE weekly prevents EFAD</td>
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<tr>
<td><strong>Mascioli, et al. 1996</strong></td>
<td>- Correction of EFAD required 2 to 8 weeks.&lt;br&gt;- For most patients, 1.2 to 1.8 g/kg every other week was sufficient to prevent EFAD</td>
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<tr>
<td><strong>Jeppesen, et al. 1998</strong></td>
<td>- 100 g IVFE weekly prevents EFAD&lt;br&gt;- Clinical symptoms of EFAD (skin problems) lacked association with T:T ratio &gt; 0.2.</td>
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<tr>
<td><strong>Ling, et al. 2002</strong></td>
<td>- Linoleic acid as 3.2% of calories intake is sufficient to prevent EFAD&lt;br&gt;- Most recent analysis of EFAD in HPN patients</td>
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