EVALUATION OF NUTRITIONAL NEEDS IN TOTAL PARENTERAL NUTRITION BASED ON NON-PROTEIN CALORIES VERSUS TOTAL CALORIES

by

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(ABSTRACT)

Whether to include or exclude the potential kilocalories in protein when calculating the energy provided by total parenteral nutrition (TPN) has been debated. Both methods are found in clinical practice. An attempt was made to study 52 patients for seven days, randomized to receive their total energy expenditure from TPN calculated for total calories (TC) or nonprotein calories (NPC). Many TPN patients were excluded or dropped from the study because of enteral nutrient intake, inability to perform metabolic cart measurements or nitrogen balance calculations, renal failure or surgery during the study. Six subjects completed at least part of the protocol (three in each group). Nitrogen balance, respiratory quotient, prealbumin, blood glucose and triglycerides were measured. Insufficient data were collected to support or dispute the superiority
of the TC or the NPC method of calculation. Possible modifications in the study design were discussed, such as using involuntary muscle function testing as the primary dependent variable.
DEDICATION

I dedicate this thesis to my father, Ross H. Smith, and my mother, Madeline L. Stevens, who taught me to value education and to value myself.
ACKNOWLEDGEMENTS

Sincere appreciation is extended to my committee chairman, Mary K. Korslund, Ph.D., for her guidance and support during this endeavor. I thank LTC Jonathan P. Kushner, M.D., and Mary Ann Novascone, Ph.D., for serving on my thesis committee and sharing their expertise.
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INTRODUCTION

The purpose of this study was twofold: (1) to compare the nutritional response and metabolic tolerance to TPN in adult patients given total parenteral nutrition (TPN) calculated with nonprotein kilocalories (NPC), ignoring the caloric value of amino acids, or TPN calculated with total kilocalories (TC), including the caloric value of dextrose, fat, and amino acids, and (2) to compare 24-hour nitrogen balance calculations for TPN patients using urinary urea nitrogen (UUN) versus total urinary nitrogen (TUN).

Whether to include or exclude the potential kilocalories in protein (amino acids) when calculating the kilocalories provided by TPN has been a philosophical decision. Both methods can be found in clinical practice; therefore, no one approach is the universally accepted standard of care.

The rationale for meeting 100% of energy needs with NPC is to provide sufficient energy substrate to minimize endogenous and exogenous protein catabolism and to optimize protein synthesis. However, this approach may increase the risk of overfeeding kilocalories since the amino acids in TPN contain four potential kilocalories per gram.

The harmful effects of long-term or severe overfeeding with parenteral nutrition are well known;\textsuperscript{1,2}
however, the consequences of short-term mild overfeeding are not known. Anabolic amounts of parenteral dextrose and fat may lead to hepatic dysfunction.\textsuperscript{1,2} Evidence that excessive caloric infusions are of importance in clinical practice has been provided by Fischer's\textsuperscript{2} observation that the incidence and severity of hepatic dysfunction may be decreasing with the modern approach of limiting energy infusions to meet (but not exceed) requirements.

In the stressed patient, glucose will be derived from amino acid substrates via gluconeogenesis. In this state, gluconeogenesis is poorly suppressed by intravenous dextrose infusions.\textsuperscript{3} Overfeeding dextrose, especially, may elevate blood glucose levels, which may suppress components of the immune defense system.\textsuperscript{3,4}

Excessive caloric infusion, particularly of dextrose, increases respiratory workload.\textsuperscript{5} This may become a clinical problem in patients with severe obstructive pulmonary disease.\textsuperscript{3}

Complications of excessive lipid infusion can include hyperlipidemia, impaired immune function and hypoxemia resulting from impaired diffusing capacity and ventilation/perfusion abnormalities.\textsuperscript{1,6} Overfeeding also increases the expense of parenteral nutrition.

On the other hand, underfeeding may result in a negative energy balance and a more negative nitrogen
balance.\textsuperscript{7} Underfeeding also is associated with lower serum protein levels, including serum prealbumin.\textsuperscript{8} Nitrogen balance and prealbumin levels have been negatively correlated with poor patient outcomes (mortality and morbidity).\textsuperscript{9,10,11,12}

We do not know if discounting kilocalories from protein in TPN solutions results in mild overfeeding or if including the potential kilocalories from protein (about 350-500 kilocalories per day) leads to slightly underfeeding the patient. More importantly, is there any clinically significant difference between these approaches in the short-term (one week or less)? Looking at metabolic indices may suggest if one of the two methods of allocating TPN kilocalories (NPC versus TC) is superior to the other in the first week of parenteral feeding.

UUN is used as an index of urinary nitrogen excretion because of its ease of determination and low cost. However, if nonurea urinary nitrogen cannot be accurately estimated in patients on TPN, then the nitrogen balance calculated from the UUN will be unreliable. The micro-Kjeldahl and chemiluminescence methods of TUN measurement may be more accurate than UUN when calculating nitrogen balance\textsuperscript{13}; however, many health care institutions, including ours, do not perform TUN analysis on-site. TUN analysis by laboratories off-site
is relatively expensive and results may not be available for two weeks after the urine sample is submitted, which is too long to be clinically useful. As a secondary purpose, this study intended to provide evidence to (1) support the continued use of UUN measurements in calculating nitrogen balance, or (2) justify replacing UUN with TUN in our hospital laboratory.
REVIEW OF LITERATURE

Historically, when calculating the kilocalories from enteral feeding, the potential kilocalories in the protein have been included. In TPN, however, the potential kilocalories from protein (amino acids) may be ignored and all of the estimated energy needs met with carbohydrate (dextrose) and fat (e.g. Intralipid). Therefore, patients receiving TPN may be getting more kilocalories than those fed enterally. Whether these additional kilocalories are beneficial, or at least benign, is not clear. Many clinical studies in nutrition support did not indicate if the kilocalories reported were calculated using TC or NPC.

Assuming that urinary nitrogen (and urea nitrogen from other sources) reflect protein carbon which is oxidized to carbon dioxide and water, Duke et al\textsuperscript{14} estimated that the mean value for the protein kilocalorie contribution was 16\% of the measured resting energy expenditure (MREE) in 28 patients with varying degrees of stress. Little information was given regarding the subjects' nutritional intake during the study period. This study design may be flawed because deamination of some amino acids (e.g., glutamine) may not always correspond to protein oxidation.\textsuperscript{15}

The use of indirect calorimetry to assess MREE is recommended in the critically ill population since
conventional equations which predict these patients' energy expenditure (EE) frequently overestimate actual requirements.\textsuperscript{15} Foster et al\textsuperscript{16} demonstrated this when MREE was assessed in 100 consecutive patients receiving TPN. A literature review revealed 191 published guidelines for NPC requirements of hospitalized patients on TPN. When these guidelines were matched and applied to the 100 individual TPN patients, the equations exceeded MREE by an average of 1076 ± 660 kilocalories per day.

Despite the potential for error in measurement, studies have confirmed that the indirect calorimeter is both a reliable and an accurate instrument.\textsuperscript{15} Indirect calorimetry, based on oxygen consumption and carbon dioxide production, correlates well with direct calorimetry (\(p<.001, r=.81\)), and the mean difference between the two methods for measuring EE is less than three percent.

With adequate caloric intake, the thermic effect of feeding (TEF) may contribute an additional 10\% to the MREE.\textsuperscript{17} An activity factor of ten percent should be added to the MREE to meet total energy requirements in most critically ill patients. Only if the patient is subject to prolonged, stressful procedures (such as wound debridement or discontinuation of mechanical ventilation) should 15\% be added. For mildly ambulatory patients, 20\% should be added to MREE.\textsuperscript{18}
Indirect calorimetry also measures the respiratory quotient (RQ) - the ratio of the volume of carbon dioxide produced to the volume of oxygen consumed per unit of time. Excessive intravenous dextrose administration increases de novo lipogenesis resulting in greater molar amounts of carbon dioxide produced per mole of oxygen consumed, thus raising the RQ to >1.0. High levels of carbon dioxide production increase the respiratory effort required to offload the carbon dioxide and can result in a respiratory acidosis and respiratory failure. Askanazi et al.\textsuperscript{19} and Cavelli et al.\textsuperscript{20} have shown respiratory distress and failure in patients, especially those with limited ventilatory reserve, who were given large amounts of parenteral carbohydrate.

RQ's exceeding 1.0 are usually indicative of overfeeding, especially overfeeding carbohydrates.\textsuperscript{5} Underfeeding can produce an RQ of <0.812.\textsuperscript{21} Until further knowledge is available, it seems reasonable to provide nutrition support that strives at an RQ in the normal physiological range between 0.81 and 1.0\textsuperscript{19} (or 0.9).\textsuperscript{22}

Large amounts of intravenous dextrose can elevate blood glucose. Glucose intolerance and hyperglycemia are common manifestations of severe illness, particularly with coexisting sepsis.\textsuperscript{23} Sustained hyperglycemia (blood glucose >220 mg/dL) will suppress the chemotactic and phagocytic actions of activated monocytes, and thus
suppress a vital component of the immune defense system.\textsuperscript{1,3,4,24} However, excess lipid may impair the reticuloendothelial system and thereby predispose to infection.\textsuperscript{25,25}

Diminished triglyceride clearance may be observed among the most gravely ill patients. It is important, therefore, to monitor lipid clearance of critically ill patients who receive a substantial proportion of their caloric intake as lipid.\textsuperscript{27,28} In people receiving TPN, hypertriglyceridemia has been defined as a serum triglyceride level >300 mg/dl.\textsuperscript{29}

Underfeeding critically ill patients can be undesirable. In 61 surgical patients who required greater than seven days of critical care, Kresowik et al\textsuperscript{11} found the mortality rate of 26 patients in positive caloric balance was 38\%, while that of 35 patients in negative caloric balance was 57\% (p<.05), with similar severity of illness in both groups. Nutritional inadequacy adversely affects muscle function,\textsuperscript{29} wound healing,\textsuperscript{30} and may increase risk for postoperative pneumonia.\textsuperscript{31}

Prealbumin, more recently renamed transthyretin, is synthesized in the liver and has a half-life of two days. Although the normal prealbumin level is 18-40 mg/dL, the level that appears important for identifying significant risk of malnutrition is below 11 mg/dL.\textsuperscript{32,33}
Prealbumin was inversely correlated with mortality in 78 patients in a medical intensive care unit (ICU). Decreases in prealbumin were associated with caloric intakes less than 2000 Kcal/day. Surgery was associated with a significant drop of five to seven mg/dL in prealbumin and a drop in nitrogen balance. With adequate feeding and resolving stress, Spiekerman discovered that prealbumin levels increased by four to five mg/dL within seven days. An increase of less than two mg/dL after one week of feeding indicated a poor response. A prealbumin of 13.5 mg/dL or greater reflected a return to stable nutritional status.

Sawicky et al found that when energy intake was >100% of estimated normal REE (calculated by the Harris and Benedict equation), prealbumin concentration significantly increased over one week in patients on TPN. When energy intake was 100-130% of REE, prealbumin concentrations increased (p<.001). This was a higher level of significance than observed when TPN provided 131-150% of calculated REE (p<.05). This study suggests that an energy intake of at least 100% of estimated REE is associated with a positive response to TPN. As in many other research reports, the authors did not indicate whether energy intake was prescribed using NPC or TC.

Changes in prealbumin also have had a positive correlation with nitrogen balance. Vanlandingham et al
demonstrated improved prealbumin concentrations in patients in positive nitrogen balance and decreased values in those with negative nitrogen balance. In this study, patients on TPN having a positive nitrogen balance demonstrated a more rapid recovery from surgical treatment and control of infection compared to patients exhibiting negative nitrogen balance.

Kresowik et al\textsuperscript{11} provided evidence that a more positive caloric balance, especially in malnourished people, generally promoted a more positive nitrogen balance. During sufficient stress, however, Bursztein et al\textsuperscript{38} reported that nitrogen balance was negative at any nitrogen intake, even with an energy supply that was greater than EE.

For stressed patients, a goal of nutritional therapy is to prevent or minimize losses of lean body mass without causing harm from overfeeding. The administration of protein at a level of 1.5 to 1.75 g/kg/day appears to be optimal for most patients with moderate to severe degrees of stress.\textsuperscript{39} Some studies show that sparing of protein is no greater when exogenous protein is provided in amounts that exceed 1.5 g/kg of body weight per day.\textsuperscript{40,41}

Renal failure, surgery, sepsis, treatment with corticosteroids, insulin therapy, cirrhosis, hepatitis, and nutritional status may alter nitrogen balance,
prealbumin, glucose, and/or triglycerides, independent of the patients' current nutritional support.\textsuperscript{38,42,43,44}

Loder et al\textsuperscript{15} focused on the relationship between UUN and TUN in preoperative, postoperative, and critically ill patients. The postoperative and stressed patients exhibited UUN/TUN inconsistencies within each group, producing unreliable estimates of the nonurea nitrogen excretion from individual patients, although group means were comparable. The most significant nonurea nitrogen losses are from urinary ammonia, creatinine, and uric acid. Fecal, integumental and body fluids other than urine account for a small amount of nitrogen losses in most people.\textsuperscript{46} The very close correlation of TUN to total nitrogen output demonstrated that the principle aim of any formula estimating total nitrogen output should be the accurate estimation of TUN.\textsuperscript{47} Therefore, the use of measured TUN may be more accurate than UUN when calculating nitrogen balance in some hospitalized patients.

\textbf{Restatement of the Purpose}

This study attempted to determine if there are any significant differences in clinical parameters (nitrogen balance, RQ, prealbumin, blood glucose control, and triglyceride level) when patients' total energy expenditure (TEE) is met by infusing a TPN formula for seven days calculated for TC versus NPC.
We also intended to examine the reliability of UUN as compared to TUN in calculating nitrogen balance in this patient population. However, because of the high price of TUN testing it was decided that TUN analysis would be eliminated from the study design.
MATERIALS AND METHODS

A. Patient selection

(1) Inclusion criteria - Adult (at least 18 years of age) patients hospitalized at Walter Reed Army Medical Center (WRAMC), without oral or enteral caloric intake, who were to begin receiving TPN.

(2) Exclusion and removal criteria -

a. Estimated creatinine clearance <50 mL/min

b. Hepatic failure manifested by encephalopathy, severe cirrhosis, active hepatitis

c. Seizures or other extreme fluctuations in EE

d. Unable to obtain reliable REE with a metabolic cart, e.g., inspired oxygen concentration >50% or supplemental oxygen with a face mask or nasal cannula

e. Unable to accurately estimate total nitrogenous losses, e.g., diarrhea >300 mL/d, or exudative wound losses exceeding 200 mL/d.

f. Surgery within 24 hr before study period or during the study

g. TPN and dextrose infusions totaling less than 90% or exceeding 110% of TEE
h. Received TPN to meet full caloric requirement any time in the week preceding entry into the study
i. TPN interrupted during the study period (including cyclic TPN)
j. Pregnancy
k. Unable to tolerate 40% of NPC as Intralipid; e.g. allergic reaction or serum triglycerides >300 mg/dL
l. Any serum glucose >400 mg/dL during the study
m. Oral or enteral kilocalorie intake during study
n. Voluntary consent for study was not obtained

B. Procedures

This research study altered the relevant standard of care in only two ways: (1) patients were randomized for determination of caloric intake and (2) breathing tests were performed at scheduled intervals to assess REE. The standard of care at WRAMC was to generally use NPC for TPN, and the breathing tests (indirect calorimetry) are performed at the discretion of individual nutrition health care providers. There was no requirement for additional blood or urine samples.
Patients who received TPN were identified by the project investigators through referrals from other health care employees, especially the WRAMC fourth floor pharmacy, which received copies of all new TPN orders. A project investigator screened the patient to determine if the subject was appropriate for the study. If so, the investigator obtained direct informed patient consent, or if the patient was unable to give consent, third party consent was obtained. (Appendix A.) If patient consent was obtained, a project investigator stratified the patient by (1) in an ICU versus not in an ICU (to roughly equalize degree of stress between groups), and/or (2) sepsis and/or (3) corticosteroid medication. (See data collection sheet in Appendix B.) Using a table of random numbers, subjects were randomly assigned to one of two treatment groups:

1. TPN calculated for NPC, n=26, or
2. TPN calculated for TC, n=26

There was no attempt to control the total number of patients in the ICU versus other locations, the number of patients with a diagnosis of sepsis, and/or the number of patients receiving corticosteroids, but since these factors have been shown to influence nitrogen balance and prealbumin, an equal number of subjects with these predisposing factors in each group is desirable.
Most patients on TPN receive 10 to 40% (maximum, 60%) of their energy as intravenous lipid during parenteral nutrition. In both groups, NPC were given as 60% dextrose and 40% fat. Caloric needs were assessed by obtaining MREE using indirect calorimetry via Deltatrac metabolic cart (Sensormedics MBM-100). Respiratory gases were sampled directly from the mechanical ventilator, or in nonventilated patients, from a canopy placed over the subjects' head. Most subjects entering this study were receiving some kilocalories from intravenous dextrose and/or half of their original TPN order. (At this hospital the policy was to provide only half of the ordered amino acids, dextrose, fat, and volume over the first 24 hr of TPN.) The MREE obtained at this time was multiplied by 1.05 (the estimated TEF); this product was then multiplied by one of the following activity factors to obtain an estimated TEE:  

1.10, if at bed rest
1.15, bed rest with prolonged stressful procedures, such as weaning from mechanical ventilation
1.20, if mildly ambulatory (at least transfers from bed to chair)

All patients were given 1.5 g protein/kg/d. Actual or most reliable recent body weight was used for the calculation; however, if >125% over high end of desirable body weight range for medium frame (using 1983
Metropolitan Height and Weight Tables\textsuperscript{50}, an adjusted weight formula was used: weight at high end of desirable weight range for medium frame plus 25\% of the weight exceeding this desirable weight.\textsuperscript{51} If the patient was overweight secondary to unusually developed muscle mass, the patient's actual or recent body weight was used in calculating TPN protein.

Blood glucose levels were requested three times a day during full TPN with the goal of maintaining serum glucose $<240$ mg/dL, using exogenous insulin, if necessary. (Appendix C.)

The investigators recommended modifying the amount of TPN kilocalories if a metabolic cart study indicated that the estimated TEE of the patient was $>10\%$ above or $<10\%$ below the previous calculation. If the RQ had been $>1.0$ or $<0.81$, the kilocalories from TPN would have been decreased by 10\% or increased by 10\%, respectively.\textsuperscript{52}

C. Data Collection

The following data were collected from all patients (see Appendix B) prior to the first full order (referred to as "day one") of TPN:

(1) Age, sex, height, weight, usual weight, desirable weight per 1983 Metropolitan Height and Weight Tables,\textsuperscript{50} weight history, physical exam findings
(2) Brief diet history, if obtainable

(3) Diagnosis, medical history, surgery and other therapies that may have influenced nutritional needs

(4) Medications, including intravenous fluids containing dextrose

(5) Laboratory data to include serum prealbumin, serum triglycerides and blood glucose (24 hr urine for UUN and creatinine was dropped from the baseline measurements because most subjects' nitrogen intake was changing during this 24 hr period, invalidating nitrogen balance assessment)

(6) MREE and RQ, using measurements from the Deltatrac metabolic cart measurement performed for at least 10 minutes with less than five percent variance of the data

(7) Activity level per patient or nurse report

(8) Protein, dextrose, fat, and kilocalories in TPN

(9) Start date for TPN

The following data was collected from laboratory analysis during the administration of TPN on days four and seven: 24 hr urine for UUN and creatinine; serum prealbumin, and serum triglycerides. Nutrition intake should be constant for at least 24-48 hr before the collection of urine for nitrogen balance assessment.
MREE and RQ was performed on days two, four, and seven.

During full TPN, any blood or serum glucose over 240 mg/dL in nondiabetic subjects was noted, as well as the units of regular insulin administered per day.

D. Analysis

Seventy-five (75) patients may have been required to enter this study to ensure 52 patients by the end of the study period. Sample size justification was based on a previous study by Vandlandingham et al\(^9\), wherein patients had a nitrogen balance change from baseline to day ten of +10.4 g/24 hr ±6.2 and serum prealbumin increased 3.5 mg/dL ±7.5 over that same 10 day period.

Controlling the probability of a Type I error at alpha = 0.05 (two-sided), a sample of 26 subjects per group would have an 80% power to detect a 0.80 standard deviation difference between the two TPN calculation methods. This would translate into a difference of five g/24 hr for nitrogen balance and six mg/dL for prealbumin.

During the study it was decided to abandon nitrogen balance calculation at baseline because subjects' nitrogen intake was increasing during the 24 hr baseline (from zero to 50% of TPN), making valid nitrogen balance calculations impossible. Nitrogen balance over 24 hr was calculated on days four and seven using the following
formula: grams of nitrogen infused in TPN minus the sum of UUN in grams and four grams for insensible losses.\textsuperscript{55}

The primary response variables were RQ, nitrogen balance (measured in g/24 hours using UUN), and serum prealbumin (measured in mg/dL). The secondary response variables were blood glucose >240 mg/dL in nondiabetic patients and serum triglycerides (measured in mg/dL).

Data were intended to be analyzed using repeated measures of analysis of variance, with the between-subject factor, TPN CALCULATION METHOD, and the within-subject factor, TIME.

Differences in demographic/clinical characteristics between the two groups were planned to be examined using t-test for continuous variables and the chi-square test for discrete variables. If data collection had been adequate, data would have been presented using descriptive statistics.
RESULTS

From May 1993 through August, 1994, 15 patients were entered into the study, and of those, a significant amount of data were collected on only six subjects. Of the nine subjects who dropped out early, five were because of resumption of oral diet, one because of surgery, one had TPN discontinued, another refused to have the canopy hood placed over his head on study day four, and one died. Among the six subjects who completed the majority of the study period, one dropped out on day five because of surgery, and another dropped out on day four because the TPN catheter fell out and was not replaced until the next day.

The following results are presented as six individual case studies:

**Subject #1**

E.M. was a 59 year old male with a history of alcoholic liver disease (no alcohol since 1991), noninsulin-dependent diabetes mellitus, metastatic colon cancer, weight loss, and decreased food intake. He presented with upper gastrointestinal bleeding, gastric outlet obstruction, and pleural effusion. At 56 kg, he was 70% of usual and desirable body weight. Bleeding had stopped, but TPN was ordered since the patient was significantly malnourished, had a gastric outlet
obstruction and small bowel access for feeding had not been obtained. Sliding scale insulin was ordered.

After direct patient consent was obtained, E.M. was stratified because of his ICU status, then randomized to the NPC study group. At that time, he was already receiving half of the TPN ordered the day before, which provided 866 NPC and 28 grams of protein over 24 hours. On that day, glucose was 181-222 mg/dl. After obtaining the MREE at baseline (day 0), the TEE was calculated and TPN was modified to provide 1767 NPC and 84 grams of protein per day.

During the study period, glucose was measured between 218-306 mg/dl. Insulin was given as needed. The patient was transferred out of the ICU on day one of full TPN. The TEE on days two, four, and seven were, respectively, 100%, 108%, and 110% of the baseline TEE. No modification of TPN was made during the study period. See Table I for results of RQ, TEE, nitrogen balance, prealbumin and triglycerides. (Serum triglycerides and prealbumin were not completed on day seven, as ordered.)
TABLE I

Results from subject #1

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Day 0</th>
<th>Day 2</th>
<th>Day 4</th>
<th>Day 7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory quotient</td>
<td>0.83</td>
<td>0.83</td>
<td>0.84</td>
<td>0.83</td>
</tr>
<tr>
<td>TEE (kilocalories)</td>
<td>1767</td>
<td>1764</td>
<td>1908</td>
<td>1956</td>
</tr>
<tr>
<td>Nitrogen balance (g)</td>
<td></td>
<td>+3.0</td>
<td>-1.1</td>
<td></td>
</tr>
<tr>
<td>Prealbumin (mg/dL)</td>
<td>12.4</td>
<td></td>
<td>10.1</td>
<td></td>
</tr>
<tr>
<td>Triglycerides (mg/dL)</td>
<td>143</td>
<td></td>
<td>80</td>
<td></td>
</tr>
</tbody>
</table>

TEE, total energy expenditure

**Subject #2**

S.L. was a 52 year old male with a history of sigmoid colectomy associated with a mesenteric artery repair, complicated by a pancreatic pseudocyst. He was admitted for colostomy closure. Post-operatively, he developed an intestinal fistula, given Somatostatin, and ordered to receive TPN. At 77 kg, S.L. was 94% of usual and 100% of desirable body weight.

At baseline (day 0), the subject was receiving a half bag of TPN, which provided 1251 NPC and 55 grams of protein. The patient was randomized to the NPC group. After the metabolic cart study, TPN was rewritten to provide 2255 NPC and 115 grams of protein per day. Results of RQ, TEE, prealbumin and triglycerides are given in Table II.
TEE on days two, four and seven was, respectively, 107%, 95%, and 109% of the baseline TEE. No modification of TPN kilocalories was made during the study. Nitrogen balance could not be calculated using UUN because of significant amounts of diarrhea which began on day two and continued throughout the study period. S.E. was febrile (100-102.5 degrees F) throughout the study. Serum triglycerides and prealbumin were not measured on day four, as ordered. Blood glucose remained less than 240 mg/dL throughout the study period.

TABLE II

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Day 0</th>
<th>Day 2</th>
<th>Day 4</th>
<th>Day 7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory quotient</td>
<td>0.75</td>
<td>0.81</td>
<td>0.84</td>
<td>0.84</td>
</tr>
<tr>
<td>TEE (kilocalories)</td>
<td>2255</td>
<td>2424</td>
<td>2136</td>
<td>2472</td>
</tr>
<tr>
<td>Prealbumin (mg/dL)</td>
<td>11.5</td>
<td>___</td>
<td>7.7</td>
<td></td>
</tr>
<tr>
<td>Triglycerides (mg/dL)</td>
<td>107</td>
<td>___</td>
<td></td>
<td>34</td>
</tr>
</tbody>
</table>

TEE, total energy expenditure

Subject #3

C.W. was a 25 year old female with a recent history of cholelithiasis and cholecystitis, treated with a cholecystectomy (seven weeks prior to this admission), followed by an adhesiolysis secondary to small bowel
obstruction. She presented to WRAMC with an enterocutaneous fistula and was ordered to receive TPN (1500 NPC and 74 grams of protein) and Somatostatin. Her usual weight had been 61.4 kg. Current weight after seven weeks of poor to fair nutritional intake was 48.6 kg (79% of usual and desirable weight).

C.W. was randomized to the TC study group. While on half of the original TPN order (740 TC and 34 grams of protein) TEE was calculated and her TPN order was changed to 1877 TC and 74 grams of protein. Results are presented in Table III. Triglycerides and prealbumin were ordered but not obtained at baseline.

### TABLE III

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Day 0</th>
<th>Day 2</th>
<th>Day 4</th>
<th>Day 7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory quotient</td>
<td>0.96</td>
<td>0.85</td>
<td>0.83</td>
<td>0.93</td>
</tr>
<tr>
<td>TEE (kilocalories)</td>
<td>1877</td>
<td>1625</td>
<td>1688</td>
<td>1713</td>
</tr>
<tr>
<td>Nitrogen balance (g)</td>
<td></td>
<td>+5.0*</td>
<td>+4.2</td>
<td></td>
</tr>
<tr>
<td>Prealbumin (mg/dL)</td>
<td></td>
<td>19.7</td>
<td>22.5</td>
<td></td>
</tr>
<tr>
<td>Triglycerides (mg/dL)</td>
<td></td>
<td>76</td>
<td>77</td>
<td></td>
</tr>
</tbody>
</table>

TEE, total energy expenditure

*Nitrogen balance was probably less positive because of fistula losses of 325 mL/24 hr
On day two of full TPN, the subject's TEE was 1625 kilocalories (87% of TC in TPN). The TPN was modified to 1625 TC. On day four, TEE was 104% of TC in TPN, therefore, no change in TPN kilocalories was indicated. An unsuccessful attempt was made to obtain the grams of nitrogen from the 325 mL of enterocutaneous fistula output, therefore, it was not possible to accurately calculate nitrogen balance on day four. By day seven, fistula output had declined to <200 mL, allowing calculation of nitrogen balance. TEE on the final study day was 105% of previous TEE calculation. Blood glucose remained under 240 mg/dL throughout the study.

Subject #4

B.P. was a 23 year old male with a 3 year history of ulcerative colitis, treated with corticosteriods who presented to WRAMC with bloody watery diarrhea. He reported a good appetite on a regular diet and no weight changes prior to this admission. Usual and current weight were 86 kg, 108% of desirable body weight. Medications included Asacol, 6-Mercaptopurine, folic acid, ferrous sulfate and an increased dosage of Prednisone.

Bowel rest was desired, so oral diet was stopped and TPN was ordered. After consent was signed, B.P. was stratified for corticosteroid medication, then randomized
to the TC study group. MREE was obtained and TEE calculated while on a half-bag of TPN, supplying 1533 TC and 57 grams of protein. TPN order was adjusted to provide 2280 TC and 129 grams of protein per day. (See results in Table IV.)

TEE was 94% of baseline on study day two, and 99% of baseline value on study day four. On day five, the patient had surgery, therefore, no additional research data were collected. Despite potential glucose intolerance from corticosteroids, blood glucose stayed below 240 mg/dL during the study.

TABLE IV

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Day 0</th>
<th>Day 2</th>
<th>Day 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory quotient</td>
<td>0.81</td>
<td>0.81</td>
<td>0.87</td>
</tr>
<tr>
<td>TEE (kilocalories)</td>
<td>2280</td>
<td>2136</td>
<td>2256</td>
</tr>
<tr>
<td>Nitrogen balance (g)</td>
<td></td>
<td></td>
<td>zero</td>
</tr>
<tr>
<td>Prealbumin (mg/dL)</td>
<td>30.4</td>
<td></td>
<td>37.7</td>
</tr>
<tr>
<td>Triglycerides (mg/dL)</td>
<td>97</td>
<td></td>
<td>66</td>
</tr>
</tbody>
</table>

TEE, total energy expenditure

Subject #5

E.B. was a 43 year old female with a history of noncirrhotic portal hypertension secondary to a thrombus.
in the portal vein. She then developed bleeding esophageal varices treated by sclerotherapy. This resulted in a paralytic ileus of the upper gastrointestinal tract with nausea and vomiting for about 3 weeks prior to admission.

Her usual weight was 94 kg, but she had dropped to 83 kg (88% of usual weight) within the past 4 weeks. Three days prior to full TPN she had surgery to resect 40 cm of necrotic jejunum and to biopsy her liver for possible abscesses. E.B. was sedated and on mechanical ventilation when TPN orders were written. Protocol consent was obtained from patient's husband. After stratification for ICU status, she was randomized to the TC group.

While on a half bag of TPN (1227 TC and 46 grams of protein), her MREE was obtained and TEE calculated. Results of RQ, TEE, nitrogen balance, prealbumin, and triglycerides are given in Table V. The TPN was modified to 2101 TC and 104 grams of protein per day.

TEE was 103%, 98%, and 99% of original calculation on days two, four, and seven, respectively. On day four, the 24 hr urine for UUN was not collected, as ordered. Thirty units of regular insulin were given over the study period to maintain blood glucose under 240 mg/dL.
TABLE V

Results from subject #5

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Day 0</th>
<th>Day 2</th>
<th>Day 4</th>
<th>Day 7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory quotient</td>
<td>0.84</td>
<td>0.98</td>
<td>0.92</td>
<td>0.89</td>
</tr>
<tr>
<td>TEE (kilocalories)</td>
<td>2101</td>
<td>2167</td>
<td>2057</td>
<td>2079</td>
</tr>
<tr>
<td>Nitrogen balance (g)</td>
<td></td>
<td></td>
<td>-0.4</td>
<td></td>
</tr>
<tr>
<td>Prealbumin (mg/dL)</td>
<td>3.9</td>
<td>5.0</td>
<td>6.7</td>
<td></td>
</tr>
<tr>
<td>Triglycerides (mg/dL)</td>
<td>70</td>
<td>144</td>
<td>158</td>
<td></td>
</tr>
</tbody>
</table>

TEE, total energy expenditure

Subject #6

D.G. was a 32 year old male with no significant medical history until he sustained severe blunt trauma to the abdomen resulting in a ruptured pancreas. His usual weight was 84 kg. Ten days following the traumatic injury he weighed 82 kg (108% of desirable body weight). Since bowel rest was desired (and the patient had already been without adequate nourishment for 10 days) TPN was ordered.

After consenting to the study protocol, D.G. was randomized to the NPC group. While receiving a half bag of TPN, providing 1565 NPC and 69 grams of protein, his TEE was calculated to be 2657 kilocalories per day. TPN was adjusted to 2657 NPC and 123 grams of protein.

Results are summarized in Table VI.
On day two, TEE was only 88% of the NPC in TPN, therefore, TPN was reduced to 2340 NPC per day. On day four D.G. had a temperature of 103 degrees F and the TEE was 117% of previous value, therefore, TPN was increased to 2875 NPC. Later that day, the TPN catheter fell out, so no more data could be used for the study. Blood glucose remained less than 240 mg/dL.

| TABLE VI |
| Result from subject #6 |
| Parameter | Day 0 | Day 2 | Day 4 |
| Respiratory quotient | 0.78 | 0.90 | 0.85 |
| TEE (kilocalories) | 2657 | 2340 | 2875 |
| Prealbumin (mg/dL) | — | — | 10.7 |
| Triglycerides (mg/dl) | 226 | 146 |

TEE, total energy expenditure

Blood glucose levels on the five nondiabetic subjects remained below the target range of 240 mg/dL. Triglyceride values were all below 300 mg/dl. The results of serum prealbumin, nitrogen balance and RQ (the primary response variables) in all six subjects are summarized in Table VII.
### TABLE VII

**Results of primary response variables**

<table>
<thead>
<tr>
<th>PAB</th>
<th>PAB</th>
<th>PAB</th>
<th>N-Bal</th>
<th>N-Bal</th>
<th>RO</th>
<th>RO</th>
<th>RO</th>
<th>RO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day: 0</td>
<td>4</td>
<td>7</td>
<td>4</td>
<td>7</td>
<td>0</td>
<td>2</td>
<td>4</td>
<td>7</td>
</tr>
</tbody>
</table>

**NPC Group:**

| #1 | 12.4 | 10.1 | 3.0 | -1.1 | 0.83 | 0.83 | 0.84 | 0.83 |
| #2 | 11.5 | 7.7 | N/A | N/A | 0.75 | 0.81 | 0.84 | 0.84 |
| #6 | 10.7 | D/C | D/C |     | 0.78 | 0.90 | 0.85 | D/C |

**TC Group:**

| #3 | 19.7 | 22.5 | 5.0* | 4.2 | 0.96 | 0.85 | 0.83 | 0.93 |
| #4 | 30.4 | 37.7 | D/C | zero | D/C | 0.81 | 0.81 | 0.87 | D/C |
| #5 | 3.9 | 5.0 | 6.7 | -0.4 | 0.84 | 0.98 | 0.92 | 0.89 |

PAB, prealbumin; N-bal, nitrogen balance; RO, respiratory quotient; NPC, nonprotein calories; TC, total calories; N/A, not applicable; D/C, discontinued from study.

* Does not include measurement of 325 mL fistula output.

Blank areas represent missed data collection.
DISCUSSION

Some of the results obtained were consistent with the patients' clinical status and treatment. The decline in prealbumin in subject #2 may have been related to infection with diarrhea.

The positive trends in prealbumin in subjects #3 and #5 may have been due to refeeding following a period of poor nutritional intake (associated with greater than 10% body weight loss). The relatively high prealbumin level in subject #4 prior to full TPN may have been secondary to corticosteroid medication and adequate food intake just prior to TPN. Although not enough data was collected to draw any conclusions, it was interesting to note that all of the subjects in the TC group demonstrated increasing prealbumin levels, despite receiving only modest amounts of dextrose and fat.

The transient positive nitrogen balance on day 4 in subject #1 may have been secondary to refeeding following a period of starvation. There was also the possibility that the urine collection was incomplete, making the nitrogen balance appear falsely positive. The slightly negative nitrogen balance on day 7 may have been due to a more complete urine collection. Subject #1 was also affected by metastatic cancer and suboptimal glucose control (up to 306 mg glucose/dL) which tend to have a negative impact on nitrogen status.
Subject #3 appeared to be in positive nitrogen balance on days 4 and 7 of TPN despite being randomized to the TC (lower kilocalorie) group.

All nondiabetic subjects maintained blood glucose levels below 240 mg/dL regardless of their treatment group. Hypertriglyceridemia was not evident at baseline or at any point during the study. No subjects had a blood glucose, triglyceride level or RQ indicative of overt underfeeding or overfeeding while on full TPN.

These case studies demonstrate some of the difficulties in designing and executing research on humans in a typical hospital setting. Failure to enter a sufficient number of subjects was primarily due to the many exclusionary criteria and fewer patients on TPN than was originally predicted. The most common reasons that subjects were excluded or dropped from the study were the following:

(1) creatinine clearance <50 mL/min
(2) unable to use the metabolic cart, generally because of supplemental oxygen (face mask or nasal cannula)
(3) unable to accurately estimate nitrogenous losses because of diarrhea or wound drainage
(4) surgery during the study
(5) oral/enteral caloric intake during the study

Written consent was refused in three qualifying patients who were uncomfortable about having the canopy hood placed over their head. None of the six case reports had complete data.
Two of the patients dropped out before day seven. Laboratory tests were not executed, as ordered, in five of the six subjects, despite efforts by the principle investigator to avoid these human errors. (Appendix C.)

This study was conducted in a facility that had a metabolic research unit, although it would have been impossible to transfer the critically ill patients to that section of the hospital. Fewer omissions would have occurred if the research team had included a nurse or technician to draw the blood, collect the urine, properly label the laboratory order forms, and deliver the labeled specimens to the laboratory. However, even if complete data had been obtained on these six subjects, the problem of insufficient sample size would have still prevented any statistical analysis of the data.

Had a pilot study been conducted, the critical problem of inadequate numbers of qualifying subjects may have been identified. An attempt was made to make this a multi-center project. Ten teaching hospitals were asked to participate, however, they were unable to comply with the study design. Many of them did not have a properly functioning metabolic cart. One institution would have been able to participate, but did not have the personnel to commit to the project.

To overcome the problem of inadequate sample size, this study could be redesigned and performed on animals, such as rats. Another option would be to use outcome measures that do
not involve so many exclusion and removal criteria and also require minimal cooperation from the patient and medical staff. One good example of this is involuntary muscle function testing which utilizes mild electrical stimulation of the ulnar nerve at the wrist with measurements of the force of contraction and/or relaxation of the adductor pollicis muscle. This test does not require the cooperation of the patient and is not influenced by sepsis, drugs (including corticosteroids), surgery, or anesthesia. Results are also not likely to be affected by renal function, hepatic function, or oxygen requirements.

Research in hospitalized patients suggests that the force-frequency curve and/or the rate of relaxation of the electrically stimulated adductor pollicis muscle were sensitive and specific measures of nutrient status. When patients who had undergone cardiac operations started to eat enough to meet daily energy requirements, as estimated by the Harris-Bennedict formula, muscle function tests normalized. The same team also showed that muscle power can be doubled by giving nutrition support to malnourished preoperative cancer patients.

Another modification might be to study long-term TPN patients and use a cross-over design to reduce the number of subjects required. Of course this population would differ significantly from the mixed population of TPN patients encountered in a typical inpatient hospital setting.
CONCLUSIONS

At this time there is no conclusive evidence that there is any advantage or disadvantage in choosing to calculate TPN by including the potential kilocalories in protein (the TC method), or ignoring the caloric contribution of protein (the NPC method).

Given the difficulty in gathering enough data for this protocol and the relatively small differences in dextrose and fat between the two methods, this research design may not be worth pursuing further. A practical approach is to initially underfeed (Kcal ≤ basal energy expenditure), then increase kilocalories gradually while monitoring metabolic tolerance (e.g., blood glucose, triglycerides, minerals, liver function tests, and cardiopulmonary status) and in some patients, measuring REE.

All candidates for TPN should have their nutritional needs assessed and monitored by professionals knowledgeable in this area. The American Society for Parenteral and Enteral Nutrition stated that "The complication rate can be minimized through careful patient selection and by having experts in specialized nutrition support oversee the feeding program". 59

A number of studies have reported advantages in having a nutrition support team (consisting of a physician and dietitian and usually including a pharmacist and nurse). Reductions in TPN complications, such as abnormal blood glucose, were
associated with the presence of a support team.\textsuperscript{60,61,62,63}

Traeger et al\textsuperscript{59} also documented improvement in achieving the documented nutrition goals when a support team dietitian provided nutrition assessment. Precisely how kilocalories should be calculated and administered in parenteral solutions will require further research to define.
LITERATURE CITED


36. Harris JA, Benedict FG: A Biometric Study of Basal

41


44. Winkler MF, Gerrior SA, Pomp A: Use of retinol-
binding protein and prealbumin as indicators of the response to nutritional therapy. *J Am Diet Assoc* 89:684-689, 1989


50. Source of basic data: 1979 Build Study, Society of Actuaries and Association of Life Insurance Medical Directors of America, 1980


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APPENDIX A

VOLUNTEER AGREEMENT AFFIDAVIT

For use of the term, see AR 40-38 or AR 40-34. The Department of Defense (DOD)

PRIVACY ACT OF 1974

Authorizing:
10 USC 3013, 10 USC 3101 and 10 USC 4871-1887.

Prerequisite Purpose:
The purpose to document volunteer participation in clinical investigations and research. SSN and home address will be used for identification and tracking purposes.

Required Uses:
The SSN and home address will be used to identify and locate volunteer. Information derived from the study will be used to document the study. Information of medical problems, medication taken, or by the provisions of medical organizations as required by law. Information may be transmitted to Federal, State, and local agencies.

Disclosure:
The furnishing of your SSN and home address is mandatory and necessary to provide identification and to assist you if future information is needed. You may be further selected. Failure to provide the information may prevent you from participating in the investigative study.

PART A(1) - VOLUNTEER AFFIDAVIT

Volunteer Subjects in Approved Department of the Army Research Studies

Volunteers under the provisions of AR 40-38 and AR 70-25 are authorized all necessary medical care for injury or disease which is the probable result of their participation in such studies.

I, ________________, SSN ________________, having full capacity to consent and having attired my ________________, birthday, do hereby volunteer to consent as legal representative for ________________, to participate in ________________________________

EVALUATION OF NUTRITIONAL NEEDS IN TOTAL PARENTERAL NUTRITION

Based on Non-Protein Calories Versus Total Calories

under the direction of SANDRA E. SMITH, R.D., C.N.S.D.

conducted at WALTER REED ARMY MEDICAL CENTER, WASHINGTON, DC 20307-5001

I have been given an opportunity to ask questions concerning the investigational study. Any such questions were answered to my full and complete satisfaction. Should any further questions arise concerning my rights as a person, I represent as a study-assisted injury. I may contact CENTER JUDGE ADVOCATE OFFICE, (202) 782-1550 or Autovon 662-1550

WALTER REED ARMY MEDICAL CENTER, WASHINGTON, DC 20307-5001

I understand that I may at any time during the course of the study revoke my consent and withdraw from the study. If I do not revoke my consent and withdraw from the study, the person I represent shall be assent to participate in the study. If I do not revoke my consent and withdraw from the study, the person I represent shall be assent to participate in the study. I understand that while the study is underway, such examinations are necessary for my/her/his physical well-being.

LIMITATIONS TO MEDICAL CARE ARE DESCRIBED IN PART B.

PART A(2) - ABSENT VOLUNTEER AFFIDAVIT (MINOR CHILD)

I, ________________, SSN ________________, having full capacity to consent and having attired my ________________, birthday, do hereby volunteer for ________________, to participate in ________________________________

Conducted at ________________________________

(Continue on Reverse)

DA FORM 5303-R, MAY 89  

PREVIOUS EDITIONS ARE OBSOLITE
PART A(2) - ASSENT VOLUNTEER AFFIDAVIT (MINOR CHILD) (CON'T)

The implications of my voluntary participation; the nature, duration and purpose of the research study; the methods and means by which it is to be conducted; and the inconvenience and hazards that may reasonably be expected have been explained to me by

I have been given an opportunity to ask questions concerning the investigational study. Any such questions were answered to my full and complete satisfaction. Should any further questions arise concerning my rights I may contact


I understand that I may at any time during the course of this study revoke my assent and withdraw from the study without penalty or loss of benefits. However, I may be requested to undergo certain examinations, in the opinion of the attending physician, such examinations are necessary for my health and well-being. My refusal to participate will involve no penalty or loss of benefits to which I am otherwise entitled.

PART B - TO BE COMPLETED BY INVESTIGATOR

INSTRUCTIONS FOR ELEMENTS OF INFORMED CONSENT: (Provide a detailed explanation in accordance with Appendix C, AR 40-38 or AR 70-25)

NATURE OF STUDY

You are being asked to participate in this research project because you are to receive your nourishment through intravenous feeding. The purpose of this study is to evaluate two different ways to estimate the amount of calories given to patients who are getting all of their calories from a solution going into their vein (intravenous feeding). The number of calories given to patients through intravenous feeding can be determined with or without including the caloric contribution from protein. We would like to determine if one method provides a better measure of caloric needs than the other. Either method is safe and used by healthcare professionals.

If you agree to participate, you will be randomized (similar to the flip of a coin) to receive your daily nutritional feedings as determined by (1) total calories or (2) nonprotein calories. Medical history and laboratory results will be collected from your record. You will be given intravenous feedings at the same times you would be given them if you were not in this study. At the beginning of the study and at days 2, 4, and 7, an instrument called a metabolic cart will be used to tell us how many calories you need and how much work your breathing muscles are doing. These measurements are made by taking small samples of the air going into your lungs, as well as air coming out of your lungs. To perform this test, you will breathe by mouth into a clear hood for approximately 30 minutes. The instrument has no affect on how you breathe.

I do □ do not □ (check one & initial) consent to the inclusion of this form in my outpatient medical treatment record.

SIGNATURE OF VOLUNTEER DATE SIGNATURE OF LEGAL GUARDIAN (if volunteer is a minor)

PERMANENT ADDRESS OF VOLUNTEER TYPED NAME OF WITNESS

SIGNATURE OF WITNESS DATE

REVERSE OF DA FORM 5303-R, MAY 89

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DURATION OF PARTICIPATION

Your participation in this study will last 1 week, or less if you are removed from intravenous feedings before that time. The breathing tests take approximately 30 minutes to perform. It is not likely that your participation in this study will affect your recovery period or your length of time in the hospital.

FORESEEABLE RISKS OR DISCOMFORTS

There are no foreseeable risks or discomforts associated with your participation in this study.

BENEFITS TO SUBJECT

You may not benefit from this study, but the information we gain may help us learn how to better estimate the nutritional requirements of patients receiving intravenous feedings. The information obtained from the breathing tests may prove useful to your physician in adjusting your ventilator, as well as in ensuring your nutritional requirements are being met.

CONFIDENTIALITY OF SUBJECT IDENTITY/RESEARCH RECORDS

Research records of your participation in this study will be maintained by the principal investigator. These records may be reviewed by the WRAMC Department of Clinical Investigation and/or the WRAMC Human Use Committee/Institutional Review Board as part of their responsibilities for ensuring the protection of research volunteers, but confidentiality will be strictly maintained. You will not be identified by name in any publication or presentation resulting from this study.

CIRCUMSTANCES UNDER WHICH PARTICIPATION MAY BE TERMINATED WITHOUT SUBJECT’S CONSENT

Your participation may be terminated without your consent if health conditions or other conditions occur that might be dangerous or detrimental to you or your health, if military contingency requires it, or if you become ineligible for military medical care as authorized by Army Regulation.

LIMITATIONS TO MEDICAL CARE

Medical care is limited and will be within the scope authorized for Department of Defense health care beneficiaries. Necessary medical care does not include domiciliary (home and nursing home) care.

SAFEGUARDS

Your doctors do not think it is likely that it will make any difference whether or not protein calories are included in your daily calorie calculation process. Your daily calorie intake will be monitored by experts in nutrition.

<table>
<thead>
<tr>
<th>SIGNATURE OF VOLUNTEER</th>
<th>DATE SIGNED</th>
<th>SIGNATURE OF LEGAL GUARDIAN, IF VOLUNTEER IS A MINOR</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>PERMANENT ADDRESS OF VOLUNTEER</th>
<th>TYPED OR PRINTED NAME AND SIGNATURE OF WITNESS</th>
<th>DATE SIGNED</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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APPROXIMATE NUMBER OF SUBJECTS INVOLVED IN THE STUDY

There will be approximately 75 patients enrolled in this study.

ADDITIONAL COST THAT MAY RESULT FROM PARTICIPATION IN STUDY

There is no additional cost to you for your participation in this study.

ALTERNATIVE PROCEDURES OR COURSES OF TREATMENT

The alternative to participating in this study is not to participate, in which case your intravenous feedings and breathing tests would be determined by your healthcare provider. Your doctor can provide detailed information about your treatment and the benefits and risks of the variety of options available. You are encouraged to discuss this with your doctor.

SIGNIFICANT NEW FINDINGS TO CONTINUE PARTICIPATION

Any significant new findings that develop during the study which may affect your willingness to continue participation will be made available to you. The results of the research will be made available to you if you so desire.

A copy of this consent form will be provided to you.

SIGNATURE OF VOLUNTEER

DATE SIGNED

SIGNATURE OF LEGAL GUARDIAN (if volunteer is a minor)

PERMANENT ADDRESS OF VOLUNTEER

TYPE OR PRINTED NAME AND SIGNATURE OF WITNESS

DATE SIGNED

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APPENDIX B

DATA COLLECTION SHEET

Name:____________________ SSN:____ _______ Ward:__ Age:__
Sex:__ Ht:_____ Wt:____ Usual Wt:____ %UBW:__ Desirable Wt:
%DBW:____ Adjusted Wt:____ Physical Exam and Diet Hx:____________
____________________________________________________________________
Problem List: Sepsis, DM, etc._______________________________________
____________________________________________________________________
Surgery/date:_______________________________________________________
Medications (include steroids and amt. of IV dextrose):__________________
____________________________________________________________________
Current TPN: Full TPN Start Date:_______ Vol:_______ ml/d
Pro:____ g  Dex:____ g  Fat:____ g  NPC:____  TC:____
Labs:  Glu______mg/dL  TG____mg/dL  PAB____mg/dL
       Cr____mg/dL  Est. CrCl____ml/min
RQ:____ MREE:______Kcal/d X 1.05 (TEF)=_____
Activity Factors: X ____ AF
1.1 (bedrest) 1.2 (ambulation) Total EE=____ (TC)
Pro dose: 1.5 g X ___kg = ____g/d X 4=____ Pro Kcal/d
NPC Group: TC=____ X 0.6=___ / 3.4 = ____ g Dex;
           TC=____ X 0.4=___ / 10 = ____ g Fat
TC Group: TC=____ - ____Pro Kcal = ____NPC X 0.6 / 3.4 =
                  ____gDex;  NPC=____ X 0.4 / 10 = ____g Fat
Stratification: (1) ICU  (2) Sepsis  (3) steroids

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DATA SHEET - Page 2  Patient's Name

DAY 1:  Date:_____  
If nondiabetic, insulin given over 24 hr=____u  
GLU:____mg/dL  GLU:____mg/dL  GlU:____mg/dL  
NPC infused/d=____  TC infused/d=____  


DAY 2:  Date:_____  
If nondiabetic, insulin given over 24 hr=____u  
GLU:____mg/dL  GLU:____mg/dL  GLU:____mg/dL  
NPC infused/d=____  TC infused/d=____  
RQ:____  >1.0  <0.81  Change in AF to:_____  
MREE:_____ x ___AF=____ TEE  ____% Prev. TEE  
>10% of previous TEE; ___ >10% below previous TEE  
If RQ is ≥1.0, decrease Kcal by 10%=____ Kcal/d  
If RQ is <0.81, increase Kcal by 10%=____ Kcal/d  
Modification of TPN?  ( ) No  ( ) Yes:  
TC=____ or NPC=____ X 0.6 / 3.4 =____g Dex  
TC=____ or NPC=____ X 0.4 / 10 =____g Fat  


DAY 3:  Date:_____  
If nondiabetic, insulin given over 24 hr=____u  
GLU:____mg/dL  GLU:____mg/dL  GLU:____mg/dL  
NPC infused/d=____  TC infused/d=____  

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DAY 4: Date:____

If nondiabetic, insulin given over 24 hr=____u
GLU:____mg/dL  GLU:____mg/dL  GLU:____mg/dL
TG:____mg/dL    PAB____mg/dL
24 hr urinary: Cr____mg
UUN:______mg

+ 4000 mg
_______mg N IN - ________mg N Out = ________mg (N-Bal)
NPC infused/d=____  TC infused/d=____
RQ:____  ≥1.0  <0.81  Change in AF to:____
MREE:_______x_____AF=____ TEE  ___% Prev. TEE
___ >10% of previous TEE; ___ >10% below previous TEE
If RQ is ≥1.0, decrease Kcal by 10%=____ Kcal/d
If RQ is <0.81, increase Kcal by 10%=____ Kcal/d
Modification of TPN? ( ) No ( ) Yes
TC=_____ or NPC=_____ X 0.6 / 3.4 =_____g Dex
TC=_____ or NPC=_____ X 0.4 / 10 =_____g Fat

DAY 5: Date:____

If nondiabetic, insulin given over 24 hr=____u
GLU:____mg/dL  GLU:____mg/dL  GLU:____mg/dL
NPC infused/d=____  TC infused/d=____
DAY 6: Date:_____  
If non-diabetic, insulin given over 24 hr=___u  
GLU:_____mg/dL  GLU:_____mg/dL  GLU:_____mg/dL  
NPC infused/d=_____  TC infused/d=_____  

DAY 7: Date:_____  
If non-diabetic, insulin given over 24 hr=___u  
GLU:_____mg/dL  GLU:_____mg/dL  GLU:_____mg/dL  
TG:_____mg/dL  PAB:_____mg/dL  
24 hr urinary: Cr:_____mg  
UUN:_____mg  
+ 4000 mg  
_____mg N IN - _____mg N Out = _____mg (N-Bal)  
NPC infused/d=_____  TC infused/d=_____  
RQ:_____ ≥1.0 <0.81 Change in AF to:_____  
MREE:_____ x _____AF=_____ TEE _____% Prev. TEE  
___>10% of previous TEE; ___>10% below previous TEE  
If RQ is ≥1.0, decrease Kcal by 10%=_____ Kcal/d  
If RQ is <0.81, increase Kcal by 10%=_____ Kcal/d  
Modification of TPN? ( ) No ( ) Yes  
TC=_____ or NPC=_____ X 0.6 / 3.4 =_____g Dex  
TC=_____ or NPC=_____ X 0.4 / 10 =_____g Fat
APPENDIX C

NURSING RESPONSIBILITIES

for

TPN RESEARCH PROTOCOL

Patient Name:________________________

1. Please record blood glucose TID from:
   ______ to ______.

2. Please begin 24 hr urine collection on:
   ______, and ______, and ______.
   For each urine collection, use SF 548 Chem III (URINE), and
   identify the patient, date, time and volume of urine
   collection, and write "24 hr UUN and creatinine".

3. Please check to assure that AM blood draws for serum
   prealbumin and triglycerides are completed on :
   ______, and ______, and ______.

If you have any questions about this protocol, feel free to
contact Sandra Smith, R.D., at voice beeper 1712, or MAJ
Kushner, MD, at digital beeper 1654.
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Professional Experience

Walter Reed Army Medical Center, Washington, D.C.
Nutrition Support Dietitian, 1990 - Present

Luis A. Heffess, M.D., Washington, D.C.

Providence Hospital, Washington, D.C.
Clinical Dietitian, in critical care, 1986-1990

Buffalo General Hospital, Buffalo, New York
Diabetes Dietitian, 1984
General Clinical Dietitian, 1981-1983

Professional Associations

American Dietetic Association, 1980 - Present

Dietitians in Nutrition Support, Dietetic Practice Group,
American Dietetic Association, 1987 - Present

American Society for Parenteral and Enteral Nutrition, 1988 - Present

Registration / Certification

Registered Dietitian, Commission on Dietetic Registration,
American Dietetic Association, 1980 - Present

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Education

Virginia Polytechnic Institute and State University,
Blacksburg, Virginia; Masters of Science in Human Nutrition and Foods, 1995

State University College at Buffalo, Buffalo, New York;
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