Predictors of Total Parenteral Nutrition-Induced Lipogenesis*

John M. Guenst, M.D.; and Loren D. Nelson, M.D., F.C.C.P.

Objective: To evaluate the incidence and cause of parenteral nutrition-induced lipogenesis.

Design: Retrospective patient review.

Setting: A 40-bed predominantly surgical ICU.

Patients: One hundred forty patients receiving central venous nutrition and mechanical ventilatory support.

Interventions: Indirect calorimetry was used to determine patient’s measured energy expenditure (MEE) and respiratory quotient (RQ). Additionally total caloric intake (TCAL), glucose infusion rate, basal energy expenditure (BEE), estimated stress factor, and calculated energy expenditure (CEE) were assessed in each patient.

Measurements and main results: Net fat synthesis was found as RQs exceeded 1 in 47 percent of patients. Statistically significant differences in oxygen consumption, CO₂ production, measured energy expenditure, total and carbohydrate caloric intake, and glucose infusion rate were found between groups of patients with an RQ ≤ or > 1. Seventy-three percent of patients with glucose infusion rates > 4 mg/kg-min had RQs > 1.

Conclusions: Net fat synthesis was found in a surprisingly large number of critically ill patients receiving central venous nutrition. Many of these patients received carbohydrate calories in excess of their measured energy expenditure, even though it appeared that they needed this level of caloric intake by clinical assessment. The high carbohydrate total parenteral nutrition (TPN) solutions with lipids provided only for prevention of essential fatty acid depletion resulted in an unacceptably high incidence of fat synthesis. The results suggest that caloric intake may be optimized in critically ill patients using indirect calorimetry. When calorimetry is not available, a total caloric intake of up to 140 percent of the BEE with glucose infusion rates not exceeding 4 mg/kg-min and fats providing 40 to 60 percent of calories will meet the energy requirements of most critically ill patients without forcing the RQ > 1.

(Chest 1994; 105: 553-59)

Nutritional support regimens are designed to provide critically ill patients with optimenergy intake and produce minimal metabolic complications. Various monitors have been proposed to assure that these goals are being met. Respiratory quotient (RQ) is the ratio of carbon dioxide production (VCO₂) to oxygen consumption (VO₂) and is an indicator of substrate metabolism. The RQs for fat, protein, and glucose oxidation are 0.7, 0.8, and 1, respectively. An RQ greater than 1 indicates net fat synthesis from carbohydrate. Complications associated with carbohydrate overfeeding include hepatic steatosis, hypercapnia, hyperglycemia, and increases in O₂ consumption and CO₂ production. Increased urinary norepinephrine excretion with excessive carbohydrate administration also suggests that overfeeding may pose an additional stress in critically ill patients.

During routine patient care, energy expenditure generally is calculated (CEE) from the basal energy expenditure (BEE) determined using the Harris-Benedict equations and a clinically estimated stress factor. More recently, indirect calorimetry has been used clinically to determine actual measured energy expenditure (MEE).

The purpose of this study was to determine the incidence and causes for net fat synthesis during total parenteral nutrition (TPN) in critically ill, mechanically ventilated patients and to suggest means by which caloric intake in this patient population may be optimized.

Materials and Methods

Patient Population

The records of 140 consecutive critically ill patients studied by indirect calorimetry while receiving TPN and mechanical ventilation were reviewed. No specific groups of patients were selected and no randomization was used to decide which patients would be studied. Often patients who had difficulty in weaning from mechanical ventilatory support as manifested by high minute ventilation and/or carbon dioxide retention were studied. The service distribution of patients was approximately 60 percent cardiac surgery, 25 percent internal medicine, and 15 percent general and vascular surgery. One hundred forty complete data sets were available in 120 of the patients. Eight patients were admitted with the primary diagnosis of sepsis and 12 other patients had primary admission diagnoses of surgical conditions associated with sepsis (ie, perforated viscus). Five patients were admitted with the primary diagnosis of decompensated COPD, 4 with pneumonia, 1 with congestive heart failure, 5 with adult respiratory distress syndrome, and 13 with unspecified respiratory failure. The other 92 patients were admitted to the ICU with primary surgical diagnoses, stroke, or renal failure. Routine postoperative patients were not studied and nearly all of the study patients had received mechanical ventilatory support.
for more than 48 h. All studies were performed in the 40-bed ICU of a large private practice hospital providing primary, secondary, and some tertiary care (St. Thomas Hospital, Nashville, Tenn.). All patients were assessed by the nutritional support team prior to the metabolic measurements. Recommendations regarding total caloric intake were made using a Harris-Benedict calculation of BEE times an estimated stress factor based on severity of illness and activity. The stress factors most commonly used by the consulting nutritional support service were based on anticipated activity of the patient plus an increase of 10 percent above BEE for routine postoperative patients, 20 percent above BEE for patients with fractures or multiple trauma, and 40 percent above BEE for patients with sepsis. Amino acid administration was calculated to achieve positive nitrogen balance. The standard hospital central venous nutrition formulation was 4.25 percent amino acids and, on consultation with the nutritional support service, supplements up to 7.5 percent amino acids were available. Dextrose concentrations were generally 25 percent but ranged from 5 percent to 25 percent. Fat emulsions were given as 10 percent and 20 percent solutions administered over 6 to 8 h, twice per week to prevent essential fatty acid deficiency. Patients were monitored with daily and weekly laboratory tests to optimize electrolytes, acid-base status, and coagulation status. Adjustments were made to composition and rate of administration of central venous nutrition as needed. Insulin was added as needed to maintain serum glucose levels between 150 and 250 mg/dl and to prevent glycosuria. The serum triglyceride concentration was monitored with the goal to maintain basal levels 6 h after the lipid infusion was terminated. Energy expenditure was generally measured at least 24 to 48 h after the patient had reached the estimated target for nutritional intake.

Substrate administration, age, sex, height, weight, urine urea nitrogen, ventilatory support level, acid-base balance, oxygen consumption, carbon dioxide production, RQ, and MEE were recorded. Nitrogen balance was calculated as the nitrogen intake (g/d) minus the urinary urea nitrogen output and 4 g for daily insensible losses.

### Table 1—Physical Data and Ventilatory Support Levels*

<table>
<thead>
<tr>
<th>All Patients</th>
<th>RQ≤1</th>
<th>RQ &gt; 1</th>
<th>t Value</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No.</td>
<td>140</td>
<td>74</td>
<td>66</td>
<td>–</td>
</tr>
<tr>
<td>Age, yr</td>
<td>66±14</td>
<td>65±14</td>
<td>67±15</td>
<td>-0.7 NS</td>
</tr>
<tr>
<td>Height, cm</td>
<td>168±7.9</td>
<td>169.2±8.6</td>
<td>168.1±9.9</td>
<td>0.5 NS</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>69.3±15.8</td>
<td>72.6±14.3</td>
<td>66.1±16.6</td>
<td>2.2 &lt;0.05</td>
</tr>
<tr>
<td>BSA, m²</td>
<td>1.79±0.21</td>
<td>1.83±0.2</td>
<td>1.75±0.22</td>
<td>0.2 &lt;0.05</td>
</tr>
<tr>
<td>Fio₂</td>
<td>0.40±0.08</td>
<td>0.40±0.08</td>
<td>0.40±0.08</td>
<td>0.1 NS</td>
</tr>
<tr>
<td>IMV rate</td>
<td>10.4±6.8</td>
<td>9.9±5.0</td>
<td>11.0±5.4</td>
<td>-0.9 NS</td>
</tr>
<tr>
<td>TV, ml</td>
<td>883±140</td>
<td>904±146</td>
<td>860±130</td>
<td>1.8 NS</td>
</tr>
<tr>
<td>Total MV, L/min</td>
<td>12.4±5.0</td>
<td>11.5±4.5</td>
<td>13.5±5.3</td>
<td>-2.2 &lt;0.05</td>
</tr>
</tbody>
</table>

*Data in all tables are mean values ± standard deviations. BSA = body surface area; IMV = intermittent mandatory ventilation rate (breaths per minute); TV = tidal volume; MV = minute ventilation.

Measured energy expenditure and RQ were used to evaluate patient response to total caloric intake (TCAL) and glucose infusion rate. Three additional indices were defined to evaluate the relationship between substrate administration and the patients’ energy requirements. The TCAL divided by MEE assesses the relationship between caloric load and actual energy expenditure. Total caloric intake divided by BEE assesses the relationship between caloric load and the Harris-Benedict derived basal energy expenditure. The actual stress factor (SF) is equal to MEE divided by the Harris-Benedict-derived BEE (actual SF = MEE/BEE).

### Table 2—Metabolic Indices and Nutritional Support Variables*

<table>
<thead>
<tr>
<th></th>
<th>All Patients</th>
<th>RQ≤1</th>
<th>RQ &gt; 1</th>
<th>t Value</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RQ</td>
<td>1.0 ± 0.1</td>
<td>0.9 ± 0.1</td>
<td>1.1 ± 0.1</td>
<td>14.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Vₜₒ₂</td>
<td>131 ± 28</td>
<td>138 ± 40</td>
<td>123 ± 23</td>
<td>2.5</td>
<td>&lt;0.025</td>
</tr>
<tr>
<td>VcO₂</td>
<td>130 ± 27</td>
<td>125 ± 26</td>
<td>137 ± 27</td>
<td>-2.3</td>
<td>&lt;0.025</td>
</tr>
<tr>
<td>BEE</td>
<td>1,384 ± 233</td>
<td>1,427 ± 221</td>
<td>1,342 ± 238</td>
<td>-1.9</td>
<td>NS</td>
</tr>
<tr>
<td>CEE</td>
<td>1,875 ± 320</td>
<td>1,901 ± 308</td>
<td>1,850 ± 330</td>
<td>0.6</td>
<td>NS</td>
</tr>
<tr>
<td>MEE</td>
<td>1,665 ± 394</td>
<td>1,781 ± 431</td>
<td>1,576 ± 313</td>
<td>3.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Estimated SF</td>
<td>1.31 ± 0.08</td>
<td>1.31 ± 0.09</td>
<td>1.30 ± 0.07</td>
<td>0.6</td>
<td>NS</td>
</tr>
<tr>
<td>MEE/BEE</td>
<td>1.20 ± 0.25</td>
<td>1.22 ± 0.26</td>
<td>1.17 ± 0.23</td>
<td>1.1</td>
<td>NS</td>
</tr>
<tr>
<td>TCAL/BEE</td>
<td>1.34 ± 0.57</td>
<td>1.17 ± 0.56</td>
<td>1.51 ± 0.541</td>
<td>-3.2</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td>TCAL</td>
<td>1,855 ± 774</td>
<td>1,873 ± 774</td>
<td>2,060 ± 720</td>
<td>-3.1</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td>Glucose intake</td>
<td>3.70 ± 1.82</td>
<td>2.89 ± 1.34</td>
<td>4.45 ± 1.88</td>
<td>-5.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>TCAL/MEE</td>
<td>1.11 ± 0.43</td>
<td>0.94 ± 0.41</td>
<td>1.30 ± 0.37</td>
<td>-5.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CHO CAL</td>
<td>1,204 ± 530</td>
<td>1,037 ± 495</td>
<td>1,383 ± 498</td>
<td>-4.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CHO%</td>
<td>69 ± 19</td>
<td>68 ± 20</td>
<td>69 ± 16</td>
<td>-0.6</td>
<td>NS</td>
</tr>
<tr>
<td>N₂ Intake</td>
<td>11.9 ± 4.8</td>
<td>10.8 ± 4.5</td>
<td>13.2 ± 4.8</td>
<td>-3.0</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td>N₂ Balance</td>
<td>-5.6 ± 7.1</td>
<td>-6.6 ± 6.2</td>
<td>-4.7 ± 7.8</td>
<td>-1.1</td>
<td>NS</td>
</tr>
</tbody>
</table>

*Vₒ₂ = oxygen consumption (ml/min/m²); VcO₂ = carbon dioxide production (ml/min/m²); BEE = basal energy expenditure (kcal/d); CEE = calculated energy expenditure (BEE × estimated SF, kcal/d); MEE = measured energy expenditure (kcal/d); SF = stress factor; TCAL = total caloric intake (kcal/d); glucose intake = glucose intake (mg/kg/min); CHO CAL = carbohydrate caloric intake (kcal/d); CHO% = percentage of nonprotein calories given as carbohydrates; N₂ Intake = nitrogen intake (g/d); N₂ Balance = nitrogen balance (g/d).

†Different from MEE/BEE ratio (p <0.003).

†Different from MEE/BEE ratio (p <0.01).

Predictors of TPN-induced Lipogenesis (Guernst, Nelson)
use in critically ill patients receiving mechanical ventilatory support.\(^\text{12}\) Clinically valid measurements of VO\(_2\) and VCO\(_2\) are attainable when the proper interface is obtained among the patient, ventilator, and the MGM device. Since this is an “open system” device, errors may be induced when patients are receiving high oxygen concentrations. No patient in this study was receiving FiO\(_2\) > 0.60 at the time of study. Thirty-minute measurements were made while the patients were hemodynamically stable and at a time representative of their overall activity. Values for energy expenditure (MEE), VO\(_2\), VCO\(_2\), and RQ were recorded on reaching steady state. The VO\(_2\) and VCO\(_2\) were indexed to body surface area to allow comparisons between patients.

**Statistical Analysis**

Measurements are expressed as mean ± SD. Student’s t test for unpaired data was used for determinations of differences in mean values between subgroups. A paired t test was used to compare mean values of data on patients within subgroups. Correlation between values was assessed by linear regression analysis. Fisher’s exact test was used to compare ratios of nonparametric data. Probability values less than 0.05 were considered statistically significant.

**RESULTS**

Physical measurements and ventilatory support levels at the time of study are shown for the 140 patients in Table 1. Two groups of patients were identified. Sixty-six of 140 (47 percent) had an RQ > 1 at the time of metabolic assessment. The other 74 patients had an RQ ≤ 1. Statistically significant differences between the two groups were observed for weight, body surface area, and total minute ventilation. There was no statistical correlation between either body weight or surface area and RQ (r = −0.25 and −0.23, p = 0.05).

Table 2 presents results of metabolic and nutritional support variables studied. Statistically significant differences between the two groups were observed for VO\(_2\), VCO\(_2\), MEE, total infused calories, glucose infusion rate, and nitrogen intake. There were no statistical differences between groups for the following: BEE, CEE, clinically estimated SF, actual SF (MEE/BEE), percentage of nonprotein calories as carbohydrate, or nitrogen balance.

The estimated and actual SFs of patients with RQs > 1 and RQs ≤ 1 were not statistically different. However, patients with an RQ > 1 had a statistically greater TCAL/BEE ratio than those with an RQ ≤ 1 (p < 0.005; Table 2). In patients with RQ ≤ 1, there was no statistical difference between their actual SF and TCAL/BEE ratio. There was a statistical difference between actual SF and TCAL/BEE ratio in those with RQ > 1 (p < 0.01, Table 2).

Table 3 shows the results for the 92 patients who received a TCAL greater than their actual metabolic needs (MEE). Statistically significant differences were observed between subgroups with RQ ≤ 1 and RQ > 1 for the percentage of nonprotein caloric intake as carbohydrate and glucose infusion rate. There were no statistical differences between the subgroups for TCAL/MEE ratio, actual SF, carbohydrate caloric intake, or MEE. For both groups of patients, MEE was significantly greater than the amount of carbohydrate caloric intake (p < 0.001, Table 3).

Figure 1A shows the relationship between actual SF (MEE/BEE) and the TCAL/BEE ratio. The correlation was statistically significant (r = 0.52, p < 0.001). The actual SF was statistically less than the TCAL/BEE ratio (1.20 ± 0.25 vs 1.34 ± 0.57, p < 0.002, Table 2). No correlation existed between actual SF and RQ (r = −0.04, p = 0.707, Fig 1B). However, there was a statistically significant correlation between TCAL/BEE ratio and RQ (r = 0.45, p < 0.001, Fig 1C). As the TCAL/BEE ratio increases above 1, the percentage of patients with RQs > 1 increases. Forty-five patients have TCAL/BEE ratios ranging from 0.8 to 1.4: 42 percent had RQs > 1. When the TCAL/BEE ratios were above 1.4, 31 of 48 patients (65 percent) had RQs > 1. Of 35 patients having TCAL/BEE ratios > 1.6, 69 per-

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**Table 3—Metabolic Indices of Patients with Total Caloric Intake > MEE**

<table>
<thead>
<tr>
<th>Patients With Total Caloric Intake &gt; MEE</th>
<th>RQ≤1</th>
<th>RQ&gt;1</th>
<th>t Value</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>92</td>
<td>33</td>
<td>59</td>
<td>0.8</td>
</tr>
<tr>
<td>TCAL/MEE ratio</td>
<td>1.35 ± 0.26</td>
<td>1.30 ± 0.20</td>
<td>1.39 ± 0.28</td>
<td>−1.8</td>
</tr>
<tr>
<td>MEE/BEE ratio</td>
<td>1.19 ± 0.22</td>
<td>1.2 ± 0.2</td>
<td>1.19 ± 0.23</td>
<td>0.2</td>
</tr>
<tr>
<td>CHO-CAL</td>
<td>1.405 ± 0.435</td>
<td>1.315 ± 0.392</td>
<td>1.455 ± 0.401</td>
<td>−1.6</td>
</tr>
<tr>
<td>MEE</td>
<td>1.627 ± 0.318</td>
<td>1.705 ± 0.290</td>
<td>1.584 ± 0.319</td>
<td>1.8</td>
</tr>
<tr>
<td>CHO %</td>
<td>65 ± 14</td>
<td>60 ± 13</td>
<td>67 ± 15</td>
<td>2.5</td>
</tr>
<tr>
<td>Glucose intake</td>
<td>4.49 ± 1.60</td>
<td>3.84 ± 1.08</td>
<td>4.5 ± 1.71</td>
<td>−2.9</td>
</tr>
</tbody>
</table>

*TCAL = total caloric intake (kcal/d); MEE = measured energy expenditure (kcal/d); BEE = basal energy expenditure (kcal/d); CHO-CAL = total carbohydrate caloric intake (kcal/d); CHO% = percentage of nonprotein calories given as carbohydrate; glucose intake = glucose intake (mg/kg/min).

†Different from MEE (p < 0.001).
percent had RQs > 1. When Fisher’s exact test is performed for RQ ≤ 1 or > 1 for TCAL/BEE ratio 0.8 – 1.4 or > 1.4, there is a statistical difference in the proportion of patients with RQ > 1 when TCAL/BEE ratio exceeds 1.4 (p < 0.0003).

A moderate correlation exists between RQ and the TCAL/MEE ratio (r = 0.54, p < 0.001, y = 0.83 + 0.16x, Fig 1D). When the total calories delivered equals the MEE, the predicted value of RQ is 0.99. Fifty-nine of 92 patients (64 percent positive predictive value) with TCAL/MEE ratios > 1 have RQs > 1. A TCAL/MEE ratio > 1 detected 59 of 66 patients (89 percent sensitivity) with RQs > 1. However, 33 of 74 patients with RQ ≤ 1 had a TCAL/MEE ratio > 1 (55 percent specificity).

A moderate correlation exists (r = 0.55, p<0.001) between glucose infusion rate and RQ (Fig 2). A glucose infusion rate of 4 mg/kg-min (actual body weight) corresponds to a predicted RQ of 1.04. Seventy-three percent of the patients having glucose infusion rates > 4 mg/kg-min had RQs > 1.

When Fisher’s exact test is applied to those with glucose infusion rates ≤ 4 or > 4 mg/kg-min, there is a statistically greater proportion of patients with RQ > 1 when glucose infusion rate exceeds 4 mg/kg-min (p < 0.0002).

**DISCUSSION**

Optimal nutritional support for critically ill patients has been a growing concern during the past decade. Improvements of life support measures and advancements in medical technology have improved survival for these patients. Nutritional assessment and support have become important elements of patient treatment and in some patients may be the limiting factor to recovery.

Much has been written about means of evaluating energy requirements and nutritional support regimens. An appropriate balance between overfeeding and underfeeding is especially important in critically ill patients. Support regimens may overestimate patients needs through errors associated with the application of the Harris-Benedict equa-
tions in disease and nutritional states which cause variation in energy expenditure,\(^6\) through linkage of caloric intake to nitrogen balance,\(^7\) by using inappropriately high SF during convalescence,\(^7\) and by using inappropriately high activity factors.\(^8\) Differences in therapy may markedly alter the relationship between perceived and actual energy requirements.

In this study, 47 percent of patients had RQs > 1, indicating net fat synthesis. Their caloric intake was statistically greater than their actual energy expenditure (MEE). Figure 1D shows that when total caloric intake exceeds MEE, the RQ is likely to increase.

The RQs were more likely to exceed 1 when carbohydrate infusion rates exceeded 4 mg/kg-min. Maximum glucose infusion rate tolerances have been reported before and appear to be prevalent in this group of patients.\(^1\)

The fact that there are no significant differences in the clinical estimate of energy needs (BEE, SF, CEE) between the two groups of patients implies that the groups were clinically assessed to be similar. Despite the apparent equality of estimated energy needs, the group with RQ > 1 actually had a slightly lower mean weight and body surface area and significantly lower MEE. Yet, this group received more total calories, more carbohydrate calories, and a higher glucose infusion rate than did the group with RQ ≤ 1.

For the total patient population, the carbohydrate composition of nonprotein calories was not significantly different between groups (Table 2). However, in the patients who received a TCAL greater than their MEE (Table 3), the carbohydrate percentage of nonprotein calories was significantly greater in patients with RQs > 1. Since the groups were separated by their relative substrate utilization after they had reached their clinically predicted nutritional target, it is apparent that overfeeding above their actual caloric needs altered substrate utilization resulting in fat synthesis.

The reason that the patients were overfed is not entirely clear. The RQ > 1 group may have appeared more stressed, thereby influencing clinicians to apply a higher estimated SF and therefore overfeed in an attempt to meet the patient’s clinically estimated caloric needs. Also, since nutritionally depleted states have been associated with energy expenditures below the predicted normal,\(^2\) some of these patients may have received nutritional support in excess of their needs in their weakened state. Finally, the patients may have received excess carbohydrate calories in an attempt to achieve a positive nitrogen balance using a solution containing a fixed carbohydrate to nitrogen ratio.

While there was no statistical difference between the mean nitrogen balances between groups, the group with a RQ > 1 achieved a nitrogen balance that was closer to neutral. The vast majority of these patients received a parenteral solution containing 25 percent dextrose and 4.25 percent amino acids. Lipid was generally given as 250 to 500 ml of 10 percent solution twice per week to prevent essential fatty acid deficiency. In order to achieve an amino acid administration of 1.5 g/kg (body weight) to a 70-kg patient, 2.47 L of solution per day must be administered. This results in 2,100 kcal/d of carbohydrate infusion (assuming a CHO:N\(_2\) ratio of 125:1). Since the mean MEE in the RQ > 1 patients was only 1,576 kcal/d, it is easy to see how patients may have been overfed carbohydrate calories.

The group of patients in this study who were overfed received an actual protein intake of 1.25 g/kg/d. At a fixed CHO:N\(_2\) ratio, they received carbohydrate calories in excess of their total energy expenditure from the parenteral dextrose/amino acid solution alone. Other caloric sources such as 5 percent dextrose solutions, intravenous lipid emulsions, and, in some, carbohydrate-containing enteral feedings contributed to their overfeeding. Whatever reason or reasons existed, the fact remains that the patients with RQ > 1 received a greater mean caloric intake but had a lower MEE than those patients with RQ ≤ 1.

The calculation of the TCAL/BEE ratio may be useful in the assessment of critically ill patients needing nutritional support. This ratio is an “implied” stress factor indicating the actual degree of caloric intake above the basal needs as estimated by the Harris-Benedict equations. Much as the estimated SF is our best guess of what the patient’s needs will be over basal requirements, the implied SF (TCAL/BEE) describes what the patient is actu-
ally receiving in relation to basal requirements.

Similarly, calculation of the TCAL/MEE ratio provides a "caloric support index" revealing the degree of actual caloric intake above the MEE. When the caloric support index is greater than 1, fat synthesis is more likely.

To avoid complications of carbohydrate overfeeding, mixed fuel regimens have been advocated.\textsuperscript{4,14-25} With a mixed fuel system, the RQ should not exceed 1 if the carbohydrate load is significantly less than the MEE.\textsuperscript{26} On the other hand, altered responses in hypermetabolism\textsuperscript{27} may account for a number of patients who were apparently overfed but had RQs \( \leq 1 \). While overfeeding of carbohydrates may cause fat synthesis, exceptions may occur in hypermetabolic patients in whom carbohydrate loading may increase both \( \text{VCO}_2 \) and \( \text{VO}_2 \) with little change in RQ.\textsuperscript{28}

Fat synthesis is an energy-requiring process\textsuperscript{29} and therefore may increase metabolic demands on the patient. In addition, overfeeding in normal subjects increases diet-induced thermogenesis from a normal of 10 percent of energy expenditure to as much as 27 percent of total energy expenditure.\textsuperscript{28} Finally, maximal increases in nitrogen balance occur at caloric intakes approaching MEE with little gain from further increases in caloric intake.\textsuperscript{29} There may be a maximum rate at which administered amino acids may be retained. Above this maximum there is no benefit to increasing nitrogen intake and further metabolic stress may result by overfeeding.\textsuperscript{30}

Meeting measured metabolic needs should optimize nutritional support for patients coping with acute illnesses. Caloric administration in excess of energy expenditure, on the other hand, creates additional physiologic stress.\textsuperscript{31,13} Increases in the likelihood of fat synthesis and fatty liver with altered hepatic function test results, and may precipitate carbon dioxide retention.\textsuperscript{6}

To avoid the complications of caloric underfeeding or overfeeding, one goal of nutritional support in the critically ill should be to match energy balance so that total caloric intake equals MEE.\textsuperscript{15,18,31,32} If meeting the patient's energy requirements with predominantly glucose-containing solutions results in fat synthesis manifested by an RQ > 1, the caloric intake from lipids may be increased to 40 to 60 percent of the total intake.\textsuperscript{23} The patient's substrate utilization may then be reassessed. This technique allows accurate initial nutritional assessment and easy follow-up in patients with varying nutritional needs.\textsuperscript{18,19} The measurement of metabolic energy expenditure remains valid under conditions of simultaneous synthesis and oxidation of lipids\textsuperscript{10} and accounts for diet-induced thermogenesis.\textsuperscript{31}

There is considerable nutritional variability among critically ill patients and the amount of stress incurred from critical illness.\textsuperscript{13,33} Nutritional support can be tailored to meet individual patient needs. Caloric substrates should be balanced between fats and carbohydrates and indirect calorimetry may help to prevent overfeeding or underfeeding complications. The total caloric intake should be based initially on a logical estimated value, monitored closely, and adjusted as necessary according to the patient's actual substrate utilization.

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The American Euro '94 program will be held June 30-July 2 in Vienna, Austria. Sponsor is the Vienna International Society for Medical Education and Preventive Medicine. For information, contact WELL DONE EVENTS, Mariannengasse 14/12, A-1090 Vienna, Austria.