Measured energy expenditure of tube-fed patients with severe neurodevelopment disabilities

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Objective: To determine measured resting energy expenditure (REE) of nonambulatory tube-fed patients with severe neurological neurodevelopmental disabilities.

Methods: Twenty patients were prospectively studied. Only steady state indirect calorimetry measurements were taken. All measurements were conducted using a canopy system. Nutritional needs were met entirely by enteral feedings via a permanent ostomy.

Results: REE was widely distributed from 16 kcals/kg/day to 39 kcals/kg/day. The mean REE (888 ±176 kcals/day) of the patients was significantly (p < 0.01) lower than predicted as estimated by the Harris-Benedict equations (1081 ± 155 kcals/day) and World Health Organization equations (1194 ± 167 kcals/day). Fat-free mass (FFM) was the best parameter for predicting REE. Two predictive equations were developed that are not significantly biased and more precise (≤ 15% error) than conventional predictive formulas.

Conclusion: Conventional formulas for estimating energy expenditure are inaccurate and generally overestimate measured energy expenditure of nonambulatory patients with severe developmental disabilities.

Introduction

Malnutrition is commonly associated with patients with neurodevelopmental disabilities and is likely due to inadequate intake and a host of medical problems including gastroesophageal reflux disease, swallowing disorders, chronic pulmonary and urinary tract infections, and spastic quadriplegia. As a result, defining the appropriate amount of calories to give to the patient with severe neurodevelopmental disabilities can be problematic. Estimates of energy requirements based on predictive equations such as the Harris-Benedict and the joint FAO/WHO/UNU Expert Consultation on Energy and Protein Requirements equations are limited in that these estimates of basal energy metabolism were derived from normal healthy subjects. Data regarding resting and total energy expenditure of children and adolescents with developmental disabilities is emerging. Resting energy expenditure of ambulatory adult patients with cerebral palsy and athetosis has been described. However, these data do not apply to our population. Currently, there are no data in the literature regarding the energy expenditure of nonambulatory adolescent and adult patients with severe neurodevelopmental disabilities that require nutrition solely by permanent ostomy. This deficit of knowledge is important to investigate because the majority of even the most severely involved children with neurodevelopmental disabilities are expected to survive until adulthood. The intent of this
study was to ascertain the measured resting energy expenditure (REE) of nonambulatory adolescent and adult tube-fed patients with severe neurodevelopmental disabilities and to assess the accuracy of conventional predictive formulas in estimating energy expenditure in this population.

Materials and Methods

Patients
Patients referred to the Pharmacist-based Nutritional Consultative Service for evaluation of enteral tube feeding via a permanent ostomy at a 380 bed state-funded regional center for developmentally disabled citizens (Arlington Developmental Center) were reviewed for potential inclusion into the study. The role and clinical impact of this clinical pharmacist-based consult service has been described elsewhere. Resting energy expenditure, laboratory and nutritional assessment were conducted as part of the routine clinical care of these patients. Patients excluded were those with malignancy, active systemic infection requiring antibiotic therapy, admission to the infirmary (a nursing ward for intensive patient observation) within 5 days prior to the measurement, fever (> 38°C), hypothermia (< 37°C) or those having a seizure on the same day prior the measurement. Hypothyroidism was excluded by measuring free thyroxine and thyroid stimulating hormone levels. Laboratory tests were requested by the primary care physician as part of the patient’s routine clinical care and were performed by an outside hospital laboratory. This study was approved and conducted in accordance with the guidelines established by the University of Tennessee Investigational Review Board. Since the energy assessment was performed as part of the routine metabolic evaluation of the patient, informed consent was waived.

Nutritional Assessment and Anthropometric Measurements
A nutritional assessment was conducted for all patients entered into the study. This assessment included examination of body fat by anthropometry; changing trends in body weight or growth in adolescent subjects; examination of serum proteins, serum electrolytes and minerals, red blood cell count (including hemoglobin, hematocrit, red blood cell indices, ferritin), prothrombin time, and selected vitamin levels; physical exam to assess fluid status, evidence of any nutritional deficiencies (e.g., skin rashes, angular stomatitis, etc.) and abdominal activity (presence of distention, bowel sounds, etc.). Current body weight was obtained by use of a body sling and height was determined in body segments due to the presence of severe scoliosis and extremity contractures (spasticity) exhibited by the patients. Body fat stores were calculated from the average of three consecutive tricep skinfold (TSF) and calf skinfold (CSF) measurements done with a Lange Skinfold Caliper® (Cambridge Scientific Industries, Cambridge, MD) according to the methods and formulas of Slaughter. Since the combination of tricep and calf skinfold measurements have been found to correlate best with body composition analysis (by isotopic dilution and bone mineral density measurements; \( r^2 = 0.80 \) and mean error of 3.8%), the following equations were used to estimate percent body fat:

\[
\text{Percent Body Fat} = \left( \frac{\text{TSF} + \text{CSF}}{2} \right) 
\]
Males: % body fat = 0.735 (sum of TSF and CSF(mm)) + 1.0

Females: % body fat = 0.610 (sum of TSF and CSF(mm)) + 5.1

This technique has been validated in children and adolescents with cerebral palsy by comparison to isotope dilution techniques.\textsuperscript{4,14} Fat-free mass was then calculated by subtracting body fat weight (derived from % body fat) from current body weight. Adolescents were confirmed as peripubescent based on a modification of the Tanner scale.\textsuperscript{20,21}

\textit{Indirect Calorimetry Measurements}

Resting energy expenditure measurements were performed by indirect calorimetry using a computer-interfaced, ventilated canopy system with a differential paramagnetic oxygen analyzer, infrared carbon dioxide analyzer, Fleish pneumotachometer, and a baffled 3 liter mixing chamber (MetaScope II, Colorado MedTech, Boulder, CO). The indirect calorimetry measurements were performed in 20-minute intervals up to a maximum of three intervals per patient until steady state measurements were achieved. Inspired room air measurements (inspired oxygen fraction or FiO2 and inspired carbon dioxide fraction or FiCO2) were performed during the initial and final 2 minutes of the interval. Expired oxygen fraction (FeO2) and expired carbon dioxide fraction (FeCO2) were measured during the middle 16 minutes of the interval. Initial and terminal inspiratory gas fraction values were averaged and used as the mean FiO2 and FiCO2 values for the interval. This process provides adjustments for the effects of small variations in FiO2 and FiCO2, barometric pressure, and minor analyzer drifts.\textsuperscript{22} Gas analyzers were calibrated immediately prior to each measurement using 95\% oxygen/5\% carbon dioxide and 100\% nitrogen reference gases. FiO2 stability was documented immediately prior to each patient measurement and a mean oxygen consumption sensitivity error of \( \leq 5\% \) was achieved before proceeding to the patient care measurement.\textsuperscript{23} Daily pneumotachograph calibration was conducted using a 3 liter syringe; three consecutive determinations with < 1\% error from predicted was accepted for successful calibration. Barometric pressure was calibrated using the institutional reference barometric pressure from the pulmonary function laboratory of the Regional Medical Center at Memphis, Memphis, TN.

Most gas exchange measurements were performed between 1000 and 1600 hours provided that at least 2 hours had elapsed from nutrient administration for those receiving intermittent feedings to minimize error from diet-induced thermogenesis.\textsuperscript{24} All patients were lying in bed or a sling or sitting inclined at rest for at least 30 minutes prior to measurement. The patients were kept in a thermoneutral environment. Steady state gas exchange measurements were used to determine oxygen consumption and carbon dioxide production rates which were then applied to the modified Weir formula to calculate REE.\textsuperscript{25} Steady state was defined as five consecutive 1-minute sampling intervals where the coefficient of variation for oxygen consumption, carbon dioxide production, and respiratory quotient were equal to or less than 5\%.\textsuperscript{26} Measured resting energy expenditure was expressed in kcals/day and as a percent of predicted energy expenditure based on the Harris-Benedict and World Health Organization (WHO) formulas\textsuperscript{12,13} generated from gender, (segmented) height (in Harris-Benedict but not WHO equations), age, and actual body
weight. Using these techniques, Feurer et al. demonstrated that 95% of 72 normal adults were within ± 15% of predicted values\textsuperscript{24} and the mean difference between measurements that are performed on the same patient at various times throughout the day were 1 ± 9%.\textsuperscript{27} Further research in studying different disease states by the principal investigator using these methods documents the reliability of determining resting energy expenditure by use of these techniques.\textsuperscript{28-32} Application of these techniques at our institution demonstrated that 90% of ten normal adults had a measured resting energy expenditure within ± 10% of predicted values and all were within ± 12% of predicted values (unpublished data).

\textit{Data Analysis and Statistics}
Continuous data were expressed as mean ± standard deviation. All statistical analyses conducted using SPSS\textsuperscript{®} for Windows\textsuperscript{TM} version 6.1 (SPSS Inc., Chicago, IL). Predicted and measured values were compared by the t-test for paired values. The Student t-test for independent variables were used to ascertain significant differences between adolescent and adult subgroups. Fisher’s Exact test was used for nominal data. Goodness of fit of the linear model between two variables was assessed from the coefficient of determination (r\textsuperscript{2}) which was derived from linear correlation using the Pearson product correlation coefficient. Stepwise multiple regression analysis using the independent variables weight, height, age, gender, fat-free mass, weight\textsuperscript{0.75}, body surface area, body temperature, body fat (kg) and % body fat were used to develop a model (Arlington equations) for predicting measured resting energy expenditure. Predictive performance of the Harris-Benedict, WHO, and Arlington equations by bias and precision was determined from the methods of Scheiner and Beal.\textsuperscript{33} The mean prediction error was employed as a measure of bias and was calculated from the residuals between predicted and measured energy expenditure. A predictive method for estimating energy expenditure was considered to be without significant bias if zero was contained within its 95% confidence interval for the prediction error. The root mean squared prediction error (absolute prediction error) was used as a measure of precision. A predicted energy expenditure method was considered precise, for clinical purposes, if the 95% confidence interval was ≤ 15% of the measured energy expenditure. A probability value (p) of ≤ 0.05 was defined as statistically significant.

\textit{Results}

\textit{Patient Characteristics}
Twenty-two patients fed by permanent ostomy referred to the consultative service were evaluated for potential inclusion into the study. Two of these patients were excluded from the study since a steady state measurement could not be achieved. Fourteen of these patients were classified as adults (≥ 18 years of age) with the remaining six patients being adolescents. The neurodevelopmental disabilities of these patients are described in Table 1. Other patient demographic information as age, current body weight, height, serum albumin concentration, and percent body fat are given in Table 2. Following nutritional assessment, it was evident that most patients were cachetic with decreased or low-normal total body fat, decreased skeletal muscle
Table 1. Developmental Diagnoses

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe to profound mental retardation</td>
<td>20</td>
</tr>
<tr>
<td>Chronic seizure disorder</td>
<td>19</td>
</tr>
<tr>
<td>Hydrocephalus</td>
<td>4</td>
</tr>
<tr>
<td>Neuroaxonal dystrophy</td>
<td>1</td>
</tr>
<tr>
<td>Cerebral palsy</td>
<td>20</td>
</tr>
<tr>
<td>Severe spastic quadriplegia</td>
<td>17</td>
</tr>
<tr>
<td>Severe spastic diplegia</td>
<td>3</td>
</tr>
</tbody>
</table>

Table 2. Patient Demographics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total</th>
<th>Adults</th>
<th>Adolescents</th>
<th>p &lt; *</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>20</td>
<td>14</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>25.9 ± 11.3</td>
<td>31.3 ± 8.9</td>
<td>13.2 ± 1.9</td>
<td>0.001</td>
</tr>
<tr>
<td>CBW (kg)</td>
<td>34.6 ± 10.4</td>
<td>37.8 ± 10.5</td>
<td>26.9 ± 4.9</td>
<td>0.03</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>140 ± 18</td>
<td>149 ± 11</td>
<td>120 ± 12</td>
<td>0.001</td>
</tr>
<tr>
<td>Serum albumin (g/L)</td>
<td>39 ± 5</td>
<td>38 ± 5</td>
<td>40 ± 6</td>
<td>N.S.</td>
</tr>
<tr>
<td>% Body fat</td>
<td>19.0 ± 7.7</td>
<td>19.4 ± 7.8</td>
<td>18.2 ± 8.4</td>
<td>N.S.</td>
</tr>
</tbody>
</table>

*Statistical significance between adult and adolescent groups.
CBW = current body weight.

Table 3. Nutrient Intake

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total</th>
<th>Adults</th>
<th>Adolescents</th>
<th>p &lt; *</th>
</tr>
</thead>
<tbody>
<tr>
<td>Energy intake (% of REE)</td>
<td>142 ± 30</td>
<td>147 ± 29</td>
<td>128 ± 24</td>
<td>N.S.</td>
</tr>
<tr>
<td>Energy intake (kcal/day)</td>
<td>1274 ± 357</td>
<td>1370 ± 362</td>
<td>1050 ± 239</td>
<td>N.S.</td>
</tr>
<tr>
<td>Protein intake (g/kg/d)</td>
<td>1.6 ± 0.4</td>
<td>1.6 ± 0.4</td>
<td>1.5 ± 0.5</td>
<td>N.S.</td>
</tr>
<tr>
<td>Protein intake (g/d)</td>
<td>53 ± 16</td>
<td>59 ± 14</td>
<td>41 ± 13</td>
<td>0.02</td>
</tr>
</tbody>
</table>

*Statistical significance between adult and adolescent groups.
REE = measured resting energy expenditure

mass, and had normal serum albumin concentrations similar to the patient with marasmus malnutrition. The adolescent patients were significantly shorter in stature, weighed less, but had a similar proportion of body fat compared to the adults (Table 2). All patients’ nutritional intake were met solely by enteral tube feeding and were generally kept nil-per-os, except for one patient who was given small intermittent snacks. The enteral feeding was given by continuous or intermittent infusion for 18 to 24 hours per day via gastrostomy or jejunostomy. Most patients received an isotonic, polymeric, nutritionally complete, 1 kcal/ml, fiber-containing formula. The amount of nutrition that was provided daily to the patients is given in Table 3.

Energy Expenditure Population Characteristics

The distribution of measured REE of nonambulatory tube fed-patients with severe neurodevelopmental disabilities is shown in Fig. 1. The data demonstrate a wide distribution in measured resting energy expenditure ranging from a minimum of 16 kcals/kg/day to a maximum of 39 kcals/kg/day. Additionally, the distribution curve appears flattened compared to a normal bell-shaped distribution curve that is observed for normal-sized healthy subjects. The majority (17 out of 20) of the population’s measured REE was within the broad range of 20 to 35
Figure 1. Distribution of measured resting energy expenditure measurements of nonambulatory tube-fed patients with severe neurodevelopmental disabilities.

Table 4 provides data regarding resting energy expenditure normalized for body weight and other associated variables for the entire population in addition to the adult and adolescent subgroups. Measured REE was significantly greater in the adolescent subgroup when both populations were normalized to body surface area (\(p < 0.05\)) and approached statistical significance (0.05 < \(p < 0.1\)) when REE was normalized to fat-free mass (Table 4). No significant differences or substantial trends were noted between subgroups when REE was normalized to current body weight, metabolic body size (weight^{0.75}), or to predicted energy expenditure derived from the Harris-Benedict and FAO/WHO/UNO equations. Table 5 examines various determinants of energy expenditure to ascertain if any differences observed between the adolescent and adult subpopulations are due to differences in these variables. As anticipated, a significant decrease in age, height, body weight, metabolic body size (weight^{0.75}), body surface area, and fat-free mass was observed for the adolescent subgroup compared to the adult subgroup. Oxygen consumption and carbon dioxide production were similar which mathematically explains the higher normalized expenditures for the adolescent subpopulation.

### Accuracy of Predictive Formulas

Table 4 indicates these predictive formulas grossly overestimate resting energy expenditure in nonambulatory neurodevelopmentally disabled tube-fed patients as the mean REE was found to be 17% to 26% lower than predicted (\(p < 0.01\)). Fig. 2 and 3 illustrate the difference between predicted energy expenditure (PEE) based on the Harris-Benedict and WHO equations and actual REE over the entire range of measured resting energy expenditures in this population. Although these formulas had a reasonable association with measured REE (\(r = 0.63, p < 0.01\) and \(r = 0.58, p < 0.01\) for the Harris-Benedict and WHO equations, respectively), their accuracy in predicting
resting energy expenditure in an individual patient is limited. To evaluate the predictive
performance of the Harris-Benedict and WHO formulas, the methods of Sheiner and Beal\textsuperscript{33} were
applied to determine their bias and precision. Both the Harris-Benedict formulas and WHO
formulas for estimating basal metabolic rate (resting energy expenditure) demonstrated
significant bias towards overpredicting measured resting energy expenditure. The 95%
confidence intervals for bias were 121 to 246 kcals/day and 137 to 249 kcals/day for the Harris-
Benedict and WHO equations, respectively. In addition, the 95% confidence interval for the root
mean squared prediction error (a measure of precision) was 16% to 31% and 26% to 45% for the Harris-Benedict and WHO equations, respectively. These predictive equations resulted in precision errors greater than what is considered as clinically acceptable.\textsuperscript{24} To assess whether a more precise and less biased model could be developed, all
independent variables listed in Tables 2, 3, and 5 were examined by stepwise multiple regression
analysis. The following formulas were generated from the analysis:

### Table 4. Normalized Resting Energy Expenditure

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total</th>
<th>Adults</th>
<th>Adolescents</th>
<th>$p &lt;$ *</th>
</tr>
</thead>
<tbody>
<tr>
<td>REE (kcals/day)</td>
<td>888 ± 176</td>
<td>934 ± 193</td>
<td>815 ± 90</td>
<td>N.S.</td>
</tr>
<tr>
<td>PEE (HB)</td>
<td>1081 ± 155**</td>
<td>1130 ± 148**</td>
<td>967 ± 109</td>
<td>0.03</td>
</tr>
<tr>
<td>REE (% of HB)</td>
<td>83 ± 13</td>
<td>83 ± 13</td>
<td>85 ± 13</td>
<td>N.S.</td>
</tr>
<tr>
<td>PEE (WHO)</td>
<td>1194 ± 167**</td>
<td>1266 ± 141**</td>
<td>1029 ± 81**</td>
<td>0.01</td>
</tr>
<tr>
<td>REE (% of WHO)</td>
<td>76 ± 12%</td>
<td>74 ± 12</td>
<td>80 ± 11</td>
<td>N.S.</td>
</tr>
<tr>
<td>REE (kcal/kg/day)</td>
<td>27 ± 6</td>
<td>26 ± 6</td>
<td>31 ± 6</td>
<td>N.S.</td>
</tr>
<tr>
<td>REE (kcal/kg$^{0.75}$/day)</td>
<td>65 ± 12</td>
<td>63 ± 12</td>
<td>70 ± 12</td>
<td>N.S.</td>
</tr>
<tr>
<td>REE (kcal/kg FFM/day)</td>
<td>34 ± 7</td>
<td>32 ± 6</td>
<td>38 ± 8</td>
<td>N.S.</td>
</tr>
<tr>
<td>REE (kcal/m$^2$/day)</td>
<td>788 ± 145</td>
<td>746 ± 125</td>
<td>844 ± 155</td>
<td>0.05</td>
</tr>
</tbody>
</table>

*Statistical significance between adult and adolescent groups.

**$p < 0.01$ compared to measured REE

REE = measured resting energy expenditure, HB = Harris-Benedict equations, PEE = predicted energy expenditure,
WHO = World Health Organization equations, FFM = fat-free mass.

### Table 5. Determinants of Resting Energy Expenditure

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total</th>
<th>Adults</th>
<th>Adolescents</th>
<th>$p &lt;$ *</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (M/F)</td>
<td>13/7</td>
<td>8/6</td>
<td>5/1</td>
<td>N.S.</td>
</tr>
<tr>
<td>Temp $^\circ$C</td>
<td>36.7 ± 0.3</td>
<td>36.9 ± 0.3</td>
<td>36.5 ± 0.3</td>
<td>N.S.</td>
</tr>
<tr>
<td>VO2 (ml/minute)</td>
<td>128 ± 25</td>
<td>134 ± 27</td>
<td>116 ± 12</td>
<td>N.S.</td>
</tr>
<tr>
<td>VCO2 (ml/minute)</td>
<td>112 ± 25</td>
<td>116 ± 28</td>
<td>104 ± 15</td>
<td>N.S.</td>
</tr>
<tr>
<td>RQ</td>
<td>0.87 ± 0.06</td>
<td>0.86 ± 0.06</td>
<td>0.90 ± 0.07</td>
<td>N.S.</td>
</tr>
<tr>
<td>CBW (kg)</td>
<td>34.6 ± 10.4</td>
<td>37.8 ± 10.4</td>
<td>26.9 ± 4.9</td>
<td>0.03</td>
</tr>
<tr>
<td>CBW (kg$^{0.75}$)</td>
<td>14.2 ± 3.1</td>
<td>15.2 ± 3.1</td>
<td>11.8 ± 1.6</td>
<td>0.03</td>
</tr>
<tr>
<td>BSA (m$^2$)</td>
<td>1.2 ± 0.2</td>
<td>1.3 ± 0.2</td>
<td>0.9 ± 0.1</td>
<td>0.01</td>
</tr>
<tr>
<td>FFM (kg)</td>
<td>27.7 ± 7.8</td>
<td>30.2 ± 7.9</td>
<td>21.9 ± 3.1</td>
<td>0.03</td>
</tr>
</tbody>
</table>

*Statistical significance between adult and adolescent groups.

Temp = body temperature (ear), VO2 = oxygen consumption, VCO2 = carbon dioxide production, RQ = respiratory
quotient, CBW = current body weight, BSA = body surface area, FFM = fat-free mass.
Total population:

\[
\text{REE (kcals/day)} = 15.8 \times \text{Fat-Free Mass (kg)} + 460
\]
\[
(r = 0.70, r^2 = 0.49, p < 0.001)
\]

Adults:

\[
\text{REE (kcals/day)} = 22.3 \times \text{Fat-Free Mass (kg)} - 9.4 \times \text{Age (years)} + 557
\]
\[
(r = 0.81, r^2 = 0.66, p < 0.001)
\]

Stepwise multiple regression analysis and a correlation matrix of the adolescent subgroup revealed no single independent variable that correlated significantly with measured resting energy expenditure. The failure to achieve a statistically significant correlation in the adolescent subgroup was most likely due to the large variability of the independent variables, small number of patients, and limited range of fat-free mass. To assess the bias and precision of the Arlington formulas, the methods of Sheiner and Beal were applied to these data. As anticipated, both formulas were markedly improved in predictive performance (both were ≤ 15%) compared to the Harris-Benedict and WHO formulas. As 0 was included in the 95% confidence interval for prediction error, the Arlington formulas were not significantly biased. However, a reduction in error and bias by application of these formulas may be solely attributable to the fact that these formulas were tested using the same population where the formulas were developed. Therefore, further research using an independent population is necessary to confirm the precision and bias of these formulas.

Discussion

Despite the growing emergence of this subgroup of patients, we are the first to report data regarding resting energy expenditure of nonambulatory adolescent and adult tube-fed patients with severe neurodevelopmental disabilities. Assessing energy needs in adolescent and adult tube-fed patients with neurodevelopmental disabilities is challenging as the severity of their disease, muscle atrophy, stunted growth, and extent of ambulation are important factors affecting their energy expenditure. Also, nutrient intake is completely controlled by the prescriber and the personnel administering it in this selective patient population. Our data indicate that there is wide variability of resting energy expenditure (Fig. 1) and that conventional predictive formulas used to estimate energy expenditure overestimate actual measured resting energy expenditure (Fig. 2 and 3).

Efforts to normalize measured resting energy expenditure to predicted energy expenditure (by the Harris Benedict and WHO equations), current body weight, metabolic body size (weight^{0.75}), fat-free mass, and body surface area failed to reduce the marked variability exhibited by this population. As anticipated, the adolescent subgroup had a significantly higher REE normalized to body surface area and statistically nonsignificant increases in REE normalized to weight and fat-free mass when compared to adults. In an effort to improve the predictive performance of
estimating energy expenditure in this population, we examined various independent variables that may contribute to resting energy expenditure in a stepwise multiple regression analysis. We performed this analysis for the entire population and by adolescent and adult subgroups. We subdivided the entire population into these subgroups since the adolescent, unlike the adult, may experience further growth and because significant differences between adults and adolescents were demonstrated for various independent determinants of energy expenditure (Tables 4 and 5). However, some of these adolescents may never experience an adolescent growth spurt. The
Figure 4. Relationship between measured energy expenditure and fat-free mass. Closed circles depict adult patients whereas adolescents are represented by the open circles. The equation for the regression line that is representative for the entire population is $y = 15.8x + 460$ ($r = 0.70, p < 0.001$).

Stepwise regression analysis for the entire population demonstrated that fat-free mass was the only statistically significant variable of all the parameters studied. Fig. 4 illustrates the correlative relationship between fat-free mass and resting energy expenditure. In the adult subpopulation, age in addition to fat-free mass was a significant factor. The coefficient of determination ($r^2$) and predictive performance was also improved in this subgroup compared to the formula for the entire population. Both of the Arlington formulas demonstrated a substantially improved predictive performance and both were found to be within an acceptable 15% error at the 95% confidence interval for clinical estimation of resting energy expenditure. This is in direct contrast to the poor performance observed by the conventional Harris-Benedict and WHO formulas whereby errors as large as 31% and 45% can be anticipated. Additionally, these conventional formulas are biased towards overestimating measured resting energy expenditure.

The inaccuracy of conventional predictive formulas was not a totally unexpected finding as this population has stunted growth and marked differences in body composition compared to normal healthy subjects. Fat-free mass contributes to approximately 55% to 88% of resting energy expenditure in normal adults and adolescents. However, fat-free mass accounted for only 49% of the variability of the resting energy expenditure in this study. Why fat-free mass contributes less to the variability in REE may be partially explained by the marked decreases in stature and skeletal muscle mass (secondary to upper motor neuron lesions) relative to organ weight. Although the patients were adolescents and adults, many exhibited a body size similar to children. The proportion of organ weight to body weight is about 15% during infancy and falls to about 8% in adolescents and 6% in adults. However, organ metabolic rate remains constant from infancy to maturity. We hypothesize that due to marked decreases in skeletal muscle mass, organ metabolism may contribute proportionately greater to resting energy expenditure in this population compared to healthy adults. Further research to confirm the hypothesis of a
disproportionate relationship between organ and skeletal muscle metabolism contribution to resting energy expenditure in this population is warranted.

Consideration of the relationship between REE and total energy expenditure (TEE) is essential when determining appropriate caloric intake. Bandini and coworkers found that nonambulatory adolescents with cerebral palsy had a TEE/REE ratio of 1.2 whereas ambulatory adolescents with cerebral palsy has a substantially higher ratio of 1.8 which was comparable to normal adolescents.\textsuperscript{15} Stallings confirmed these data in more subjects that included both children and adolescents with cerebral palsy.\textsuperscript{2} It may be reasonable to assume that the TEE/REE ratio is similar in this population; however, total energy expenditure may not always be higher than measured resting energy expenditure in some patients with severe neurodevelopmental disabilities. Some of the patients followed by our service had intermittent nonshivering hypothermia necessitating warming of the body with the use of heating blankets and wool caps. Despite its presumed rarity, poikiliothermia may be more common in patients with severe neurodevelopmental disabilities who have suffered from years of modestly controlled seizure disorders, have severe mental retardation, and spastic quadriplegia.\textsuperscript{28} We have identified six patients from our total referral service of about 30 patients that periodically exhibit this disorder. One patient had severe chronic hypothermia and her measurement had to be postponed several times until a day where significant hypothermia was not evident. This patient with severe chronic hypothermia was measured when hypothermic and normothermic to ascertain a better estimate of “actual” resting expenditure.\textsuperscript{28} She continued to gain weight and had abundant fat stores despite receiving a total caloric intake approximately equal to her measured normothermic REE.\textsuperscript{28} Additionally, some patients with severe seizure disorders may receive substantial doses of medications that are potentially sedating (e.g., phenobarbital) which may also decrease measured resting energy expenditure. Therefore, despite a presumed TEE/REE ratio of 1.2, this relationship may need to be individually examined in the nonambulatory tube-fed patient with severe neurodevelopmental disabilities.

The development of the predictive Arlington formulas may be more reflective of the entire population if more patients were studied; however, no other patients that met the entry criteria were available. The number of patients in this highly selective population available for study, although growing, is still limited. Arlington Developmental Center is a 380 bed state facility for the severe developmentally disabled citizens of the western portion of Tennessee. All of the available patients that met the study entry criteria were investigated. It is recommended that these patients be measured to assess resting energy expenditure; however, in the event that indirect calorimetry is not immediately available, the Arlington formulas may provide a better estimate of measured resting energy expenditure than other conventional formulas. Further research by other developmental centers to validate the accuracy of these equations in this selective population is encouraged.
Conclusions

The nonambulatory tube-fed adolescent and adult patient with severe neurodevelopmental disabilities is a growing population that present with unique medical and physical problems that make nutritional intervention problematic. The measured resting energy expenditure of nonambulatory tube-fed patients with severe neurodevelopmental disabilities is widely variable. Conventional methods to estimate caloric expenditure are an unreliable estimate of measured resting energy expenditure. It is recommended that resting energy expenditure be measured in this population. In the event that indirect calorimetry is not immediately available, this paper presents a predictive method that may be less biased and more precise than the Harris-Benedict and World Health Organization formulas for estimating resting energy expenditure in this population.

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References


