The Harris Benedict equation reevaluated: resting energy requirements and the body cell mass[1-3]

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ABSTRACT The Harris Benedict equations (HBE) were derived from indirect calorimetric data obtained in 239 normal subjects. Using these data and additonal data published by Benedict, which were obtained from subjects spanning a wider age range (n = 98), the present study evaluated the relationship between measured resting energy expenditure and age, sex, and predicted body cell mass (BCM). When the additional subjects from the subsequently published series are included, the regression equations, standard error of the estimate, and 95% confidence limits are similar to the original equations. The HBE estimate resting energy expenditure of a normal subject with a precision of 14%. Resting energy expenditure is directly related to the size of the BCM and is independent of age and sex. The variables of height, weight, age, and sex in the HBE reflect the relationship between body weight and the BCM. Indirect calorimetry and body composition measurements were performed in both normally nourished and malnourished patients (n = 74) to assess the accuracy of the HBE in malnourished patients. Malnutrition is associated with an increase in resting oxygen consumption (VO_2) which becomes apparent only when VO_2 is expressed as a function of the BCM. There is no difference in resting VO_2 between the sexes when expressed as a function of BCM. A regression equation was derived from the Harris Benedict data to predict resting VO_2 from age, height, weight, and sex. Predicted VO_2 was not significantly different from measured VO_2 for the normally nourished patients (n = 33) whereas in the malnourished (n = 41) predicted VO_2 underestimated the measured value. The HBE accurately predict resting energy expenditure in normally nourished individuals with a precision of ±14%, but are unreliable in the malnourished patient. *Am J Clin Nutr* 1984;40:168-182.

KEY WORDS Basal metabolism, body composition, energy, malnutrition, metabolism

Introduction

Malnutrition is common in the hospitalized patient, developing as a complication of the disease process and/or as a result of diagnostic and therapeutic maneuvers. Aggressive nutritional support will both prevent and treat the malnourished state. The success of nutritional support depends on the delivery of adequate calories and protein by either the enteral or parenteral route. Two methods are commonly used to determine the caloric or energy requirements of the individual patient. The first uses the Harris Benedict equations which give an estimate of resting energy expenditure (REE). The second method involves measurement of REE, by indirect calorimetry.

In 1919, Harris and Benedict published their classic monograph on basal metabolism in normal subjects (1). Metabolic parameters were determined by indirect calorimetry on 136 men and 103 women. From these measurements they derived regression

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formulae which estimated REE from height, weight, age, and sex. Total energy expenditure is estimated by adding the additional energy cost associated with activity, fever, trauma, and malnutrition (2).

Indirect calorimetry, which involves the measurement of metabolic gas exchange, is simple to perform and results in a reliable measurement of REE (3, 4). In the resting, postabsorptive subject, the rate of oxygen consumption is a measure of REE, because for all classes of nutrients, a direct relationship exits between the energy generated and the volume of oxygen consumed.

The body cell mass (BCM), is the total mass of metabolically active cells, and is therefore that component of body composition which is responsible for all of the oxygen consumption, carbon dioxide production, and the work performed by the body. Moore (5), demonstrated that total exchangeable potassium (K_e), which is equivalent to total body potassium, is a measure of the BCM. An excellent correlation has been demonstrated between K_e and both the intracellular water volume (5) and REE (6).

According to the Harris Benedict equations there is a decrease in REE with aging. In addition, separate equations were derived for male and female subjects implying a difference in energy expenditure related to sex. In the present study we examined the original Harris Benedict data in order to investigate the relationship between REE and both sex and age, and the relationship between the BCM and REE. In addition, the accuracy of the Harris Benedict equation in predicting REE was evaluated in both normally nourished and malnourished patients.

Materials and methods

The Harris Benedict equation

The Harris Benedict monograph reported for each subject the age, height, weight, body surface area, pulse rate, carbon dioxide production and oxygen consumption per minute, and heat production per 24 h, expressed as calories. In the original monograph, the published data were obtained in 239 subjects, 136 men and 103 women. Two further series were published subsequently by Benedict in 1928 and 1935 with similar data on additional subjects (7, 8). This resulted in a total series of 337 subjects, 168 men and 169 women. The two latter series included subjects with a wider age range (**Table 1**).

TABLE 1
Age data for Harris Benedict subjects

	Men		Women	
	Mean age	n	Mean age	n
Series I (1919)	27 ± 9*	136	31 ± 14	103
Series II (1928)	34 ± 16	27	32 ± 12	33
Series III (1935)	81 ± 7	5	76 ± 6	33
Total	30 ± 14	168	40 ± 22	169

* SD.

TABLE 2
Body composition regressions*

Men

$TBW = 0.7945\,(wt) - 0.0024\,(wt)^2 - 0.0015\,(age)\,(wt)$

$ICW = 0.623\,(TBW) - 0.0016\,(age)\,(TBW)$

$ECW = TBW - ICW$

$K_e = 150\,(ICW) + 4\,(ECW)$

$BCM = 0.00833\,(K_e)$

Women

$TBW = 0.6981\,(wt) - 0.0026\,(wt)^2 - 0.0012\,(age)\,(wt)$

$ICW = 0.553\,(TBW) - 0.0007\,(age)\,(TBW)$

$ECW = TBW - ICW$

$K_e = 150\,(ICW) + 4\,(ECW)$

$BCM = 0.00833\,(K_e)$

* TBW, total body water (l); ICW, intracellular water (l); ECW, extracellular water (l); K_e, total exchangeable potassium (mEq); BCM, body cell mass (kg).

In the present study the Harris Benedict data were used to correlate REE (kcal/day), as the dependent variable, with age, height, and weight as the independent variables by means of multiple linear regression. Separate equations were derived for both men and women. This was carried out separately for the original group of 239 subjects and for the combined group of 337 subjects. The significance of each regression was determined by an analysis of variance. The 95% confidence limits about the regression were calculated as 1.96 times the SE of the estimate. In addition, for each regression the multiple correlation coefficient was calculated and the statistical significance of each regression coefficient was evaluated (9). All of the calculations were carried out with a Digital PDP/11 computer (Digital Equipment Corp, Maynard, MA).

The BCM for each of the 337 Harris Benedict subjects was calculated using the regression equations developed by Moore et al (10) (**Table 2**). The relationship between REE and the BCM was evaluated by correlating the calculated BCM with REE. Separate correlations were performed for the 168 men and the 169 women.

To evaluate the effect of age, sex, and the BCM on REE, multiple linear regression was used to correlate REE as the dependent variable with age and the BCM as independent variables. Separate equations were derived for men and women. Age was also correlated with BCM expressed as a fraction of body weight for both men and women, to establish the relationship between the BCM and aging. Finally, to evaluate the relationship between REE and sex, REE and the BCM were correlated separately for men and women. The significance of the difference between the regression lines determined from the resultant equations was determined by analysis of variance.

Reference entity for energy exchange

Body composition was determined by multiple isotope dilution in 74 nonseptic, afebrile general surgical patients before the onset of nutritional therapy with total parenteral nutrition. None of the patients was receiving medication that would significantly alter metabolic gas exchange. A multiple isotope dilution technique was used to measure total body water and total exchangeable sodium (Na_e) as previously described (11). An indirect method was used to calculate total K_e from TBW, Na_e, and the ratio in whole blood of the sodium plus potassium content divided by the water content (12). Na_e provides an estimate of the extracellular mass (ECM) and K_e provides an estimate of the BCM. The ratio of Na_e to K_e was used to define the presence or absence of malnutrition (10, 15). In 25 normal volunteers the mean Na_e/K_e was 0.98 ± 0.02 with an upper 95% confidence limit of 1.22. As a result, malnutrition is defined by a ratio of more than 1.22 while a patient with a ratio of less than 1.22 is considered to be normally nourished. All studies were performed after obtaining written informed consent.

In all patients oxygen consumption and carbon dioxide production were measured on the day of the body composition measurement. The measurements were performed with the patient resting and in the supine position. All patients were receiving a small amount of glucose calories as 5% dextrose in water intravenously but were otherwise fasting. Measurements of gas exchange were performed by the open circuit method of indirect calorimetry. To minimize hyperventilation during gas collection, all patients underwent a period of acclimatization to breathing through a mouthpiece with a disposable Hans-Rudolph type valve (OEM Medical Inc, Richmond, VA) with the nasal airway occluded. This period of acclimatization was continued until the patients were all breathing normally. There was no obvious difference in breathing patterns between the malnourished and normally nourished patients. Expired gas was collected in a Douglas bag for four periods of 2 min each. The concentration of oxygen and carbon dioxide in inspired air and mixed expired gas were measured, within 1 h, using a mass spectrometer (Perkin Elmer 1100, Perkin-Elmer Medical Instruments, Pomona, CA). Expired gas volume was measured with a dry gas meter (JH Emerson & Co, Cambridge, MA) which was accurate to within 0.25 l in 20 l. Oxygen consumption was determined from the minute volume and gas concentration corrected for standard temperature and pressure and expressed as ml/min (13). For all patients, including those on a respirator, the accuracy of the oxygen consumption measurement was estimated at less than 5%. However, measurements were not performed on patients who were on respirators with an inspired oxygen that exceeded 40%.

Body weight and height for each patient was recorded and body surface area was calculated for each subject according to the formula developed by Dubois and Dubois (14):

$$S = 71.84\ W^{0.425} \times L^{0.725}$$

where S is body surface area in cm^2, W is body weight in kg, and L is height in cm.

Mean oxygen consumption for the normally nourished and the malnourished patients was expressed in ml/min as a function of body weight [$ml \cdot min^{-1} \cdot (kg)^{-1}$], as a function of body surface area [$ml \cdot min^{-1} \cdot (m^2)^{-1}$], and as a function of BCM [$ml \cdot min^{-1} \cdot (kg\ BCM)^{-1}$]. The significance of the difference between the means was determined by unpaired "Student's" *t* test.

Predicted versus measured oxygen consumption

Equations to predict the resting oxygen consumption per minute from height, weight, and age were derived, for men and women, using the total combined Harris Benedict data (n = 337). Resting oxygen consumption as the dependent variable was correlated with height, weight, and age as the independent variables by means of multiple linear regression. Separate equations were derived for both men and women.

These regression equations were used to predict resting oxygen consumption for the 74 patients. Patients were divided into two groups based on the presence or absence of malnutrition, as determined by the Na_e/K_e ratio. For this analysis the data from men and women were combined. The correlation between predicted resting oxygen consumption and measured oxygen consumption was performed by standard linear correlation for both the normally nourished and the malnourished patients.

Predicted oxygen consumption, as a function of the BCM (ie oxygen consumption per kg of BCM), was calculated for each of the 74 patients. Moore's regression equations and the equations derived from the Harris Benedict data were used to predict body composition and oxygen consumption, respectively. These values were compared to the measured oxygen consumption per kg of measured BCM for the normally nourished and the malnourished patients. Values are reported as the mean ± the SEM. Significance of the difference between the means for the four groups was determined by analysis of variance and Scheffe's test.

Results

The Harris Benedict equation

The correlation of REE as the dependent variable with height, weight, and age by means of multiple linear regression represents a recalculation of the Harris Benedict equation. **Table 3** lists the published Harris Benedict equations for males and females (equations 1 and 3) with the recalculated regression formulas for men and women (equations 2 and 4, Table 3). A similar regression analysis was performed with the additional subjects from the two subsequent series which span a wider age range, ie, the total series of 168 men and 169 women (equations 3 and 6, Table 3). All of the

TABLE 3
Harris Benedict regression equations

Men

Equation 1. Harris Benedict equation based on 1919 data ($n = 136$)
$REE = 66.473 + 5.003\ (ht) + 13.752\ (wt) - 6.755\ (age)$

Equation 2. Original 1919 data recalculated ($n = 136$)
$REE = 77.607 + 4.923\ (ht) + 13.702\ (wt) - 6.673\ (age)$
$r = 0.86$ $F = 122.4$ $p < 0.001$ 95% $CL = \pm 210.5$ kcal

Equation 3. Total data ($n = 168$)
$REE = 88.362 + 4.799\ (ht) + 13.397\ (wt) - 5.677\ (age)$
$r = 0.88$ $F = 192.3$ $p < 0.001$ 95% $CL = \pm 213.0$ kcal

Women

Equation 4. Harris Benedict equation based on 1919 data ($n = 103$)
$REE = 655.096 + 1.850\ (ht) + 9.563\ (wt) - 4.676\ (age)$

Equation 5. Original 1919 data recalculated ($n = 103$)
$REE = 667.051 + 1.729\ (ht) + 9.740\ (wt) - 4.737\ (age)$
$r = 0.77$ $F = 37.8$ $p < 0.001$ 95% $CL = \pm 211.9$ kcal

Equation 6. Total data ($n = 169$)
$REE = 447.593 + 3.098\ (ht) + 9.247\ (wt) - 4.330\ (age)$
$r = 0.83$ $F = 119.2$ $p < 0.001$ 95% $CL = \pm 201.0$ kcal

TABLE 4
Resting energy expenditure for 70-kg man

Ht = 170 cm
Wt = 70 kg
Age = 50 yr

Equation 1—Table 3
$REE = 66.473 + 5.003\ (ht) + 13.752\ (wt) - 6.755\ (age)$
$= 1542$ kcal/day

Equation 2—Table 3
$REE = 77.607 + 4.923\ (ht) + 13.702\ (wt) - 6.673\ (age)$
$= 1540$ kcal/day
95% Confidence limits = 1329 to 1750 kcal/day

Equation 3—Table 3
$REE = 88.362 + 4.799\ (ht) + 13.397\ (wt) - 5.677\ (age)$
$= 1558$ kcal/day
95% Confidence limits = 1348 to 1769 kcal/day

equations are similar. A sample calculation for a 70-kg man is presented in **Table 4** using equations 2 and 3, ie, the recalculated Harris Benedict equation and the equation generated from the larger series of men, respectively. The estimated values for REE using either equation are virtually identical.

In the present study the multiple correlation coefficients and the SE of the estimate were also determined (Table 3). For the original series of 136 men the multiple correlation coefficient is 0.86 which is highly significant, ($p < 0.001$, F ratio = 122.4). The 95% confidence limits are ±210.5 kcal/day. The multiple correlation coefficient for the regression obtained for men using data from all three published series ($n = 168$), is 0.88 ($p < 0.001$, F ratio = 192.3). The 95% confidence limits are ±213.0 kcal/day. For the original series of 103 women the multiple correlation coefficient is 0.77 ($p < 0.0001$, F ratio = 37.8), with 95% confidence limits of ±211.9 kcal/day. For the combined series of 169 women the correlation coefficient is 0.83 ($p < 0.0001$, $F = 119.2$) and the 95% confidence limits are ±201.0 kcal/day. The 95% confidence limits estimate the precision of the calculated REE. In the example presented in Table 4, the 95% confidence limits represent 13.7% of the estimated REE.

To examine the relationship between REE and the BCM in the Harris Benedict subjects, the BCM for each of the 337 subjects was calculated using the regression equations developed by FD Moore. The calculated BCM was correlated with REE as measured in each Harris Benedict subject. Separate correlations were performed for men and women. There was a highly significant ($p < 0.001$) correlation between REE and BCM for both men and women (**Fig 1**).

The REE as the dependent variable was correlated with age and BCM as the independent variables. The following highly significant ($p < 0.001$) multiple linear regression equations were obtained:

Men ($n = 168$):

$$REE = 75.9 + 1.3\ (age) + 53.7\ (BCM)$$

$r = 0.86$ $p < 0.001$

Women ($n = 169$):

$$REE = 490.8 - 1.5\ (age) + 45.8\ (BCM)$$

$r = 0.82$ $p < 0.001$

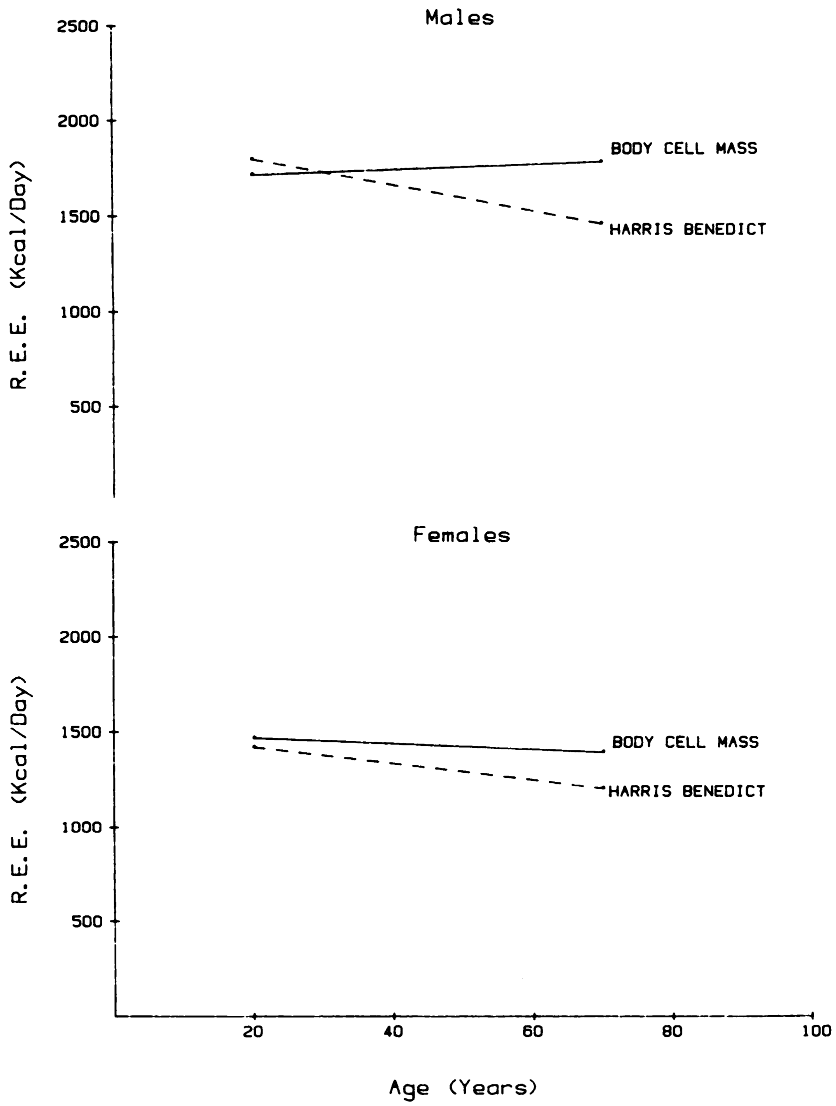

FIG 1. The regression and 95% confidence limits for the calculated BCM on the measured REE for the Harris Benedict males and females. For both sexes there was a highly significant correlation ($p < 0.001$) with correlation coefficients of 0.86 and 0.80 for the men and women respectively.

The regression coefficient associated with the BCM was statistically significant in both equations ($p < 0.001$), while the coefficient associated with age was statistically significant ($p < 0.05$) for women only. However, in both sexes the magnitude of the regression coefficients associated with age was small, indicating that age minimally affected the REE. Because these regression equations contain more than one independent variable, they can only be plotted in a multidimensional space. However, by holding one or more independent variables constant, the relationship between the dependent variable and a single independent variable can be plotted on a two-dimensional graph. With the Harris Benedict equation, height and weight are held constant and in the second equation, the BCM is held constant. In this way the effect due to aging inherent in each equation can be demonstrated (**Fig 2**). With the Harris Benedict equation, where REE is predicted from height, weight, age, and sex there is an apparent reduction in REE with

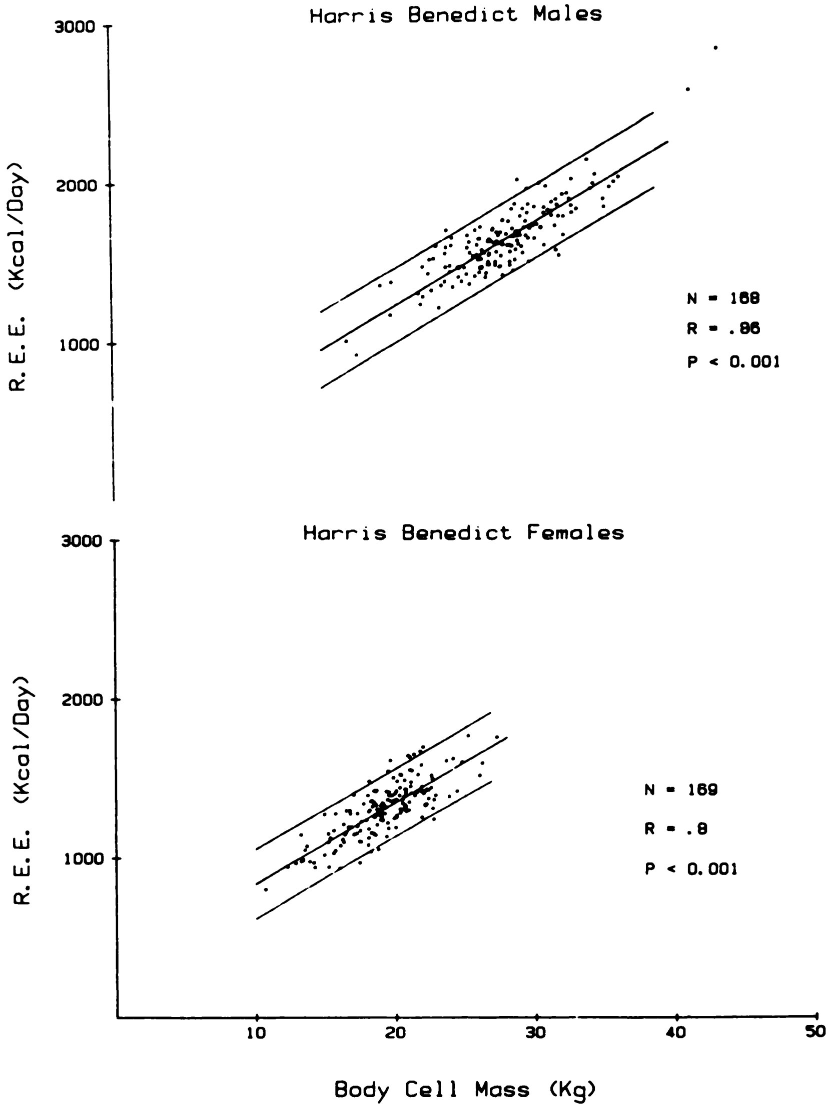

FIG 2. The relationship between age and the REE, when determined from the BCM and age (*solid line*), which was derived by setting the BCM constant at 30 kg for men and 22 kg for women. The *broken line* represents the aging effect inherent in the Harris Benedict equation with height held constant at 180 cm for men and 160 cm for women and weight held constant at 70 kg for men and 60 kg for women.

advancing age when height and weight remain constant. However, when REE is predicted from age and BCM, REE does not change with advancing age, with a constant BCM.

The relationship between the BCM and body weight as a function of advancing age was examined using the Harris Benedict data. In both men and women body weight did not change with age (**Fig 3**). However, the BCM as a fraction of body weight decreased significantly with age for both men and women (**Fig 4**). In both sexes there is a constant decline in the proportion of body weight due to the BCM with aging.

To examine the influence of sex on energy requirements, REE for all Harris Benedict subjects, men and women, was plotted against their calculated BCM. The results are shown in **Figure 5**. It is evident from this plot that the data points for both men and women are clustered about the same regres-

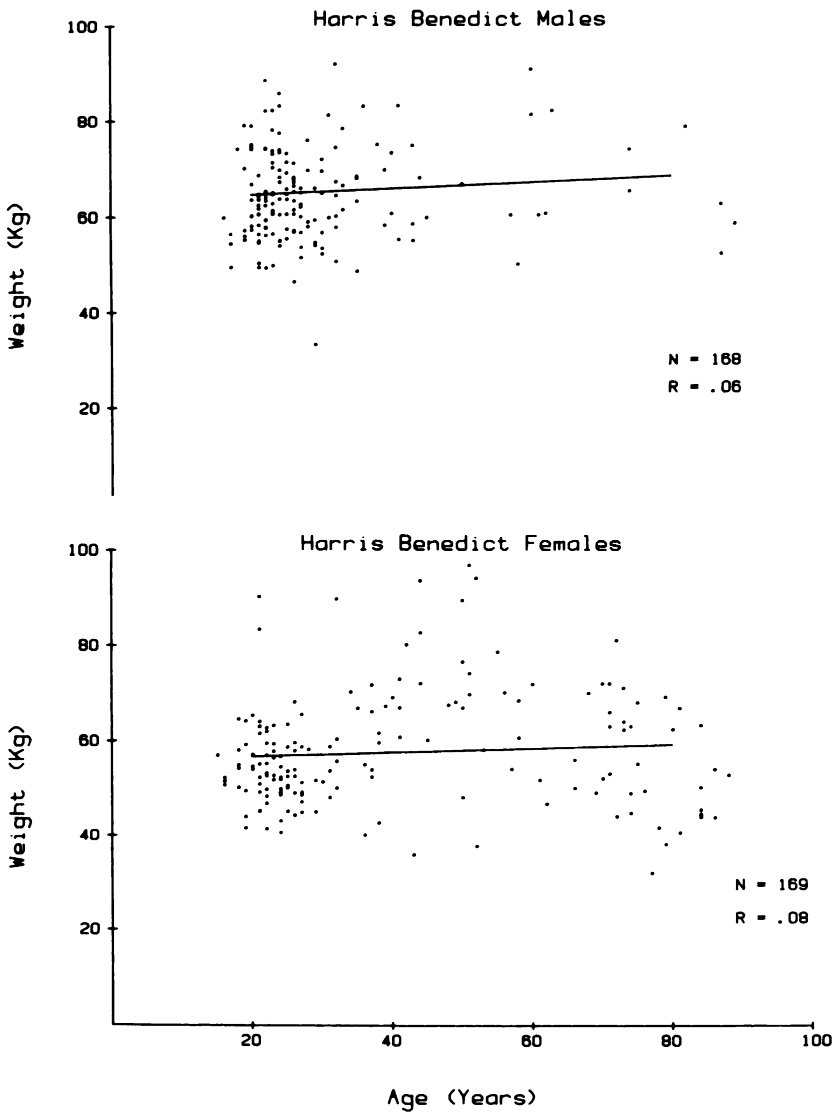

FIG 3. The correlation between body weight and age for both the Harris Benedict men and women. The body weight did not change significantly with advancing age.

sion line. The REE of the women is lower than that of the men primarily because the BCM of the women tends to be smaller. Furthermore, the regression of REE on BCM in the men was not significantly different from the regression obtained for the women by analysis of variance ($t = 0.13$).

Men (n = 168):

$REE = 171 + 51.7\,(BCM)$ $r = 0.86$ $p < 0.001$

Women (n = 169):

$REE = 325 + 51.1\,(BCM)$ $r = 0.80$ $p < 0.001$

Reference entity for energy exchange

The body composition data of the 74 patients studied before nutritional therapy with total parenteral nutrition are tabulated in **Table 5** and compared to similar data obtained from 25 normally nourished volunteers. In these patients 33 were normally nourished while 41 were malnourished. Patients were classified as malnourished on the basis of a $Na_e/K_e > 1.22$. The Na_e/K_e ratio is a senstitive index of the nutritional state (15), as it is a measure of the (ECM), ex-

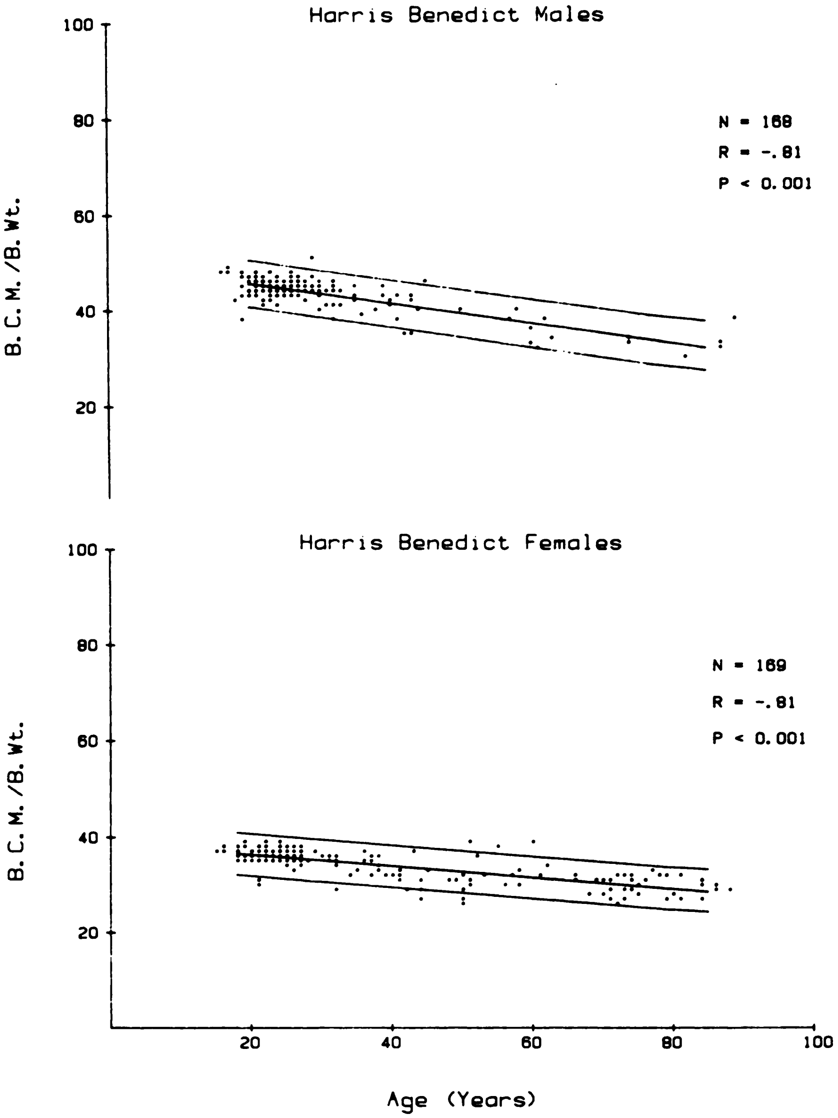

FIG 4. The correlation between BCM, expressed as a percentage of body weight with advancing age for both the Harris Benedict men and women. With aging there is a significant ($p < 0.001$) decline in the proportion of body weight due to the BCM, with correlation coefficients of −0.81 for both sexes.

pressed as a function of the BCM. With malnutrition, the ECM increases, while the BCM contracts, resulting in an increased Na_e/K_e. The malnourished patients in the present study show a statistically significant ($p < 0.05$) expansion of the ECM with a significant ($p < 0.05$) erosion of the BCM when compared to both the normal volunteers and the normally nourished patients. These changes are reflected by the Na_e/K_e ratios. In the malnourished group the mean ratio is significantly greater ($p < 0.05$) at 1.77 ± 0.09 than that of the normally nourished patients with a ratio of 1.08 ± 0.02. The mean ratio of the normal controls (0.98 ± 0.02) does not differ significantly from the ratio of the normally nourished patients.

As illustrated in Table 5, mean oxygen consumption expressed in ml/min was significantly greater ($p < 0.05$) in the normally nourished as compared to the malnourished groups (214 ± 10 and 185 ± 7 $ml \cdot min^{-1}$).

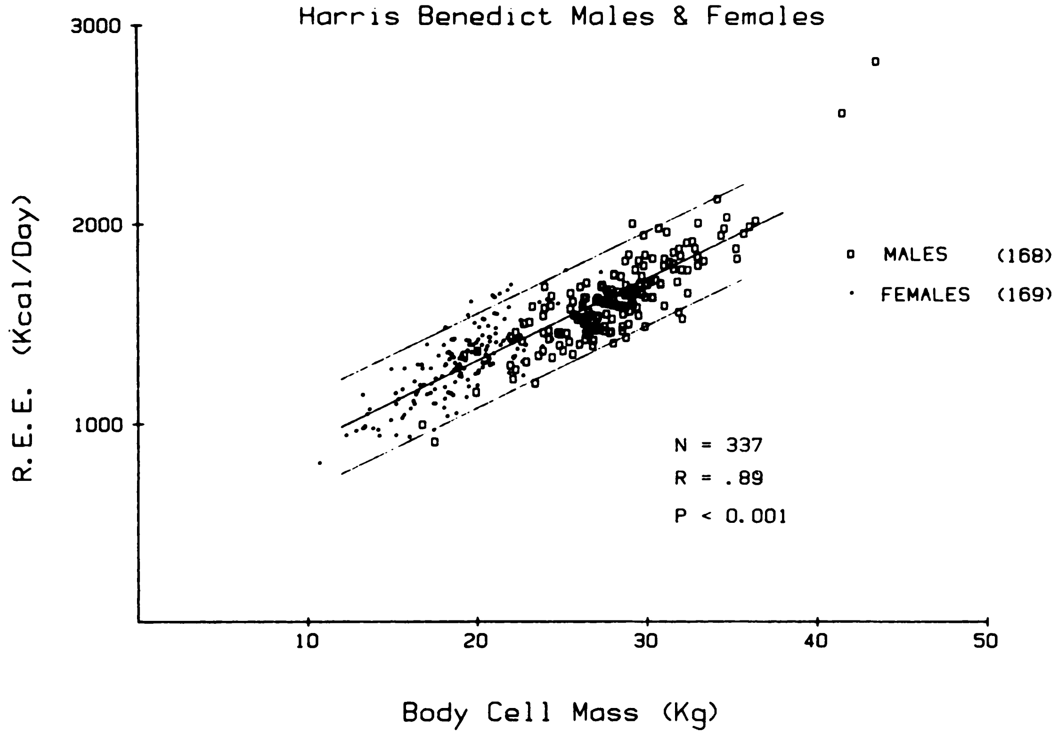

FIG 5. The REE for all 337 Harris Benedict subjects, men (*squares*) and women (dots) plotted against their calculated BCM, demonstrating that both sexes cluster about the same regression line. The REE for women is lower than that of the men because of the smaller size of the BCM in women.

TABLE 5
Body composition and oxygen consumption data of patient population

	Normal volunteers	Normally nourished	Malnourished
n	25	33	41
Wt (kg)	70.4 ± 2.5	70.8 ± 3.6	60.0 ± 2.1*
Body fat (kg)	20.1 ± 1.4	21.9 ± 2.3	12.5 ± 1.7*
TBW (l)	36.8 ± 1.4	35.7 ± 1.4	34.6 ± 1.2
ECM (kg)	25.8 ± 1.0	27.2 ± 1.1	31.4 ± 1.2*
BCM (kg)	24.6 ± 1.1	21.7 ± 1.0†	16.0 ± 0.6*
K_e/TBW (mEq/l)	80.0 ± 1.0	72.6 ± 0.6†	55.7 ± 1.5*
Na_e/TBW (mEq/l)	77.5 ± 1.0	78.1 ± 0.7	93.8 ± 1.8*
Na_e/K_e	0.97 ± 0.02	1.08 ± 0.02	1.77 ± 0.09*
VO_2 (ml·min)		214 ± 10	185 ± 7‡
VCO_2 (ml/min)		200 ± 11	165 ± 7‡
R/Q		0.90 ± 0.03	0.89 ± 0.02
VO_2/body wt ($ml \cdot min^{-1} \cdot kg^{-1}$)		3.2 ± 0.2	3.1 ± 0.1
VO_2/surface area [$ml \cdot min^{-1} \cdot (m^2)^{-1}$]		122 ± 5	110 ± 4
VO_2/BCM ($ml \cdot min^{-1} \cdot kg^{-1}$)		9.9 ± 0.3	11.8 ± 0.6‡

* Significantly different ($p < 0.05$) from the normal volunteers and the normally nourished by analysis of variance and Scheffe's test.

† Significantly different ($p < 0.05$) from the normal volunteers and the malnourished by analysis of variance and Scheffe's test.

‡ Significantly different ($p < 0.05$) from normally nourished by unpaired "Student's" *t* test.

All values reported as mean ± SEM. VO_2, resting oxygen consumption; VCO_2, resting carbon dioxide product; R/Q, respiratory quotient.

Mean oxygen consumption when expressed as either ml/kg body weight (3.2 ± 0.2 and 3.1 ± 0.1 $ml \cdot min^{-1} \cdot (kg\ body\ weight)^{-1}$ or as ml/m^2 of body surface area (122 ± 5 and 110 ± 4 $ml \cdot min^{-1} \cdot (m^2)^{-1}$) was not significantly different in the two groups. However, there was a difference in the mean oxygen consumption when expressed as ml/kg BCM with the malnourished group having a significantly ($p < 0.05$) higher mean oxygen consumption, 11.8 ± 0.6 compared to 9.9 ± 0.3 $ml \cdot min^{-1} \cdot (kg\ BCM)^{-1}$ in the normally nourished patients.

Predicted versus measured oxygen consumption

The Harris Benedict equation predicts REE in kcal/day. Since this measurement was unavailable to us in our laboratory, REE was estimated by measuring oxygen consumption. The relationship between resting oxygen consumption and weight, height, age, and sex was determined from the original Harris Benedict data. For both men and women, the oxygen consumption, expressed as ml/min, was correlated, as the dependent variable, with height, weight, age, and sex as the independent variables. The resultant regression equations can thus be used to predict resting oxygen consumption in ml/min from height, weight, age, and sex (**Table 6**). The correlation coefficients, SE of the estimate, and the 95% confidence limits were similar to those obtained with REE as the dependent variable (Table 3).

Using the regression equations listed in Table 6, the resting oxygen consumption was predicted for each of the 74 patients studied. In the normally nourished patients a highly significant correlation ($p < 0.001$) existed between measured and predicted resting oxygen consumption, with a correlation coefficient of 0.76 and a regression line which approximated the line of identity (**Fig 6**). In the malnourished group, although a significant ($p < 0.01$) correlation existed between the measured and predicted resting oxygen consumption, the correlation coefficient was only 0.43 and the regression line was quite different from the line of identity (Fig 6).

Ideally oxygen consumption data should be expressed as a function of the BCM, the oxygen consuming, work performing component of body composition. As a result the above analysis was repeated with the resting oxygen consumption expressed as a function of the BCM. The predicted oxygen consumption expressed as ml/kg BCM was calculated for the normally nourished and the malnourished patients using the regression equation derived from the Harris Benedict data (Table 6). The BCM was calculated using the regression equations of Moore (Table 2). The measured oxygen consumption was expressed as a function of the mesured BCM. The predicted and measured oxygen consumptions were compared by an analysis of variance and Scheffe's test (**Table 7**). In the normally nourished group there was no difference between the measured and predicted oxygen consumption, when expressed as a function of the BCM. The mean measured oxygen consumption per kg BCM for the malnourished group was, however, significantly higher ($p < 0.05$) than the predicted value for the same group. Furthermore the measured VO_2, per unit BCM in the malnourished patients was significantly ($p < 0.05$) different from both the predicted and measured values for the normally nourished group. In contrast the predicted VO_2/kg BCM for the malnourished group was similar to that in the normally nourished group.

TABLE 6
Resting oxygen consumption

Men
$VO_2 = 12.04 + 0.687\,(ht) + 1.929\,(wt) - 0.802\,(age)$
$n = 168 \quad r = 0.88 \quad F = 191.7 \quad p < 0.0001$

Women
$VO_2 = 63.23 + 0.457\,(ht) + 1.318\,(wt) - 0.621\,(age)$
$n = 169 \quad r = 0.82 \quad F = 114 \quad p < 0.0001$

VO_2, resting oxygen consumption in ml/min.

Discussion

In their original 1919 monograph Harris and Benedict expressed reservations concerning the applicabilty of their predictive formulae to elderly individuals. This concern prompted them to carry out similar measurements in two additional groups of subjects with a wider age range. These data were published in 1928 and 1935. However, no revision of the 1919 regression equations appeared in the literature despite the availability of the additional subjects spanning a wider age range. This was due undoubtedly to the enormous task involved in performing the required computation without the aid of modern digital computers. In the present study we derived the Harris Benedict equation by using the original 1919 Harris Benedict data to correlate REE, as the dependent variable, with height, weight, age, and sex as the independent variables. This task was simplified by using a modern computer. The data from the two additional series that used identical methodology permitted us to perform a similar calculation with larger numbers of male and female subjects across a wider age range.

The regression equations derived using the original 1919 data (equations 2 and 5, Table 3) are virtually identical to the equations obtained with the data from the larger number of subjects (equations 3 and 6, Table 3). The REE obtained with both of these equations is identical to the estimate obtained with the equation published in the original

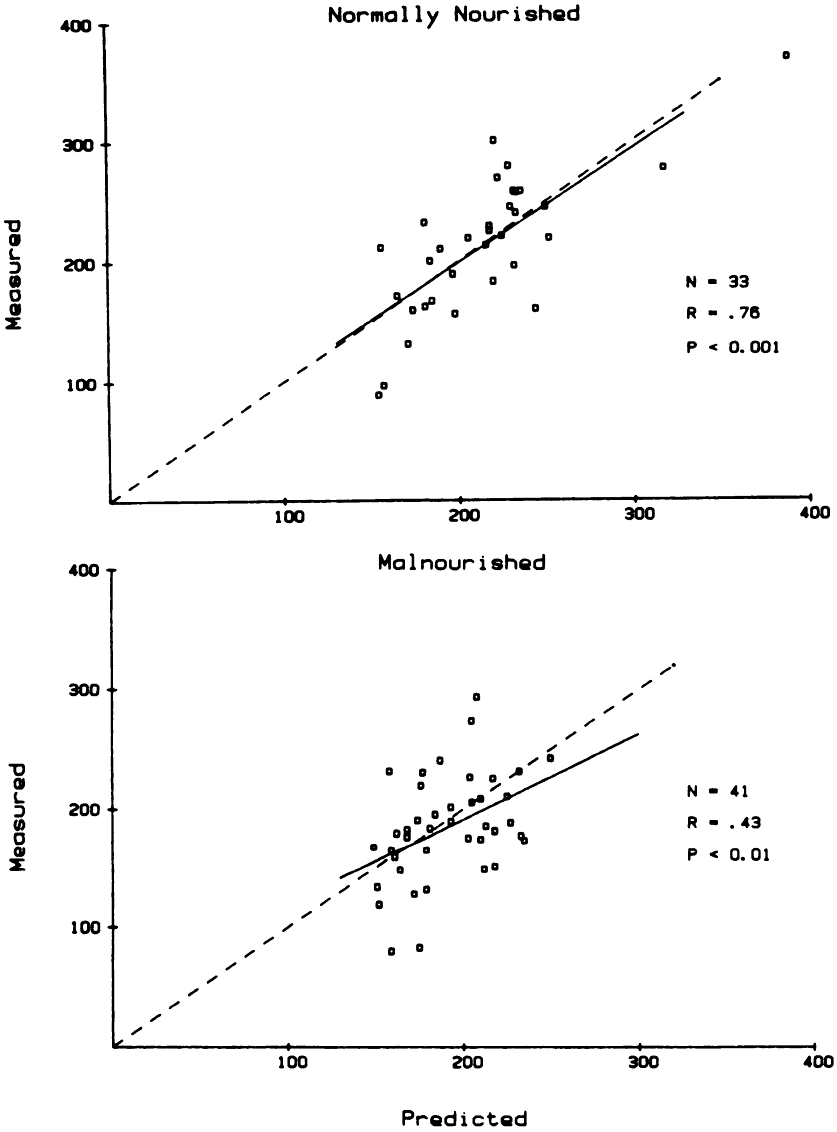

FIG 6. The correlation between measured VO$_2$ and predicted VO$_2$ (ml/min) for both normally nourished ($Na_e/K_e < 1.22$) and malnourished patients ($Na_e/K_e > 1{,}22$). A statistically significant relationship existed between the two parameters. However, in the normally nourished group the regression line was almost identical to the line of identity (*broken line*) whereas in the malnourished patients the regression line was different from the line of identity.

Harris Benedict monograph. The correlation coefficients, SE of the estimate, and the 95% confidence limits are similar for all the equations listed in Table 3. The Harris Benedict equation is therefore equally valid for both younger and older individuals. The 95% confidence limits of both the original equation and that derived from the larger group of subjects represent ±14% of the estimated REE. The Harris Benedict regression thus estimates REE of a normal individual with a precision of 14%.

Multiple linear regression was used to derive the regression equations, and therefore they are based on the assumption that a linear relationship exists between REE and the independent parameters that were used to derive the regression. However, the rela-

TABLE 7
Predicted versus measured oxygen consumption

	Measured	Predicted
Normally nourished $Na_e/K_e < 1.22$	9.93 ± 0.34	9.10 ± 0.11
Malnourished $Na_e/K_e > 1.22$	11.80 ± 0.6*	9.26 ± 0.12

* Significantly different ($p < 0.05$) from other values by analysis of variance and Scheffe's test.

All values reported as mean ± SEM. Units are $ml \cdot min^{-1} \cdot kg\ BCM^{-1}$.

tionship may not be truly linear and therefore at the extremes of age the resultant estimates may be in error. Benedict (8) reported that in elderly women (age range 66 to 88 yr) basal metabolism was constant irrespective of age when body weight exceeded 74 kg. Dubois (16), however, concluded that the linear relationship of the Harris Benedict equations actually overestimated energy requirements in the elderly.

The BCM represents the total mass of living cells. It includes the cellular components of muscle and viscera and in addition the cellular fraction of adipose tissue, bone, cartilage, and tendon. The BCM is, therefore, that component of body composition that is responsible for all of the metabolic gas exchange, ie, oxygen consumption and carbon dioxide production. All of the energy exchange and work performed within the body occurs within the BCM, whereas no work is performed by the extracellular supporting component of body composition. The primary function of the ECM is support and transport. Therefore, the BCM is the ideal reference point for energy expenditure.

In the present study the BCM was estimated from K_e. K_e is linearly related to the size of the BCM as 98 to 99% of K_e is within the intracellular compartment, and the potassium concentration within this compartment varies within a narrow range. A small, and as yet undetermined, fraction of K_e is related to glycogen stores. The potassium associated with body glycogen reflects changes in BCM that occur as a result of changes in intracellular glycogen stores. K_e is not a measure of either total body protein or total body nitrogen, as there is no potassium associated with the 30% of total body nitrogen which in the normal individual is located in the extracellular compartment.

The regression equations developed by Moore et al were used to calculate the BCM for each of the Harris Benedict subjects. These regression equations were derived from data obtained from a group of normal volunteers and have been demonstrated to predict accurately the body composition of the normal adult. Thus, it is valid to use these regression equations to calculate the BCM of the Harris Benedict subjects, who were a representative sample of the normal population. For both the men and women there was an excellent correlation between the calculated BCM and REE (Fig 1). The regression was highly significant ($p < 0.001$) with narrow 95% confidence limits about the regression. In order to examine the independent contribution of both age and BCM on REE a multiple linear regression was carried out with REE as the dependent variable and age and BCM as the independent variables. The magnitude of the regression coefficient associated with each independent variable indicates their relative influence on REE. Thus, the small regression coefficients associated with age for both men and women indicate that age plays an insignificant role in both sexes as a determinant of REE. This was demonstrated graphically in Figure 2, where age was plotted against REE, for a constant BCM. It is apparent that age negligibly affects the REE.

In contrast, when plotting age against REE for the Harris Benedict equation, with all of the independent parameters except for age held constant, age exerts a significant effect on REE (Fig 2). This arises because the independent variables in the Harris Benedict equation, namely weight, height, age, and sex, provide an estimate of the BCM. In the normally nourished individual, the BCM is directly related to body size. However, this relationship between the BCM and body weight is not a constant one throughout life. In the Harris Benedict subjects, body weight did not change significantly with advancing age (Fig 3). However, the BCM, as a fraction of the body weight did decrease significantly with increasing age for both men and women (Fig 4). It is apparent that age is a factor in the original Harris Benedict equation not because of a decline in REE associated with and secondary to the aging process. Rather, age is a factor to account for the changing relationship between the BCM and body weight with advancing age.

Different regressions are required for men and women when relating REE to weight, height, and age. However, when REE is correlated with BCM separately for men and women, the resultant regression lines are not significantly different by an analysis of variance. This was demonstrated by Figure 5 where REE is plotted against BCM for all 337 Harris Benedict subjects, both men and women. The women and men distribute evenly about the regression line, demonstrating that REE is similar in the two sexes. The different Harris Benedict equations for the two sexes arise because of the different relationship between body weight and BCM in the two sexes. Generally, in women as opposed to men, body fat occupies a larger proportion of the body weight, while the BCM is a smaller fraction of body weight.

Dubois and Benedict (16, 17) introduced the concept of the oxidizing protoplasmic mass as a reference entity in studies of energy exchange. Rubner in 1902 (18) in the German literature had proposed the concept of the active tissue mass. Behnke et al (19) later popularized the concept of the lean body mass. Moore et al defined the BCM as the oxygen consuming, metabolically active component of body composition and developed a multiple isotope dilution technique that provided an accurate, reliable, and reproducible measure of the BCM.

Oxygen consumption is usually expressed as a function of either body wieght or body surface area. In the present study oxygen consumption and body composition were determined in 74 patients. When oxygen consumption was expressed as either a function of body weight or as a function of the body surface area, there was no difference between the normally nourished and malnourished patients. However, when oxygen consumption was expressed as a function of the BCM there was a significant elevation in the malnourished group. This is consistent with previous data from our laboratory (20) and in sharp contrast to the generally held view that malnutrition is associated with a decreased or unchanged oxygen consumption. All patients were receiving minimal caloric infusions and therefore any increase in oxygen consumption secondary to large glucose and protein infusion was avoided. All of the patients studied were clinically stable, afebrile, and none had undergone recent operation.

The BCM, in gross anatomic terms can be subdivided into the skeletal muscle and the visceral components, with the skeletal portion occupying a much larger proportion of the BCM. It has been estimated that the visceral organs, liver, brain, heart, and kidney are responsible for 60 to 70% of basal oxygen consumption and that skeletal muscle consumes 16 to 30% (21). Malnutrition results in a greater relative loss of the skeletal component. Thus the rise in oxygen consumption with malnutrition, when expressed as a function of the BCM, may be due to the changing relationship within the BCM of its two main components. Malnutrition most probably results in a preponderance of the visceral subdivision with its higher oxygen consumption.

Malnutrition results in a loss of body fat, a loss of the BCM, and an expansion of the ECM. The sum of these changes is reflected in the change in body weight. Because of the expansion in the ECM and the variable loss of body fat that occurs in malnutrition, the loss of body weight is not an accurate reflection of the loss of BCM. Since REE is directly related to the size of the BCM, the use of body weight as the reference entity for metabolic gas exchange is unreliable, especially in the malnourished patient. Relating REE to body weight assumes a normal body composition. In malnutrition this assumption is not valid. Body surface area as a reference entity introduces similar errors because weight and height are used in calculating surface area. Furthermore, classification of patients into such catergories as normometabolic or hypermetabolic on the basis of energy expenditure normalized for body weight or body surface area may not in fact be valid.

The Harris Benedict equation is frequently used to determine energy requirements from weight, height, age, and sex. These independent parameters are used to estimate the BCM. The estimate obtained is valid in the normally nourished patient but probably invalid in the malnourished patient. To evaluate the validity of the Harris Benedict equation in malnourished individuals, studies were carried out in 74 patients. Because we lacked the facilities to determine REE, we measured instead oxygen consumption and carbon dioxide production. Body composition was measured at the same time. A relationship between oxygen consumption and weight, height, age, and sex was obtained using the Harris Benedict data. The equation obtained is analogous to the Harris Benedict equation. In the normally nourished patients, the resting oxygen consumption predicted by this equation was similar to the measured values. There was an excellent correlation between the two, with the resultant regression approximating the line of identity (Fig 6). However, in the malnourished patients, the regression equation did not accurately predict the resting oxygen consumption. Rather, it tended to underestimate the resting oxygen consumption. Although a statistically significant correlation existed between the predicted and measured resting oxygen consumption, the resultant regression was significantly different from the line of identity (Fig 6). Similar results were obtained when the resting oxygen consumption was expressed as a function of the BCM, the oxygen consuming component of body composition. In the normally nourished patients there was no difference in the measured and predicted oxygen consumption whereas in the malnourished patients the predicted and measured means were significantly different. In the malnourished patients, the predicted mean was 22% less than the mean measured oxygen consumption.

In 200 cancer patients Knox et al (22) compared measured REE, determined by bedside indirect calorimetry, with that predicted by the Harris Benedict equation. In 82 patients there was no difference between predicted and measured REE, normalized for metabolic body size (body weight$^{0.75}$) (23). These patients were defined as normometabolic. In 52 patients, predicted REE normalized for metabolic body size underestimated the measured REE by 18%. These patients were defined as hypermetabolic. It could be argued that the hypermetabolic patients were malnourished. As compared to the normometabolic patients, the hypermetabolic patients were older, had their disease for a longer period of time, and had a significantly smaller mean body weight, percentage ideal body weight and serum albumin.

Stewart et al (24) found a similar relationship in critically ill ventilated patients and in normal controls. Estimated energy expenditure was predicted using the Harris Benedict equation. Indirect calorimetry using the Douglas bag technique was used to measure energy expenditure. In 20 normal controls, there was no difference in the predicted and measured energy expenditure. However, in 10 critically ill ventilated patients, predicted energy expenditure significantly underestimated the measured value by 18%.

The data in this study and others therefore seriously question the reliability of the Harris Benedict equation in malnourished patients. Equations for predicting REE were derived from a normal, healthy population and thus are best applied to similar populations. To assess REE accurately in the ill and malnourished patient, direct measurement is preferable to the use of the Harris Benedict equations.

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