

Copyright
by
Valerie Anne Hodges
2004

**The Dissertation Committee for Valerie Anne Hodges Certifies that this is
the approved version of the following dissertation:**

**Evaluation of Protocols for Assessing Energy Needs in
Overweight and Obese Adults**

Committee:

M. Beth Gillham, Supervisor

Margaret Briley

RoseAnn Loop

Richard Willis

Jack Wilmore

**Evaluation of Protocols for Assessing Energy Needs in
Overweight and Obese Adults**

by

Valerie Anne Hodges, B.S., M.S.

Dissertation

Presented to the Faculty of the Graduate School of
The University of Texas at Austin
in Partial Fulfillment
of the Requirements
for the Degree of

Doctor of Philosophy

The University of Texas at Austin

May, 2004

Dedication

To Adam and Grace:

My Dream Come True

Acknowledgements

There is no way to express how much I love, honor, and cherish my husband, **Adam Hodges**. Adam, I hope you're able to read between the lines, because this can only be a feeble attempt at thanking you for wanting this for me as much as I want it for myself. Thank you for falling in love with me, marrying me, and bringing Grace into the world with me, in spite of what has seemed like a never-ending project. Thank you for your service, bravery, and honor. Grace will respect you beyond words one day, as I do today. Thank you for being a better Husband and Father than I have ever dreamed of having.

To my family. My parents, **A. J. and Patricia Hebert**, have supported whatever I have wanted for myself and have always helped me make it happen. I love you more than I can possibly express. As I sit here putting the final touches on this work, Grace is waking up, and Mom, without hesitation, you are on your way to pick her up and make it all better. Thank you both for the hours of rocking and walking Grace while I have sat at the computer. This truly would not have been completed without your help and love. Thank you for always telling me I could do anything and be

anything, and making me believe it. And to my sister, **Vanessa Littleton**, for giving up your days off to make my trips to Austin possible. Thank you for loving Grace and giving me peace when leaving her for the day.

Thank you **Dr. Gillham** for helping me see another way when I didn't think there was one. You have always known just the right words to make me better and my work better. Thank you for supporting all of my goals – not just the ones pertaining to school, and thank you for sticking out the storm and enjoying the sunshine with me. Your guidance, encouragement, and desire to see me complete this goal are invaluable.

To **Jaimie Davis** for being the best research partner I could have wished for. Your determination is inspiring and your energy is addictive. Thank you for experiencing this project with me and for always willing to be the ear on the other end of the line. I'm fortunate to have experienced this with you.

To **Alison Padget** for paving the way to fall in love, get married, bring a child into the world, and still finish graduate school. Thank you for your continued friendship and always offering a voice of reason.

To **Dr. Briley** for being the sweetest face I could find on the 3rd floor. You and Clyde have added so much to this experience, and I am thankful you have shared several years of my life with me. Thank you for seeing me get married and begin the best part of my life and encouraging me both academically and personally.

To **Dr. Loop**, you have given the best advice “this too shall pass.” Thank you for continuing to encourage me and always being available.

To **Dr. Willis** for helping me understand statistics beyond what I thought was possible. I sincerely appreciate your willingness to help me work through my statistics crisis.

To **Dr. Wilmore** for advising from afar. Thank you for lending your expertise and for staying just a mouse click away with quality suggestions.

To those who serve and protect our country, and their spouses; thank you.

**Evaluation of Protocols for Assessing Energy Needs in
Overweight and Obese Adults**

Publication No. _____

Valerie Anne Hodges, Ph.D.
The University of Texas at Austin, 2004

Supervisor: M. Beth Gillham

Accurate estimation of energy needs in overweight and obese adults is essential for long term weight management and during hospitalization, when in the presence of metabolic stress, significant underfeeding encourages loss of lean tissue. Modification of the Harris-Benedict equation (HBE) published in 1919 and derivation of new equations have attempted to accurately predict energy requirements in overweight/obese individuals. Objectives for this research were to examine protocols for adjusting weight in the HBE and to evaluate more recently developed predictive equations,

for accuracy in estimating basal energy expenditure (BEE) of overweight and obese adults.

Subjects were 53 overweight/obese and 53 normal weight healthy adults matched for gender, height, and age. Indirect calorimetry and dual energy x-ray absorptiometry were used to assess BEE and body composition, respectively. Study specific (SS) equations to predict BEE for normal and overweight/obese adults were derived using linear multiple regression. A hypothesis that excess fat-free mass (FFM), i.e., FFM above that carried at normal weight, in overweight/obese subjects would provide a tailor-made adjustment for weight in the HBE proved false. Mean excess FFM in our population was 17% while others had observed that adding 25% of the excess weight to standard body weight (SBW) in overweight/obese adults to be inadequate.

SS, Owen and Mifflin equations predicted measured BEE (MBEE) within $\pm 10\%$ for about 75% of all normal weight subjects and about 65% of the overweight/obese subjects. Overweight/obese subjects were partitioned into two groups, those >125 to 150% and $>150\%$ of SBW, and weight was adjusted by adding 25% and 60% of the excess weight to SBW for the two

groups, respectively. The HBE equation with the adjusted weights predicted MBEE within $\pm 10\%$ for 78% of those subjects >125 to 150% of SBW and more than 60% of those $>150\%$ SBW.

Although newer equations predict MBEE within $\pm 10\%$ in about 75% and 65% of the cases for normal weight and overweight/obese individuals, respectively, they are unlikely to replace utilization of the HBE in practice. Results of the present study indicate accuracy for the HBE similar to that of the newer equations in assessment of overweight/obese subjects with additions of 25% and 60% of excess weight applied to SBW for individuals >125 to 150% and $>150\%$ SBW, respectively.

Table of Contents

List of Tables	xiv
List of Figures	xvi
Chapter 1: Introduction	1
Chapter 2: Review of Literature	5
Energy Assessment Techniques	6
Fick Method	7
Direct Calorimetry	8
Indirect Calorimetry	8
Doubly-Labeled Water	9
Summary of Energy Measurement Techniques	10
Prediction Equations	10
Summary of Determination of Energy Expenditure	37
Body Composition Measurement Techniques	39
Skinfold Measurement	39
Densitometry	43
Bioelectrical Impedance	44
Biochemical Evaluation	45
Dual Energy X-ray Absorptiometry	47

Fat-free Mass and Resting Energy Expenditure	49
Chapter 3: Evaluation Of Protocols For Assessing Energy Needs In Overweight And Obese Adults	55
Abstract.....	56
Introduction.....	59
Subjects and Methods	62
Anthropometric Measurements	64
Calorimetry.....	64
Repeatability of Calorimetry Measurements.....	66
Body Composition.....	67
Regression Equations	67
Statistical Analysis	68
Results.....	69
Body Composition.....	69
Regression Equations	71
Discussion.....	75
Chapter 4: Measured Basal And Resting Metabolic Rates In A Healthy Adult Population	87
Abstract.....	88
Introduction.....	91

Methods	94
Steady State And Energy Expenditure Calculations	96
Heart Rate Data	97
Reproducibility of Calorimetry Measurements	98
Statistical Analysis	98
Results.....	99
Heart Rate Data	99
Steady State and Energy Expenditure Calculation.....	100
Discussion	101
Chapter 5: Summary and Conclusion.....	111
Appendices.....	120
Appendix A: Recruitment Flyer	121
Appendix B: Campus Wide Mass E-mail.....	123
Appendix C: Consent Form	125
Appendix D: Body Composition Print Out.....	128
Appendix E: Indirect Calorimetry Instrument.....	130
Appendix F: DXA Instrument	132
Bibliography	134
Vita	141

List of Tables

Table 2.1 Advantages and disadvantages of some available techniques for measuring and predicting energy expenditure	7
Table 2.2 Published prediction equations used to estimated energy expenditure.....	11
Table 2.3 Publications reporting the accuracy of predicted BEE using standard body weight compared to measured REE, BEE, RMR.....	18
Table 2.4 Publications reporting accuracy of predicted REE compared to measured REE.....	29
Table 2.5 Stress factors in obese subjects by Barak et al.	35
Table 2.6 Advantages and disadvantages of various body composition measurement techniques	40
Table 3.1 Gender specific weight, height, age, percent standard body weight, and BMI for overweight/obese and normal weight subjects	82
Table 3.2 Body composition data for overweight/obese and normal weight subjects.....	83
Table 3.3 Measured resting energy expenditure in overweight/obese and normal weight groups compared to predictive equations from the current study, Mifflin et al., Owen et al., HBE using actual weight, and HBE using weight adjustment of 25 and 50%.	84
Table 3.4 Mean, mean difference, and accuracy of the SS-O, Mifflin, and Owen equations, HBE using actual weight, and HBE with weight adjustments of 25 and 60% excess weight partitioned into percent standard weight for height of ≥ 125 to 150% and $>150\%$	86

Table 4.1 Age, weight, height, and BMI for males, females, and all subjects.....	108
Table 4.2 Heart rates reported as beats per minute before and during indirect calorimetry measurements.....	108
Table 4.3 Mean basal and resting energy expenditure values and oxygen consumption (VO ₂) for minutes 6-15, 10-20, 10-30, and 20-30 for males, females, and all subjects	109

List of Figures

Fig 2.1 Accuracy of Harris-Benedict using adjusted body weight in obesity, over the range of BM by Frankenfield et al.	42
Fig 3.1 Accuracy of Study Specific, Mifflin, Owen, and HBEs in overweight/obese and normal weight subjects	92
Fig 4.1 Measured Energy Expenditure for basal and resting conditions. Within subject condition and within subject period as tested by repeated measures analysis of variance	119

Chapter 1: Introduction

The complexity of physiologic factors that influence basal energy expenditure (BEE) make predicting an individual's BEE a challenging task, especially for those who are overweight. Multiple equations are available to assist clinicians in estimating BEE based on age, sex, height, and weight. The most widely used of these is the Harris-Benedict Equation (HBE) (1). Adjustments to these equations for obesity are commonly used for individuals 25% or more above their standard weight for height (SBW) (2). SBW is calculated for males at 106 pounds for the first 5 feet of height plus 6 pounds for each additional inch and for females at 100 pounds for the first 5 feet of height plus 5 pounds for each additional inch. In absence of empirical evidence, it is commonplace to add 25% of excess body weight to the subject's SBW and use that adjusted weight in predictive equations such as the HBE (1) to estimate BEE. The mathematical equation that depicts this concept is referred to as the Karkeck formula (3):

$$[(\text{Actual Body Weight} - \text{SBW}) \times 0.25] + \text{SBW}$$

Statement of Problem

Little or no experimental evidence has been collected to investigate the anthropometric basis for using adjusted weight to improve the prediction of BEE in overweight or obese individuals. To date no one has examined differences in fat-free mass (FFM) (total mass minus fat mass) in an overweight population compared to a normal weight group matched for height, age and gender as a means of precisely adjusting weight for overweight and obese individuals in commonly used predictive equations such as the HBE.

Overview of Research

This project was designed to evaluate a tool frequently used to assess energy and protein needs among those who are overweight or obese. With little access to direct or indirect measurements of BEE or body composition in hospitals, private practice clinics, and other related healthcare facilities, persons providing nutritional care generally use predictive equations to estimate BEE.

For more than eight decades the HBE (1) has been widely used for estimation of BEE. Multiplication of physical activity and injury factors by

BEE as estimated by the HBE is the accepted practice for calculating total energy requirements. Individuals whose weight is significantly above SBW offer an additional challenge. In this group BEE is assumed to be over- or underestimated if calculations are based on actual weight or SBW, respectively. The consensus among healthcare professionals is that the appropriate value is somewhere between actual body weight and SBW, but to date little data exists to establish this value.

The missing piece for establishing a sound guideline for predicting BEE in overweight individuals may be found in the amount of energy required by FFM, in particular the percent of FFM found in excess weight $[(\text{FFM above that carried at normal weight} / \text{SBW}) * 100]$. The present study will attempt to capture the percent excess FFM in overweight individuals and use that data to calculate an adjusted weight for application in the HBE. The unique contribution of this work resides in the assessment of normal and overweight individuals matched for gender, height, and age. Prediction equations are based on individuals' gender, height, and age as well as weight. Controlling for all variables except weight by matching over- and normal weight participants allows assessment of average FFM in

excess weight in overweight individuals compared to their normal weight controls.

RESEARCH GOALS

Research goals for the project are:

1. To assess the validity of the Karkeck equation that suggests that correcting body weight by adding 25% of excess weight to SBW will improve accuracy of prediction equations in estimating BEE in overweight and obese adults.
2. If warranted, develop a revised equation for estimating the best weight to use in overweight adults when estimating energy and protein needs.

Hypothesis

Measurement of FFM and BEE in normal and overweight individuals matched for height, age, and gender will result in the validation of a commonly used adjustment equation or identification of an adjustment that when used in predictive equations better estimates BEE in overweight and obese individuals.

Chapter 2: Review of Literature

As the prevalence of overweight individuals steadily increases in nearly all ethnic groups, intervention becomes progressively more important to prevent or control diseases that are associated with being overweight. An estimated 129.6 million U.S. adults, 62% of women and 67% of men, are overweight (4, 5). Along with this increased prevalence comes the increased need for nutritional intervention. One component associated with nutritional intervention is the assessment of energy and protein requirements. Assessment of basal energy expenditure (BEE) is most frequently accomplished using regression equations based on body weight alone or weight and one or more of the factors height, sex, and age. When calculating BEE for overweight clients, applying actual weight likely would suggest an excessively high caloric estimate whereas calculations based on standard weight for height (SBW) (2) may result in a caloric total insufficient to maintain current weight. In acutely ill overweight patients, rapid weight loss that might ensue from underfeeding is likely to be loss of mostly lean tissue and therefore detrimental. Actual weight of overweight

individuals needs to be appropriately adjusted before that value is incorporated into a prediction equation.

A common method for adjusting weight in overweight individuals was to add 25% of excess weight to SBW. The adjustment considered the increased fat-free mass (FFM) that accompanied excess weight and was based on an informal examination of body composition data from the literature (3). Is this modification an accurate assessment of the contribution of excess weight to one's metabolic rate? To answer this question, techniques for measuring and predicting energy expenditure and techniques available for measurement of body composition will be reviewed. Studies evaluating body composition and the contribution excess weight makes to BEE in an overweight population will be assessed also.

Energy Assessment Techniques

Assessment of basal energy expenditure (BEE) is the basic component of assessment of energy needs and subsequent nutritional intervention. Two methods for determining BEE include *measurement*, by specialized instruments, and *estimation*, using prediction equations. The existence of multiple techniques for both measurement and estimation of

energy needs provides healthcare personnel and researchers a variety of options. The advantages and disadvantages of various techniques for measuring energy expenditure are outlined in Table 2.1.

Table 2.1 Advantages and disadvantages of some available techniques for measuring and predicting energy expenditure		
Method	Advantages	Disadvantages
Direct Calorimetry	<ul style="list-style-type: none"> •Accurate and precise •Direct measurement of energy expenditure 	<ul style="list-style-type: none"> •Expensive •Cumbersome •Requires controlled environment •Few chambers in existence
Indirect Calorimetry	<ul style="list-style-type: none"> •Accurate •Compact and somewhat portable •Allows relatively rapid data collection 	<ul style="list-style-type: none"> •Expensive •Eliminates claustrophobic subjects •Does not measure substrate use
Doubly-Labeled Water	<ul style="list-style-type: none"> •May be used in free-living subjects •Accurate •Non-invasive •Requires little effort from subject 	<ul style="list-style-type: none"> •Expensive •Must estimate contribution of macronutrient oxidation •Measures overall mean of energy expenditure over 2-3 weeks; impossible to measure 24-hour expenditure thus not typically useful for basal or resting energy expenditure assessments
Prediction Equations	<ul style="list-style-type: none"> •No financial cost •Quick •Easy to use 	<ul style="list-style-type: none"> •Not as accurate as measurement techniques •Particularly subject to error in critically ill and obese populations

Direct Calorimetry

Direct calorimetry quantifies BEE by measuring heat given off by a subject and estimating the sum of evaporative (condensation and water vapor) and non-evaporative (gradient layer chamber walls) measurements. Measurements are obtained from the confines of a highly sophisticated calorimetry chamber designed to measure all heat entering or leaving the chamber. Measurements of heat loss from a single subject may be made over 24 hours to a week or more, but participants are restricted to the artificial environment for the duration of the data collection period. Although considered highly accurate, the limited availability of calorimetry chambers and the complexity of a calorimeter chamber make its use clinically impractical and of limited opportunity in present-day research (6-9).

Indirect Calorimetry

Based on respiratory gas exchange, indirect calorimetry measures energy expenditure by assessing the difference in volume of oxygen in inspired and expired air. Because of the direct relationship between oxygen consumption and caloric burn (burning 1 kilocalorie requires 208.06 milliliters of oxygen), the volume of oxygen used is interchangeable with the caloric burn rate (6-11). Resting energy expenditure (REE) or BEE may

be determined by substituting the volume of oxygen used and the volume of carbon dioxide produced into the abbreviated Weir equation (12).

Doubly-Labeled Water

Since its discovery in the late 1940s by Lifson et al. (13) enthusiasm has grown for the use of doubly-labeled water (DLW) as an approach to measuring *total* energy expenditure in free-living subjects. Although its use was initially limited by exorbitant cost, the early 1980s provided for incorporation of a more cost-effective isotope, which decreased the financial burden from \$700 to \$800 to between \$300 and \$400 per sample (9, 14), a value still not cost-effective for clinical use.

The principle of the DLW method is the consumption of an accurately weighed oral dose of $^2\text{H}_2^{18}\text{O}$ after collection of an initial urine sample. Based on the model that hydrogen is eliminated as water and oxygen is excreted as both water and expired carbon dioxide, elimination rates of labeled hydrogen and oxygen isotopes may be measured and carbon dioxide production rate calculated. Urine samples collected 12-14 days after initial dosing provide a gauge of water turnover measured by the loss of $^2\text{H}_2$ and the combined loss of water and carbon dioxide quantified by the disappearance of ^{18}O . The difference between these two values corresponds

to the subject's production rate of carbon dioxide, which can be mathematically converted to total energy expenditure (6, 8, 9, 13).

Summary of Energy Measurement Techniques

Direct calorimetry and indirect calorimetry possess the ability to obtain energy expenditure data without invasive blood collection or confinement to an artificial environment. In addition, the portability of an indirect calorimeter allows for measurement of a variety of persons including ventilator dependent and spontaneously breathing hospitalized patients and nonhospitalized individuals. In contrast to the high cost per subject associated with doubly labeled water indirect calorimetry imposes a one-time initial purchase cost with periodic refills of calibration gas plus maintenance.

Prediction Equations

The expense, invasiveness and unavailability of the previously described measurement techniques force most clinicians to rely on predictive equations for estimating energy requirements. Based on weight, height, age, gender, activity, and/or injury and/or disease, multiple formulae have been devised in an attempt to estimate BEE. Less commonly used equations include one developed by Ireton-Jones and Turner for hospitalized patients and nonhospitalized individuals (15), and those developed by the

World Health Organization (16), Owen (17, 18), Mifflin and St. Jeor (19), and the Institute of Medicine (20) as shown in Table 2.2.

Table 2.2 Published prediction equations used to estimated energy expenditure		
Author	Equation	
Ireton-Jones and Turner for obese hospitalized patients, (15)	$606 S + 9 ABW - 12 A + 400 V + 1,444^a$	
Ireton-Jones and Turner for obese nonhospitalized patients, (15)	$294 S + 11 ABW + 791$	
World Health Organization, (16) Female	3-10 years old	$22.5 W + 499^b$
	10-18 years old	$12.2 W + 746$
	18-30 years old	$14.7 W + 496$
	30-60 years old	$8.7 W + 829$
	>60 years old	$10.5 W + 596$
Male	3-10 years old	$22.7 W + 495$
	10-18 years old	$17.5 W + 651$
	18-30 years old	$15.3 W + 679$
	30-60 years old	$11.6 W + 879$
	>60 years old	$13.5 W + 487$
Owen et al., (17, 18)	Males: $879 + 10.2(WT)^c$ Females: $795 + 7.2(WT)$	
Mifflin and St. Jeor, (19)	Males: $10(WT) + 6.25 (HT) - 5(\text{age}) + 5^d$ Females: $10(WT) + 6.25(HT) - 5(\text{age}) - 161$	
Institute of Medicine, The Panel on Macronutrients, (20)	Males 19 years and older: $864 - 9.72 * \text{Age} + \text{PA} * (14.2 * \text{WT} + 503 * \text{HT})^e$ Females 19 years and older: $387 - 7.31 * \text{Age} + \text{PA} * (10.9 * \text{WT} + 660.7 * \text{HT})$	

^aS = sex (male = 1, female = 0); ABW = actual body weight (kg); A = age (years)

V = ventilatory status (ventilatory dependent = 1, spontaneously breathing = 0)

^bW = weight in kilograms

^cWT = weight in kilograms

^dHT = height in centimeters; WT = weight in kilograms

^eWT = weight in kilograms, HT = height in meters, PA = physical activity

In 1991 Ireton-Jones and Turner (15) published a regression equation for obese hospitalized and nonhospitalized individuals. BEE was measured in 65 hospitalized obese adults and 65 nonhospitalized obese adults. Each group had body weights 30% or more above their SBW. BEE was measured by indirect calorimetry at one-minute intervals until three consecutive minutes were within 10% of each other. The three measurements were averaged to obtain the measured basal energy expenditure (MBEE). Using regression analysis they concluded age, stature, and SBW were poorly correlated with MBEE in nonhospitalized individuals. In contrast they found actual body weight and gender to be significantly correlated with MBEE, $R^2 = .52$ and $p < .03$. In the hospitalized group, age, actual body weight, sex, and ventilatory status were significantly correlated with MBEE, $R^2 = .55$ and $p < .006$.

In 1981 the Joint Food and Agriculture Organization of the United Nations, World Health Organization, and United Nations University (FAO/WHO/UNU) (16) reevaluated energy and protein requirements published by the 1971 Joint FAO/WHO/UNU. The 1981 committee compiled an extensive set of approximately 11,000 basal metabolic rate

(BMR) measurements from the literature. Data represented males and females of various ages, weights, and stature; all subjects were considered to be healthy individuals. Because BMR varies with age equations were formulated for six different age ranges. Increased body fat throughout the life span in females as compared to males necessitated division of the equations by gender. Regression equations indicated that body weight was the most useful indicator of BMR in all age groups. Inclusion of height or body surface area did not improve the fit of the regression equation, and height, independent of weight, showed little effect on the predicted value of BMR.

Owen et al. (17, 18) examined caloric requirements in men and women and published two gender specific equations. Sixty lean and obese males with ranges of age, height, and weight of 10 to 82 years, 163 to 188 centimeters, and 60 to 171 kilograms participated in this study (18). Body composition was obtained by both underwater weighing and skin fold thickness measurements. BEE was measured via an indirect calorimeter after a 12 to 13 hour overnight fast at the testing facility. Subjects rested 30 minutes prior to the start of a ten-minute calorimetry measurement session.

The first 4-5 minutes were discarded and the final 5-6 minutes were used to determine 24-hour BEE. Subjects were divided into lean ($BMI \leq 30$) and obese groups ($BMI > 30$) to examine the impact of body composition on BEE. Weight, body surface area, lean body mass, body cell mass, and FFM measured by both densitometry and skin fold calipers were highly interrelated ($r > .85$); a single or combination of these variables predicted BEE equally well. Age was insignificant and excluded as a variable in the prediction equation. Body weight was highly correlated with other body composition measurements ($r > .85$) and BEE ($r = .75$). Since weight is accurately and easily determined it was used to derive a male specific prediction equation. The relationship between weight and BEE in lean versus obese males was statistically not significant. As a result one regression line with weight as the sole predictor was developed for both lean and obese males.

Owen et al. (17) also developed a BEE prediction equation specific to women. Forty-four lean and obese healthy females participated in calorimetry and body composition measurements identical to the methodology previously mentioned in the male sample. Females were

divided into lean and obese groups under the same parameters as described by Owen et al. (18). Weight, body surface area, lean body mass, body cell mass, and FFM measured by both densitometry and skin fold thickness were highly interrelated ($r > .80$). Stepwise regression analysis determined the combination of body surface area and weight ($r = .79$) to be the most highly correlated with BEE, however it was not statistically different from regression analysis for weight alone ($r = .74$). As with the male population, results from regression analysis for lean versus obese females did not differ statistically and therefore these researchers produced a single prediction equation specific for women.

In 1990 Mifflin and St. Jeor (19) published a prediction equation for healthy individuals based on REE and body composition data from 264 normal weight ($80 < 119\%$ SBW) and 234 obese ($\geq 120\%$ SBW) subjects. Percent body fat was assessed using skinfold measurements taken at three selected sites. FFM was calculated as the difference between body weight and fat mass (FM). BEE was measured by indirect calorimetry after a 12-hour fast and a 12-hour abstinence from exercise. The time of day measurements were obtained was not presented. Measurements continued

until a three-minute steady state was achieved. Parameters of the steady state or calculation of the subject's REE from the three-minute steady state were not discussed. Percent FFM was highly correlated with REE ($r=.80$). The authors felt obtaining FFM measurements in outpatient settings was impractical and difficult. Exclusion of FFM from the stepwise multiple regression analysis produced an equation based on weight, height, age, and sex. These variables accounted for 71% of the variability in REE ($R^2=.71$).

In 2002, the Panel on Dietary Reference Intakes for Macronutrients (20) presented gender specific equations for normal weight and overweight/obese individuals. The panel requested total energy expenditure data by doubly labeled water from published authors. Over 20 investigators responded with a collective database of over 700 subjects. All subjects were free-living healthy individuals who were maintaining their body weight. Normal and overweight/obese groups were based on subjects' body mass index (BMI), 18.5 kg/m² to 24.99 kg/m² and >25 kg/m², respectively. The normal weight database included a total of 407 subjects, 169 males and 238 females. The overweight/obese database included a total of 360 subjects, 165 males and 195 females. Overweight/obese equations as well as normal

weight equations were developed based on age, gender, height, weight, and physical activity variables. The overweight/obese equations were not significantly different from the equations derived from combined normal and overweight/obese data ($p=.96-.99$) or normal weight data alone ($p>.99$). Therefore, male and female predictive equations for all adults 19 years of age or older were presented.

The Harris-Benedict Equation (HBE) (1) is a prediction equation that estimates energy needs based on weight, height, gender and age. Applied almost universally in clinical nutrition, the HBE is a widely accepted method for estimating BEE. The HBE, a regression equation developed in 1919 by Harris and Benedict, has been reviewed and examined extensively for its accuracy compared to accepted methods of measurement (21-26). As shown in Table 2.3, previously published reports reached differing conclusions on the accuracy of the HBE in predicting BEE.

To clarify terminology for previously published reports, reference to energy expenditure will be presented as stated in each paper cited, i.e. REE, resting metabolic rate (RMR), BEE, or basal metabolic rate (BMR).

Table 2.3 Publications reporting the accuracy of predicted BEE using standard body weight compared to measured REE, BEE, RMR^a

Author, Year	Instrument	Patient Condition, Number of subjects(n)	Weight	Results	Statistical Analysis
Daly, 1985, (21)	Direct and Indirect Calorimetry	Healthy ambulatory outpatients n=127	90 – 125% standard body weight	HBE overpredicted REE by 14.1%±12.6% compared to direct calorimetry (DC) and 11.35%±11.15% compared to indirect calorimetry (IC)	p<.001 ^b r=.83 ^c p<.001 ^c
Pavlou, 1986, (26)	Indirect Calorimetry	Healthy males n=31	121 – 170% standard body weight; mean % standard body weight = 144±15.6	HBE (2108±270) overpredicted RMR (1942±298); 64% of subjects had RMR within ±10% of HBE value	P<.001 ^b
Vermeij, 1990, (23)	Indirect Calorimetry	50 healthy subjects 10 hospitalized patients diagnosed with liver cirrhosis n=60	Mean=158.4±30.8 lbs (healthy subjects) Mean=90.2-244.2 lbs (hospitalized patients)	BEE average of 10±45kcal/day higher than HBE in healthy group; In cirrhotic patients HBE was 93±10% of mean measured BEE; REE 8-10% higher than BEE	NS ^d
Taaffe, 1995, (24)	Indirect Calorimetry	Healthy ambulatory women 60-82 years of age n=116	Mean=155±22.9 lbs (104 - 223 lbs) (BMI = 18.9-39.4)	HBE (1315±108) accurately predicted BEE (1285±155); HBE explained 50% of variance of BEE	R ² =.50 ^e p=.0001
De Lorenzo, 2001, (22)	Indirect Calorimetry	Normal weight and obese ambulatory outpatients n=127 males n=193 females	Males: 134-270 lbs Females: 97-234 lbs	HBE accurately predicted RMR in males (mean diff 13±644) and slightly underestimated RMR in females (mean diff -59±589); similar pattern in obese subjects (means not provided)	NS
Frankenfield, 2003, (25)	Indirect Calorimetry	Nonobese and obese healthy adults n=130	Range of BMI 18.8 – 96.8	HBE range of agreement (ROA) = ±10% of RMR; Nonobese: 27%↑, 4%↓ ROA; Obese: 30%↑, 6%↓ ROA; mean % difference ↑ as BMI ↑	--

^a measurements occurred after 8, 10, or 12 hour fast, ^bpaired *t* test, ^ccorrelation, ^dnot significant, ^eregression analysis

Protocols for resting and fasting prior to measurement also will be presented. At times terminology appears to be inconsistent between basal and resting states. Since the HBE was designed to predict BEE, it is essential to know if subjects in these studies were measured under basal conditions (data collected in the morning upon awakening, after a 12-18 hour fast, and before any physical activity) (27) or resting conditions (data collected after fasting several hours and within 24 hours of strenuous physical activity.)

Daly et al. (21) observed the HBE to overestimate BEE by a mean of $11.35 \pm 11.15\%$ and $14.1 \pm 12.6\%$ compared to indirect and direct calorimetry, respectively. Subjects were 127 healthy men and women, 90-125% of SBW, and between the ages of 18 and 67 years of age. BEE for each subject was measured via direct and indirect calorimetry. Subjects began an overnight fast at 8:00PM the evening prior to the study. They arrived at the calorimetry facility between 8:00 and 8:30AM the next morning. Subjects rested 15 to 30 minutes prior to calorimetry measurements. Indirect calorimetry measurements were monitored every two minutes until stable for a minimum of 6 minutes. The final 3 minutes were averaged for a mean

BEE value. Procedures for determining stable measurements were not disclosed. Compared to indirect calorimetry, data from the HBE significantly over predicted the MBEE by an average of $11.35 \pm 11.2\%$ ($p < .001$). In spite of the significant difference between values there was a significant correlation between MBEE and predicted energy expenditure ($r = .83$, $p < .001$). Likewise, BEE measured by direct calorimetry was over predicted by the HBE ($14.1 \pm 12.6\%$, $p < .001$) but significantly correlated at $r = .84$ and $p < .001$.

Pavlou et al. (26) measured and predicted REE in 31 moderately obese males. Mean age was 48 ± 8 years. They averaged $44 \pm 15.6\%$ above SBW. After an 8 to 12 hour fast and prior to measurement of REE, subjects rested quietly for 30 to 45 minutes in a darkened quiet room. REE was measured in 30-second intervals by an indirect calorimeter. The last 10 minutes of a steady state period were averaged to produce the mean measured REE value. Procedures for determining a steady state were not provided. Mean measured REE was 1942 ± 298 compared to that predicted by HBE at 2108 ± 270 . Measured REE was found to be significantly lower than REE calculated by the HBE ($p < .001$).

Vermeij et al. (23) compared the HBE with both BEE and REE in healthy and cirrhotic patients. All subjects were measured on two consecutive days. On the resting day subjects were measured three times; 1-2 hours after breakfast (REE 1), before lunch (REE 2), and before dinner (REE 3). On the basal day subjects were measured after a minimum 8-hour overnight fast and travel to the testing site. Indirect calorimetry measurements began after a 30-minute rest in a supine position. Subjects were measured for a total of 30 minutes. The first 10 minutes were excluded and the final 20 minutes averaged for a measured energy expenditure value. The HBE was found to accurately predict BEE in the healthy control group. MBEE averaged 1645 ± 315 kcal compared to an average of 1635 ± 270 kcal as predicted by the HBE ($p < .9$). Results for cirrhotic patients followed a similar pattern. MBEE averaged 1530 ± 235 kcal compared to the average prediction of 1419 ± 303 kcal by the HBE ($p < .07$, 93% of measured mean). Measured REE of healthy subjects exceeded MBEE 8 to 10% (REE 1 = 1808 ± 365 kcals, 10%; REE 2 = 1782 ± 384 kcals, 8%; REE 3 = 1775 ± 316 kcals, 8%).

Taaffe et al. (24) compared the HBE with BEE in 116 healthy older white females, aged 60 to 82 years. BMI ranged from 18.9 to 39.4 kg/m². BEE was measured using indirect calorimetry after a 10 hour fast and an overnight stay at the testing facility. After 7 to 8 hours of bed rest and before rising respiratory gases were captured in a Douglas bag for 10 minutes after a 5-minute adjustment period. Based on analysis from oxygen and carbon dioxide contained in the bag BEE was calculated using the Weir equation. The HBE was found to accurately predict BEE in these subjects. BEE measured an average of 1285±155 kcal compared to an average of 1315±108 kcal predicted by the HBE.

De Lorenzo et al. (22) compared measured RMR to predicted RMR in normal and obese individuals. RMR was defined as “the energy expenditure 10-12 h after a meal, the subject lying supine and completely at physical and mental rest in a thermoneutral environment.” Subjects reported to the testing site in the early morning. Before measurements began subjects remained supine in a quiet room for 25-30 minutes. Using an indirect calorimeter, oxygen used (VO₂) and carbon dioxide produced (VCO₂) were measured for 30 minutes. A steady state was achieved if “VO₂ and VCO₂

did not vary more than 5% from the mean value of the 3-minute measurement period.” Only data from subjects in an apparent steady state were included. In both groups the HBE accurately predicted measured RMR with only a slight overestimation (mean difference= 13 ± 644 kcal, not significant) in males and a slight underestimation (mean difference= -59 ± 589 kcal, not significant) in females. This pattern continued in obese females ($\text{BMI}\geq 30\text{ kg/m}^2$) and overweight males ($\text{BMI}\geq 25\text{ kg/m}^2$ and $< 30\text{ kg/m}^2$). The HBE slightly underestimated RMR in obese females and overestimated RMR in overweight males (means not provided).

Most recently, Frankenfield et al. (25) evaluated prediction values from the HBE compared to MBEE in nonobese and obese individuals. BEE was measured by indirect calorimetry. Subjects were measured between 8 and 11 AM after a 12-hour fast. No resting period prior to measurement was noted. Measurements were taken for 30 minutes. The first 5 minutes were discarded, and the remaining 25 minutes were averaged for a resting state provided that the coefficient of variation was $\leq 10\%$. If a 25 minute resting state was not achieved, a 5-minute segment with a coefficient of variation of $< 5\%$ was accepted. Results were assessed based on agreement

between measured and predicted BEE. Range of agreement was set at $\pm 10\%$ of BEE. Among normal weight individuals measured and predicted BEE were within $\pm 10\%$ in 69% of the subjects; predicted BEE was 10% or more above the measured value in 27% of the subjects and $\geq 10\%$ below BEE in 4% of the subjects. Measured and predicted BEE for 64 percent of obese individuals were within range, while the predicted values were above range for 30% of the subjects and below range for 6% of the subjects. In 67% of males with a BMI > 50 the HBE overestimated MBEE by more than 10%. The mean percent difference increased as BMI increased (BMI $< 30 = 13.3 \pm 0.8\%$, BMI 30-40 = 16.4 ± 1.4 , BMI $> 40 = 26.2 \pm 1.6$).

Harris and Benedict (1) published their equation in 1919 based on MBEE from a healthy adult population. It is reasonable that healthy individuals today are different from those in 1919. Dietary intake, physical fitness levels, body composition, and increased life spans are potential explanations for differences in modern measured values and those predicted by the HBE. An additional likely explanation for variations in MBEE data is the methodology used to calculate an average value. Each study calculated a mean BEE based on a determined steady state, however, there

is no standardized procedure for obtaining a steady state. There is agreement that at a minimum the initial 5 minutes of measurements should be eliminated; yet mentioned much variation exists for calculations beyond exclusion of the initial five minutes. An additional problem associated with administering indirect calorimetry is the condition of the subject at the time of measurement. It is likely that subjects in some studies are in a resting state when they are measured rather than a basal state. Even though the conditions for basal are clearly defined as data collected in the morning upon awakening, after a 12-18 hour fast, and before any physical activity (27) no consistent definition exists for resting energy expenditure. The HBE estimates BEE. Calorimetry data obtained in a resting state would not accurately compare to values predicted with the HBE.

Turley, McBride, and Wilmore (28) acknowledged the wide variation in protocols observed throughout the literature and the possibility of inconsistent results associated with differing methodologies. These authors specifically examined RMR in subjects spending the night at the testing site (C) or transporting from home (H) on the morning of measurement. However, the condition when subjects spent the night in the

clinic met the classic definition for BMR. Four males and six females were measured on six occasions. Three measurements followed an overnight stay at the testing facility and three measurements were conducted after the subjects transported themselves to the testing site following an overnight stay at their homes. Subjects were instructed to fast for 12-hours, eat the same meal each evening, obtain at least 7 hours of sleep, and refrain from exercise for 24-hours before each measurement. In addition, on the mornings subjects slept at their homes they were instructed to wake slowly, expend as little energy as possible, and promptly drive to the facility arriving between 0530 and 0730. During the onsite overnight stay subjects were awakened between 0530 and 0730, allowed to use the restroom, and escorted to the testing room. Up to 17 hours before and throughout each measurement subjects' heart rates were monitored in 60-second intervals. Before measurement began, participants rested in a semirecumbant position ≥ 30 minutes. Data were collected for 30 minutes. Measurements were accepted if VO_2 values were within ± 25 ml/min. If this standard was not met the trial was repeated under the same conditions. In addition, if any VO_2 value was not within ± 30 ml/min of the mean VO_2 for that trial the

entire trial was eliminated. Mean (H) and (C) RMR did not differ averaging 4.4 ± 0.83 kJ/min and 4.4 ± 0.92 kJ/min, respectively. Mean rate heart rates for (H) and (C) at 50.6 ± 3.7 and 50.2 ± 4.7 beats per minute, respectively, were not different. In addition to finding no advantages to subjects staying overnight in a testing facility prior to indirect calorimetry measurement these results support the ability to obtain basal results in individuals sleeping off site before measurements and transporting themselves to the testing facility.

The HBE was designed using a population of healthy normal weight individuals (1). The accuracy of the HBE in other populations such as overweight individuals is open to question. Various adjustments to the weight used in the HBE have been employed, but uncertainty and controversy about the accuracy achieved by adjusting actual weight persists. The most widely accepted adjustment equation used today is the Karkeck formula (3). This formula was originally designed as a result of an informal review of published literature on body composition and metabolic requirements. This adjustment is based on the assumption that excess weight includes FFM plus other unknown factors result in the following equation: $[(\text{Actual Weight} - \text{SBW}) \times 0.25] + \text{SBW}$. Even though the author

intended the formula for internal use only at the teaching hospital where she practiced, in the absence of validated adjustments for obese adults, use of the Karkeck formula spread rapidly. In 1986 the formula was presented in a national newsletter (3) for practitioners caring for patients with renal disease. Because it filled a need in clinical practice this equation has become a widespread assessment tool in clinical nutrition practice. The formula was a recommended assessment tool by the American Society for Parenteral and Enteral Nutrition in a 1988 publication (29).

Few studies have investigated the accuracy of the Karkeck formula. Table 2.4 summarizes four studies that have specifically explored the use of adjusting weight by the Karkeck formula for incorporation into a prediction equation.

Cutts et al. (30) evaluated 110 ventilator-dependent adult patients at three hospitals in Missouri. Indirect calorimetry results were reviewed retrospectively from medical records. “Measurements were performed according to each institution’s protocols, which were similar.” Detailed protocols were not described. A resting state ≥ 30 minutes was maintained prior to measurements. In subjects above their SBW, an effort was made to

Table 2.4 Publications reporting accuracy of predicted REE compared to measured REE

Author, Year	Subject Condition	Methods	Number of Subjects; BMI	Weight Variations	Results
Cutts et al., 1997, (30)	Ventilator-dependent adults	Retrospective study of indirect calorimetry – resting state for ≥ 30 minutes prior to measurement	110 subjects; 29 subjects $< 101\%$ standard body weight, 35 subjects 101-129% standard body weight, 31 subjects 130-159% standard body weight	Variations used in the HBE: 25% adjusted & actual weight	Prediction equations using actual weight over predict energy requirements; HBE using adjusted weight under predicted energy requirements (empirical data not presented); 130-159% weight above weight indicates $> 47\%$ variability of prediction equations.
Glynn et al., 1999, (31)	Obese, hospitalized individuals	Retrospective chart review of indirect calorimetry – 12 to 15 minute measurement	57 subjects; BMI 30 – 50 kg/m ²	Variations used in the HBE: standard, actual, 25% and 50% adjusted weights	BMI stratified into 4 levels: 1 = BMI $\geq 30 < 35$ kg/m ² 2 = BMI $\geq 35 < 40$ kg/m ² 3 = BMI $\geq 40 < 50$ kg/m ² 4 = BMI ≥ 50 kg/m ² ; Level 4 significantly differed from levels 1-3 for HBE and was excluded from further analysis; HBE using 50% adjustment with 1.3 stress factor most closely resembled measure energy expenditure, 38/57 subjects (67%) were $\pm 10\%$ of measured energy expenditure; $r = .85$

Table 2.4 Publications reporting accuracy of predicted REE compared to measured REE, continued

Author, Year	Subject Condition	Methods	Number of Subjects; BMI	Weight Variations	Results
Barak et al., 2002, (32)	Hospitalized patients with various disease characteristics	Indirect calorimetry – 30 minute measurement	79 underweight subjects BMI = <18.5; 326 normal weight subjects = BMI 18.5-30; 162 obese subjects BMI = >30	Calculated stress factor from indirect calorimetry data (MEE) and HBE; stress factor based on the ratio: MEE/HBE; Variations used in the HBE: 25, 33, and 50% adjusted weight	STRESS FACTORS: Underweight 1.24 ± 0.25 for men and 1.19 ± 0.26 for women; Normal weight 1.24 ± 0.25 for men and 1.26 ± 0.26 for women; Obese (25, 33, 50% adjustment), 50% adjusted body weight most comparable with normal and underweight stress factors 1.26 ± 0.32
Frankenfield et al., 2003, (25)	Nonobese and obese healthy individuals	Indirect calorimetry – 30 min measurement after a 12-hour fast compared to HBE with adjusted weight	83 nonobese subjects (BMI <30), 94 obese subjects: BMI >30 (n=47), BMI 30-40 (n=20), BMI >40 (n=27)	Variations used in the HBE: 25% adjusted and actual weight	HBE in agreement with BMR if $\pm 10\%$; Actual Wt = Nonobese: 27% \uparrow , 4% \downarrow agreement; Obese: 30% \uparrow , 6% \downarrow agreement, Adjusted Wt=BMI 30-40: 5% \uparrow , 35% \downarrow agreement, BMI>40 100% \downarrow agreement; mean % difference \uparrow as BMI \uparrow (BMI 30-40, 19.5 ± 2.1 and BMI >40, 26.7 ± 1.2)

ascertain if excess weight was due to excess fat or overhydration. If patients were found to be overhydrated a dry weight was estimated, and if excess fat standard weight was adjusted to include one quarter of excess weight. In subjects found to be both overhydrated and overfat, a dry weight was determined then adjusted for excess weight. BEE was predicted using the HBE substituting weight variations of actual weight (HBE-A) and overhydrated or overfat adjustments (HBE-AD) as previously described. Twenty-nine subjects were <101% SBW, 35 subjects were 101 to 129% SBW, and 31 subjects were 130 to 159% SBW. The accuracy of HBE-AD and HBE-A was compared to MBEE and reported as a percentage. Results of 100% imply accurate assessment by the HBE compared to indirect calorimetry measurements, >100% would support overfeeding, and <100% would suggest underfeeding. Calculations using HBE-A in overweight individuals (>130% SBW) predicted BEE above indirect calorimetry results whereas the HBE-AD underpredicted BEE (empirical data was not presented). Regression analysis of measured and predicted BEE for groups 101 to 129% and 130 to 159% SBW yielded R^2 values of .21 and .47,

respectively. These data suggest adjusted-weight more strongly explains the variability of BEE as weight increases above SBW.

Glynn et al. (31) completed chart reviews of 61 obese hospitalized patients assessed by the Nutrition Support Service of Rhode Island Hospital. Indirect calorimetry measurements in moderately to severely obese ($\text{BMI} \geq 30 \text{ kg/m}^2$) patients were compared to the HBE. Calorimetry data were collected for 12 to 15 minutes. Neither a resting protocol nor the method used for calculation of average steady state value was presented. Weight variations used in the HBE included actual weight, SBW, SBW plus 25% excess body weight, and SBW plus 50% excess body weight. The sample was stratified into four levels of obesity as follows: level 1 = $\text{BMI} \geq 30$ and < 35 , $n = 40$, level 2 = $\text{BMI} \geq 35$ and < 40 , $n = 9$, level 3 = ≥ 40 and < 50 , $n = 7$, and level 4 = $\text{BMI} \geq 50$, $n = 4$. Obesity was found to have a significant affect on the accuracy of a predictive formula compared to MBEE. Post-hoc analysis found level 4, $\text{BMI} \geq 50 \text{ kg/m}^2$, significantly different ($p < .05$) from levels 1, 2 and 3 for the HBE using actual weight and HBE using average of SBW and actual weight. As a result, subjects with a BMI in level 4 were excluded from further analysis. The final sample was composed of 57

participants, 32 of which could breathe spontaneously and 25 of whom were ventilator dependent. Mean MBEE was 2036 ± 414 kcal with a range of 1340 to 3310. A variety of stress factors and weight adjustments were calculated using the HBE and proportioned within $\pm 10\%$. SBW plus 50% of weight above SBW, modified with a stress factor of 1.3, was found to be the best predictor of MBEE (38 out of 57 or 67% of subjects were within $\pm 10\%$ MBEE). In addition, a strong correlation was found between MBEE and the HBE calculated using SBW plus 50% weight above SBW ($r=.85$, $p=.001$).

Barak et al. (32) examined stress factors and body weight adjustments used to predict BEE in hospitalized patients. Indirect calorimetry data was retrospectively reviewed on 567 patients at the University of Chicago Hospitals between 1991 and 2000. Patients at least 16 years of age with a variety of critical diagnoses were categorized as underweight ($BMI < 18.5 \text{ kg/m}^2$, $n=79$), normal weight ($BMI 18.5$ to 30 kg/m^2 , $n=326$) or obese ($BMI > 30 \text{ kg/m}^2$, $n=162$). A resting period prior to indirect calorimetry measurement was not described. Calorimetry measurements were performed for 30 minutes. The first 10 minutes were discarded and the last 20 minutes averaged. MBEE was calculated using the

Weir equation. In normal weight subjects MBEE was divided by predicted BEE, determined using the HBE, to produce a mathematical stress factor. A stress factor of 1.24 ± 0.25 for men and 1.26 ± 0.26 for women was calculated. In obese individuals, five variations of the HBE were calculated using the following weight variables: actual weight, SBW, SBW plus 25% excess body weight, SBW plus 33% excess body weight, and SBW plus 50% excess body weight. Five stress factors were calculated for these subjects using a calculated HBE based on the previously mentioned weight variations. As shown in Table 2.5, the stress factor derived from indirect calorimetry data divided by the HBE calculated using 50% of the difference between actual and SBW yielded stress factors most comparable to those of normal weight individuals, 1.26 and 1.28 for females and males, respectively.

Frankenfield et al. (25) examined the validity of an HBE for REE in 83 nonobese and 94 obese individuals. Nonobese subjects had an average BMI of 24 (15.9-29.6). Obese participants were divided into the following three groups: BMI>30 (n=47), BMI 30-40 (n=20), and BMI>40 (n=27). In 36% of subjects BMI was >30 and 57% of subjects had a BMI >40.

Table 2.5 Stress factors in obese subjects by Barak et al. (32)

Weight Adjustment	Female Stress Factor ^a ± SD ^b	Male Stress Factor ± SD
Actual weight ^c	1.09 ± 0.28	1.10 ± 0.22
Standard weight ^d	1.53 ± 0.40	1.55 ± 0.35
25% adjusted weight ^e	1.38 ± 0.35	1.39 ± 0.26
33% adjusted weight ^f	1.34 ± 0.34	1.35 ± 0.25
50% adjusted weight ^g	1.26 ± 0.32	1.28 ± 0.23

^aMathematical stress factors determined by measured REE by indirect calorimetry / HBE using ^{b,c,d,e,f}

^bSD = standard deviation

^cActual body weight

^dStandard body weight as estimated by the Hamwi, (2) method (females = 100 lbs for the first 5 feet plus 5 lbs for each additional inch; males = 106 lbs for the first 5 feet plus 6 lbs for each additional inch)

^eStandard body weight plus 25% of the difference between actual and standard body weight

^fStandard body weight plus 33% of the difference between actual and standard body weight

^gStandard body weight plus 50% of the difference between actual and standard body weight

Indirect calorimetry was utilized to measure REE in the morning after a 12-hour fast. Subjects were asked to refrain from exercise during the fasting period. Participants were measured for 30 minutes. The initial 5 minutes of measurement were automatically discarded. The remaining data was accepted if it had a co-efficient of variation of $\leq 10\%$. If this criterion was not maintained, a 5-minute interval with a coefficient variation of $< 5\%$ was averaged. Predicted REE was calculated in all subjects using the HBE. The HBE predictive value was considered accurate if it fell within a $\pm 10\%$ range of measured REE. Among nonobese individuals estimated and predicted

REE in 69% of the subjects were within $\pm 10\%$ of measured REE; for 27% of these subjects HBE values were above range, and for 4% of the subjects the HBE values were below range. Estimated and measured REE for 64% of obese individuals were within range, while the HBE values for 30% of the obese subjects were above range, and 6% of the obese subjects were below range. In 67% of males with a BMI >50 the unadjusted HBE overestimated REE by more than 10%. The mean percent difference increased as BMI increased, e.g. BMI $<30=13.3\pm 0.8\%$; BMI 30-40= $16.4\pm 1.4\%$; and BMI $>40=26.2\pm 1.6$.

In individuals with a BMI >30 the HBE adjusted with 25% of weight above SBW underpredicted REE in obese subjects as shown by Frankenfield et al. (25) in Figure 2.1, particularly for those with a BMI >30 kg/m². In individuals with a BMI >40 a 25% weight adjustment in the HBE produced a 100% incidence of underprediction of REE for both men and women. Mean percent difference \pm standard error of mean between predicted and measured REE in subjects with inaccurately calculated values were 25 ± 1.3 , 19.5 ± 2.1 , and 26.7 ± 1.2 for individuals with a BMI of ≥ 30 , 30-40, and >40 , respectively.

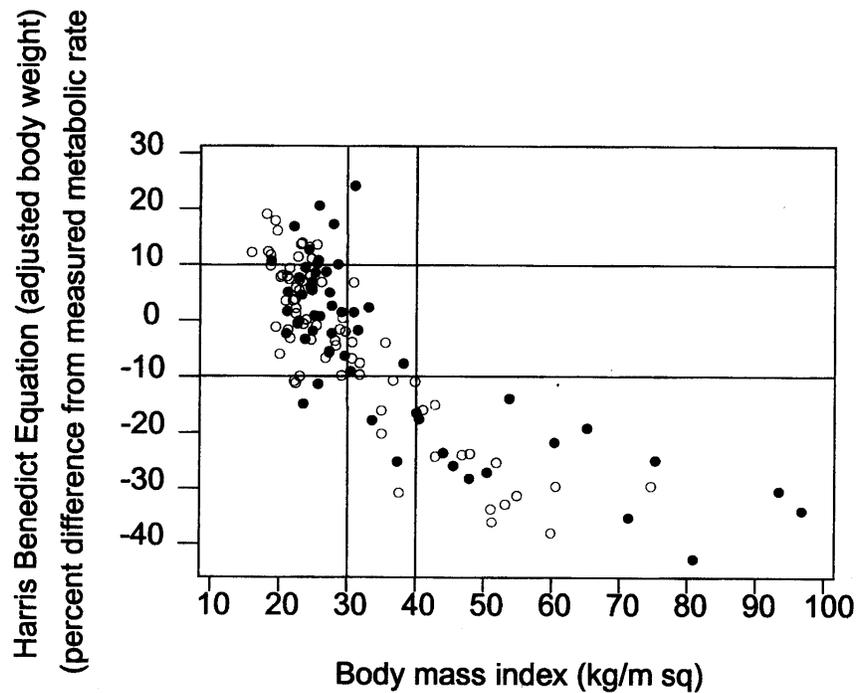


Figure 2.1. Accuracy of Harris-Benedict using adjusted body weight in obesity, over the range of BMI. Horizontal band between +10% and -10% of measured resting metabolic rate indicates range considered accurate. Vertical lines at BMI 30 and 40 separate the obesity groups. Solid circles represent men, open circles represent women. Frankenfield et al. (25).

Summary of Determination of Energy Expenditure

There is little disagreement that estimating BEE in overweight individuals is problematic. The HBE, developed on healthy normal weight

adults, may give skewed results that inaccurately assess BEE in overweight individuals. This equation relies on total body weight and does not consider FFM versus FM; therefore overestimation in the overweight population is to be expected. In addition, Frankenfield et al. (25) report that using an adjusted weight of SBW plus 25% of excess weight underestimates BEE especially as weight increases, while others have suggested that a 50% adjustment is the best predictor of MBEE (31, 32).

Body composition, particularly FFM, has proven to have an influence on BEE (19, 33-40). It is well recognized that an increase in FFM accompanies excess adipose tissue. This and other factors contribute to the increased BEE in the overweight population. Therefore, it is reasonable that predictive equations developed for normal weight populations should be adjusted or reformulated for the overweight or obese. Examination of body composition and the relation it has to BEE may shed further light on this problem.

Evidence in support of FFM as a primary predictor of BEE has made the measurement of body composition increasingly important in nutrition assessment (39-41). An adjustment to body weight in overweight clients,

based on assumptions of metabolically active FFM, is a widely accepted variation of predictive equations. Quantifying FFM in overweight individuals may bridge the inconsistencies between measured and predicted BEE in this population.

Body Composition Measurement Techniques

Multiple techniques exist for measuring body composition, each possessing advantages and disadvantages as shown in Table 2.6. Unfortunately, methods that require instruments that are small, mobile, and least expensive have a large margin for error and rely on interpretation from the administrator. Techniques that have proven accurate require equipment that is large, immobile, sometimes invasive, and very expensive. As a result the availability of accurate measurements of body composition are limited in healthcare settings.

Skinfold Measurement

Among the various methods for estimating percent body fat, skinfold thickness is one of the most reasonable and widely utilized in the clinical setting. In addition to being convenient, the equipment used for measurement is relatively inexpensive and require little storage space.

Table 2.6 Advantages and disadvantages of various body composition measurement techniques		
Measurement Technique	Advantages	Disadvantages
Skinfold Measurements	<ul style="list-style-type: none"> •inexpensive, fast, non-invasive, accurate with well trained and experienced technician, requires little space 	<ul style="list-style-type: none"> •requires biological assumptions, poor precision in the obese population, requires well trained and experienced personnel for accuracy
Densitometry	<ul style="list-style-type: none"> •two-compartment model, based on mathematics 	<ul style="list-style-type: none"> •requires much cooperation from subject; not appropriate for children, elderly, or fragile individuals; assumes intestinal gas, residual volume difficult to measure
Bioelectrical Impedance	<ul style="list-style-type: none"> •fast, inexpensive, non-invasive, requires no exertion from subject, 	<ul style="list-style-type: none"> •Results based on hydration; subjects must be compliant consuming fluids and abstaining from dehydrating agents
Total Body Water	<ul style="list-style-type: none"> •safe, simple, non-invasive 	<ul style="list-style-type: none"> •isotopes expensive; based on assumption of constant water content; potential for isotope contamination by atmospheric H₂O prior to analysis
Urinary Creatinine Excretion	<ul style="list-style-type: none"> •applicable in hospitalized patients 	<ul style="list-style-type: none"> •influenced by diet; requires much subject cooperation; 24-hour urine collection must be accurate
3-Methylhistidine	<ul style="list-style-type: none"> •applicable in hospitalized patients 	<ul style="list-style-type: none"> •influenced by diet; requires much subject cooperation; 24-hour urine collection must be accurate
Dual Energy X-Ray Absortometry	<ul style="list-style-type: none"> •fast, non-invasive, requires little input from the subject 	<ul style="list-style-type: none"> •instrument is extremely costly to purchase; •uses radiation

Measurements may be performed quickly and easily. Although these mentioned benefits make skinfold thickness one of the preferred non-invasive body composition estimation models, the potential for human error renders this method less than ideal (7).

The attempt to estimate total body fat with skinfolds relies heavily on the assumption subcutaneous adipose tissue, and the fraction of total body fat contained in that compartment is fairly directly representative of total body fat. Measuring the thickness of a double fold of skin and compressed subcutaneous adipose tissue at a single site and inferring total body fat from that data requires the assumption of five parameters: compressibility, skin thickness, adipose tissue patterning, fat fraction in adipose tissue, and a predictable relationship between internal and subcutaneous fat (42). Compressibility, a common occurrence when performing skinfold measurements, is a decrease in readings after initial application of the caliper. It is suggested this dynamic event is a result of interstitial fluid shift under pressure from the caliper. Significant differences in compressibility have been demonstrated at different sites on one subject and at one particular site among a group of subjects (43). Skin

thickness refers to a double layer of skin of unknown depth and has been shown to vary at different sites. Although its contribution to total skinfold thickness is small, it may introduce large errors, particularly in lean individuals (44). Adipose tissue patterning would be of little issue if the subcutaneous adipose tissue layer was constant in all individuals (7, 42). Given the unique variability of patterning in each person, the number of measurements needed to represent adipose tissue patterning is a major concern. Equations using readings from multiple fat storage regions, including a lower limb site, provide a general representation of overall pattern (42). The uncertainty associated with the percentage of water and fat content that make up adipose tissue thickness requires assumption of fat fraction in adipose tissue (42, 44). The water content of adipose tissue is suggested to vary from approximately 14 to 34 percent (42). Predicting body fat using skinfold thickness measurements assumes fat content of adipose tissue is constant when in reality no two identical skinfold thicknesses have the same fat concentrations (42, 43). Since skinfold calipers only estimate external fat it is necessary to assume a proportionate relationship between internal and subcutaneous fat or a negligible

contribution by internal fat compared to subcutaneous fat (42, 43). Although subcutaneous adiposity has been found to correlate with measurements from particular skinfold sites (42) the Brussels Cadaver Analysis Study (CAS 1) (42) provided little data to suggest an absolute relationship between internal and subcutaneous fat. Practice and repetition may produce consistency in skinfold thickness measurements; however, biological uncertainties hinder obtaining the most accurate body composition data by this methodology.

Densitometry

Based on Archimedes' Principle, densitometry is a technique that estimates body density given that FFM and FM are greater and less dense than water, respectively (45). This approach assumes that densities of FFM and FM are constant within the individual when in reality density of both bone and muscle vary within and between individuals. (45).

Although densitometry has generally been considered the gold standard of body composition measurement, this claim is becoming less common as newer measurement techniques become available. Subject cooperation is the variable most likely to influence the accuracy of

densitometry. Subjects must be willing to expire as much air as possible and remain motionless while submerged in a tank of water. The successes of this technique require subjects to be extremely comfortable in water and have enough strength to pull themselves underwater and remain submerged while seated on a suspended chair following expiration of air. This technique would be limited and inappropriate in elderly, pediatric, or critically ill populations.

Bioelectrical Impedance

Based on the conduction of an applied electrical current, bioelectrical impedance analysis (BIA) measures the resistance to the alternating current passed through the body by electrodes positioned on a hand and foot. Highly conductive lean mass, which contains large amounts of water and electrolytes, provides a low resistance to the electrical current. In contrast, FM and bone are highly resistant to the electrical pathway. BIA measures resistance as the current travels through the water contents of lean mass and FM. Since the water content of fat is less than that of lean mass the resistance is much higher. Given that the resistance is dependent on the aqueous environment one may conclude the resistance, or impedance, is

proportional to total body water volume (TBW). Prediction equations are used to convert a measured impedance to a corresponding TBW. Using a given hydration factor lean mass may be calculated from the estimated TBW and FM as the difference between body weight and lean mass. Most modern BIA instruments calculate TBW, lean mass and percent body fat (7, 46, 47).

The largest limitation associated with BIA is the assumption of constant hydration among subjects. Since resistance is based on the body's water content dehydration will result in an overestimation of FM. Therefore subjects must be compliant with adequately hydrating themselves, abstaining from dehydrating agents such as alcohol or caffeine, and refraining from heavy exercise that may cause excessive perspiration. In spite of these shortcomings, BIA has been found to be accurate and reliable (7, 46, 47).

Biochemical Evaluation

Total body water (TBW). TBW is an indirect measure of body composition evaluated when a known concentration and volume of a tracer is given and allowed to equilibrate with water in the body. Analysis of the

concentration of the tracer in a sample of blood, urine, or saliva allows TBW to be calculated using the formula $C_1V_1 = C_2V_2$ where C_1 = concentration of the tracer administered, V_1 = volume of the tracer administered, C_2 = concentration of the tracer in the sample, and V_2 = TBW (volume of water in the body) (7, 45, 48). Based on the assumption that FFM contains an average water content of approximately 73.2% (7, 36) FFM may be calculated by dividing TBW by 0.732. FFM is the difference between body weight and FFM (36).

Urinary Creatinine Excretion. The origin of urinary creatinine and its association with lean muscle mass may be traced back to its precursor creatine. Ninety-eight percent of the body's creatine is found in skeletal muscle and subsequently metabolized to form creatinine that is excreted in urine without alteration. Measurement of a 24-hour sample of urine should indicate total body creatinine and total muscle mass. Although the relationship between urinary creatinine and muscle mass is established, this technique is not without weaknesses. The influence dietary meat has on urinary creatinine concentration is the most notable issue. Intra-individual variations in creatinine output in both free-living and meat-free diets of 11

to 20% and 11%, respectively, have been observed; therefore, subjects' diets should be meat-free or constant during data collection. In addition, urine sample collections must be accurately timed since as little as 15 minutes can represent an error of 1% (7, 45, 48).

3-Methylhistidine. Similar to urinary creatinine, *3-Methylhistidine* is a derivative of muscle protein that is quantitatively excreted in urine, and, when measured in a 24-hour urine sample, reflects muscle and FFM. 3-Methylhistidine is produced after methylation of histidine residues in the actin and myosin of muscle fibers. After catabolism of these muscle containing proteins, 3-Methylhistidine is released and excreted in urine. Limitations are similar to those previously described for urinary creatinine excretion. Individual intra-variability is suggested to be 10% to 20%, diets should remain meat-free for the entire measurement period, and urine collections should be precisely 24-hours in duration (7, 45, 48, 49).

Dual Energy X-Ray Absorptiometry (DXA)

Dual energy x-ray absorptiometry (DXA) is a relatively new method for measuring body composition. In contrast to the previously described two-compartment (fat and fat-free) models, DXA is based on a three-

compartment model; detecting FM, bone mineral mass, and lean mass. Utilizing low-dose radiation that passes above and below the subject DXA measures both regional and total body tissue. It is a non-invasive and safe method that demands little effort from the participant and is advantageous for populations in which densitometry is too challenging, i.e. elderly, children (45, 48, 50, 51).

DXA is an accurate and precise method for obtaining body composition measurements and is becoming the preferred method for assessing body composition (38, 39, 41, 48, 50). In addition to separating FFM into lean and bone mass, lean mass may further be separated into visceral and muscular parts (50). Svendsen et al. (52) found DXA to measure bone mass, FM, and lean mass with a precision of 0.9%, 4.6%, and 1.5%, respectively. Kistorp et al. (50) found body composition measured by DXA explained 89.8% of the variation in BEE compared to 88.1% by bioelectrical impedance.

In addition to being an accurate and precise technique for measuring body composition, particular attributes of the DXA scan favor its use for the selected population in the present study. This technique required

considerably less exertion from the subject compared to densitometry, was easier to administer in an overweight population compared to skinfold thickness, and did not rely on hydration levels for accuracy as with BIA. In addition, cost per scan was a minimal financial burden compared to techniques incorporating tracers or isotopes.

Fat-Free Mass and Resting Energy Expenditure

Several investigators have observed that FFM was a major predictor of BEE. Mifflin et al. (19) developed a prediction equation for estimating REE. In a sample of 264 normal weight and 234 obese males and females, percent FFM was highly correlated with REE ($r=.80$). In addition using stepwise multiple-regression analysis FFM was the best single predictor of REE ($R^2=.64$) and produced the equation $REE = 19.7 * FFM + 413$.

Foster et al. (33) examined REE and body composition in 80 obese females with a mean BMI of 38.9 ± 7 . Stepwise regression analysis demonstrated FFM alone accounted for 26% of the variance in REE. The addition of FM only explained a 4% increase of variance for REE ($R^2=.30$).

Ravussin et al. (34) examined 24-hour total energy expenditure, RMR, and body composition in 10 control subjects ($103 \pm 2\%$ SBW), 6

moderately obese subjects ($129 \pm 1\%$ SBW), and 14 obese subjects ($170 \pm 5\%$ SBW.) Total energy expenditure, RMR, and body composition were measured using an airtight respiratory chamber, an open circuit ventilated hood indirect calorimeter, and skinfold thickness, respectively. Mean RMR was significantly higher ($p < .01$) in obese subjects (1816 ± 84 kcal/day) compared to normal weight control subjects (1464 ± 97 kcal/day). Regression analysis found FFM significantly correlated with REE, explaining 68% of the variation.

In another study, Ravussin et al. (35) measured 24-h BEE in a direct calorimetry chamber and measured body composition by densitometry in 177 subjects. Seventy-four females and 103 males with a mean weight and percent body fat of 96.9 kg and 32%, respectively, participated in the study. Mean body weight was 96.9 kilograms (41.3-178.1). FFM was the best determinant of 24-h BEE, accounting for 81% of the variance. Addition of sex or age in a stepwise multiple regression analysis did not increase the explanation of variability.

Bernstein et al. (36) measured RMR via indirect calorimetry and body composition via TBW and TBP in 154 obese women and 48 obese

men. RMR was measured after a 12-hour fast and after 30-minute resting period. Univariate correlation demonstrated weight and FFM to be most highly correlated with RMR in both males ($r=.78$ and $r=.74$) and females ($r=.66$ and $r=.65$). When the sexes were combined correlation of FFM with RMR increased ($r=.81$).

Based on a review of studies with large (>100) and small (10-50 subjects) sample sizes Cunningham (37) compiled and studied data from multiple publications that examined the relationship between REE and FFM and FM. A wide range of weights and ages as well as both males and females were included in the data sets. Results suggested FFM explained approximately 85% of individual variation in REE. In addition he reviewed studies with large data sets for which FFM was the prime REE predictor and using regression analysis developed the equation $REE = 370 + 21.6 * FFM$. This equation was supported by both large (>100 subjects) and small (10-50 subjects) sample studies and explained 65-90% of REE variance and was suggested applicable for any population of adults.

Nielsen et al. (38) found that adjusting FFM extracellular fluid did not increase the ability of FFM to predict REE. Their sample population

consisted of 153 healthy women (BMI range 21.0-32.0) and 100 healthy men (BMI range 23.0-29.9). REE was measured using an indirect calorimeter. Subjects spent the night in the research clinic, consumed their evening meal between 5:00 and 7:00 pm, and had nothing by mouth except water until after the calorimetry measurements the following morning. Methods for calculating a steady state or average REE value were not presented. Body composition was measured with DXA. In both men and women, FFM was strongly correlated with REE with r values of .62 and .65, respectively. FM was similarly correlated in women with an r of .63. Adjusted FFM (FFM – extracellular fluid) demonstrated a weaker correlation ($r=.37$) with REE compared to FFM. Likewise, adjusted FFM substituted for FFM in a multiple regression analysis produced a weaker prediction of REE indicating that adjusting FFM for extracellular fluid did not improve the prediction of REE.

Halliday et al. (40) measured REE and body composition in 22 women with a mean weight of 90.2 ± 18.6 kilograms. Body composition was measured by creatinine excretion, TBK and TBW. TBK lean body mass was most strongly correlated with REE ($r=.84$, $p<.001$) but TBW lean body

mass was highly correlated with REE ($r=.76$, $p<.001$). In addition, body weight, surface area, and sex and age were correlated with REE, all with r values of $.79$. FM determined by TBW and TBK was least correlated with REE at $r=.59$ and $r=.62$, respectively. Regression analysis of REE on lean mass and FM was conducted to assess the independent variability of lean mass and FM. Ninety-four percent of the variation in REE was explained by lean mass alone and 51% of the variation was explained by FM alone. These results corroborated those of others that lean mass has a much stronger relationship to REE compared to FM.

Increased BEE or REE in overweight individuals are attributed primarily to excess weight (34, 53, 54). Excess weight may be divided into two categories: energy requiring FFM and relatively metabolically inactive FM. Significant differences are reported between MBEE and predicted BEE when actual weight and SBW are incorporated into prediction equations. Calculation of BEE based on actual weight allocates excess energy to non-energy requiring FM, and therefore, supports further weight gain. In contrast, calculation of BEE based on SBW deprives energy

requiring FFM of needed energy and support weight loss mostly of lean mass over the short term, an ill advised event in acutely ill patients.

The present study is designed to determine what percent of excess weight in persons 25% or more above their SBW is composed of FFM, measure BEE, and assess the validity of adjusting SBW by +25% of excess weight for the HBE in overweight adults. If warranted, an alternate equation for estimating BEE in overweight individuals will be developed.

**Chapter 3: Evaluation Of Protocols For Assessing Energy Needs
In Overweight And Obese Adults**

ABSTRACT

Objectives To examine protocols for adjusting weight in the Harris-Benedict equation (HBE) and to evaluate recently developed predictive equations, including those specific for this study (SS), one for normal weight and one for overweight/obese subjects, for accuracy in estimating basal energy expenditure (BEE) of overweight and obese adults.

Design Indirect calorimetry and dual energy x-ray absorptiometry (DXA) were used to assess measured BEE (MBEE) and body composition, respectively. Identification of fat-free mass (FFM), total mass minus fat mass, in overweight/obese and normal weight individuals allowed calculation of mean excess FFM (FFM above that carried at normal weight) in overweight/obese subjects. Accuracy of equations developed in this study, those developed by Owen, Mifflin, and Harris-Benedict, and the HBE using weight adjustments of adding 25% and 60% of excess weight to standard weight for height (SBW) were assessed in normal weight and overweight/obese subjects. A predictive value within 10% of MBEE was considered accurate.

Subjects/Setting Fifty-three overweight or obese healthy adults that were >125% SBW with body mass index (BMI) ranging from >25 to 45 kg/m² were matched for gender, height (± 1 inch) and age (± 1 year) with healthy adults of normal weight, $\pm 10\%$ of SBW, and BMI's ranging from 19 to 26 kg/m².

Statistical Analysis Performed Linear multiple regression was used to derive new predictive equations for normal and overweight/obese subjects. A one-way analysis of variance was used to analyze differences in predictive equations compared to MBEE. Significance was defined at 0.05.

Results Based on body composition data from normal and overweight/obese subjects, mean excess FFM in overweight/obese individuals was 17%. Since others have found adjusting SBW by at least 25% of the excess weight under predicted MBEE for 72% of the overweight/obese subjects, factors in addition to FFM are responsible for increased BEE in this population. SS, Owen, and Mifflin equations predicted MBEE within $\pm 10\%$ for about 75% of all normal weight subjects and about 65% of the overweight/obese subjects. The HBE with

weight adjustments to represent SBW plus 25 or 60% of excess body weight accurately predicted MBEE for 78% of those >125 to 150% SBW and for 63% of those >150% SBW, respectively.

Applications/Conclusion Although newer equations predict MBEE within $\pm 10\%$ for about 75% and 65% of normal weight and overweight/obese individuals, respectively, they are unlikely to replace utilization of the HBE in practice. Results of the present study indicate similar accuracy for HBE in assessment of overweight/obese clients when 25% and 60% of excess weight is added to SBW for individuals >125 to 150% and >150% SBW, respectively.

INTRODUCTION

As the prevalence of overweight individuals steadily increases in nearly all ethnic groups, intervention becomes progressively more important to prevent or control diseases that are associated with excess weight (4). One component associated with intervention is assessment of energy requirements. The complexity of physiologic factors that influence basal energy expenditure (BEE) make predicting an individual's BEE a challenging task, especially for those who are overweight or obese. Most frequently BEE is estimated with predictive equations based on body weight alone or weight and one or more additional factors such as height, sex, and age.

The predictive equation published by Harris and Benedict (HBE) (1) in 1919, is widely used among practitioners in health care. The HBE was developed on healthy adults of normal weight and may give skewed results that inaccurately assess BEE in overweight individuals. The HBE relies on total body weight and does not consider fat-free mass (FFM) versus fat mass (FM); therefore overestimation of energy needs in the overweight population is to be expected. Adjustments for obesity are commonly used

when the HBE is employed among those who are >125% of their standard weight for height (SBW) as defined by Hamwi (2). One adjustment widely employed in clinical dietetics since 1984, prescribes adding 25% of the excess body weight to the subject's SBW and then using that adjusted weight in predictive equations such as the Harris-Benedict (3). At least one published study reported that using an adjusted weight of SBW plus 25% of excess weight underestimated BEE, especially as weight increased (25) while others have suggested that a 50% adjustment, an average of actual and SBW, is the best predictor of measured BEE (MBEE) (31, 32). More recently developed but less commonly used predictive equations include those generated by Owen (17, 18), and Mifflin et al. (19). Neither of these equations distinguish between normal weight and overweight or obese individuals. However, when evaluated by Frankenfield et al. (25), both more accurately predicted BEE within $\pm 10\%$ of measured values than Harris-Benedict based on actual weight or adjusted by 25% of excess for those greater than 125% their SBW.

The missing piece for establishing a sound guideline for predicting BEE in overweight individuals may reside in the amount of energy required

by additional FFM associated with excess weight. This tissue is likely responsible for a significant portion of increased BEE of overweight/obese individuals of same sex and height.

The present study was designed to capture the average extra FFM expressed as a percent of SBW in overweight individuals and use that data to calculate an adjusted weight for application in the HBE. To accomplish this goal, both body composition and BEE were measured in normal and overweight individuals matched for gender, height, and age. It was hypothesized that controlling for several prominent variables that contribute to BEE other than weight when matching over- and normal weight participants would allow identification of differing BEE between normal and overweight/obese adults. Body composition analysis in these matched pairs would allow the identification of excess FFM in overweight and obese individuals by subtracting the FFM of the normal weight control from that of their overweight or obese match. That value could be converted to a percent of excess weight if divided by the overweight or obese subjects weight minus their SBW and multiplied by 100. This FFM composed of extra muscle, circulatory, and other tissue related to increased FM increases

BEE in overweight/obese adults to a greater degree than FM and possibly would represent an appropriate adjustment for weight in overweight and obese subjects in the HBE or other predictive equations.

Investigational reports that have attempted to identify a weight adjustment for overweight and obese subjects related to the excess FFM present in these subjects that would improve the accuracy of predictive equation in this population are limited. To our knowledge, the problem has not been addressed in an overweight population compared to a normal weight group matched for height, age, and gender. Objectives of the current study are to 1) identify and/or validate an appropriate adjustment to weight for estimating BEE in overweight/obese individuals with the HBE, 2) provide a new set of equations that will more accurately predict BEE in individuals >125% of their SBW than is possible with current procedures and 3) to evaluate accuracy of study specific (SS), Owen (17, 18) and Mifflin (19) equations, and HBE (1) with two weight adjustments.

SUBJECTS AND METHODS

A total of 106 generally healthy volunteers (70 females and 36 males) participated in this study. Subjects were recruited by posting flyers

at local gyms, spas, running clubs, and hospitals, and distributing a campus wide mass e-mail at the local university. Fifty-three volunteers (35 females and 18 males) >125% of their SBW, qualified for the overweight/obese group. Fifty-three individuals (35 females and 18 males) matched for gender, height (± 1 inch) and age (± 1 year) whom were within ten percent of their SBW were accepted for the normal weight group. Individuals who may have an excessive amount of muscle mass, such as body builders and elite athletes, were excluded because of discrepancies in body composition when compared to the general population. Pregnant females were excluded from participation because of the radiation emitted by the DXA instrument. To avoid discomfort and subsequent inaccuracy of indirect calorimetry measurements, individuals who were claustrophobic or experienced anxiety in small places such as the clear plastic hood used in our calorimetry measurements were excluded. This research was conducted with approval from the Human Subjects Review Board at the University of Texas at Austin and informed written consent was obtained from each subject before measurement.

Anthropometric Measurements

All participants were weighed on the same Physician Dual Ready Scale (Model 337, Detecto, Webb City, Missouri) located in a campus laboratory. Weight was recorded to the nearest quarter of a pound. Height was measured to the nearest sixteenth of an inch using a wall-mounted stadiometer. SBW was calculated as defined by Hamwi (2). Subjects were measured without shoes, with empty pockets, and light clothing.

Calorimetry

Resting energy expenditure (REE) was measured using an open-circuit canopy ventilated indirect calorimeter system (Deltatrac Metabolic Monitor, serial number 65001, Sensor Medics Corporation, Yorba Linda, CA.) The calorimeter was allowed to warm up at least thirty minutes before measurements were made. Relative humidity at 55 to 60% at the test sites was within the instrument's tolerance of 10 to 90%. Gas calibration was conducted, as specified by the manufacturer, before the first measurement of each testing day using concentrations of 4% carbon dioxide and 96% oxygen except for one data collection session where 13 subjects, 3 from the overweight/obese group and 10 from the normal weight group, were

measured. For this session the standard gas was not available, and a mixture containing 5.2% carbon dioxide and 94.8% oxygen was used instead.

REE was obtained between 7:30 and 11:30 a.m. in the morning or between 3:30 and 6:30 p.m. after subjects had fasted, with the exception of water, for at least three hours and abstained from vigorous physical activity for 24 hours. Participants were instructed to rest on a lounge chair in a supine position with arms and hands in a comfortable position. A light blanket was available in the event the subject was too cool. A brief oral explanation of the calorimeter and the process of obtaining metabolic data were provided to each individual. To provide visual stimulation to help participants stay awake during the measurement period, a National Geographic or Discovery Channel video was shown.

A clear plastic canopy was placed over the subject's head so that it rested on their shoulders, and adjusted until the subjects was comfortable. The thin plastic collar attached to the canopy was folded under the pillow and tucked around the participant so that the air inlet was the only passageway for air exchange. All measurements were performed for a

minimum of 15 consecutive minutes. At the conclusion of the calorimetry measurement, subjects were offered a light snack and juice.

REE was calculated using the abbreviated Weir equation (12) from the mean of minutes 6 to 15 unless the coefficients of variation for volume of oxygen (VO_2) was $\geq 10\%$. In those cases, a mean of 5 continuous minutes from the same time period with coefficients of variation $\leq 5\%$ was utilized. Additional data collected in our laboratory indicated that energy expenditure under resting conditions for minutes 6 through 15 averaged about 12% above that measured under basal conditions. To facilitate comparison of our data with equations developed under basal measurements, the resting values were reduced by 12% and will be referred to as BEE.

Reliability of Calorimetry Measurements

In order to verify that differences observed between BEE and REE in our laboratory were related to the conditions of measurement rather than variation in repeated measures, eight subjects were measured under identical resting conditions at the same time on different days. The two measurements were highly correlated ($r=.97$), and no significant differences

between measurements were observed ($p>.847$). Percent mean difference for the two measurements was 1.3% with a range from 0 to 3%.

Body Composition

Body composition was measured using dual energy x-ray absorptiometry (DXA) (Prodigy Pro, GE Medical Systems LUNAR, Madison WI, Encore 2002 Software). A certified radiology technician performed all DXA scans. Participants were asked to remove all jewelry, excess clothing, shoes, and to remain as stationary as possible in the supine position on the DXA scan bed.

Regression Equations

Measured BEE (MBEE) values were compared with BEE derived from four regression equations, the HBE (1), Owen et al. (17, 18), Mifflin et al. (19), and those developed from this sample population (SS). Based on percent SBW, overweight/obese subjects were partitioned into the following subgroups: >125 to 150% and >150%. Adjustments were made to weight by adding 25% and 60% of excess weight to SBW, e.g. for the 25% adjustment, [(actual weight – SBW * .025) + SBW].

Statistical Analysis

Data were analyzed using Statistical Program for the Social Sciences (SPSS) (SPSS 11 for Mac OS X, Version 11, Chicago, IL: SPSS, Inc. 2003.) Results were reported as mean \pm standard deviation; α was set at 0.05. Percent SBW and body mass index (BMI) in overweight/obese and normal weight groups were compared using independent *t* tests. Multivariate analysis of variance (MANOVA) was used to analyze body composition data. Multiple regression analysis was used to identify strong predictors of BEE. Based on unstandardized beta coefficients, weights were assigned to each variable, and predictive equations for both normal weight and overweight/obese groups were generated. BEEs estimated from equations developed by Owen et al. (17, 18), and Mifflin et al. (19), and the HBE with and without weight adjustments, and SS equation for normal weight (SS-N) and overweight/obese (SS-O) were compared to MBEE using a one-way analysis of variance with Scheffe multiple comparisons post hoc test. Mean difference was calculated between predicted BEE and MBEE; a predictive value within 10% of MBEE was judged to be accurate.

RESULTS

Height, weight, age, percent SBW, and BMI, are presented in Table 3.1. Normal weight and overweight/obese individuals were matched for gender, height (± 1 inch) and age (± 1 year). On average, the normal weight group was 0.6 inches taller than the overweight/obese group. Mean age for the two groups was essentially identical. Percent SBW was about 53% higher in overweight/obese subjects on the average than in those of normal weight. Mean BMI in overweight/obese subjects was 12 kg/m^2 higher on the average than that of matched normal weight individuals. Four male subjects classified as normal weight had a BMI of 26 kg/m^2 . These subjects were not excluded from the normal weight group because they met the inclusion criteria of weight within $\pm 10\%$ of SBW. Percent SBW for these subjects ranged from 105 to 107% and percent FM for these subjects ranged from 19 to 26%.

Body Composition

Body composition data are presented in Table 3.2. Significant effects in percent FM and percent FFM were observed for group, gender, and group by gender. As a group, overweight/obese subjects had about 54

pounds more FM and 18 pounds less FFM than their normal weight matched controls. A significant gender effect was observed for percentages of FM ($p<.001$) and FFM ($p<.001$). Average percent FM of 21% for normal weight males was unexpected. However, four male subjects, ages 60 to 68 years, had a percent FM $>24\%$. These subjects were not excluded from the normal weight group because they met the inclusion criteria of weight within $\pm 10\%$ of SBW. Percent SBW for these subjects ranged from 105 to 110%.

One goal of this study was to quantify FFM found in excess weight of an overweight/obese population. The essence of this study was the recruitment of subjects matched for height, age, and gender, so that the FFM of each normal weight subject could be subtracted from that of the overweight/obese match. That value could then be expressed as a percent of excess weight by dividing weight by the overweight/obese subjects actual weight minus their SBW and multiplying by 100, as shown in the following equation:

$$\% \text{ excess Fat-Free Mass} = \text{FFMo} - \text{FFMn} / (\text{AWTo} - \text{SBWo}) * 100$$

where FFM_o equals FFM in the overweight/obese group, FFM_n equals FFM in the normal weight group, AW_o equals actual weight of the overweight/obese group and SBW_o is the SBW of the overweight/obese group. Average percent FFM in excess weight for the overweight/obese group was approximately 17±14%. This suggested 17% of excess weight in overweight/obese subjects is FFM, and a weight adjustment of SBW plus 17% of excess weight incorporated into the HBE might accurately predict BEE in clients >125% SBW. Since Frankenfield et al. (25) in assessing the accuracy of adjusted body weight in the HBE demonstrated that adding 25% of excess weight to SBW underestimated MBEE in many overweight/obese subjects, the 17% weight adjustment was judged inadequate and eliminated from further analysis of predictive equations in the study population. Given the similarities of height, weight, and age in the two groups of the current study, apparently additional unknown factors in addition to excess FFM contribute to increased BEE in overweight/obese individuals.

Regression Equations

Table 3.3 presents the gender specific mean, mean difference, and statistical analysis of predictive BEE determined by various equations

compared to MBEE. Based on data from subjects in the present study, multiple linear regression analysis was used to develop SS-N and SS-O. For overweight/obese individuals weight, height, age, and gender explained 75% of the variance in MBEE and generated the formula: $SS-O = 860 + (9.7 * wt (kg)) - (1.6 * ht (cm)) - (6 * age) - (315 * S)$, where S = 1 for females and 0 for males. In the normal weight population weight, height, age, and gender were able to explain 77% of the variance in MBEE and produced the formula: $SS-N = (6.9 * wt (kg)) - (7 * ht (cm)) - (2.2 * age) - (182 * S) - 59$, where S = 1 for females and 0 for males. None of the predicted means for BEE differed statistically from MBEE except HBE for the overweight/obese subjects when actual weight was employed.

Figure 3.1 presents accuracy of predictive equations analyzed in the current study. Predicted BEE values were considered accurate when they differed from MBEE by no more than 10%. As expected, the SS equations derived from the study sample using weight, height, age, and gender as predictors, predicted MBEE more frequently than the other equations examined. In normal weight subjects, rates of accurate prediction for the Owen and Mifflin equations (17, 18, 19) were comparable to the SS

equation. Errors in prediction occurred most frequently using the HBE, which overestimated BEE by more than 10% in almost half of the cases.

In the overweight/obese group, the Owen equation (17, 18) accurately predicted MBEE in as many subjects as the SS-O equation while Mifflin (19) and the HBE adjusted for 25 and 50% were accurate in about as many cases. The HBE using actual weight over predicted energy needs for three-fifths of subjects. The HBE adjusting weight using 25% of excess weight underestimated MBEE in almost one-third of the cases. The HBE using weight adjustment of 50% excess weight both under and over predicted MBEE in nearly 20% of subjects.

In the present study, overweight/obese subjects' SBW ranged from 128 to 218% and BMI ranged from 26 to 45 kg/m². It is not surprising that a single adjustment failed to accurately predict MBEE in subjects with extreme variations of weight. In an attempt to evaluate the accuracies of predictive equations as weight increased, overweight/obese individuals were divided into two groups with percent SBW of >125 to 150% and > 150%. These values were chosen based on linearity of fit for weight and MBEE,

which disappeared to a great extent when weight ranged above 150% SBW or a BMI of 35 kg/m².

Using MBEE and weight, height, and age for each subject, the HBE was solved in reverse, with the following formula, to calculate a weight adjustment.

$$X = \{MBEE - (66 \text{ for males \& } 655 \text{ for females}) - [(5 \text{ for males \& } 1.8 \text{ for females})(ht \text{ in cm})] + [(6.8 \text{ for males \& } 4.7 \text{ for females})(age \text{ in years})]\} / 13.7 \text{ for males \& } 9.6 \text{ for females}$$

and

$$X / SBW * 100 = 57\% \text{ on the average in our population}$$

The accuracy of the HBE for subjects >150% SBW was assessed using an adjustment of SBW plus 60% of excess weight.

Table 3.4 presents an examination of selected predictive equations in overweight/obese subjects partitioned by percent SBWs of >125 to 150% and >150%. Among subjects >125 to 150% SBW, SS-O, Owen, and the HBE adjusted with 25% excess weight was accurate for about three-quarters of the cases. The Mifflin equation predicted accurately in about 65% of the cases, while the HBE using actual weight predicted accurate values for fewer than one-fifth of cases.

The HBE adjusted with SBW plus 25% excess weight accurately predicted MBEE in less than half of all subjects >150% SBW whereas the HBE adjusted with 60% of excess weight accurately predicted BEE in over 60% of these same subjects. Rates of accuracy for the other equations tested except the SS-O and Owen equations among those >150% SBW were about 50%. SS-O and Owen approached an accuracy rate of 60%. The HBE using actual weight over predicted BEE by more than 10% for almost one-half of the subjects while the HBE adjusted for 25% of excess weight under predicted needs by more than 10% for one-half of the subjects. With the 60% adjustment, the HBE underestimated needs for less than 10% of the subjects; rate of overestimation was almost 30%, however.

DISCUSSION

The accuracy of predictive equations in normal weight individuals has been examined in multiple studies. Daly et al. (21) and Pavlou et al. (26) concluded that the HBE (1), the equation most commonly used in clinical practice, over predicted BEE while others found that it accurately predicted BEE (22-25). The HBE was produced in 1919 based on a healthy normal weight adult population. As lifestyles become less active and body

weight increases, attention has turned to derivation of new predictive equations or adjustment to the HBE in the assessment of overweight/obese individuals.

These results suggest that when predicted and measured mean differences are the criteria SS-N, Mifflin equation, Owen equation, or HBE predict BEE equally well for normal weight individuals. Similarly, SS-O, Mifflin equation (19), Owen equation (17, 18), and the HBE using 25% or 50% weight adjustment predict BEE equally well for overweight/obese individuals. Adjustment to HBE equation in overweight/obese individuals is supported by Barak et al. (32) and Glynn et al. (31) who agree BEE in overweight clients are most accurately calculated when SBW plus 50% of excess weight is incorporated in the HBE.

However, a more rigorous method for evaluating predictive formulae is to plot the accuracy of the equations in predicting BEE within 10% of the measured value, as shown in Figure 3.1. Results of this analysis suggest that SS-N derived from this sample population and the equations produced by Owen (17, 18) and Mifflin (19) are more accurate predictors of BEE in normal weight subjects than the HBE which over predicted BEE by more

than 10% for 47% of the subjects. Among overweight/obese subjects, SS-O and the equations produced by Owen et al. (17, 18) and Mifflin et al. (19) appeared to be more accurate predictors of MBEE than the HBE using actual weight, which over predicted BEE for 60% of the subjects. The HBE adjusting SBW with 25% and 50% excess weight improved on the HBE using actual weight but did not appear to improve on accuracy rates of SS-O or the Owen (17, 18) or Mifflin (19) equations. Mifflin (19) over predicted for about one-third of the subjects while the HBE using 25% of excess weight under predicted for a similar number.

Accuracy of predicting BEE for overweight/obese individuals may be improved by giving special consideration to the degree of overweight/obesity as shown in Table 3.4. Adjustments are typically made in individuals >125% SBW. Our data indicate that individuals at 125% SBW may not be accurately assessed using the same equation used for those >150% SBW. Glynn et al. (31) and Frankenfield et al. (25) noted a tendency for increased error with standard prediction equations as body weight increased. Although the predicted and measured means did not differ significantly, and percent of subjects for which predicted and

measured values agreed within 10% did not differ greatly, scatter plot data from the present study indicated that error was more likely to occur using the HBE with a 25% adjustment as weight increased. When the overweight/obese subjects were partitioned, mean difference between measured and predicted BEE using the HBE with a 25% adjustment increased from 7 kcal/day in individuals >125 to 150% SBW to 153 kcal/day in those >150% SBW. The HBE with a weight adjustment of 60% of excess weight added to SBW predicted MBEE within 10% more frequently for those subjects at >150% SBW than the HBE using a weight adjustment of either 25 or 50% of excess weight.

Data from the present study generated a SS equation for estimating BEE in normal and overweight/obese adults. In addition, Owen (17, 18) and Mifflin (19) equations were similarly accurate predictors of MBEE across all subjects. However, use of these recently developed equations in practice continues to be limited. Since results of these predictive equations vary in different populations, and the accuracy of predicted BEE depends on how much a particular subject differs from the mean in the population used

to produce the equation, one equation is not likely superior to another in all adults.

The unique characteristic of the present study was that overweight/obese subjects matched for gender, height, and age with normal weight individuals. This deliberate protocol allowed examination of MBEE with variations attributed to weight rather than height, age, or gender. This distinction in weight was examined as variations in body composition, as assessed by DXA. Employment of a reliable and accurate DXA instrument increased the confidence in data collection and results produced from body composition measurements and allowed for the inclusion of subjects who would not have participated had densitometry been required. Although the goal of determining what percent of FFM is contained in excess weight and a subsequent recommendation for a more accurate adjustment to the HBE for assessment of overweight/obese individuals did not materialize, the study did set the scientific community on notice that factors other than excess FFM are responsible for a considerable portion of the increased BEE in overweight/obese adults.

A major shortcoming of this study is the minimal number of subjects with a BMI greater than 35 kg/m². Seventy-two percent of overweight/obese subjects had a BMI from 26 to 35 kg/m² and 19% were concentrated at 35 kg/m². Only 8% of subjects had a BMI >40 kg/m². A larger representation of subjects with BMIs >35 kg/m², or SBW >150%, especially males, would have increased our ability to predict BEE for that segment with greater confidence.

The HBE is the oldest, most well recognized, and highly utilized prediction equation. Adoption of newer equations as the standard for assessment of BEE is likely to be slow. Although SS equations for this investigation and Owen (17, 18) and Mifflin (19) equations result in predicted BEE within ±10% of MBEE in about 75% of normal weight and 65% of overweight/obese subjects, it is unlikely that any of these equations have the potential to replace the HBE in the near future. Therefore, our attention was directed toward the most accurate weight adjustment to be incorporated into the HBE. Although a weight adjustment of adding 25% of excess weight to SBW enjoys wide use among practitioners, it loses predictability in subjects >150% SBW. Instead, our results show clinicians

may use the HBE for assessment of BEE in overweight/obese clients provided the proper weight adjustments of 25 and 60% are applied to individuals >125-150% SBW and >150% SBW, respectively.

Table 3.1 Gender specific weight, height, age, percent standard body weight, and BMI for overweight/obese and normal weight subjects

	Overweight/Obese			Normal Weight		
	Men n=18	Women n=35	All Subjects n=53	Men n=18	Women n=35	All Subjects n=53
Weight (lb)	235±21 ^a (202–272) ^b	199±31 (151–276)	211±32 (151–276)	175±15 (151–197)	127±10 (111–148)	144±26 (111–197)
Height (in)	70.7±3 (65–74)	64.4±2 (61–69)	66.5±4 (61–74)	71.3±2 (67–76)	65.0±2 (62–68)	67.1±4 (62–76)
Age (years)	40±10 (20–60)	40±14 (20–69)	40±13 (20–69)	40±10 (21–58)	40±14 (19–68)	40±13 (19–68)
%SBW ^{c, d}	138±8 (128–155)	164±23 (129–218)	155±23 (128–218)	101±5 (91–107)	102±5 (90–111)	102±5 (90–111)
BMI (kg/m ²) ^{d, e}	33.1±5 (31–36)	33.9±2 (26–45)	33.6±4 (26–45)	24.3±1 (22–26) ^f	21.2±1 (19–23)	22.3±2 (19–26)

^a mean ± standard deviation

^b range (minimum-maximum)

^c SBW = standard weight for height (2)

^d significant group effect (p<.001)

^e BMI = body mass index

^f 4 males subjects with BMI = 26 kg/m² were included in this group because they met inclusion criteria of ±10% SBW

Table 3.2 Body composition data for overweight/obese and normal weight subjects^a

	Overweight/Obese			Normal Weight		
	Men n=18	Women n=35	All Subjects n=53	Men n=18	Women n=35	All Subjects n=53
Fat Mass (lbs) ^{b, c}	79±14 ^d (60-112) ^e	94±21 (58-144)	89±20 (58-144)	36±8 (17-50)	34±8 (21-57)	35±8 (17-57)
% Fat Mass ^{b, c}	34±4 (28-45)	47±5 (34-56)	43±8 (28-56)	21±4 (10-26)	27±6 (16-39)	25±6 (10-39)
Fat-Free Mass (lbs) ^{b, c}	154±15 (131-186)	104±14 (81-147)	121±28 (81-186)	138±13 (118-160)	93±9 (77-114)	108±24 (77-160)
% Fat-Free Mass ^{b, c}	66±4 (55-73)	53±5 (44-66)	57±8 (44-73)	79±4 (74-90)	73±6 (61-84)	75±6 (61-90)

^a fat and fat-free mass (lean + bone mineral content)/total body weight;

^b significant group effect (p<.001)

^c significant gender effect (p<.001)

^d mean ± standard deviation

^e range (minimum-maximum)

Table 3.3 Measured basal energy expenditure^a in overweight/obese and normal weight groups compared to predictive equations from the current study, Mifflin et al., Owen et al., HBE using actual weight, and HBE using weight adjustments of 25 and 50%.

	Mean		Mean difference		P value ^{b,c}	
	Males	Females	Males	Females	Males	Females
Study Specific Equations^d	kcal/day					
Normal Weight (SS-N)	1659±88	1216±66	-1	< 1	NS	NS
Overweight/Obese (SS-O)	1941±127	1444±164	6	6	NS	NS
Fat-Free Mass Equations						
Normal Weight	1647±91	1205±78	11	10	NS	NS
Overweight/Obese	2084±110	1575±141	-136	-125	NS	NS
Mifflin et al. (19)						
Normal Weight	1733±115	1249±94	75	-33	NS	NS
Overweight/Obese	1993±148	1565±172	-46	-115	NS	NS
Owen et al. (17, 18)						
Normal Weight	1690±71	1212±32	-32	3	NS	NS
Overweight/Obese	1967±96	1448±100	-19	3	NS	NS
HBE Actual Wt (1)						
Normal Weight	1798±141	1319±76	140	-103	<.038	NS
Overweight/Obese	2163±183	1630±154	-215	180	<.018	<.002
25% adjusted HBE^e (3)						
Overweight/Obese	1859±163	1376±74	88	74	NS	NS
50% adjusted HBE^e						
Overweight/Obese	1961±168	1461±109	-13	-11	NS	NS

^a Mean and standard deviation for MBEE in kcal/day for: Normal weight female (n=35) = 1215±124; Normal weight male (n=18) = 1658±176; Overweight/obese female (n=35) = 1450±232; Overweight/obese males (n=18) = 1948±201

^b One-way analysis of variance (ANOVA) with Scheffe multiple comparisons post hoc test

^c NS = not significant; significant at p<.05

^d SS Equations = study specific equation

^e [(actual weight – SBW) * 25 or 50%] + SBW

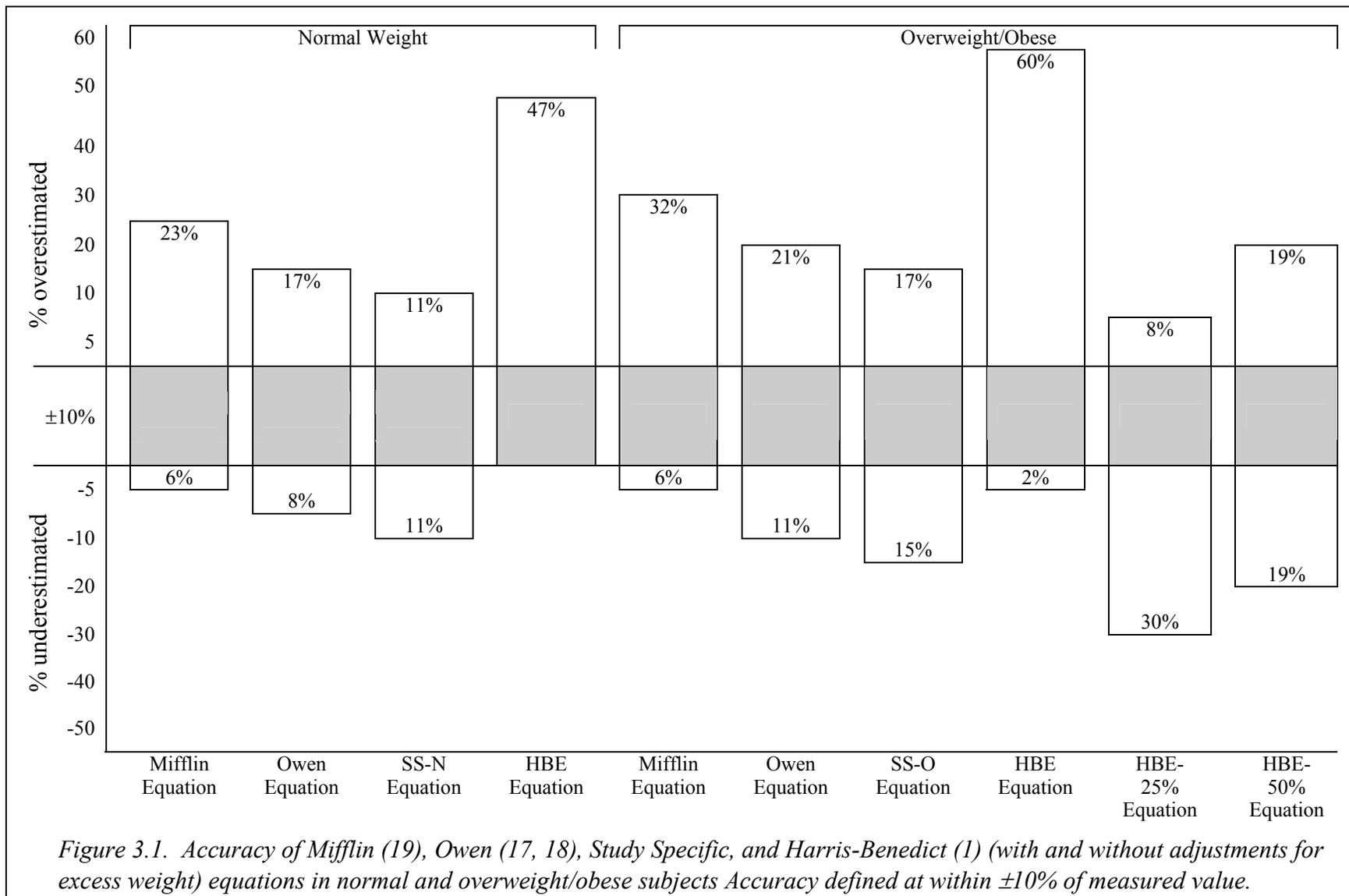


Table 3.4 Mean, mean difference, and accuracy^a of the SS-O equation, Mifflin equation, Owen equation, Hrris-Bendict Equation using actual weight, and with weight adjustments of 25, 50, and 60% excess weight among subjects partitioned into percent SBW of >125 to 150% and >150% compared to MBEE^b.

	Mean ^c	Mean Difference	Underestimated	Accurate within ±10%	Overestimated
>125 to 150% SBW^c		kcal/day		% of cases	
females=11 males=16					
SS-O ^d	1695 ± 346 ^e	19	7	78	15
Mifflin et al. (19)	1777 ± 323	101	0	63	37
Owen et al. (17, 18)	1720 ± 322	44	7	74	19
HBE-Act (1) ^f	1907 ± 376	231	4	19	78
HBE-25% (3) ^g	1669 ± 300	-7	11	78	11
>150% SBW					
females=24 males=2					
SS-O	1528 ± 162	-32	23	58	19
Mifflin et al.	1642 ± 155	82	12	54	35
Owen et al.	1525 ± 142	-35	19	58	23
HBE-Act	1712 ± 153	152	4	50	46
HBE-25%	1407 ± 104	-153	50	46	4
HBE-50% ^h	1508 ± 118	-52	29	54	17
HBE-60% ⁱ	1548 ± 123	-12	8	63	29

^a accuracy define at within ±10% of MBEE

^b MBEE >125 to 150% SBW = 1676±370 kcal/day; MBEE >150% SBW = 1560±262

^c SBW = standard body weight for height (2)

^d SS-O = study specific overweight/obese equation

^e mean±standard deviation

^f HBE-Act = Harris-Benedict Equation using actual weight

^g HBE-25% = HBE using standard weight plus 25% weight above standard

^h HBE-50% = HBE using standard weight plus 50% weight above standard

ⁱ HBE-60% = HBE using standard weight plus 60% weight above standard

**Chapter 4: Measured Basal And Resting Metabolic Rates
In A Healthy Adult Population**

ABSTRACT

Objective To quantify differences between basal (BEE) and resting energy expenditure (REE), identify a minimum length of time for accurate measurement of energy expenditure with indirect calorimetry, and recommend standardized procedures for defining REE.

Design BEE and REE were measured for a minimum of 30 minutes via indirect calorimetry. For basal measurements participants fasted ≥ 10 hours, slept a minimum of 7 hours, and abstained from strenuous exercise for at least 24 hours. Resting measurements were made after 24 hours without exercise and a three-hour fast. Using the abbreviated Weir equation, twenty-four hour energy expenditure was calculated from a steady state for minutes 6 to 15, 10 to 20, 10 to 30, and 20 to 30 from each session. Steady state was defined as a coefficient of variation in volume of oxygen (VO_2) $< 10\%$ for 10 consecutive minutes or five consecutive minutes with a coefficient of variation $\leq 5\%$.

Subjects/Setting Twenty healthy adults, 10 males and 10 females participated. Subjects slept at either the testing site or at their home. In

the latter case, participants drove to the testing site within one-half hour of awakening.

Statistical Analysis Performed A 2 X 4 repeated-measures analysis of variance was used to test within subject condition (BEE versus REE) and within subject period effects (minutes 6-15, 10-20, 10-30, and 20-30.) Significance was set at $p < .05$.

Results Significant condition ($F=21.1$, $p < .001$) and period ($F=7.85$, $p < .005$) effects were observed, but the condition by period effect ($F=2.6$, $p < .292$) was not significant. Mean 24-hour energy expenditure in duplicate periods differed by 10 to 12% between BEE and REE.

Applications/Conclusion Adjusting REE measurements by 10 to 12% is a tool clinicians may use to estimate BEE when REE is the only measured value available. In addition, a 20-minute measurement discarding minutes 1 through 10 when this period meets specified steady state criteria is an adequate duration of measurement. We recommend the adoption of a standard definition of REE. Criterion employed in and recommended from the current study include: ≥ 3 hour fast with the exception of plain water, abstinence from strenuous exercise at least 24

hours before measurement, and a defined steady state of a coefficient of variation in $\text{VO}_2 < 10\%$ for 10 consecutive minutes or five consecutive minutes with a coefficient of variation $\leq 5\%$.

INTRODUCTION

Indirect calorimetry has been employed in multiple studies to measure basal energy expenditure (BEE) and resting energy expenditure (REE). A variety of accepted methodologies for collecting calorimetry data exist, but the lack of standardized procedures raises concern over the interpretation of clinical results and comparison of data reported in various studies (15, 17-19, 21-26, 30-32). Inconsistencies in length of measurement, pre-measurement restrictions, and calculation of a steady state have been found to vary among published protocols and have the potential to considerably affect the measured energy expenditure value. Even though values obtained under different protocols may not differ statistically, differences often equal 100 to 200 kilocalories per day. Since a deficit or excess of this magnitude can result in the gain or loss of 10 to 20 pounds over a year, identification of procedures for obtaining more accurate estimates is critical.

Restrictions placed on subjects before measurement are the basis for defining BEE and REE. BEE is clearly defined as the energy required by the body at complete rest after a 12 to 14-hour overnight fast with

measurements made in a comfortable and relaxed environment soon after the subject has awakened (20). In contrast, REE is a more liberal term for energy expenditure collected under the same conditions as BEE with the exception of the overnight fast. Many authors and clinicians define conditions for BEE and REE similarly except for allowing subjects to sleep somewhere other than the testing site the previous night or to move from the room where they slept at the site to another room for measurement. However, Turley et al. (28) demonstrated that when other conditions were the same, measured BEE did not differ when subjects slept at or away from the test site.

Other investigators and clinicians employ differing definitions for REE. In intensive care units, REE often is measured in patients being fed continuously. Some investigators require short fasts of 3 to 4 hours, as well as exercise restrictions ranging from 12 to 24 hours. If one assumes that these REE measurements represent basal conditions, the metabolic contribution of the thermic effect of food and/or elevated oxygen consumption related to physical activity may be neglected.

Because many predictive equations were developed under basal conditions, it is important to ensure measured values intended for use in estimating BEE or evaluating predictive equations accurately reflect basal conditions. However, adhering to pre-measurement basal conditions is potentially problematic. In a free-living population a 12-hour fast and an early morning measurement are likely barriers to measuring BEE. A protocol in which energy expenditure could be measured throughout the day and modified to reflect basal conditions likely would be beneficial in clinical practice.

Published differences in REE definitions include fasting 3 to >12 hours, activity before measurement, time of day for analysis, morning versus afternoon, and time of rest before the start of measurement, i.e. 30 minutes to one hour. Inconsistencies also exist in the length of time for data collection and methodology used to calculate 24-hour REE or BEE values. Reported length of measurement varies from 15 to 60 minutes. Most protocols determine energy requirements based on a steady state from volume of oxygen (O₂) uptake. However, no standardized procedure is well established for obtaining a steady state. General agreement exists that a

minimum of the initial 5 minutes measured should be discarded. Beyond excluding the initial 5 minutes, previous studies have reported steady states based on consecutive minutes that achieve <10% change in VO_2 and carbon dioxide production (VCO_2) from the measured mean, consecutive measurements with a coefficient of variation $\leq 10\%$, a small segment of 5 or more consecutive minutes with a coefficient of variation <5%, or 30 consecutive minutes of VO_2 within ± 25 mL/min (22, 23, 25, 28).

The primary purpose of this study was to establish an empirical difference between measured BEE and REE, identify a minimal optimal length of time for data collection, as well as minutes to be discarded and evaluated in that period, and recommend standardized methodology for REE measurements.

METHODS

Participants were recruited from a sample previously studied by these researchers as well as referrals from friends and family members. Potential subjects were excluded if they were pregnant or if they were taking a medication that did not allow fasting for ≥ 10 hours. A cohort of twenty healthy adults, 10 males and 10 females met the criteria for participation.

This research was conducted with approval from the Human Subjects Review Board at the University of Texas at Austin and informed written consent was obtained from each subject before measurement.

Employing indirect calorimetry, energy expenditure was assessed twice on each of the 20 subjects, once under basal and once resting conditions. Basal conditions were defined as fasting except for plain water ≥ 10 hours, abstinence from strenuous exercise ≥ 24 hours, a minimum of 7 hours of sleep the previous night. Measurements were obtained within 30 minutes of awakening, and no significant activity occurred during this period. Resting conditions were defined as fasting except for plain water ≥ 3 hours, and abstinence from strenuous exercise ≥ 24 hours. Measurements were made within 24-hours of each other in random order, i.e., for some subjects BEE was measured initially followed by REE; in others the order was reversed. For basal measurements, subjects slept at either the testing site or at their home. In the latter case, participants drove to the testing site within one-half hour of awakening. Basal measurements began between 6:00 and 7:00 a.m. For all data collection periods subjects were measured using an open-circuit canopy ventilated indirect calorimeter (Deltatrac

Metabolic Monitor, serial number 65001, Sensor Medics Corporation, Yorba Linda, CA). Relative humidity of 55-60% at the measurement location was within the instrument's tolerance of 10 to 90%. Gases were calibrated, as specified by the manufacturer, before each measurement session using concentrations of 4% carbon dioxide and 96% oxygen. Room temperature was adjusted for each subject's comfort per individual request, and a light blanket was available if requested. Subjects were measured while awake but resting in a semirecumbent position. A clear plastic canopy was placed over the subject's head so that it rested on their shoulders, and was adjusted until comfortable. The thin plastic collar attached to the canopy was folded under the pillow and tucked around the participant so that the air inlet was the only passageway for air exchange. In order to provide visual stimulation and help participants stay awake during the measurement period, a National Geographic or Discovery Channel video was shown.

Steady State And Energy Expenditure Calculations

VO_2 and VCO_2 were downloaded to a personal computer. Using the abbreviated Weir equation (12), twenty-four hour energy expenditure was

calculated from the mean of minutes 6 through 15, 10 through 20, 10 through 30, and 20 through 30, for both basal and resting conditions. For these consecutive minute segments a “steady state” criterion of coefficients of variation for $VO_2 \leq 10\%$ was applied. For individuals who failed to meet the standard, a mean of 5 consecutive minutes within the same time period with a coefficient of variation $\leq 5\%$ was accepted.

Heart Rate Data

To validate adequate sleep as well as relaxation during basal and resting states, subjects wore heart rate monitors (Polar E600, Polar USA, Lake Success, New York) before and during each BEE and REE analysis period. Heart rate measurements were initiated 10 hours before BEE analysis and 3 hours before REE measurements; heart rate data were collected every 15 seconds and downloaded to a personal computer at the conclusion of each calorimetry session. For some subjects, the heart rate monitors failed to record data for the full night before the BEE measurement. Therefore, for BEE, mean heart rate was calculated during the last hour of sleep and during indirect calorimetry; for REE, heart rate was calculated over 3 hours before and during data collection.

Reliability of Calorimetry Measurements

In order to verify that any difference observed between basal and resting states did not represent variation in repeated measures, eight subjects were measured under identical resting conditions at the same time on different days. Pearson's correlation was performed to assess the relationship between repeated measures on different days at the same time of day. Mean REE measured during visit 1 and visit 2 were 1143 ± 123 and 1141 ± 131 kcal/day, respectively. The two measurements were highly correlated ($r=.97$), and no significant differences between visits were observed ($p<.847$). Mean percent difference for the two measurements was 1.3% and differences ranged from 0 to 3%.

Statistical Analysis

Data were analyzed using Statistical Program for the Social Sciences (SPSS) (SPSS 11 for Mac OS X, Version 11, Chicago, IL: SPSS, Inc. 2003.). Paired sample *t*-tests were used to analyze differences in sleeping and awake heart rates before and during basal measurements, and before and during resting measurements. A 2 X 4 repeated-measures analysis of variance was used to test within subject condition (BEE versus REE) and

within subject period effects (minutes 6-15, 10-20, 10-30, and 20-30) for VO₂ and energy expenditure. All measurements evaluated were available for each subject; there were no missing data points. Significance was defined at $p < .05$.

RESULTS

A total of 20 subjects were studied; gender was evenly distributed with 10 men and 10 women. Seven of the subjects were >125% their standard body weight (SBW) (2) and had a body mass index (BMI) greater than 25 kg/m². Gender specific height, weight, age, and BMI are presented in Table 4.1.

Heart Rate Data

Table 4.2 provides data on heart rate during basal and resting measurements, as well as the last hour during sleep before basal data collection and three hours before resting measurement. Heart rate during sleep did not differ significantly from that recorded during basal measurement. In contrast, heart rate recorded before resting measurement was about 10% higher than during data collection.

Steady State and Energy Expenditure

Table 4.3 illustrates VO_2 and REE values for the total sample and differentiated by gender. Because the assumption of Sphericity was violated, the Greenhouse-Geisser test of within-subjects effects, which applies a correction for lack of Sphericity, was used for analysis. There was a significant condition effect ($F=31.4$, $p<.001$), which indicated VO_2 was significantly higher when measured under resting conditions than when measured under basal conditions. Likewise, there was a significant period effect ($F=10.8$, $p<.004$), which indicated a difference in period 6 through 15, 10 through 20, 10 through 30, and/or 20 through 30 in either or both BEE and REE. Since the condition by period interaction ($F=2.5$, $p<.111$) was not significant, further detailed analysis of differences within periods was precluded.

On the same basis as that for VO_2 , the Greenhouse-Geisser test of within-subjects effects was used for analysis of energy expenditure under basal versus resting conditions. Significant condition ($F=21.1$, $p<.001$) and period ($F=7.85$, $p<.005$) effects were found; however, no significant condition by period effect ($F=2.6$, $p<.292$) was observed. The condition

effect indicated that VO_2 and energy expenditure was significantly higher under resting as compared to basal conditions. Percent mean difference between REE and BEE was calculated at ~10 to 12%. The absence of a condition by period interaction prevented further investigation into the specific periods that differed within BEE and REE conditions. However, resting means, as shown in Table 4.3, and the graphic trend illustrated in Figure 4.1 suggest that average REE in minutes 6 through 15 is likely higher compared than that in minutes 10 through 20, 10 through 30 and 20 through 30 under the same conditions. Amplitude of this difference between BEE periods is much smaller as illustrated by the relatively flat slope in Figure 4.1.

DISCUSSION

Results of our study show a clear difference between BEE and REE measurements and indicate the need for about a 10 to 12% reduction in measured REE values when the desire is to estimate BEE. Data from the current study are supported by Vermeij et al. (23) who found slightly smaller average differences (8-10%) between BEE and REE values. These investigators compared morning, noon, and afternoon REE measurements to

morning BEE measurements in a healthy adult population and found REE measurements to be significantly higher than the BEE measurements at 10%, 8%, and 8%, respectively. Subjects recruited by Vermeij et al. (23) were hospital and university staff and students and were reported to have spent most of the day seated. These subjects likely had less varied activities than the free ranging subjects recruited for the current study. Haugen et al. (55) found a 5-6% ($p < .002$) difference between basal and resting measurements as defined in the present study and collected in the morning and afternoon, respectively. Activities of their subjects between measurements were not described. Differences in results produced by Haugen et al. (55), Vermeij et al. (23), and the current study also may be explained in part by the thermic effect of food due to fasting criteria variations at 4 hours, 1-2 hours, and 3 hours, respectively.

Among the inconsistencies in indirect calorimetry measurement protocols is the procedure for bringing subjects to a steady state upon which 24-hour energy requirements are based. Years ago standard procedures called for the subjects to rest for one-half to one hour before measure, but time pressures of the current clinic or laboratory mediate against this

practice. Subjects may rest as little as 5 to 10 minutes before data collection begins. Almost universally at least the initial five minutes of measurement are discarded. Some investigators have taken a more conservative approach and elected to discard the initial 10 minutes. Findings from the current study support the latter method. The repeated measures profile plot in Figure 4.1 suggests that at least under resting and possibly under basal conditions, energy expenditure in period 6 through 15 differed significantly from periods 10-20, 10-30 and 20-30, but that periods 10-20, 10-30 and 20-30 did not differ amongst one another. These results indicate discarding the first 10 minutes of any measurement will allow subjects to achieve a steady state by relaxing and eliminating elevated energy expenditure related to erratic breathing patterns. In addition, after the initial 10 minutes of measurement, gas exchange does not change significantly with an increase in the duration of measurement. Results from this study suggest the final 10 minutes from a 20-minute measurement period is adequate to estimate BEE or REE.

Of particular importance in explaining variations in results between studies are the restrictions and conditions under which subjects are

measured. While pre-measurement BEE restrictions are clearly defined, there are a multitude of criteria for REE measurements. The length of fast before measurement and time of day for testing are inconsistent among documented protocols. Results from the current study support measurement at various times throughout the day. When morning measurements under basal conditions are not possible, clinicians may measure at other times during the day and estimate basal values by applying an 8-12% reduction to REE measurements. Ideally, practitioners would determine experimentally a percent mean difference between BEE and REE under conditions in their laboratory or healthcare facility by measuring 10 to 20 subjects typical of their clientele under morning basal conditions after an overnight fast and morning or afternoon resting conditions after fasting 3 hours or more. Medication and exercise conditions for resting conditions should be consistent with that required for basal measurements.

Although dietary intake was not evaluated in the current study, Westerstrate (56) reports a minimal thermic effect of food 3 hours after a small meal (<400 kcals). Reed and Hill (57) investigated thermic effect of food in 131 subjects who ingested meals of various sizes and composition.

These investigators found 60% of thermic effect of food had been measured after 3 hours, 78% after 4 hours, and 91% after 5 hours and concluded thermic effect of food response disappears in ≥ 6 hours in most people. From a clinical standpoint, clients are likely to comply with eating a small meal with perhaps specified composition 3 or more hours before their appointment as an alternative to a 12-hour overnight fast.

A shortcoming associated with the present study was the lack of control over pre-measurement meals. In retrospect, our protocol would have included requirement of a pre-measurement meal of ≤ 400 kcals (56) and completion of a diet record 24 hours before measurements to confirm adherence to intake parameters. This additional information would have allowed identification of excessive intake that may have contributed to energy expenditure because of postprandial response.

The objectives for the present study were achieved. Differences in energy expenditure under basal and resting conditions were evaluated. Measured REE was significantly higher than MBEE by a factor of 10 to 12%. In addition, the mean energy expenditure in minutes 10 through 20 did not appear to change appreciably with longer measurements up to 30

minutes. These results have implications in clinical nutrition practice when maintaining a 10 to 12 hour fast and/or obtaining a measurement over extended time is medically and economically inappropriate, inconvenient, or problematic. Adjusting REE measurements by a correction factor is a tool clinicians may use to estimate BEE when REE is the only measured value available.

The lack of standardized procedures for measuring energy expenditure via indirect calorimetry raises concern over the interpretation of clinical results and comparison of data reported in various studies. We recommend adoption of consistent criteria for REE and recommend the following: ≥ 3 hour fast except plain water, abstinence from strenuous exercise at least 24 hours before measurement, a 20-minute measurement discarding minutes 1 through 10 and evaluating minutes 10 through 20 when this period meets specified steady state criterion. Steady state criterion in the present study were for VO_2 with a coefficient of variation $<10\%$ for minutes 10-20 or 5 consecutive minutes with a coefficient of variation $\leq 5\%$. Establishment and adherence to standardized procedures for indirect calorimetry measurements, especially those for resting conditions,

will increase confidence when comparing data between studies and clinical sites and allow variations in results to be attributed to equipment and/or subject variation rather than differing methodologies.

Table 4.1 Age, height, weight, and BMI for males, females, and all subjects

	Age	Height	Weight	BMI^b
	years	cm	kg	(kg/m ²)
Males	41 ± 14 ^a	179 ± 2.3	81 ± 5.9	26 ± 1.7
Females	43 ± 17	162 ± 6.1	70 ± 14.6	27 ± 4.9
All subjects	42 ± 15	170 ± 9.4	76 ± 12.3	26 ± 3.6

^a mean ± standard deviation

^b BMI = body mass index

Table 4.2 Heart rates reported as beats per minute before and during indirect calorimetry measurements^a

	Before BEE^b	During BEE^c	Before REE^d	During REE^c
	beats per minute			
Males	56 ± 9	60 ± 10	72 ± 11	69 ± 12
Females	62 ± 2	65 ± 6	81 ± 15 ^e	72 ± 14
All Subjects	59 ± 7	62 ± 8	77 ± 13 ^e	70 ± 13

^a mean ± standard deviation

^b last hour of overnight sleep

^c awake but at rest

^d normal daily activity

^e significantly different from rate recorded during REE (p<.002)

Table 4.3 Mean basal and resting energy expenditure values and oxygen consumption (VO₂) for minutes 6-15, 10-20, 10-30, and 20-30 for males, females, and all subjects^a

Minutes	BEE Measurement					
	Males	Females	All Subjects ^{b,c}	Males	Females	All Subjects ^{b,c}
	VO ₂ (mL/min)			kcal/24 hours		
6-15	248±47	209±53	229±53	1775±269	1494±355	1634±339
10-20	243±49	208±55	225±54	1752±273	1483±267	1618±338
10-30	242±51	208±60	225±57	1748±284	1483±396	1615±362
20-30	242±53	208±64	225±60	1736±289	1480±421	1608±375

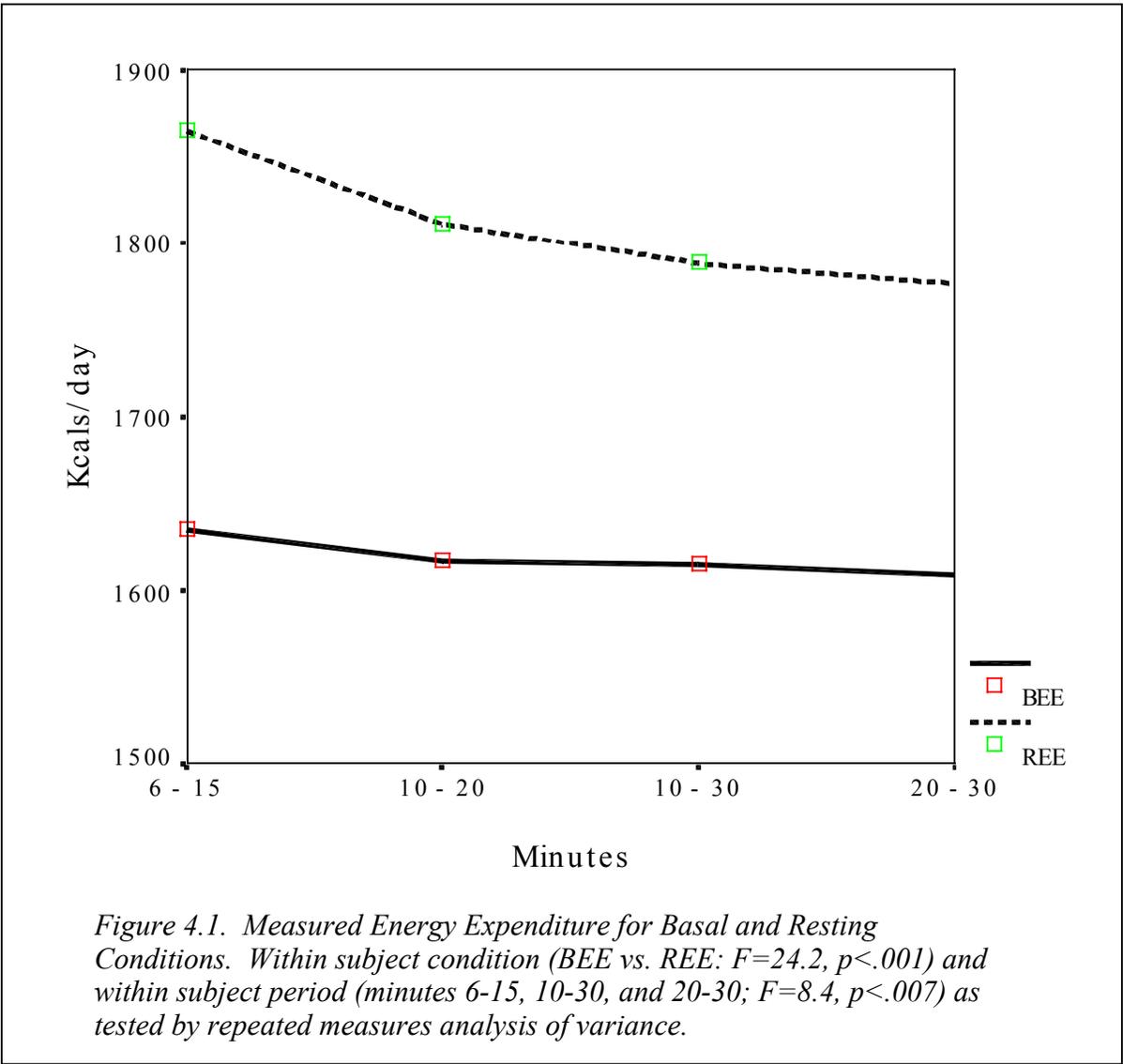
Table 4.3. Mean basal and resting energy expenditure values and oxygen consumption (VO₂) for minutes 6-15, 10-20, 10-30, and 20-30 for males, females, and all subjects^a, continued

Minutes	REE Measurement					
	Males	Females	All Subjects ^{b,c}	Males	Females	All Subjects ^{b,c}
	VO ₂ (mL/min)			kcal/24 hours		
6-15	290±48	238±56	264±57	2042±239	1688±373	1865±355
10-20	279±50	231±54	255±57	1991±289	1633±353	1812±364
10-30	280±56	231±53	255±59	1977±311	1616±289	1796±346
20-30	275±57	228±52	252±58	1957±338	1609±290	1783±355

^a mean ± standard deviation

^b significant condition effect (BEE versus REE), p<.001

^c significant period effect (6-15, 10-20, 10-30, and 20-30), p<.005



Chapter 5: Summary and Conclusions

Accurate estimation of energy needs in overweight and obese adults is essential for long term weight management and during hospitalization, when in the presence of metabolic stress, significant underfeeding encourages loss of lean tissue. Predictive equations for determining basal energy expenditure (BEE) have been scrutinized for years. The Harris-Benedict equation (HBE) (1) has continued to be widely used despite criticism that it is inaccurate for today's healthy adults that do not fit the profile of the population for which it was developed. Certainly, today many individuals are heavier, older, and more sedentary than Harris and Benedict's 1919 sample population. With the increased incidence of obesity among modern adults, many have questioned the accuracy of the HBE in assessing BEE, especially in overweight and obese individuals. A common method for modification of estimated BEE in overweight and obese individuals is to assume 25% of excess weight is metabolically active, and add that weight to standard body weight (SBW) (2) when estimating energy requirements (3).

Protocols for adjusting weight in the HBE and recently developed predictive equations were evaluated for accuracy in estimating BEE of overweight and obese adults in the present study. Subjects were 53 overweight/obese adults, 35 females and 18 males, and 53 normal weight healthy adults, matched for gender, height, and age. Energy expenditure was measured using an open-circuit canopy ventilated indirect calorimeter system. Resting energy expenditure (REE) was obtained in the morning, from 7:30 to 11:30 a.m., and in the evening, from 3:30 to 6:30 p.m., after subjects had fasted, with the exception of water, for at least three hours and had abstained from vigorous physical activity for 24 hours. Data were collected for a minimum of 15 minutes. REE was calculated from the mean of minutes 6 through 15 unless the coefficients of variation for VO_2 were $\geq 10\%$. In those cases, a mean of 5 continuous minutes from the same time period with a coefficient of variation $\leq 5\%$ was utilized. Energy expenditure in the current study was collected under resting conditions; however, because the predictive equations selected for comparison reported basal energy expenditure (BEE), conversion of the resting values to basal was

required. A correction factor, for adjusting REE to BEE was determined experimentally.

For this investigation, BEE and REE were measured via indirect calorimetry, for a minimum of 30 minutes, in 20 adults, 10 males and 10 females. For basal measurements, made in the early morning, participants fasted ≥ 10 hours, abstained from strenuous exercise for 24 hours, and slept a minimum of 7 hours the night before data collection. Resting measurements, collected in the late afternoon, were made after a minimum 3-hour fast and 24 hours without strenuous exercise. Within subject condition (BEE vs. REE) and within subject period effects (minutes 5-15, 10-20, 10-30, and 20-30) were analyzed using a 2 X 4 repeated-measures analysis of variance. Significant condition ($p < .001$) and period ($p < .005$) effects were observed for VO_2 and kilocalories per day; however, no significant condition by period effect was observed. Mean 24-hour energy expenditure in the four periods differed by 10 to 12%. These results allowed us to reduce REE values collected in our study by 12%. These values, hereafter referred as BEE, were used when comparing data with equations developed under basal conditions.

The present study of overweight/obese and normal weight subjects matched for height, age, and gender allowed quantification of fat-free mass (FFM) in excess weight of the overweight subjects in an attempt to provide a tailor-made adjustment for weight in the HBE. To accomplish this objective percent fat mass (FM) and FFM were obtained using dual energy x-ray absorptiometry. Results suggested that on the average $17\pm 14\%$ of excess body weight of the overweight/obese group was FFM, therefore, by our hypothesis, adding 17% of the difference between actual and SBW of those subjects to the SBW was predicted to account for added FFM and provide an accurate adjustment of weight for estimation of BEE with the HBE. Fankenfield et al. (25), however, had concluded that a 25% weight adjustment frequently under predicted BEE in the overweight/obese population. Obviously, additional not yet identified factors account for the increased BEE observed in overweight/obese adults as compared to their matched normal weight controls.

Attention was directed to assessing accuracy of study specific (SS) equations derived from the current study for normal (SS-N) and overweight/obese individuals (SS-O) and other recently developed, but not

commonly used, predictive equations. Predictive equations were considered accurate if predicted BEE was within $\pm 10\%$ of measured BEE (MBEE). As expected, the SS equations derived from the study sample using weight, height, age, and gender as predictors, predicted MBEE more frequently than the other equations examined. In normal weight subjects, rates of accurate prediction for the Owen and Mifflin equations (17, 18, 19) were comparable to the SS equation, about 75% of the cases. For these same subjects, the HBE overestimated BEE by more than 10% in almost half of the cases.

While the HBE using actual weight over predicted BEE for three-fifths of subjects, the SS-O, Owen (17, 18) and Mifflin (19) equations and the HBE adjusted by adding 25 and 50% of the excess weight to SBW accurately predicted MBEE in 62 to 68% of the cases. However, the HBE adjusting weight using 25% of excess weight underestimated MBEE in almost one-third of the cases while the HBE using a weight adjustment of 50% excess weight both under and over predicted MBEE in nearly 20% of subjects.

Scatter plots indicated that more errors occurred with the various prediction equations as subjects' weight increased above SBW. Glynn et al.

(31) and Frankenfield et al. (25) noted a tendency for increased error with standard prediction equations as body weight increased. To explore alternatives that might better predict BEE in subjects >150% of their SBW, overweight/obese subjects were partitioned into groups of >125 to 150 and >150 percent SBW because the linearity between weight and MBEE declined considerably among those >150% SBW as opposed to those >125 to 150% of SBW.

An average adjustment of weight for the HBE to estimate MBEE in subjects >125% of SBW was calculated by incorporating each subject's data into the gender appropriate HBE and solving for weight. That weight divided by the subject's SBW and expressed as a percent provided the ideal adjustment for that subject. Average adjustment for the overweight/obese group was $57 \pm 15\%$. Weight of those members of the overweight/obese group who were >150% SBW was adjusted by adding 60% of their excess weight to their SBW and tested in the HBE. The HBE using a weight adjustment of SBW plus 25% of excess weight accurately predicted MBEE in 78% of subjects >125 to 150% SBW while HBE using a weight adjustment of SBW plus 60% of excess weight was more accurate in

subjects >150% SBW, predicting MBEE within $\pm 10\%$ in 63% of all individuals, an increase of 9% from the accuracy rate achieved when a weight adjustment of SBW plus 50% of excess weight was applied for these subjects.

In the present study our SS equations for BEE in normal and overweight/obese adults and equations published by Owen (17, 18) and Mifflin (19) performed about equally as predictors of MBEE across all subjects. Whereas, Frankenfield et al. (25) found the Mifflin equation (19) to produce the smallest error among morbidly obese individuals (BMI>40), we found the Owen equation (17, 18) produced fewer cases over or under the MBEE in our population. Accuracy of these equations is likely to differ slightly in different populations, especially as height, weight, and age in the test group differ from those parameters in the group for which the equation was derived.

Although proven to be accurate, the SS equations derived in the present study, and those equations less commonly used, are unlikely to replace utilization of the HBE in practice. Further large sample studies are needed to evaluate the use of weight adjustments in overweight/obese

individuals, especially in subjects with a BMI > 40 kg/m². However, in the present study, adjusting weight by adding 25% and 60% of excess weight to SBW for subjects >125 to 150% and >150% SBW, respectively, in the HBE equation gave the adjusted HBE's the ability to predict BEE within ±10% for more than 75% of those >125 to 150% of their SBW and more than 60% of those >150% of their SBW. Mean difference between MBEE and predicted BEE using HBE with a 25% adjustment were 7 kcal/day in subjects >125 to 150% SBW and 12 kcal/day in subjects >150% SBW using HBE with a 60% weight adjustment.

In summary, two studies were conducted and provide clinicians and researchers with recommendations for collecting BEE and REE and predicting energy expenditure, especially in overweight and obese subjects. The investigators hypothesized determining the percent FFM in excess weight would provide a tailor-made weight adjustment to be incorporated into the HBE. Although this hypothesis proved false, results of the primary study indicate good accuracy for the HBE in assessment of overweight/obese clients when 25% and 60% of excess weight is added to SBW for individuals >125 to 150% and >150% SBW, respectively.

In support of the primary research, a secondary study produced results to recommend adjusting REE values by 10 to 12% to estimate BEE when REE is the only measured value available. Data from this investigation indicates that indirect calorimetry data collected for at least 20 minutes does not differ noticeably from longer measurements up to 30 minutes once the first 10 minutes are discarded. In addition, we recommend the adoption of a standard definition for REE. Criteria employed and recommended from data from the secondary study include: ≥ 3 hour but less than an 8-hour fast to distinguish data from basal measurements, abstinence from strenuous exercise at least 24 hours before measurement, and a steady state demonstrated by an acceptable method. In the present study, steady state was defined by a coefficient of variation $<10\%$ in VO_2 for 10 consecutive minutes or five consecutive minutes with a coefficient of variation $\leq 5\%$, after discarding the initial 10 minutes.

Appendices

Appendix A

RECRUITMENT FLYER



IT'S ABOUT YOUR HEALTH.

UT Clinical Research Study

**Seeking overweight adults (18 to 70)
to participate in a short study (1 day for ~ 2 hrs)**

**Receive a FREE body fat composition
test and a calorie analysis**

(valued at \$250)

**Please contact Jaimie Davis, R.D.
to see if you qualify.
phone: 512-694-4160
email: jaimiedavis@earthlink.net**

Appendix B

CAMPUS WIDE MASS E-MAIL

Would you like to know your % body fat and how many kilocalories you need to maintain or lose weight? Get this vital health information by volunteering to participate in a clinical nutrition research study. Testing will take approximately 1-2 hours and will be conducted on campus at Belmont Hall. If interested, and to see if you qualify, please respond to this e-mail with the following information: weight, height, and age.

Hope you will join us!

Thank You,
Project Staff
Human Ecology Department
The University of Texas at Austin

Appendix C

CONSENT FORM

CONSENT FORM

For persons participating in the study called

Examination of a Commonly Used Adjustment Equation for Predicting Energy Needs

You are invited to participate in a study that investigates the amount of lean tissue included in total body mass. Our names are Jaimie Davis and Valerie Hodges and we are graduate students at The University of Texas at Austin in the Department of Human Ecology, working under the supervision of Beth Gillham, Ph.D. We hope to determine the amount of lean tissue that makes up total body weight, and use that information to predict how many calories someone needs in one day. You will be one of approximately 100 subjects chosen to participate in this study.

If you elect to participate, you will be asked to do the following. We will perform a calorimetry measurement to see how many calories you use while at rest. You will be asked to schedule your appointment at least two hours after your last meal or snack. This test will require that you relax in a lounge chair and breathe normally for approximately thirty minutes. After you relax, a large clear plastic dome will be placed over your head to measure oxygen intake and carbon dioxide output for 30 minutes. We will measure your height and weight also. You will then have your body composition measured by a Dual Energy X-ray Absorptiometry (DXA) scan, a new technique that provides an accurate and precise measurement of body composition by passing two low dose x-rays across your reclining body. You will be asked to lie down on your back and remain motionless for 10 to 20 minutes. Both tests will be performed on the University of Texas campus by trained technicians. At the time of your appointment you will be asked to complete a diet history, physical activity, and general health questionnaire. This will take approximately 20 minutes of your time.

Possible risks to be expected from your participation in this study are minimal. There is the remote chance of discomfort if you will feel claustrophobic with a plastic dome over your shoulders and head or have difficulty lying still for up to 20 minutes. At no time will you be tested against your free will. Appropriate precautionary measures and supervision will protect against injury. If you are claustrophobic or experience anxiety in small places you may wish not to participate in this study.

You will be provided the results of these tests, which would cost you about \$200 at a clinic or fitness program. The co-principal investigators for this study are Valerie Hodges and Jaimie Davis. If you have any further questions you may contact them at (512) 694-4160 and (512) 659-7779, respectively. In addition, if you have questions about your rights as a research participant, please contact Clarke A. Burnham, Ph.D., Chair, The University of Texas at Austin Institutional Review Board for the Protection of Human Subjects, 512/232-4383.

Data compiled from your performance will be kept in strict confidence at all times. Only Valerie, Jaimie, and their Supervising Professor, Beth Gillham, will have access to the information. Numbers rather than names will identify all information collected. The list that ties the study numbers to the individual subjects will be kept in a locked file in the researchers' office. Any information that is obtained in connection with this study and that can be identified with you will remain confidential and will be disclosed only with your permission.

Your decision whether or not to participate will not affect your future relations with The University of Texas at Austin. If you decide to participate, you are free to discontinue participation at any time without prejudice. A copy of this consent form will be given to you for your files.

You are making a decision whether or not to participate in the study called "Examination of a Commonly Used Adjusted Equation for Predicting Energy Needs." Your signature indicates that you have read the information provided on the previous page and have decided to participate. You agree to complete both DXA scan and calorimetry techniques. To the best of my knowledge I am not pregnant at the time of measurement. You may withdraw from the study at any time after signing this form, should you choose to discontinue participation.

You may keep a copy of this form.

Signature of Participant

Signature of Investigator

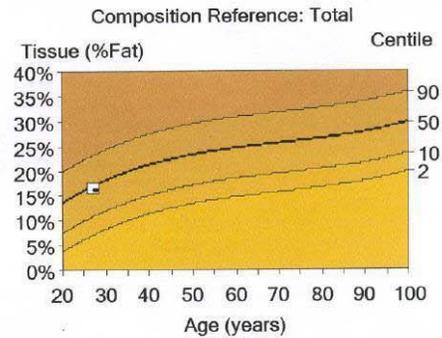
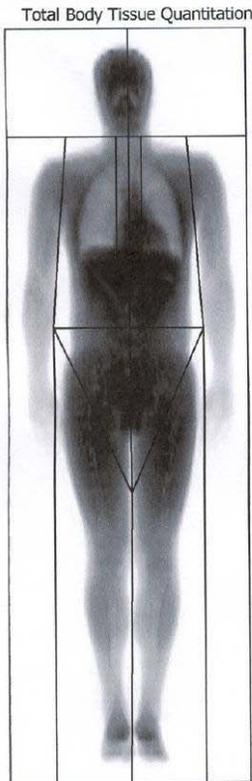
Date

Appendix D

BODY COMPOSITION PRINT OUT

Fitness Institute of Texas
Dept. of Kinesiology & Health Education
University of Texas at Austin

Patient:	[Redacted]	Attendant:	Archie Baker
Birth Date:	12/25/1975 27.1 years	Measured:	1/30/2003 6:10:18 PM (6.70)
Height / Weight:	68.0 in. 160.0 lbs.	Analyzed:	1/30/2003 6:11:01 PM (6.70)
Sex / Ethnic:	Male White		



Region	Tissue (%Fat)	Centile ^{2,3}	T.Mass (kg)	Fat (g)	Lean (g)	BMC (g)
Arms	6.4	-	-	467	6,861	423
Legs	17.2	-	-	3,789	18,225	1,236
Trunk	19.3	-	-	6,875	28,774	994
Total	16.7	47	72.6	11,581	57,946	3,111

COMMENTS:

Image not for diagnosis
 Printed: 1/30/2003 6:11:10 PM (6.70) 76:0.15:153.85:31.2 0.00:-1.00
 4.80x13.00 11.0:%Fat=16.7%
 0.00:0.00 0.00:0.00
 Filename: hodgeg_h9jxibb40.dfb
 Scan Mode: Standard

2 -USA/NHANES, Total Body Reference Population
 3 -Matched for Age, Weight (males 25-100 kg), Ethnic

Appendix E

INDIRECT CALORIMETER



Appendix F

DXA



BIBLIOGRAPHY

1. Harris JA, Benedict FG. *A Biometric Study of Basal Metabolism in Man*. Carnegie Institute of Washington, Washington, DC. 1919; Publication No. 270:1-266.
2. Hamwi GJ. Changing Dietary Concepts. *In Diabetes Mellitus: Diagnosis and Treatment*, vol 1, Danowski TS (ed). American Diabetes Association, New York, 1964:73-78.
3. Karreck J. Adjusted weight for obesity. *American Dietetic Association Renal Dietitians Practice Group Newsletter*. 1984;3(1):6.
4. National Institutes of Health, July 2003.
<http://www.niddk.nih.gov/health/nutrit/pubs/statobes.htm>
5. Flegal KM, Carroll MS, Ogden CL, Johnson CL. Prevalence and trends in obesity among US adults, 1999-2000. *JAMA*. 2002;288:1723-1727.
6. Schutz Y, Jéquier E. 1994. Energy needs: assessment and requirements. Shils ME, Olson JA, Shike (eds) *Modern Nutrition in Health and Disease*, 8th ed. Philadelphia: Lea & Febiger.
7. Lee RD, Nieman DC. *Assessment of the Hospitalized Patient*. 2nd ed. 1996. The McGraw-Hill Companies, Inc., St. Louis.
8. Seale JL, Rumpler WV, Conway JM, Mile CW. Comparison of doubly labeled water, intake-balance, and direct- and indirect-calorimetry methods for measuring energy expenditure in adult men. *Am J Clin Nutr*. 1990;52:66-71.
9. Murgatroyd PR, Shetty PS, Prentice AM. Techniques for the measurement of human energy expenditure: a practical guide. *Int J Obes*. 1993;17:549-568.

10. Isbell TR, Klesges RC, Meyer AW, Klesges LM. Measurement reliability and reactivity using repeated measurements of resting energy expenditure with a face mask, mouthpiece, and ventilated canopy. *J Parenteral Nutr.* 1991;15(2):165-168.
11. Harris CL. Weaning with indirect calorimetry. *Respiratory Support in Critical Care.* 2003;3(12). www.clinicalwindow.com.
12. Weir JB. New methods for calculating metabolic rate with special reference to protein metabolism. *J Physiol.* 1949;109:1-9.
13. Lifson N, Gordon GB, McClintock R. Measurement of total carbon dioxide production by means of D2O18. *J Appl Physiol.* 1955;7:704-710.
14. Metabolic Solutions, Inc., 460 Amherst Street, Nashua, NH 03063. http://www.metsol.com/energy_expenditure.htm, March 27, 2003.
15. Ireton-Jones CS, Turner WW. Actual or ideal body weight: which should be used to predict energy expenditure? *J Am Diet Assoc.* 1991;91:193-195.
16. FAO/WHO/UNU. *Energy and Protein Requirements.* Report of a Joint FAO/WHO/UNU Expert Consultation. WHO Technical Report Series No. 724. 1985.
17. Owen OE, Kavle E, Owen RD, Polansky M, Caprio S, Mozzoli MA, Dendrck ZV, Bushman MC, Boden G. A reappraisal of caloric requirements in healthy women. *Am J Clin Nutr.* 1986;44:1-19.
18. Owen OE, Holup JL, D'Alessio DA, Craig ES, Polansky M, Smalley KJ, Kavle EC, Bushman MS, Owen LR, Mozzoli MA, Kendrick ZV, Bowden G. A reappraisal of caloric requirements of men. *Am J Clin Nutr.* 1987;46:75-85.

19. Mifflin MD, St. Jeor ST, Hill LA, Scott BJ, Daugherty SA, Koh YO. A new predictive equation for resting energy expenditure in healthy individuals. *Am J Clin Nutr.* 1990;51:241-247.
20. Institute of Medicine of the National Academies. Dietary reference intakes for energy, carbohydrate, fiber, fat, fatty acids, cholesterol, protein, and amino acids. The National Academies Press, Washington, D.C., 2002.
21. Daly JM, Heymsfield SB, Head CA, Harvey LP, Nixon DW, Katzef H, Grossman GD. Human energy requirements: overestimation by widely used prediction equation. *Am J Clin Nutr.* 1985;42(12):1170-1174.
22. De Lorenzo A, Tagliabue A, Andreoli A, Testolin G, Comelli M, Dwurenberg P. Measured and predicted resting metabolic rate in Italian males and females, aged 18-59 y. *Eur J Clin Nutr.* 2001;55:208-214.
23. Vermeij CG, Feenstra WA, Oomen AMFA, De Graaf EJR, Zillikens MC, Swart GR, Bruining HA. Assessment of energy expenditure by indirect calorimetry in healthy subjects and patients with liver cirrhosis. *J Paren Enteral Nutr.* 1991;15(4):421-425.
24. Taaffe DR, Thompson J, Butterfield G, Marcus R. Accuracy of equations to predict basal metabolic rate in older women. *J Am Diet Assoc.* 1995;95:1387-1392.
25. Frankenfield DC, Rowe WA, Smith JS, Cooney RN. Validation of several established equations for resting metabolic rate in obese and nonobese people. *J Am Diet Assoc.* 2003;103(9):1152-1159
26. Pavlou KN, Hoefler MA, Blackburn GL. Resting energy expenditure in moderate obesity predicting velocity of weight loss. *Ann Surg.* 1986;203(2):136-141.
27. Boothby WM, Sandiford I. Normal values for standard metabolism. *Am J Physiol.* 1929;90:290-291.

28. Turley K, McBride PJ, Wilmore JH. Resting metabolic rate measured after subjects spent the night at home vs at a clinic. *Am J Clin Nutr.* 1993;58:141-144.
29. Kushner RF, Wall-Alonso E, Alverdy J. Obesity: In *The A.S.P.E.N. Nutrition Support Practice Manual*, Merritt RJ, Rombeau JL (eds). A.S.P.E.N., Silver Springs, MD, 1988, pp 21/1-21/11.
30. Cutts ME, Dowdy RP, Ellersieck MR, Edes TE. Predicting energy needs in ventilator-dependent critically ill patients: effect of adjusting weight for edema or adiposity. *Am J Clin Nutr.* 1997;66:1250-1256.
31. Glynn CC, Greene GW, Winkler MF, Albina JE. Predictive versus measured energy expenditure using limits-of-agreement analysis in hospitalized, obese patients. *J Parenteral Nutr.* 1999;23(3):147-154.
32. Barak N, Wall-Alonso E, Sitrin MD. Evaluation of stress factors and body weight adjustments currently used to estimate energy expenditure in hospitalized patients. *J Parenteral Nutr.* 2002;26(4):231-237.
33. Foster GD, Wadden TA, Mullen JL, Stunkard AJ, Wang J, Feurer ID, Pierson RN, Yang MU, Presta E, Van Itallie TB, Lemberg PS, Gold J. Resting energy expenditure, body composition, and excess weight in the obese. *Metabolism.* 1988;37(5):467-472.
34. Ravussin E, Burnand B, Schutz Y, Jequier E. Twenty-four-hour energy expenditure and resting metabolic rate in obese, moderately obese, and control subjects. *Am J Clin Nutr.* 1982;35:566-573.
35. Ravussin E, Lillioja S, Anderson TE, Christin L, Bogardus C. Determinants of 24-hour energy expenditure in man. *J Clin Invest.* 1986;78:1568-1578.

36. Bernstein RS, Thornton JC, Yang MU, Wang J, Redmond AM, Pierson RN, Pi-Sunyer FX, Van Itallie TB. Prediction of the resting metabolic rate in obese patients. *Am J Clin Nutr.* 1983;37:595-602.
37. Cunningham JJ. Body composition as a determinant of energy expenditure: a synthetic review and a proposed general prediction equation. *Am J Clin Nutr.* 1991;54:963-969.
38. Nielsen S, Hensrud DD, Romanski S, Levine JA, Burguera B, Jensen MD. Body composition and resting energy expenditure in humans: role of fat, fat-free mass and extracellular fluid. *Int J Obes.* 2000;24:1153-1157.
39. Müller MJ, Bosity-Westphal A, Kutzner D, Heller M. Metabolically active components of fat-free mass and resting energy expenditure in humans: recent lessons from imaging technologies. *Obes Rev.* 2002;3:113-122.
40. Halliday D, Hesp R, Stalley SF, Warwick P, Altman DG, Garrow JS. Resting metabolic rate, weight, surface area and body composition in obese women. *Int J Obes.* 1979;3:1-6.
41. Müller MJ, Illner K, Bosity-Westphal A, Brinkmann G, Heller M. Regional lean body mass and resting energy expenditure in non-obese adults. *Eur J Nutr.* 2001;40(3):93-97.
42. Martin AD, Ross WD, Drinkwater DT, and Clarys JP. Prediction of body fat by skinfold caliper: assumptions and cadaver evidence. *Int J Obes.* 1985;9(suppl 1):31-39.
43. Himes JH, Roche AF, Siervogel RM. Compressibility of skinfolds and the measurement of subcutaneous fatness. *Am J Clin Nutr.* 1979;32:1734-1740.
44. Clarys JP, Martin AD, Drinkwater DT, Marfell-Jones MJ. The skinfold: myth and reality. *J Sports Sci.* 1987;5:3-33.

45. Lukaski HC. Methods for the assessment of human body composition: traditional and new. *Am J Clin Nutr.* 1987;46:537-556.
46. Segal KR, Gutin B, Preta E, Wang J, Vanitallie TB. Estimation of human body composition by electrical impedance methods: a comparative study. *J Appl Physiol.* 1985;58:1565-1571.
47. Kushner RF, Schoeller DA. Estimation of total body water by bioelectrical impedance analysis. *Am J Clin Nutr.* 1986;44:417-424.
48. Ziegler EE, Filer LJ. *Present Knowledge in Nutrition.* 7th ed. Chapter 2: Body Composition. Forbes GB. 1996. ILSI Press, Washington, DC. Pp 7- 12.
49. Lukaski HC, Mendez J. Relationship between fat free weight and urinary 3-methylhistidine excretion in man. *Metab.* 1980;29:758-761.
50. Kistorp CN, Toubro S, Astrup A, Svendsen OL. Measurements of body composition by dual-energy x-ray absorptiometry improve prediction of energy expenditure. *Ann NY Acad Sci.* 2000;904:79-84.
51. Illner K, Brinkmann G, Heller M, Bosy-Westphal A, Müller MJ. Metabolically active components of fat free mass and resting energy expenditure in nonobese adults. *Am J Physiol Endocrinol Metab.* 2000;278:E308-E315.
52. Svendsen OL, Haarbo J, Hassager C. Accuracy of measurements of body composition by dual energy x-ray absorptiometry *in vivo.* *Am J Clin Nutr.* 1993;57:605-608.
53. James WPT, Bailes J, Davies HL, Dauncey MJ. Elevated metabolic rates in obesity. *Lancet.* 1978;5:1122-1125.

54. Hoffmans M, Pfeifer NA, Gundlack BL. Resting metabolic rate in obese and normal weight women. *Int J Obes*. 1979;3:111-118.
55. Haugen HA, Melanson EL, Tran ZV, Kearney JT, Hill JO. Variability of measured resting metabolic rate. *Am J Clin Nutr*. 2003;78:1141-1144.
56. Weststrate JA. Resting metabolic rate and diet-induced thermogenesis: a methodological reappraisal. *Am J Clin Nutr* 1993;58:592-601.
57. Reed GW, Hill JO. Measuring the thermic effect of food. *Am J Clin Nutr* 1996;63:164.169.

Vita

Valerie Anne Hodges was born in Wharton, Texas, to AJ and Patricia Hebert. She attended school in Palacios, Texas, graduating from Palacios High School in 1992. In 1996 she graduated with a Bachelors of Science degree in Nutritional Sciences from Texas A&M University in College Station, Texas, completed an American Dietetic Association accredited Dietetic Internship at the University of Connecticut in Storrs, Connecticut in 1997, and earned a Masters of Science degree in Nutrition in 1998 from Texas A&M University. She held the position of Clinical Dietitian at Matagorda General Hospital in Bay City, Texas before entering the Graduate School at The University of Texas at Austin. She worked as a Teaching Assistant with the Coordinated Program in Dietetics and in introductory nutrition classes.

The author is married to Captain Adam Hodges, United States Army. They have a beautiful daughter, Grace Anne.

Permanent address: HC 2 Box 402, Palacios, Texas 77465

This dissertation was typed by the author.